Systemic Therapy
for At Risk Teens

RESEARCH PROTOCOL

START (Systemic Therapy for At Risk Teens): A national randomised controlled trial to evaluate multi-systemic therapy in the UK context

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Trial Summary

In this study we will compare multisystemic therapy (MST) with carefully documented management as usual (MAU) for adolescents who meet criteria for being at 'high risk' of requiring out of home care, specifically when this risk is associated with antisocial behaviour including conviction as a young offender. MST, an intervention specifically designed for young people who exhibit antisocial behaviour and their families, was originally developed in the United States as an approach for helping adolescents seen to be at elevated risk of becoming young offenders and who are already receiving multi-agency interventions. A major strength of this approach is that it integrates key elements from a number of different individual treatments as well as family based psychological treatments, making it a robust means of engaging with a group of young people from a range of environments whose difficulties and needs are heterogeneous and complex. It typically lasts for between 3 and 6 months and assists not only families but also schools, neighbourhoods, and community resources to help the young person overcome their antisocial problems. It is delivered by specially trained professionals who work with only a few families at a time.

Although the evidence from the United States suggests that MST is a very promising treatment the question of whether it will be similarly effective in the UK has not been fully investigated. In order to asses the efficacy of MST in the UK context, we will compare it with the multi-agency interventions that are currently provided for these adolescents through the NHS from specialist youth offending teams and from social services and education services. In order to make sure that we achieve the fairest and least biased assessment of the potential benefits of MST we will randomly allocate adolescents to either MST or standard care.

We will conduct this research across 9 pilot sites, each overseen by a team of therapists who will have received a specialist training in MST ensuring high quality delivery of the intervention. We know that out of home placement in most cases represents an unhelpful outcome for antisocial adolescents (be it incarceration, hospitalisation, residential schooling or assignment to residential local authority care) and so we want to use the preservation of the family as the main measure of benefit, although we realize that in some cases out of home placement might be the most appropriate outcome. MST aims to reduce the level of offending in the target population, and so we will also use offending rates as a key measure to determine whether or not the intervention is effective. We will look at other possible benefits of MST such as the impact on the young person's educational progress, his or her mental health and well-being and that of the family. In order to assess what the benefits of MST and MAU might be we will also take considerable care to describe the interventions delivered to both groups in the study accurately and will attempt to chart the subjective experience of all stake holders in the project (service users, providers and commissioners of services). We will analyse the data from the trial to determine whether the expected benefit of MST is achieved and whether it represents an economically viable option.

Randomisation to 18 month follow up;

Primary Aim: We aim to carry out a pragmatic trial that will inform policy makers, commissioners of services and professionals about the potential of MST in a UK context, investigating whether the provision of MST could reduce the incidence of out of home placements for young people at risk of being removed from their homes because of antisocial behaviour, severe mental health problems, educational problems or unmet need. The trial will take referrals of families with an adolescent with severe antisocial behaviour problems who is considered to be at risk of custodial or other forms of out of home care. The trial will answer the question of whether MST can contribute to significantly reducing the rate of out of home placement

Secondary Aim: We will investigate whether MST is associated with (a) decrease in antisocial behaviour, (b) increase in young person's well-being, (c) improved educational outcomes and (d) improved family functioning. Moreover, we aim to establish the cost of MST relative to management as usual, and the cost-effectiveness of providing this intensive form of intervention against the background of costs incurred in the 18 months period following randomisation.

The immediate objectives of the trial are: (1) to confirm recruitment of ten MST service providers and agree on an acceptable protocol for randomisation of cases (month 3); (2) to recruit and train outcome assessors (OAs) to a predetermined level of reliability (month 4); (3) to identify a representative clinical sample of 700 young people to be recruited from ten sites (month 21); (4) to randomise 350 cases to MST and 350 to MAU (month 21 – this figure allows for a significant number who may not consent to enter the trial); (5) to assess outcome of randomised cases at 6, 12, 18, 24,30 and 36 months post recruitment (month 39); (6) to estimate the total social, health, educational and criminal justice cost of interventions at 18 months post-randomisation (month 42); (7) to identify the key cost and outcome drivers and the value for money of the treatments at 18 months (month 44) and (8) to analyse data, write reports and prepare papers for publication in peer reviewed journals 4 years after the commencement of the trial (month 48).

Two to Five years post randomisation;

Primary Aim: The primary outcome is criminal conviction as registered on the Police National Computer.

Secondary Aim: Secondary outcomes will include (a) antisocial behaviour as indicated by arrest, cautions, self-report, (b) emotional well-being, including the presence or absence of psychiatric problems, (c) education and training outcomes, (d) social network, specifically the quality of relationships with parents and peers (e) self-efficacy (f) physical health, together with (g) work adjustment and (h) early (unplanned) pregnancy or fatherhood. The use of services and associated costs will be monitored. We will estimate the total social, health, educational and criminal justice cost of interventions at 48 months post-randomisation, when we will also identify the key cost and outcome drivers and value for money of the treatments.

Results and Implications of Systematic Review of MST

There is genuine equipoise concerning the potential of MST in a UK context. MST is offered by one therapist, who potentially offers a range of techniques, dependent on the clinical picture. These include marital and family therapies, parent training, behavioural and cognitive approaches, supportive therapy and case management (which may involve liaison with outside agencies). Nine treatment principles govern delivery, including an emphasis on systemic strengths, the promotion of responsible behaviour, the targeting of sequences of behaviour in multiple systems responsible for maintaining behavioural problems, and continuous evaluation from multiple perspectives.

A number of good-quality RCTs of this approach suggested that this was the most effective treatment for delinquent adolescents in reducing recidivism and improving individual and family pathology (Borduin, 1999; Henggeler, Cunningham, Pickrel, Schoenwald, & Brondino, 1996; Henggeler, Melton, & Smith, 1992; Henggeler, Melton, Smith, Schoenwald, & Hanley, 1993; Henggeler et al., 1986). It certainly appeared to be substantially more effective than individual treatment even for quite troubled and disorganised families (Borduin et al., 1995). MST shares a particular strength with other systemic family approaches in reducing attrition rates in this highly volatile group (Henggeler, Pickrel, Brondino, & Crouch, 1996). The success of this programme was noted to be quite striking: at an average 4-year follow-up, recidivism in those who completed MST was significantly reduced (22.1%) relative to recipients of individual therapy (71.4%). Although 26% of the MST group were arrested, their crimes were usually less serious than was the case in the 71% of the individual therapy group who had been charged (Borduin, 1999)

MST has remarkable strengths. These include but are by no means limited to the intensive commitment of therapists to a family's problems, the small caseloads and attention to quality control, the ongoing reporting of outcome by family members, meeting the challenge of the most severe psychosocial and psychiatric problems head-on, a clear link between hypothesised pathogenic and treatment mechanisms, an intensive but time-limited therapeutic format, generically but well-trained practitioners, etc. Initial reviews of the approach were highly favourable (Borduin, 1999; Fonagy, Target, Cottrell, Phillips, & Kurtz, 2002; Roth & Fonagy, 1996), but more recently reviews have been more mixed and critical (Littell, 2005; Littell, 2006; Littell, Popa, & Forsythe, 2005). The number of reviews is actually greater than the number of studies with a ratio of at least 1:3. Because the available meta-analyses are partial and do not incorporate the more recent investigations, leading perhaps to misleading power calculations, we undertook a further systematic review of our own to estimate effect sizes obtained from MST when compared to MAU as a control condition. We also contrasted these figures with those obtained from treatments of anti-social problems by alternative treatment approaches (coping, affect regulations and social skills training) obtained as part of our research for a new edition of 'What Works for Whom? A Critical Review of Treatments for Children and Adolescents'. The present meta-analysis of MST includes nine studies, i.e. all the more recent reports as well as the Canadian report (Leschied & Cunningham, 2002). The following studies were included in this review; (Borduin & Schaeffer, 2001; Borduin et al., 1995; Henggeler, Halliday-Boykins, & Cunningham, 2006; Henggeler, Melton, Brondino, Scherer, & Hanley, 1997; Henggeler et al., 1992; Henggeler, Pickrel, & Brondino, 1999; Ogden & Hagen, 2006; Rowland et al., 2005; Timmons-Mitchell, Bender, & Kishna, 2006). The meta-analysis found near-significant reductions in the number of arrests post-treatment, re-arrests and incarceration/conviction (for effect sizes, 95% CIs and p values see Table 1). The effect size of reduction of problem behaviours as rated by teachers is particularly impressive for both internalising and externalising behaviours ($p = .0001$). MST may influence individual wellbeing as well as behaviour. By contrast re-arrest rates in young women supported in multidimensional foster care significantly decrease ($p = .02$), as do behaviour problems treated with social skills training ($p = .003$), or parent training ($p = .000001$), and or functional family therapy ($p = .001$). However, it should be noted that the client groups in MST trials appear to be more severe than almost all of the other trials, although of course this is hard to assess from journal reports alone. Most pertinent in this context, MST trials looking at family preservation and the avoidance of psychiatric hospital admission have yielded extremely strong effects in a remarkable unique study (Henggeler et al., 1999) (RR(random) =0.51 (95% CI .94 to .19; $p = .002$). Overall, looking across the trials the figures from our systematic review suggest that the conclusions of those reviewers who are unwilling to ascribe unique efficacy to MST are probably unduly cautious. In our view there is reasonable evidence to suggest that MST is better than management as usual, and no treatments that we have identified in our systematic review are better than MST. However, as was stated above, questions remain about the applicability of MST to the particular set of complex clinical problems which characterise the UK context.

Whilst the 2007 review by Utting et al. (Utting et al., 2007) was also positive in identifying MST as an evidence-based approach for children at risk of developing antisocial personality disorder and associated problems including substance misuse and time spent in custody, a number of issues emerge from reviews of these studies that point to issues for further exploration in an RCT: (1) inflation of effect sizes in some trials because of exclusion of participants who did not engage with MST (i.e. a failure to do intent-to-treat analyses); (2) the possible influence in efficacy trials of the developer's deep involvement and commitment to the success of the intervention, and the feasibility of transporting treatments that require such intensive supervisory oversight from the developers to real-world settings; (3) the importance of developer involvement in ensuring adherence to the nine MST treatment principles that are believed to account for the effect size difference between efficacy (d=.81) and effectiveness studies (d=.26); (4) the extent to which the 9 MST principles discriminate MST from standard care, particularly as many standard care packages in the UK share these principles which are principles of good practice not unique to MST (a schematic current care pathway for young people in the UK is given in figure 1 below); (5) the absence of empirical data to demonstrate that the MST therapist adherence measure (TAM)

actually evaluates adherence to MST principles, as opposed to measuring simply good therapeutic practice by better supervised, better trained, and more experienced clinicians; (6) the limited evidence of the importance of fidelity which appears unrelated to outcome unless rated by therapists, whose ratings are of course known to be confounded by the extent to which a family "permits" a therapist to stick to manual; (7) the limitations of a manual of principles rather then a specific protocol in drawing conclusions about the contrast between MST and treatments as usual as similarities and differences are challenging to specify; (8) the limitations of evidence for transportability with one major trial (Ontario study) showing no treatment effects and the Norwegian study although showing strong effects, also presenting major transportability issues since children under 15 in Norway are not charged with criminal offences and antisocial behaviour is dealt with by the child welfare system offering no "objective" treatment indicators of criminal offending; (9) further generalisability issues arising from large differences between comparison groups across studies according to the level of organisation of MAU services; (10) the high level of arrest rates at 18 months follow-up, even in successful trials such as the Hawaiian RCT (MST 66.7% and MAU 86.7%), despite the highly significant drop in the likelihood of re-arrest in the MST condition.

