PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a cohort study of adolescent mental health service users with a nested cluster-randomised controlled trial to assess the clinical and cost effectiveness of managed transition in improving transitions from child to adult mental health services (The MILESTONE study)
AUTHORS	Singh, Swaran; Tuomainen, Helena; De Girolamo, Giovanni; Maras, Athanasios; Santosh, Paramala; McNicholas, Fiona; Schulze, Ulrike; Purper-Ouakil, Diane; Tremmery, Sabine; Franić, Tomislav; Madan, Jason; Paul, Moli; Verhulst, Frank; Dieleman, Gwen; Warwick, Jane; Wolke, Dieter; Street, Cathy; Daffern, Claire; Tah, Priya; Griffin, James; Canaway, Alastair; Signorini, Giulia; Gerritsen, Suzanne; Adams, Laura; O'Hara, Lesley; Aslan, Sonja; Russet, Frédérick; Davidović, Nikolina; Tuffrey, Amanda; Wilson, Anna; Gatherer, Charlotte; Walker, Leanne

VERSION 1 – REVIEW

REVIEWER	Patience H. White, MD, MA Got Transition: Center for Health Care Transition Improvement Professor of Medicine and Pediatrics George Washington University School of Medicine and Health Sciences Washington DC USA
REVIEW RETURNED	10-Mar-2017

GENERAL COMMENTS	This is a research proposal to evaluate the longitudinal course of outcomes of adolescents approaching the transition boundary and to evaluate a model of managed transition to improve outcomes compared to usual care. There is no data in this submission so this is a request to publish an untested model. It would be better to publish this model when there is some data to guide the readers if it is worthy of utilization. There are some fundamental issues with the model that need to be addressed to better understand the model and the analysis. Transition is about planning, transfer and then integration into the new adult system/practice. This model discussed some of the planning components that include shared understanding, systematic identification and a readiness assessment(TRAM), but no discussion of what would be offered to the youth/young adults to address the issues found in the TRAM, for example, a plan of care and/or educational process to improve the skills the youth needs to handle their illness and care in the adult system. For the transfer component there is mention that adult and pediatric providers “have a common understanding “ with appropriate information transfer. This should be spelled out knowing that one of the key barriers in the literature for adult providers (especially generalist physicians) in accepting young adults is not

	receiving the appropriate information such as a medical summary, care plan and information about the condition and ability to consult back with the pediatric providers if needed. This was not articulated in this proposal and thus makes this proposal difficult to reproduce. Lastly, in the literature the careful integration into the adult system is as important as the planning component. There is no mention of the process of integration into the adult system and the timing to that first appointment that may be critical to the success of the integration. Thus, the model proposed is one that is not complete and should be further flushed out given the recent medical transition literature. Also, there was no explanation as to what "usual care "entails to help the reader understand what the real difference is between this approach and usual care. There are some concerns about a potential bias in the results by having the clinician and the TRAM be the deciding factor as to who will transfer. For example, perhaps only those youths that are "easier' to transfer will be recommended to transfer. This has been shown to be the case in transition clinic experiences that are being evaluated in studies for efficacy. Similarly, the analytic approach is not well described. Many of the assessments are over lapping in what they are asking and practically will take too long to be useful in replication in busy practices. There was no mention if the data could be used to determine if one assessment tool was better than another in predicting transition outcome. The assessments seemed more about the global health and well-being than about the transition process and experience. It has been shown that the transition could be successful by all quantitative measures but if an unrelated to transition event occurs, such as a parent losing their job, the measured quality of life for the youth would be registered as poor. Considering the questions in HoNOSCA, the reviewer wondered if the results gathered by a research assistant and the youth would be reliable. More quantitative outcomes that are well reported in the literature such as adherence with medications, appointments, etc. should be considered. There was no mention in the analysis to understand if some components of the model are better than others in relationship to the