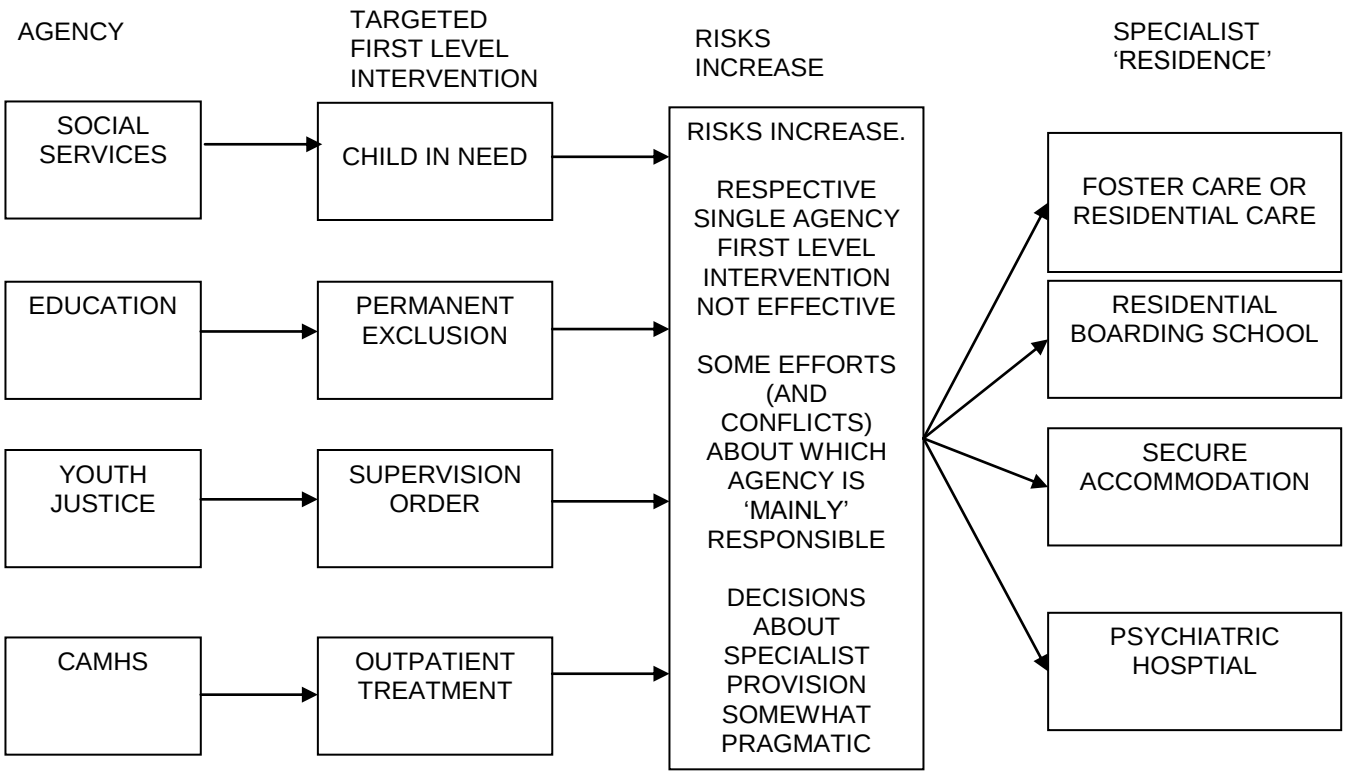
Table 1: Summary of MST RCTs

	N (MST, Standard Care)	Effect Size	95% CI	*P*< (Overall Effect)
Incarceration/conviction end of treatment (Henggeler et al., 1992) (Henggeler et al., 1997) (Leschied & Cunningham, 2002)	335, 316	0.51	(0.23, 1.16)	0.11
Incarceration/conviction 1.7 year follow-up (Henggeler et al., 1997)	82, 73	0.75	(0.52, 1.07)	0.11
Incarceration (days/weeks) (Henggeler et al., 1992) (Henggeler et al., 1997) (Leschied & Cunningham, 2002)	325, 298	-0.30	(-0.71, 0.11)	0.15
Rearrested 12-18 month follow-up (Borduin et al., 1995) (Henggeler et al., 1992) (Leschied & Cunningham, 2002) (Timmons-Mitchell et al., 2006)	393, 372	0.70	(0.45, 1.09)	0.12
Rearrested 8-14 year follow-up (Borduin et al., 1995) (Borduin & Schaeffer, 2001)	116, 105	0.53	(0.31, 0.90)	0.02

Number of arrests short term follow-up (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997) (Henggeler et al., 1999) (Henggeler et al., 2006) (Rowland et al., 2005) (Timmons-Mitchell et al., 2006)	354, 325	-0.39	(-0.81, 0.02)	0.06
Number of arrests 4 year follow-up (Henggeler et al., 1999)	43, 37	-0.33	(-0.77, 0.11)	0.14
Self Reported Delinquency end of treatment (Henggeler et al., 1992) (Henggeler et al., 1997) (Henggeler et al., 1999) (Henggeler et al., 2006) (Rowland et al., 2005)	227, 214	-0.18	(-0.42, 0.07)	0.15
Self Reported Delinquency 6 month follow-up (Henggeler et al., 1999)	58, 60	0.05	(-0.31, 0.41)	0.77
Self Reported Delinquency 2 year follow-up (Ogden & Halliday-Boykins, 2004)	43, 26	-0.26	(-0.75, 0.23)	0.30
Self Reported Delinquency 4 year follow-up (Henggeler et al., 1999)	43, 37	-0.33	(-0.77, 0.11)	0.14
MPRI: Peer Bonding (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997)	185, 152	-0.38	(-1.16, 0.40)	0.34
MPRI: Maturity (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997)	185, 152	0.04	(-0.18, 0.25)	0.75
MPRI: Peer Aggression (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997)	173, 149	-0.13	(-0.35, 0.09)	0.24
Revised Behavior Problem Checklist (RBPC) (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997)	173, 149	-0.50	(-1.42, 0.42)	0.29
CBCL: Parent Reports (2 years after pre-assessment)				

CBCL 89-Item Problem Scale (Ogden & Halliday-Boykins, 2004)	43, 26	-0.51	(-1.01, -0.02)	0.04
CBCL Externalizing (Ogden & Halliday-Boykins, 2004)	43, 26	-0.17	(-0.66, 0.32)	0.49
CBCL Internalizing **(**Ogden & Halliday-Boykins, 2004)	43, 26	-0.69	(-1.19, -0.19)	0.007
CBCL: Teachers Reports (2 years after pre-assessment)				
TRF 89-Item Problem Scale (Ogden & Halliday-Boykins, 2004)	43, 26	-1.10	(-1.62, -0.58)	< 0.0001
TRF Externalizing (Ogden & Halliday-Boykins, 2004)	43, 26	-1.09	(-1.61, -0.57)	< 0.0001
TRF Internalizing (Ogden & Halliday-Boykins, 2004)	43, 26	-1.14	(-1.67, -0.62)	< 0.0001
FACES-III Adaptability (Ogden & Halliday-Boykins, 2004)	61, 35	-0.34	(-0.76, 0.08)	0.11
FACES-III Cohesion (Ogden & Halliday-Boykins, 2004)	61, 35	-0.08	(-0.49, 0.34)	0.71
General Psychiatric Symptoms (SCL/BSCL) (Borduin et al., 1995) (Henggeler et al., 1992) (Henggeler et al., 1997)	185, 152	-0.14	(-0.56, 0.27)	0.50
Psychiatric Symptoms: TAS 4 year follow-up: Externalizing Scale (Henggeler et al., 1999)	43, 37	0.16	(-0.28, 0.60)	0.47
Internalizing Scale (Henggeler et al., 1999)	43, 37	0.11	(-0.33, 0.55)	0.61

Fig 1: Schematic Care Pathway for Anti-social Young People



Design and Methodology (Randomisation to 18 month follow up)

Overview: We are undertaking a superiority trial comparing multisystemic therapy (MST) with carefully documented management as usual (MAU) for adolescents who meet criteria for being at 'high risk' of requiring out of home care, specifically when this risk is associated with antisocial behaviour including conviction as a young offender. Each of the 9 MST pilot sites will be staffed by a team of therapists who will have been trained in MST and all sites will have agreed at least in principle to participate in a rigorous RCT. We anticipate referrals from youth offending teams, CAMHS and occasionally from social services and education services.

We will randomise approximately half the qualifying cases to MST; the other half will receive management as usual (MAU). It is not assumed that MAU will be uniform across the ten sites and specific profiles of service delivery will have to be monitored for each person randomised to this arm. Recruitment will take place for 18 months commencing between 3 and 6 months after the inauguration of the programme at each site. The study will run for four calendar years and the capacity for MST is assumed to be 40 clients in the first year and 50 in subsequent years at each of the sites. The number of eligible cases will be substantially higher; based on our past experience of MST implementation, the proportion of families accepting this treatment is likely to be 25-33% of those to whom it is offered. In the sample size and power calculations we have assumed that most if not all of the MST treatment capacity at each site will go towards cases participating in the trial who have agreed to randomisation. We would be extremely concerned if pilot sites were to offer MST to large numbers of candidates who had not consented to randomisation. Not only would that make the sample potentially skewed but it would act to reduce recruitment to the study, since families would know that they could increase their chances

of obtaining the treatment by refusing consent to the trial. Given the therapeutic equipoise that exists between MST and MAU for this group of young people in the UK contact we believe that this is an ethically appropriate and defensible position.

Our primary outcome is incidence of out of home care, but we recognize that out of home care cannot be considered a negative outcome in all cases. We have therefore identified key forensic, family function and individual well being indicators which will be assessed at 6, 12, 18, 24, 36and 48 months after randomisation. It is important to delimit as far as possible the key moderators of the effects of MST and we will explore the moderating effects of callous and unemotional traits and severity of anti-social behaviour. In order to understand the way this new intervention impacts on current services, from the viewpoint of both the users and providers, we will also undertake a qualitative, interview based investigation of the key stakeholders in the service systematically sampled from the 9 sites.

Design: This will be a randomised controlled trial. Allocation will be by minimisation, controlling for number of past convictions, gender and age at onset of criminal behaviour. Minimisation will be necessary to limit the impact of factors that could easily influence treatment response. Treatment centre will also be included in the minimization stratification to control for differences between centres. Recruitment and treatment will take 18 months. Treatments will be offered over a period of three to six months for individual families. The primary outcome will be out of home placements at 18 months. Key outcomes will include court or pre-court disposal rates as at 18 months following randomisation with further follow-ups included in the initial consent, as long-term prevention is a central goal of the intervention. Other secondary endpoint measures will be total service and criminal justice sector costs over 18 months post-randomisation, wellbeing, drug misuse, and family functioning.

Setting: Treatments will be offered by services collaborating in this MST trial at the 9 pilot sites. The study will be conducted in three research hubs or centres: London (UCL and IoP), Cambridge and Leeds. Cambridge and Leeds will be responsible for data collection from 5 pilot sites while London will collect from 4, selected on the basis of geographical convenience.

Target population: In general we will aim to increase generalisability by using the minimum number of entry criteria. The task of establishing an adolescent target population based on the status of being on the edge of care is a challenging one as, in most contexts, this term gestures towards a heterogeneous group. At the same time, we also recognise that the referral routes of Forensic, Social Services, CAMHS or Education often identify the same young people and families with very similar needs when they have reached a particular crisis point. The quality of the crisis may be associated with the specific service (e.g. forensic services are triggered by convictions, education services by repeated school exclusions) but the underlying causes in terms of family disorganisation combined with antisocial behaviour by the young person are similar and the outcomes in terms of risk of out of home care are shared.

Taking this into consideration we have defined four alternative inclusion criteria for eligibility for randomisation into MST or MAU depending on the source of the referral. We are confident based on our shared clinical experience that the families identified in these routes will be similar and that the target population will be a relatively homogenous one. They will share at least 3 of the following features indicative of 'risk status' that can be considered severe and which serve as generic inclusion criteria: (a) Excluded or at significant risk of school exclusion; (b) High levels of non attendance at school (c) An offending history or at significant risk of offending; (d) Previous episodes on the Child Protection Register; (e) Previous episodes of being looked after; (f) Previous referral to FGC to prevent young person from becoming looked after; (g) History of siblings being looked after. We will put in place demographic, clinical and family functioning measures to assess these attributes and test the assumption of relative homogeneity notwithstanding different referral paths. We hope that at most sites a multi-agency panel will consider referrals. Referrals considered suitable by the panel will be included in the trial if they meet the following general inclusion criteria: (1) Young person aged 11-17 years; (2) Sufficient

family involvement for MST to be applied, excluding adolescents already in local authority care or foster accommodation unless this is a long term placement of over 3 years. For sufficient family involvement to be applied an adult primary caregiver needs to be clearly identified as having a long-term commitment to that YP in providing care. If that young person cannot reasonably be defined as having a long-term parenting figure, for example, being placed in the care of a family friend or individual with no prior caretaking experiencing with that young person, then it should be clear how the parent or prior parenting figures remain part of the intervention. We would ask that the following considerations are borne in mind for each case - a) is the young person being placed with an adult figure who will provide sufficient family involvement and all that entails b) If this person is outside of the immediate family constellation, how will a family or extended family member remain involved; c) is there a credible plan for parenting that will persist beyond the intervention.

We discourage families to be entered in to the trial where there is no stable parenting figure in place, however in certain circumstances, when there is a clear plan for the young person to be placed immediately back in the home prior to randomisation i.e. if a young person has a short term admission to care/accommodation in either a residential or foster placement an exception will be made for them to be included., (3) No existing agency involvement (e.g. the family is already engaged with a therapist) which would interfere with MST and (4) Meets ONE of the following set of criteria indicating suitability for MST: (a) Persistent (weekly) and enduring (6 months or longer) violent and aggressive interpersonal behaviour OR (b) A significant risk of harm to self or to others e.g. self harming, substance misuse, sexual exploitation, absconding, OR (c) at least one conviction and three warnings, reprimands or convictions in the last 18 months; OR (d) current diagnosis of externalising disorder and a record of unsuccessful outpatient treatment, OR (e) permanent school exclusion.

In the event that there is no multi-agency panel and the treatment team is asked to decide if the case is acceptable, a guideline for inclusion analogous to the considerations above could be used depending on the nature of the referral. This would of course create the need for even more complex negotiations with multiple groups but we anticipate that at the end of those discussions the inclusion criteria for the four agencies might include the following:
(1) *Recruitment via Children's services:* Looked after children can be looked after on a voluntary basis (section 20) or under a legal framework following court proceedings. The process for the latter is currently changing with introduction of the Public Law Outline which requires the LA to have undertaken a pre-specified set of tasks before care will be considered by the court. It also 'gives notice' to the families that care is being considered and that they need to comply with required assessments or interventions if they wish the child to remain in the family. We therefore propose that the MST RCT would be most appropriate for children designated as 'Children In Need' and who have an allocated social worker. The inclusion criteria would be broadly as above and would include additional criteria (3&4): (1) Young person aged 11-17 years; (2) sufficient family involvement for MST to be applied, excluding adolescents already in local authority care or foster accommodation, (3) no existing agency involvement (e.g. the family is already engaged with a therapist) which would interfere with MST; (4) Adolescent designated as 'Child in Need' where this is associated with antisocial behaviour on the part of the adolescent; (5) Exhibiting extremely challenging behaviour by EITHER Persistent (weekly) and enduring (6 months or longer) violent and aggressive interpersonal behaviour AND/OR a significant risk of harm to self or to others e.g. self harming, substance misuse, sexual exploitation, absconding;
Recruitment via Forensic services: Those recruited via forensic services will have forensic histories indicating both severity and chronicity. Thus the inclusion criteria, in addition to the generic criteria 1, 2 and 3 above, would comprise (1) at least one conviction within the last twelve months, or referral via a supervision order with MST as specified activity, (2) a warning, reprimand and/or conviction on at least three occasions in the 18 months.
Recruitment via Child Mental Health services could have the following specific criteria: (1) current diagnosis of conduct disorder, substance misuse, major depression or anxiety; (2) history of at least one unsuccessful outpatient intervention; (3) EITHER history of school exclusion OR assessment as child in need.

Recruitment from Educational services could have the following specific criteria: (1) currently permanently excluded from School, (2) history of having been excluded from at least one other school for aggressive conduct;

Exclusion criteria will include: (1) history or current diagnosis of psychosis, (2) generalised learning problems (clinical diagnosis) as indicated by IQ below 65, (3) risk of injury or harm to a worker, (4) presenting issues for which MST has not been empirically validated, in particular substance abuse in the absence of criminal conduct or sex offending as the sole presenting issue.

Procedure and Sample size: A minimum of 700 participants (350 in each arm) will be recruited. The sample size calculation is motivated by the secondary outcome (achieving reductions of re-conviction) as reliable figures for the reduction of out of home placement associated with MST are not available (see above). The expected difference in proportion of our trial is derived from the major US effectiveness trials as Brandon Centre trial (BCT) data will not be available until late 2009.

Sample size: We assume that each site will have at least 140 families per year referred for treatment. On the basis of past experience and assumptions outlined below (see Figure 2) we assume that about 30% of referred families will meet criteria and agree to randomisation, this implies that each site will be able to recruit and treat about 70 families over one and a half years. This means that we expect to be able to recruit and assess 700 participants (350 in each arm). Assuming that 30% of the MAU arm will have out-of-home placements, this sample size will give 86% power to detect a 10% difference in out-of-home placements (a reduction from 30% to 20%). To take account of within-therapist correlation of outcomes in the MST arm, we assumed an ICC of 0.02 and a total of 30 therapists, giving design effects of 1.22 in the MST arm and 1 in the TAU arm, and thus reducing the power to 83%.

Methods of recruitment and consent: The process of recruitment is fundamental to the success of this research trial. In addition to criteria that apply to recruitment for any trial (the clear application of eligibility criteria, a standard procedure for obtaining informed consent, etc), recruitment for this trial must be especially sensitive to the community context and be based on effective partnerships with referral agencies and strong relationships with the young people and their families. Given the relatively large number of sites and limited possibility of statistically moderating site-specific effects, the trial team will have to work in strong collaboration with the MST team at each site to achieve the high levels of accrual necessary to ensure sample comparability and reasonable generalisability. The mechanism for recruitment will have some of the features of the multiple gating procedure in use in the Brandon Centre MST. One possible model for this type of multiple gating is the following: decisions about eligibility for the trial would be made at three points: (a) by the multi-agency panel, (b) at an explanatory visit by the MST team and (c) by the OA following the baseline assessment. Experience suggests that each of these screens tend to throw up different criteria for ineligibility and their use in combination minimizes the considerable recruitment effort. For example, the panel review tends to identify referrals for issues where MST has not been empirically validated (e.g. sex offending as the sole presenting issue), while OA assessment is necessary to confirm IQ and psychiatric diagnosis. The visit by the MST team most commonly identifies risk of possible injury to worker or incompatible agency involvement precluding inclusion in the trial.

The following then is a recruitment protocol based on 5 years of experience at the Brandon Centre to optimise take-up of MST services. We assume that a multi-agency panel will be in place at each site, taking referrals from both Youth Offending Teams, CAMHS and children's services and perhaps increasingly from Education. This panel will be in charge of identifying new cases that meet the eligibility criteria for MST. If there is no multi-agency panel the MST team would form its own referrals group. We assume that without careful attention there may be substantial differences between sites as to the criteria the panel will use to accept referrals for

MST. This is a potential source of bias and could, if criteria interact with suitability, generate built-in between site differences. We intend to use the expertise that we have built up both in London and in Cambridge to work with each multi-agency panel and create a homogenous recruitment protocol for the panels to work to which would also be consistent with the eligibility criteria for the trial. We are currently in discussion with the sites regarding this protocol. The key components of such a protocol would include a standard referral form including information pertaining to inclusion and exclusion criteria which will form the first screen to the trial focusing on establishing severity and chronicity. Following the acceptance of the referral by the Panel, a standard initial letter in the first language of the family from the multi-agency panel will be sent to parents and separately to the young person if s/he is 16, informing them about the trial, standard explanatory visit and a standard consenting procedure. Recruitment begins with this letter which would be sent to all those identified by a panel to be probably suitable for MST. The letter from the panel (or the MST referral team) would invite participation, and informs families and the young person that someone from the MST team (preferably the MST supervisor) will contact them unless they do not wish to participate in the trial. The letter would include material in age and culturally appropriate language in the form of a leaflet for both the parents and the young person explaining the trial and what involvement in the trial would mean at that particular site. Information sheets have been constructed and designed with input from young people and their parents/carers who have used MST in order to make them as useful and accessible as possible. Separate, specifically adapted sheets are included for different age ranges; one for children aged 11−15 and one for young people aged 16−17, containing the same information as the parent/carer sheet but in age−appropriate language. Information sheets have been constructed and designed with input from young people and their parents/carers who have used MST in order to make them as useful and accessible as possible. The MST supervisor and therapist will be on hand at consent meetings to explain anything in the information sheets and consent forms that is unclear. After a brief period of time (1-2 weeks) the family would be contacted by a member of the MST team to explain in person what participation might involve and to arrange an appointment. This is the second stage of the multiple gating procedure and the MST worker might identify exclusion criteria at this stage (e.g. risk of possible injury to worker, incompatible agency involvement, severe substance dependence). Consent forms would not be signed at this appointment because experience has shown that actual take-up of treatment increases dramatically and early dropouts are reduced if the family feels they have been given adequate time to consider their participation. Unless the family expresses a decision not to participate at the time of the visit, a phone contact would be made by the OA no less than 3 days after MST and the trial have been explained to families or within 7 days should the family wish for more time to think about the trial. This would be the time for reviewing the consent form and if signed, completing pre-randomisation questionnaires and measures. At this second visit, the final evaluation for eligibility is made (screen 3). When all the instruments have been completed and trial eligibility confirmed, the OA makes a call to the trial centre to obtain the allocation.

The ethical principles of which the MST Supervisor, MST Therapists and Outcomes Assessor must be aware when speaking to the young person and his or her carer about participation in the study are:

There is no negative consequence for those who decline to participate;
There is no negative consequence for those who do participate;
Potential participants are informed of all that is expected of them, including benefits and risks that may be associated with participation;
Consent to participate is freely and voluntarily given, with full appreciation of the above;
Participants understand that they can withdraw their consent to continued participation at any point in the process;
All information gathered about them will remain confidential; and
Anonymity is assured in that individual participants will not be identified in any report or document produced.

Second, the MST Supervisor, MST Therapists and Outcomes Assessor understand that, for the MST clinical trial, the implications of these standards are that potential participants must understand:

What MST entails, including the amount of time spent in the home, the intensity and duration of intervention and what is expected of the participants;
That young people who decline to participate in the clinical trial will receive the same level of intervention they would normally expect from the YOS (i.e. they will not be penalised for declining consent);
That half those who sign the consent forms will receive whatever intervention would have been available to them if no MST study had been underway;
That the decision about who gets MST is made randomly so each person has an equal chance of being selected;
That the services offered to the control group are not a placebo or are not inferior but rather constitute the typical services available to young offenders as MAU;
That participation in the clinical trial entails filling out questionnaires to gather background information and after discharge from treatment or approximately five months if not allocated to MST;
That the young person's school will be approached for information;
That the parent or carer and the young person are free to drop out of the MST condition;
That all information participants provide will remain confidential except in three circumstances: 1) A person under 16 is at risk as defined in the Children Act 1989
2) a person voices a fixed intention to harm a specific other person that must be communicated to the police; or 3)the information is demanded by the judge; and
That at six-month, one-year, two-year and three-year intervals the law-breaking behavior of the young person will be checked and that this information will not be revealed to anyone outside the research group.

The verbal explanation of the study given by the MST Supervisor, MST Therapists and Outcomes Assessor to the young person and her/his parent or carer is a crucial part of the process whereby they are able to give valid consent to take part in the study. In seeking consent, the MST Supervisor, MST Therapists and Outcomes Assessor ensure the decision is made on an informed basis. Due to the vulnerability of the young person and her/his parent or principal carer, there are a number of potential misunderstandings that could lead to their giving consent on an uninformed basis and to which the MST Supervisor, MST Therapists and Outcomes Assessor must be alert, namely:

1. The young person and her/his parent or carer may think they are obliged to take part because the study is part of the young person's sentence, i.e. they may not understand the voluntary nature of the study.
2. They may think that refusal to participate will have further negative consequences for the young person.
3. They may think that if they drop out of the study that this will have negative consequences for the young person, for instance that the young person will be breached and taken back to court.
4. They may think that agreement to participate means that they automatically get MST.
5. They may not understand that the MST intervention involves the participation of the parent or carer as well as the young person.
6. The young person and his/her parent or carer may not realise the young person's decision as to whether to participate carries the same weight as the parent or principal carer and that, if the young person refuses to give consent, participation cannot go ahead even if the parent or carer agree to give their consent.
7. The capacity of the young person to understand the nature of the study will vary accoridng to her/his age. For example, a young person aged 13 years is unlikely to understand or grasp the nature of the study in the same way as a young person aged 16 years.

To guard against these and other pitfalls MST Supervisor, MST Therapists and Outcomes Assessor considers the following action points:

1. Those who have agreed to discuss the study having received the MST information leaflets may sign the consent form at the first meeting with the MST Supervisor, MST Therapists and Outcomes Assessor. Some potential participants may express an interest in the study but prefer to have time to think over their participation.
2. At the meetings, the pitfalls described above should be addressed as part of the explanation of the study given to the young person and her/his parent or carer.
3. Before the consent forms are signed, the MST Supervisor goes through the information sheet and the consent forms with the parent or carer to ensure she/he understands the study. The MST Therapist, who like the MST Supervisor is trained to work with young people, goes through the information sheet with the young person. the MST therapist interprets the information sheet to ensure that the young person understands what is involved: that her/his participation is entirely voluntary; that she/he can withdraw from the study at any time without being penalised; that at any time she/he can refuse to have her/his criminal record accessed; that should she/he get MST, this intervention is independent of services offered by the YOS; that we may offer to help in a number of areas, including education, social activities, substance abuse and anger management if these are problems that contribute to her/him getting into trouble but that he/she can refuse help in one area without jeopardising help in other areas.

Finally, the MST supervisor and therapists follow the following guidelines regarding withdrawal from the study by the young person and her/his parent or carer:
1. The decision of the young person and her/his parent or carer to withdraw from the clinical trial should at all times be respected.
2. If the young person and her/his parent or carer consistently refuse to carry out recommendations of the MST therapist, this should be interpreted as them not wanting to continue with the project.
3. If the young person and her/his parent or carer consistently refuse to make appointments with the MST Therapist, this should be interpreted as not wanting to continue with the project.
4. Withdrawal from the study is a barrier to future participation.
5. The data from the participants who withdraw consent should be kept until the end of the study. Once the study is over their data must be removed.

Accrual: Anticipated recruitment paths are shown in Figure 2. We have made very conservative assumptions based on the Brandon Centre MST Trial (Baruch and Butler, personal communication) throughout. It is likely that with time fewer inappropriate referrals will be made but we assume that only 80% of those referred by YOTS, Children's Services, Educational Services and CAMHS will be considered appropriate referrals by a Multi-Agency Panel or the MST team. For the moment we assume that 20% will clearly not meet the 'at severe risk' citeria or meet exclusion criteria and fail screen 1. Data from the BCT (which takes only chronic forensic referrals) suggests that approximately 1 in 5 cases considered by a panel to be appropriate for the trial go through to providing consent and 1 in 3 families to whom MST was explained in person by an MST worker agree to participate. We anticipate that in the more heterogeneous recruitment context of this trial, the ratio of referrals to randomised will be closer to 33%. In the BCT on average over 50% of cases deemed eligible in the multiple screening are expected to eventually consent. 20% refuse the offer of an explanatory visit. Of those who are visited 25% are expected to be clearly not eligible but 50% of those eligible consent and go onto accept baseline assessment and randomisation. Qualitative study of the recruitment process in the BCT (Baruch & Butler, personal communication) indicated that 57% of those declining to proceed to baseline assessment claim that there were no recent, current or anticipated difficulties with the young person's behaviour, often adding that it had improved significantly since the offence that triggered the referral. The remainder of the eligible families give a variety of explanations: not having enough time to commit to MST, receiving adequate support from other services, claiming not be able to persuade the son or daughter to consent to the intervention, expecting that the

situation would change, not wishing anybody to work in the family home or planning to move out of the borough soon. 88% of those consenting and undertaking baseline assessment will be expected to participate in the trial with 12% excluded because they did not meet criteria. Thus we assume no more than about a third of those referred will participate but that 55% of appropriate referrals meeting criteria will participate with approximately 40% of those referred being excluded as failing to meet criteria. It should be noted that although these assumptions mean that only a relatively small number of those referred will be included in the trial, data indicates that immediate dropout from treatment for severe conduct problems is in any case very high (Kazdin & Wasser, 2000). Thus, those receiving MST are likely to be a much higher proportion of those adolescents who, in the real world would be willing to engage with therapeutic services for treatment. To recruit 700 adolescents who are considered at severe risk of out of home placement we would expect approximately 2,117 to be referred to the MST multi-agency panel. This means about 200-225 families referred to each site over the study period. It should be remembered that these may be conservative assumptions that reflect the severe forensic problems that characterise the BCT sample.

Randomistion: Eligible consenting participants will be randomised on a 1:1 basis by the Clinical Trials Unit at UCL using a secure, automated 24 hour telephone randomisation service that will ensure allocation concealment. A computer-generated adaptive minimisation algorithm that incorporates a random element will be used with the following stratification factors: treatment centre, gender, age (11-14, 15-17), age at onset of severe conduct problems (2-11, 11+), number of past convictions (≤2/≥3). These strata have been selected because previous research (see Background) has shown that younger age of onset and greater number of previous convictions are associated with poorer prognosis and there is insufficient evidence concerning gender mix, particularly in the older age groups, to ensure that simple randomisation would generate comparable groups. Minimisation should ensure that there will be an even distribution of adolescents across the two arms of the trial.

Planned Intervention: Multi-systemic therapy is an integrative, manualised, licensed programme with a substantial evidence base for engaging young people exhibiting anti-social behaviour and their families. Adolescents with severe conduct problems (violence, drug abuse, school expulsion) will be treated over a period of 3-6 months with a community-based multi-component treatment programme focused on the family but also engaging schools, neighbourhoods and community resources and administered by specifically trained professionals with relatively low caseloads. Young people and families requiring this approach are assumed to be resistant to engagement by existing services even though intensive outreach services may be required, probably associated with complex family problems including substance misuse and mental health problems that are likely to affect parenting. Adolescents and their families will receive a minimum of 3 and a maximum of 6 months of input from the MST team. The frequency of contact with the MST workers will be monitored but not controlled. It is expected that, as with MAU, some families will require briefer periods of treatment or may prematurely terminate treatment unilaterally. MST is going to be delivered by a team of at least 3 specially trained clinicians under the supervision of an MST supervisor, with weekly one hour conference calls for consultation with an MST services staff member. In addition, it is expected that MST therapists will have the support of local consultation from mental health professionals with post-graduate qualifications in disciplines such as social work, psychology or counselling. In view of the breadth and complexity of this input, it will be essential to monitor consultation as well as contact time of the MST team in order to arrive at accurate assessments of health and social care costs. It is essential that MST therapists and MST supervisors should not be allowed to see participants in the MAU arm of the trial, although professional consultants to the MST team may well be engaged in provision of MAU.

Management as usual MAU will be the standard care offered to adolescents and their families who meet eligibility criteria for the trial. This treatment is likely to be diverse and may involve no therapeutic intervention or individual or family orientated work. It is likely to be delivered by a wide range of practitioners with quite different theoretical orientations. The average duration of

these interventions is also likely to vary. It is expected that practitioners will be working in line with best practice as specified in relevant SCIE and NICE guidance. It is unlikely that treaters in MAU will receive the extent or quality of supervision available for MST therapists. However, it is by no means clear that even during the trial period MAU interventions are likely to be less intensive or less costly than MST. However, they are likely to be delivered in a less focused and far less well specified manner. For this reason MAU interventions will be carefully monitored using a service use schedule designed specifically for the trial that will record contact with all services (health, social, YOT, education, voluntary sector etc), including number of contacts (and possibly average duration of contacts). This will give a realistic sense of the level of intensity of MAU, whatever that may be, and, used in conjunction with the MST arm, will give an indication of shifts in intensity, i.e. does the addition of MST reduce the need for other supports. As this will be a pragmatic trial involving a number of collaborating services even within each site, it will not be possible to specify in advance what management as usual will be.

We have chosen an individually randomised design in favour of a cluster randomised approach as we anticipate that there will be minimal risk of contamination between the two treatment arms. However, we are not certain what the framework for administering MST will be, how and in what services it is likely to embedded and the risk of contamination may vary. In order to address this potential bias, site-specific strategies may be necessary to ensure that MST principles and practice do not directly influence the treatment of those randomised to the MAU condition. We assume that MAU will be variably influenced by principles of good practice which are articulated by the MST nine principles. In the measures section we describe how we intend to deal with the likely overlaps between the two arms of the trial. Presently, interventions in the MAU group are likely to be somewhat different from manualised MST interventions. Many forms of treatment that are specifically contraindicated by MST (e.g. supportive counselling, individual psychodynamic psychotherapy) might well be offered to the MAU group in a CAMHS or Children's Services context.

Participant Adherence:

Dropping out of treatment is common during interventions for antisocial problems (Kazdin & Wassell, 2000; Kazdin & Wasser, 2000) MST has a far superior record of maintaining cases in treatment when compared with MAU (86% vs 79%). Based on 6 studies the RR is highly significantly favouring MST (RR=.69, 95% CI: 0.49, .98). In the BCT following the careful recruitment procedure outlined above, well over 90% of those recruited for either arm of the trial have been retained for the purposes of data collection. We recognise that participation in the various treatment protocols will have lower adherence than data collection as data collection visits are incentivised for both families and young persons by modest compensation for time and travel. To ensure a comprehensive intent to treat analysis the primary outcomes consist of data recorded formally (e.g. out of home placements) which can be measured even if participants have dropped out of treatment and research appointments. In the current trial we have conservatively assumed a 5% dropout at each measurement point, totalling a 15% attrition overall that would effect analysis of secondary outcomes (see Figure 2).

Measures:

Follow-up assessments will be at 6, 12, 18, 24, 36 and 48 months post randomisation, with primary outcomes collected until 5 years post randomisation.

(a) Principles of measurement: The measures will be made across multiple domains (specific to criminal behaviour, family function, user satisfaction, comorbid problems and economic costs), using multiple methods (interviews, questionnaires, records), and multiple sources (adolescent, parent, teachers) to maximise the clinical validity of the outcome assessments and minimise bias arising from any single source of information. Where possible, measures will be made by individuals blind to treatment allocation. Many of the measures have been selected because they are part of an ambitious project under-way in the Parenting Academy (Scott, Dabbs et al.) with a range of samples, including with a large sample of looked after children, which will provide UK norms against which the current sample may be compared.

(b) *Domains of measurement:*

Screening, diagnosis and potential moderators:
Demographics Interviews (DIP and DIT developed specifically for this project) will cover general information, information about forensic history, schooling and economic information. Psychiatric disorders will be identified and a psychosis screen provided by the Development and Well-Being Assessment (DAWBA) (Goodman R, Ford T, Richards H, et al. 2000), which also incorporates a general measure of wellbeing, the Strength and Difficulties Questionnaire (SDQ) (Goodman, 1999) in its administration and the K-SADs and SCID I &II will be used at the 3 year follow up to identify current psychiatric disorders (First, et al.1997). We will use specific measures to assess hyperactivity and Impulsivity, the Conners ADHD DSM-IV scales (Conners, 1995) from parents and teachers. ODD/CD will be monitored using the self-report delinquency measure, and callous and unemotional traits using an updated version of the Anti-social process screening device (Essau, Sasagawa, & Frick, 2006), while depression will be monitored using the Short Moods and Feelings questionnaire (Messer et al., 1995). Non-compliance and increasingly serious forms of antisocial behaviour, together with young people's perceptions of law-abiding behaviour and institutions, will be measured using the Anti-social Beliefs and Attitudes Scale (ABAS), a broad-based measure designed to assess antisocial beliefs and attitudes in pre-adolescents and adolescents (Butler, Leschied and Fearon, 2007). Child Psychometrics will be obtained using two subtests from Wechsler Abbreviated Scale of Intelligence (The Psychological Corporation, 1999) for IQ. Peer delinquency will be assessed using the Peer Delinquency Questionnaire (Smith & McVie, 2003) and the quality of the child-parent attachment relationship using the Child Attachment Interview (Shmueli-Goetz, Target, Fonagy, & Datta, in press). The latter measured will be obtained only on 10% of the young people involved in the study. The quality of the parent-adolescent relationship and parenting practices will be evaluated using the Family Assessment Device (FAD;Epstein, Baldwin & Bishop, 2007) and the Alabama Parenting Questionnaire (APQ; Frick, P.J., Christian, R.E., & Wootton, J.M. 1999). Parental disruption will be indicated by the short-form of the Conflict Tactics Scale (Jaffee, Moffitt, Caspi, Taylor, & Arseneault, 2002), while level of expressed emotion in the home (as conceptualised in the Camberwell Family Interview) will be assessed using the Level of Expressed Emotion Questionnaire (Gerlsma & Hale, 1997; Hale, Raaijmakers, Gerlsma, & Meeus, 2007). An assessment of parental psychopathology will be obtained using the General
Health Questionnaire (GHQ 28; Goldberg, Gater, &Ustun, 1997).

It is estimated that this battery would require approximately 2 hours with the parents, combining interview and questionnaire administration. The measurement burden for the child is 15 minutes in psychometric testing, and approximately 1 hour and 45 minutes in questionnaire completion and interview. For the 10% of the sample of young people completing the child attachment interview, the total time increases to approximately 2 hours and 15 minutes.

Family functioning measures: Family function is an important outcome of the intervention. There are again several approaches to this domain available. We opted to use the 12 item general functioning scale of the McMaster Family Assessment device (Epstein, Baldwin, & Bishop, 1983) to be completed by parents and index subject. The measure has been used with families with young people with severe antisocial behaviours and with emotionally disordered children and has discriminant and some predictive validity (Martin, Bergen, Richardson, Roeger, & Allison, 2004; Tamplin & Goodyer, 2001). We predict that MST will achieve increases in positive emotional quality and communication between parents and young people as well as increases in parent confidence and skills in addressing challenging/problematic adolescent behaviour.

Adolescent wellbeing outcomes: Key adolescent behavioural outcomes have been teacher and parent rated in previous studies and we also intend to repeat the SDQ (Goodman, 1997) as an alternative to the longer Child Behaviour Checklist (Achenbach, 1991). We consider educational outcomes (school attendance, Teacher's report) to be particularly critical secondary outcome measures. We will also repeat measures to assess peer relations. These include the Peer

Delinquency Questionnaire (Smith & McVie, 2003) which cover perceptions of adolescent's friendships. We predict that MST will achieve decreases in associations with other antisocial peers and increases in positive peer relations and greater commitment to pro-social activities (e.g. education). This prediction is consistent with the model and hypothesised mediating mechanisms (Huey et al 2006) and are relevant to social policy initiatives and concerns.

The primary outcome will be the proportion of cases assigned to long-term (3 months+) out of home placements in specialist residential provision at 18 months following randomisation including placement into local authority care, incarceration, long-term hospitalisation and residential schooling. Adolescents on the edge of care are often placed in boarding schools or even psychiatric hospitals because of a variety factors that currently prevent or in the past have prevented them coming into care earlier so that alternative solutions are sought (e.g. a family may have successfully resisted a previous attempt by LA to obtain a care order etc.). The Children Plan produced by the Department of Children in November conceptualised all integrated children's services as being universal, targeted or specialist. We expect this trial to give information on how many children from MAU and MST required specialist residential provision either immediately or during follow-up period. The Norwegian study identified the relative risk of out of home placements associated with MST 2 years after randomisation to be .59 (95% CI: .32, 1.06) with almost half (48%) of children in the MAU condition being taken into care. The reduction in end of treatment incarceration estimated on the basis of 3 US studies carries an RR of .34 (95% CI: ..20, .56) at treatment termination and .75 (95% CI: .52, 1.07) at 18 months follow-up. The MAU incarceration rate was about 50%. These figures are hard to apply directly to the UK context where both out of home child welfare placements and incarceration is less likely then in the US (50% in MAU). This makes power calculations challenging but following the recommendations for power calculations of Kreamer and colleagues (Kraemer, Mintz, Noda, Tinklenberg, & Yesavage, 2006) We suggest specifying an apriori clinically significant reduction of around 15% in specialist residential provision to be of clinical significance.

The research team strongly feels that while the rate of out of home placement is an important primary outcome, it is not in every instance an indication of the failure of the system to provide adequate support to the young person and her/his family. Findings have to be interpreted in the context of other outcomes, including general wellbeing, which may in some cases improve following out of home placement. Thus while out of home placement is a critical indicator (and the only measure that can be collected on the entire sample even if the families are lost to data collection interviews), it cannot be considered to be the final arbiter of effectiveness. Placement into specialist residential provision in our view reflects four types of outcome based on two separate factors; the first is about family functioning and the second concerns decisions about where the young person lives. If, following intervention, the family functions in a way that more adequately meets the young person's needs and the young person continues to reside in the family, this constitutes an unequivocally preferred outcome. If, despite intervention, family functioning remains unchanged and is unable to meet young person's needs and the young person is placed out of the family, this constitutes a failure of the intervention (preservation of the family did not succeed) but it is likely to be the best outcome for the young person under the circumstances. The third possible outcome is that, despite intervention, family functioning is still unable to meet the young person's needs but the young person remains in the family. This is the critical instance where an apparently good outcome (family preservation) in fact reflects a non-preferred (poor) outcome for the young person. The fourth outcome, perhaps less likely, is that the intervention results in better family functioning after intervention but the young person still placed out of home. This will hopefully be rare but could be an 'effective' intervention with respect to psychological outcomes but not with respect to family preservation. In the light of this argument, while we intend to retain out of home placement as the primary outcome, we intend to interpret the family preservation information in the context of the information collected with the self-report wellbeing instruments. So, instances when there is no out of home placement but home observation data and self-report measures suggest that the young person's situation is markedly sub-optimal, the outcome would be coded as a treatment failure as would the second-category of outcome listed above.

There may be further concerns attached to using out of home placement as a primary outcome. It is possible to envision a situation whereby the presence of the MST team would influence the likelihood of court or other systems deciding to place the young person away from the family. It is also possible that the presence of the MST team, affording a more accurate view of family function, may precipitate the placement of the young person outside the home. These types of influences which suggest that the primary outcome measure may be 'reactive' with the planned intervention would compromise randomisation, and compromise the trial. In order to minimise these problems we have placed the endpoint of the study at 18 months in order to see if the impact of MST may be felt over the course of the year that follows the intervention. It is unlikely that over this period the measure (long-term placement out of home) would be reactive with the intervention.

The other domains we consider key to the intervention are (a) forensic outcomes, (b) adolescent wellbeing outcomes and (c) family functioning outcomes. In addition of course, in line with the research brief, we consider the economic data collected alongside these outcomes to be key.

Key Forensic Outcome: We have considered a range of forensic outcomes related to the antisocial behaviors which remain a key part of the definition of the target population. Perhaps the most meaningful key forensic outcome would be reconviction rates which over a short term follow-up based on 3 studies favours MST compared to standard care with an RR of .51, (95%CI .23, 1.16). The likelihood of reconviction during the course of treatment is 30% and over 18 months from randomisation is about 50% based on a combination of US and Canadian studies. . We will use time to offences (categorised as per annual statistical reports Youth Justice Board, 2007) that resulted in a pre-court disposal (Reprimand or Final Warning) or a court disposal. Access to this information will have been approved by the YJB. In collaboration with the YJB, we will also examine whether MST reduces use of custodial sentences and hence service costs.

Additional forensic outcome measures that have been used in previous RCTS include arrests (based on archival data) of survival rates to first arrest (time to arrest), number of arrests or dichotomously coded arrest (arrested or not). In some studies seriousness of crime (tariff) for which the individual was arrested was also included. An obvious alternative forensic outcome would be number of arrests where the mean reduction associated with MST in previous studies was significant (SMD=-.39, 95%CI -.81, .02, based on 7 studies; N=677). Arrest as an outcome measure is known to be confounded by the efficiency of police forces and to some extent policies of policing. Incarceration (based on archival data) has been used as a dichotomous or continuous measure period of time in prison or institution. A number of alternative measures had been used in the literature which can be collected in the present study and would enable us to compare outcomes in the hope that further meta-analytic and mega-analytic studies may be conducted. 18 months has been selected as the time for primary outcome measurement to enable identification of any changes subsequent to cessation of therapy but it will also facilitate the collection of more meaningful forensic data more likely. The choice of disposal as the key forensic outcome is justified because other indicators (arrest rates, duration of incarceration, episodes of incarceration, self-reported delinquency) and other indicators used in MST research are more prone to reporting and other biases.

(c) *Economic evaluation:* Health economic analysis will be conducted by the Centre for the Economics of Mental Health at the Institute of Psychiatry (IoP), London. Introduction. Economic evaluation techniques will be used to explore the relative costs and cost-effectiveness of the alternative management strategies – MST and MAU. The evaluation will take a broad perspective, including all health, social services, education and voluntary sector services, plus costs falling on the criminal justice sector, costs resulting from crimes committed, and out-of-pocket expenses to the young people and their families.

Data on MST contacts will be collected directly from pilot schemes to avoid participants revealing their group allocation to the research assessors. Data on the use of all other services will be collected in interview using the Child and Adolescent Service Use Schedule (CA-SUS), developed and successfully employed by the applicants in previous evaluations with young people with complex mental health and social care needs (Barrett, Byford, Chitsabesan, & Kenning, 2006; Byford et al., 2007; Clark et al., 2005; Harrington et al., 2000). The CA-SUS will be adapted to the current population through review of the literature and pilot testing, to ensure comprehensive coverage and face validity.

The cost of the trial interventions will be calculated through a detailed micro-costing (or bottom-up) approach using standard costing methodology (Beecham & Knapp, 1992; Drummond, O'Brien, & Stoddart 1997), which will involve estimation of indirect time spent on individual cases, including preparation, meetings, telephone calls and supervision, as well as detailed recording of direct face-to-face contact. Unit costs will be calculated using data on salaries, employer on-costs (National Insurance and superannuation), conditions of service and appropriate administrative, managerial and capital overheads (Curtis, 2007). National unit costs will be applied to all other resources used by participants, where available (e.g. British Medical Association & Royal Pharmaceutical Society of Great Britain, 2007; Curtis, 2007; Department of Health, 2007; HM Prison Service, 2007; Home Office, 2005).

(d) *The MST Adherence Measures:* The MST team in South Carolina have developed a form measuring MST adherence derived from the nine principles, to be completed by the parent(s). This will be used to measure adherence in the trial. We understand that these data are likely to be available to the research team. It would seem costly and wasteful to undertake a separate coding for adherence which would in any case need to be validated by the originators of the treatment.

(e) Characterising MST and MAU interventions: We will carefully characterise the nature and delivery of interventions in both the MST and MAU arms of the trial. Families will be asked to complete the Expectancies Questionnaire (Client and Therapist version of a 5 item questionnaire that assess client and therapist expectancies of treatment success and satisfaction with treatment) (Shaw et al., 1999) , the California Psychotherapy Alliance Scale (CALPAS) a 24 item measure assessing 4 dimensions of therapeutic alliance (Gaston, Thompson, Gallagher, Cournoyer, & Gagnon, 1998) and The Reasons for Termination checklist developed on the bases of work by Moras (1986). In addition, using the key features of effective programs identified by Utting et al., we will develop a fidelity measure of MST which will enable accurate characterisation of the MST intervention itself and potentially allow for the identification of key programme elements associated with positive outcome. The fidelity measure will characterise key aspects of the functioning of the MST service that have been identified in the literature as necessary for the effective implementation of MST. These characteristics will also be present, probably to a lesser degree in MAU services and we will use the same measure to characterise important dimensions of the care delivered in MAU. The use of a common measure will therefore allow for the comparison between MST and MAU along important dimensions of care and potentially provide information on common aspects of service function associated with outcome. Such an approach has been used by members of the team to characterise other complex interventions in mental health (Killaspy et al., 2006). It will be of particular value in assessing the key functions of a complex intervention such as MST when it is deployed in another health care system from that which it was developed (Hawes & Dadds, 2006).

(*f) Qualitative measures of commissioners, referrers, providers, parents, adolescents and other staff views about MST:* One of the aims of this evaluation is to identify typologies or describe characteristics of the implementation of MST interventions adopted by the pilot sites and explore the association of their different components with specified outcomes (e.g. cost, average therapeutic gain) which will be of value in a national rollout of MST. As the number of sites is not sufficient for a reliable quantitative approach to be taken to this question we hope to use qualitative approaches to identify and create typologies of the barriers to MST implementation in

order to maximise the lessons that might be learnt with these pilot sites. We aim to use methodologies we have evolved in the context of an SDO commissioned evaluation of pilot sites for innovative PD services (Crawford et al, press) (Crawford et al., 2007) ; Crawford et al. (application). We intend to interview key stakeholders at each site which includes service heads for YOTS, Children's Services, CAMHS, MST supervisor and representative therapist, representative parents and young people and colleagues in the services within which MST will be embedded. The first round of interviews would be conducted in autumn of 2008 and will seek to forge collaborative partnerships with key project staff in each area, engaging them in the process of characterising the program models they have decided to implement and their decision-making rationale in terms of perceived barriers and facilitators. The primary focus will be on systemic and inter-agency factors, on the collection of multiple perspectives and on the identification of shared and different perceptions across different stakeholders. Soft Systems Methodology (SSM) (Checkland & Scholes, 1990) will be used to analyse the principal themes and issues apparent at this level and this stage of the project which will feed forward into the second round of interviews in Autumn 2009. In the second-stage interviews the focus will be on the detail of implementation of the site's program model, looking at what is being done and how, what facilitators and barriers have been experienced. Data collected at this stage will be used to elaborate the systems models developed from the first-stage interviews and a framework approach to content analysis (Ritchie & Spencer, 1993) will be applied to identify dimensions and levels of implementation across programmes that can be quantified for analysis of relationships with outcome variables. Subsequently in Years 2, 3 and 4 we will use checklists and other tools developed as a result of the above analysis to gain relevant information from key stakeholders to monitor changes in service models and relevant staffing. In order to obtain additional information about the experience of (a) MST and (b) being in an RCT of this treatment we propose to use the semi-structured interview developed by Butler and colleagues in the BCT (Casagli, 2007; Lawrie, 2005). This 45-minute interview elicits the parents' and the young person's experience of MST or control treatments, their view of costs and of benefits. It will be administered to a random, representative sub-sample of families, about 4 per year at each site, by a person independent of the intervention but not blind to treatment allocation. We will extend this approach also to cover staff experience of delivering MST.

An optional qualitative interview will also involve a small sub-sample of families (approximately 12 families) recruited into the START Trial to look at what their experience of receiving MST was like in regard to their and their sons/daughters gang involvement. The interviews aim to specifically explore the experience of MST according to families where the young person has been, or remains to be gang-involved and MST therapists will also be interviewed from two of the nine sites involved in the trial about their experience of working therapeutically with these families. This will be conducted by a person independent of the intervention but not blind to treatment allocation.

It is widely accepted that gang involvement acts as an amplificatory factor for delinquent behaviour (Battin et al., 1998), whilst gang involvement is also highlighted as part of a longer-term trajectory of worsening behaviour (Loeber et al., 1993; Howell & Egley, 2005). With proven effectiveness targeting the behavioural problems that predict and are amplified by gang membership, family support programmes, such as MST, might also prove effective in preventing gang membership or promoting desistance from the gang (Howell & Egley, 2005; Shute, 2008).

Despite this, whether such approaches might prove successful or whether gang-involvement acts as a mediating factor on the success of the intervention has not been investigated. This smaller qualitative study aims to use qualitative interviews to look at the MST model in relation to these families, exploring their experience of MST and looking at what aspects of the model are applicable and helpful for this population as well as additional challenges which it may pose.

Sixty minute semi-structured interviews will be conducted with both the families (young person and parent/carer) and the MST therapists. The data will then be analysed for themes using Framework analysis (Ritchie & Spencer, 1994).

Design and Methodology (Annual follow up from 2-5 years)

The annual follow-up period from 2 years post randomisation will extend the primary outcome window to 60 months and carry out an evaluation of a broadened range of outcomes of both MST and MAU to 48 months. We will conduct annual full-blind outcome evaluations up to 48 months post-randomisation. Data on service use will be collected using the Child and Adolescent Service Use Schedule (CA-SUS) and Children & Young People, Resources, Evaluation and Systems Schedule (CYPRESS) (Pilling et al., 2012). Data will be used to characterise services and provide currently lacking information on transitions from child to adult services, identifying correlates of a smooth transition (continuation of appropriate services across the 18-year barrier) and testing the hypothesis that transition is important to relatively better outcomes. A a semi-structured interview will explore young people's and primary caregivers' views of change or the absence of change in key outcome domains and the families experiences of services and of the transition between services..

The following domains will be assessed using a comprehensive battery of measures anticipated to take approximately 2-3 hours per assessment (measure in brackets): (i) antisocial behaviour (arrests, reprimands, final warnings or convictions, self-reported delinquency scale, Antisocial Process Screening Device/ICU (Frick & Hare.,2001) (Kimonis, et al.,2008), Achenbach Adult Behaviour Scale (Achenbach, et al.,2013) and emotional well-being and adjustment (Achenbach Youth or Adult Self-Report Scale (YRS)(Achenbach et al.,2013;Achenbach.,1991); Adolescent Resiliency Questionnaire (ARQ) (Gartland et al.,2011); Mental health (services receipt interview, KSADS/SCID (Kaufman et al.,1996; First et all.,1997); (ii) education (school records, interviews, National Pupil Database) and work adjustment ((CLES-A (First et al.,1999), Achenbach Youth or Adult Self-Report Scale(Achenbach et al.,2013;Achenbach.,1991) and the work and relationships information form). (iii) social network (Peer delinquency questionnaire (Smith et al.,2003), Family Adaption and Cohesion scales (Gorall et al., 2006), ARQ (Gartland et al.,2011)) and family outcome (Sib-SDQ (Goodman et al.,1998), Alabama Parenting Questionnaire (Frick.,1991), ARQ (Gartland et al.,2011)), self efficacy (ARQ) (Gartland et al.,2011)) and parenthood (interview); and (iv) physical health (SF-36) (McHorney, Ware.,1995). Diagnostic status will be determined by the K-SADS until participants reach 18 and by the SCID thereafter.

Collecting comorbidity data will inform us of the impact of comorbid disorders on the primary outcome, enabling us to characterise over time the relation between initial trial outcome and subsequent antisocial behaviour, and the presence of these different disorders, and key participant characteristics, e.g. attachment, family relationships and service utilisation. This will have implications for the design of future interventions. Data on MST contacts will be collected directly from the pilot schemes to avoid participants revealing their group allocation to the research assessors. Receipt of all other services is monitored using the Child and Adolescent Service Use Schedule (CA-SUS)

The overall service will be characterised by CYPRESS (Children & Young People, Resources, Evaluation and Systems Schedule) and additional case record extraction measures designed specifically for the trial on the intended and actual MAU as well as the duration and frequency of the intervention. CYPRESS is used to characterise services offering complex interventions for children and young people with conduct disorder and other behavioural problems and check that the necessary elements are in place to deliver the intended objectives of a programme. It aims to understand to what degree particular characteristics are intrinsic to such services, and what relationships exist between particular characteristics and outcomes. This data collection will be carried out annually in person, which will inform us about the extent to which MST services are able to sustain the model and provide information in relation to staff training, employment and turnover, which will be helpful in workforce planning.

Health economic analysis will be continue to be conducted by the Centre for the Economics of Mental Health at the Institute of Psychiatry, London, to explore the relative costs and cost-effectiveness of MST and MAU. The evaluation will take a broad perspective, including all health, social services, education and voluntary sector services, plus costs to the criminal justice sector, costs resulting from crimes committed, and out-of-pocket expenses to the young people and families.

Optional Qualitative Interviews-The subset of young people and primary caregivers who participate in the qualitative part of the study will receive a semi-structured interview at approximately 42 months (plus or minus 2 months) which will be administered independently. The key domains of the quantitative outcome data will help shape the qualitative semi-structured interview schedule. There will be three primary domains for this enquiry which have been identified because of their putative causal significance in the aetiology of conduct problems: the quality of the parent-adolescent relationship (FACES, ARQ family scale)(Gartland et al.,2011; Gorall et al.,2006), the young person's ability to foster relationships outside the family, including those with non-delinquent peers (SRD, ARQ Peer scale) (Gartland et al.,2011; Smith , McVie.,2003) and perceived ability to meet future challenges (ARQ Self or self-efficacy scale related to confidence (Gartland et al.,2011), social skills and optimism for the future).

The qualitative interviews will focus on the quantitatively assessed central constructs within each of the domains. For example, within the parent-adolescent relationship domain, the constructs of engagement vs. disengagement, high vs. low levels of cohesion and effective vs. ineffective communication will be explored. In relation to the peer domain, interviews will explore the nature of the young person's friendships and the ways in which those who engage with delinquent peers perceive and experience these relationships vs. those who desist from engaging in delinquent peer involvement. In the self-efficacy domain, we will explore the young person's perceived ability vs. perceived inability to meet the developmental challenges of early adulthood such as having supportive relationships and meeting their achievement goals for the future. Finally the interview will also ask questions about the young person's experience of the transition to adult services. While the interview questions will be guided by these constructs they will be transformed into exploratory user-friendly questions.

For example, some sample questions for the third domain are as follows:
1. What do you think it means to become an adult? (prompt: what is the main difference between being a child and being an adult)
2. When you think about your future, what comes to mind? (prompts: time frame, job opportunities).
3. How much control do you think you have over how that future will unfold? (prompt: what abilities do you think you will be drawing on?)
4. Do you think there is help you can draw on to help you as you go through the process of becoming an adult? (prompts: parents, peers, institutions)

While the qualitative arm has clearly been shaped by the quantitative component, it will also have its own integrity. The interviewer will start with the questions on the schedule, but their primary task will be to explore in detail the personal lived experience of the participant within the broad parameters of the domains.

The young people and caregivers will be interviewed separately. They will be interviewed about their experiences of (a) good and bad outcomes across the domains listed above, (b) engagement and contact with services and difficulties encountered, particularly in relation to transition from child to adult services. We will work with MAC-UK young advisors to develop the best format for data acquisition from this group of purposively sampled adolescents. We will also sample 36 clinicians who will be interviewed in the first year of the study in relation to barriers they encountered in implementation and delivery of services. The transcribed interviews will undergo a synthesis of IPA and framework analysis (Smith et all.,2009; Ritchie, Spencer ,1994)),

the results of which can then be examined alongside the results of the quantitative analysis of secondary outcome

Trial management: There will be 3 Centres: London (UCL and IoP), Leeds and Cambridge. A trial manager at postdoctoral level will be appointed at the UCL site. There will be 4 RAs based at the three research sites (London, with one RA at UCL and one at Iop, Cambridge and Leeds). London will cover 4 MST sites and the others 5 each. They will work semi-independently from others to ensure blindness in coding and interviewing. They will be able to support each other in doing assessments in order to maximise the possibility of blindness (also enforced by instruction to families) so that site A will have an OA from team 1 and someone doing qualitative interview with the same family from Team 2. Economic analysis will be based at the IoP and mediational analysis in Cambridge and the IoP. OAs and the trial co-ordinator will meet weekly across sites by telephone conference. There will be a trial advisory committee including international experts from both Europe and North America.

Setting up of the Trial Steering Committee (TSC): In the first phase of the study we will set up a TSC to monitor the progress of the project and advise the research team on matters arising during subsequent phases of the study. The TSC will meet at least quarterly and perhaps more regularly during the preparatory and final stages of the project. The group will be made up of researchers, statisticians, service users and carers, and representatives of professional/ provider organisations, including each link person from the 9 pilot projects. Service users and carers will be drawn from a variety of local groups and national organisations (e.g. Young Minds). The TSC will play a central role in helping us finalise the content of topic guides to be used in the qualitative components of the study. The TSC would also have opportunity to comment upon and inform the final project report. Unwaged service users and carers will receive travel and other expenses and honoraria in accordance with guidance for involving service users.

Risks and anticipated benefits for trial participants and society, including how benefits justify risks: There is minimal risk from randomisation and treatment. Both MST and MAU will be delivered by experienced professionals used to working with young people of this age with severe conduct problems. Those who agree to participation in the trial will be involved in a number of time-consuming interviews and assessments (up to 3 hours for baseline assessment, 2 hours for follow up assessments) which may be somewhat burdensome but do not carry specific risk. Given that participant families will agree to provide access to confidential information including the young person's arrest and conviction records, there is potential risk of accidental breakdown of confidentiality which must be met by stringent data-handling safeguards. Benefits to participants will include the provision of intensive high quality care from uniquely trained and supervised clinicians in the MST arm of the trial. Benefits to society will be predominantly through the potential for discovering a clinically and economically effective intervention for a social problem that causes considerable distress not only to the family members involved, but to the social group directly affected by the criminal activities and is a very significant cost to public services as well as the individuals and families concerned.
Informing potential trial participants of possible benefits and known risks: This will be, as outlined above, through the provision of written material as well as discussion with the recruiting MST clinician.
Obtaining informed consent from participants: See above. Informed written consent will be obtained from both the young person who has been referred and at least one parent or carer with legal responsibility.
Time period for retention of relevant trial documentation: University College London, as study sponsor, will be responsible for archiving records which will be kept for at least 20 years as per the Research Governance requirements.
Expected Serious Adverse Event: Epidemiological data suggest that with a sample of this size it is possible that some young people will be involved in violent crime and inflict or experience

serious injury during the course of the study. In the event of a death associated with the trial, the independent Data Monitoring and Ethics Committee would consider the implications for continuation of the trial. In addition it is possible that families (or indeed coroners) may wish to speak to someone representing the research project about such deaths as well as to local MST staff who have provided treatment. If required the site PIs would be available for such meetings.

Research Governance: UCL has taken on sponsorship and will delegate responsibilities as appropriate to the Principal Investigator, the Centre for Outcomes Research and Effectiveness (CORE), and participating research centres through a Research Sponsorship Agreement. The Trial Management Team housed within CORE will ensure that all approvals (R&D and ethical approvals and other necessary agreements) will be in place at each site through the four participating centres prior to family enrolment. Oversight of the trial will be established in line with MRC GCP guidelines. Oversight will be ensured through the following structure: (a) a core Project Team made up of the PI, trial coordinator and one RA from each Centre, (b) the Trial Management Group (TMG) including the senior co-PIs from each Centre and the trial coordinator , (c) the independent Trial Steering Committee (TSC), and (d) a Data Monitoring and Ethics Committee (DMEC). The TMG will be responsible for the development of trial protocols and their implementation, and will meet at least fortnightly during set-up and monthly or bi-monthly through-out the trial. The function of the TSC will be to provide independent oversight of the trial. It will be chaired independently and will have an independent statistician, independent clinician and service user representation. The TSC will approve the final protocol and meet once during set-up and 6-monthly after recruitment. The DMEC will provide independent review of the safety and ethics of the trial and the interim analysis. The DMEC will comprise an independent statistician and two independent clinicians and will meet once during set-up and annually during the recruitment period. The trial will be conducted to MRC GCP and CORE Standard Operating Procedures which ensure the monitoring and safety of trial participants, internal validity through robust trial conduct and quality assurance systems and high quality reporting to CONSORT standards.

Data analysis (randomisation to 18 month follow up): The primary outcome, out-of-home placement, will be described by a Kaplan-Meier graph and summarised by the proportions with out-of-home placement by 18 months. The primary analysis will be Cox regression, adjusting for key predictors which will be pre-specified from a list including centre, site, the minimisation variables, and other risk indicators. We will use interaction tests to explore whether the intervention effect differs according to pre-specified sub-grouping variables (gender, age, presence of criminal record and referral path). Clustering by therapist will be allowed for by computing robust standard errors (but these will be ignored if they turn out to be smaller than conventional standard errors) (Roberts, 1999). Secondary outcomes at each time will be analysed by linear or logistic regression as appropriate. We will also use random effects models to explore differences between randomised groups in trajectories over time. Analyses will be by intention-to-treat: that is, including each individual in their randomised group regardless of the intervention actually received, and performing sensitivity analyses to explore the impact of any missing data.

Health economics data analysis: Despite the often skewed nature of costs, mean costs will be compared using standard parametric tests and the robustness of the results confirmed using bootstrapping (Efron & Tibshirani, 1993). The advantage of this approach, as opposed to logarithmic transformation or non-parametric tests, is the ability to make inferences about the arithmetic mean, which is more meaningful from a budgetary perspective (Thompson & Barber, 2000). Details of special school placement will also be recorded as part of the economic data collection. Because schools vary greatly, we generally ask for specific details regarding all non-mainstream schools, including name and address of school so that we can check/verify the type of school, as necessary.

The primary economic evaluation will explore cost-effectiveness in terms of the primary outcome. A secondary cost-utility analysis will be undertaken using Quality Adjusted Life Years (QALYs)

calculated using the EQ-5D (EuroQol) measure of health related quality of life (Brooks, 1996; Williams, 1995). Analyses will be undertaken from the societal perspective. Whilst an NHS/Personal Social Services perspective is preferred for submissions to the National Institute of Health and Clinical Excellence, this perspective is likely to be too narrow to capture all relevant costs and effects of this population. However, this narrower perspective will also be reported.

Cost-effectiveness will be explored initially through the calculation of incremental cost-effectiveness ratios (ICERs) – the difference in mean costs divided by the difference in mean effects (Van Hout et al, 1994). Repeat re-sampling from the costs and effectiveness data will then be employed to generate a distribution of mean costs and effects for the two treatments (Efron & Tibshirani, 1993), which can be used to calculate the probability that each of the treatments is the optimal choice, subject to a range of possible maximum values (ceiling ratio) that a decision-maker might be willing to pay for a unit improvement in outcome. Cost-effectiveness acceptability curves will be presented by plotting these probabilities for a range of possible values of the ceiling ratio (Fenwick, Claxton, & Sculpher, 2001). These curves incorporate the uncertainty that exists around the estimates of mean costs and effects as a result of sampling variation and uncertainty regarding the ceiling ratio.

Accurate description of MAU is a key element of the proposed research. Analysis of the service use data collected as part of the economic evaluation will be used to explore patterns of service use and, through multivariate regression analysis, to identify characteristics of young people and their families that are related to total costs. This analysis will help to clarify what MST is being compared to and will help services to better identify and target those young people who are likely to be particularly expensive to support.

Data analysis (annual follow up 2- 5 years)

The primary outcome, time to first conviction, will be described by a Kaplan-Meier graph and summarised by the proportion with convictions by 60 months. Cox regression adjusting for pre-specified key predictors will estimate treatment effects. Secondary outcomes up to 48 months post-randomisation will be analysed by linear or logistic regression as appropriate. We will also use random effects models to explore differences between randomised groups in trajectories over time. Data on service use collected using the CA-SUS will be supplemented by a critical pathway analytic approach mapping participants' journey from initial referral to experience of adult services

The primary economic evaluation will explore cost-effectiveness in terms of the primary outcome. A cost-utility analysis will also be undertaken, using QALYs calculated using the EQ-5D (EuroQol) measure of health related quality of life (Brooks.,1996)). Analyses will be undertaken from a societal perspective. Cost-effectiveness will be explored initially by calculating incremental cost effectiveness ratios (ICERs) –difference in mean costs divided by difference in mean effects (Van Hout.,1994). Repeat re-sampling from the costs and effectiveness data will then be used to generate a distribution of mean costs and effects for the two treatments, which can be used to calculate the probability that each of the treatments is the optimal choice, subject to a range of possible maximum values (ceiling ratio) that a decision-maker might be willing to pay for a unit improvement in outcome. Cost-effectiveness acceptability curves will be presented by plotting these probabilities for a range of possible values of the ceiling ratio Fenwick et al., 2001).

The qualitative interviews will all be transcribed before undergoing a synthesis of IPA and framework analysis (Smith., 2009; Ritchie., 1994) as successfully employed in Smith's previous

funded health research. This enables analysis to begin with a closely focused and psychological examination of the first set of transcripts using IPA. This then feeds into a framework analysis of subsequent transcripts as the balance shifts from an inductive to a more deductive phase and accommodates a large amount of qualitative data. This hermeneutic circle of analysis is completed by a final micro analysis of selected subset of cases illuminated by the complete corpus analysis.

At the end of phase 1 of the qualitative analysis, the results will be available in a series of matrices defined by variable, participant and theme which can then be examined alongside the results of the quantitative analysis of secondary outcomes. This process will take the form of a mutual interrogation and illumination. The primary output from this will be an integrated empirical paper combining quantitative and qualitative analysis. The qualitative arm will then be completed with the production of a detailed, interpretative narrative.

As well as interviewing young people and primary caregivers on their views of change or the absence of change in key outcome domains, we will explore their experiences of services and of the transition between child and adult services. We will complement the interview data from young people and caregivers around their experiences of services with semi-structured interviews of MST and MAU staff around barriers to service implementation. The interviews with staff will be conducted using a semi-structured interview based on the domains of CYPRESS, a service characterisation instrument that we have designed and validated, which will enable us to describe service configurations associated with particularly good outcomes both in the MAU and MST arms of the trial and increase the accuracy of cost estimates for the programme. The interviews will be with senior staff and case managers and the data will be analysed thematically in the same manner as the narratives collected from the semi-structured qualitative interviews with young people and caregivers.

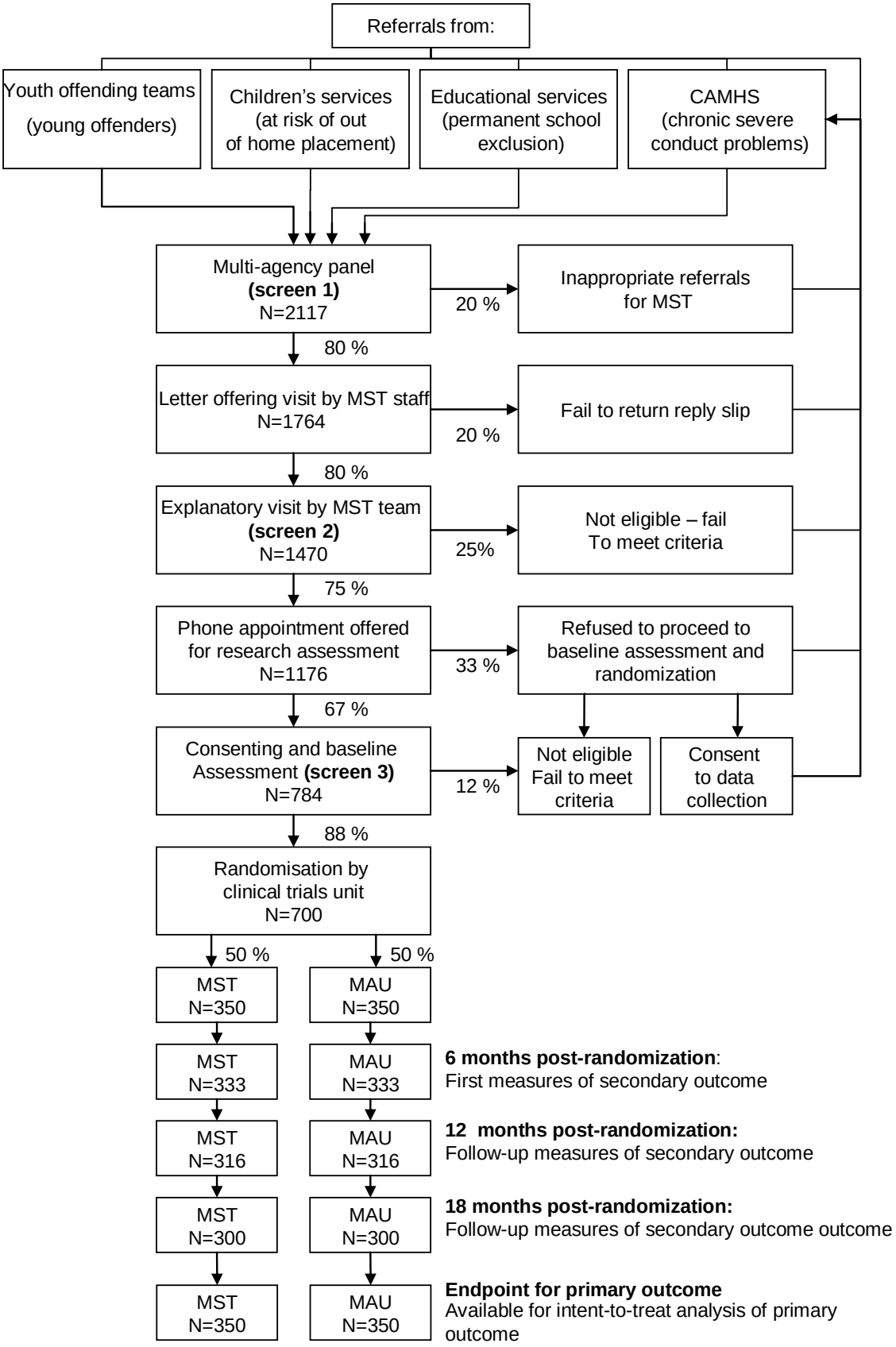
A mixed methods approach (Creswell., 2010)) to integrate the qualitative interview data with the primary and secondary outcome measures to expand our understanding of the relationship between the variables set out above and (a) participants' and families' experience of the problems, (b) the impact of any skills acquired on participants' abilities to cope with these problems and (c) their relationship to access to services and participants' ability to engage. This will contribute to the refinement of interventions and inform the design and delivery of future services.

While a quantitative score will be obtained for each MST and MAU service based on TAMS and outcomes statistics, we will analyse interview transcripts using IPA in order to capture the rich thematic data (on service characteristics, team operations, interventions and sustainability) that is obtained from clinicians when using the semi-structured interview based on the CYPRESS Measure.

Data Monitoring and Ethics Committee (DMEC): An independent DMEC is being established to review the safety and ethics of the trial and will meet prior to the start of recruitment and annually thereafter. Detailed unblinded reports will be prepared by the statistician for the DMEC to monitor safety data, recruitment and drop-out rates. The formal statistical interim analysis of the primary endpoint will be reported to the DMEC after at least half the required number of events has occurred.

Scheduling: See Roadmap document below.

Figure 2: Anticipated screening and consenting procedure and attrition rates



Systemic Therapy for At Risk Teens: Roadmap

Month 1-3

Consultation with sites: • Agree study methods with service providers • Recruit Trial Co-ordinator who will liaise with local sites • Contact potential DMEC and TSC members • Finalise consent and patient information forms • Pilot client recruitment protocol at lead sites • Participate in MST training and setting up of MST supervisors' group • Develop and test case report forms and randomisation systems

Month 3-6

• Recruit and train RAs • Participation in MST training and setting up of MST supervisors' group • R&D approval and research sponsorship agreement • Setting up of trial steering committee, TMG and DMEC • Database development and database reports

Month 4-27

• Ongoing recruitment - geographically staggered early start sites at each Centre • Administration of pre-treatment measures • Randomisation

Month 4-33

• Treatment – duration of 3-6 months for families randomised to MST

Month 7-45

• Collect treatment characteristic information - 3 months post randomisation • Collect Economic Data - 3 months post randomisation and 3 monthly up to final data collection

Month 10-33

• Primary and secondary outcome assessment at 6 months post randomisation - minimum of 2 weeks after family complete MST

Month 16-39

• Primary and secondary outcome assessment at 12 months post randomisation

Month 22-45

• Primary and secondary outcome assessment at 18 months post randomisation

Month 22-45

• Assessment of total social, educational and health costs at 18 months post randomisation

Month 45-48

• All final follow up data collection complete • Data cleansing • Liaison with participants and user groups concerning outcomes
• Statistical and economic analysis

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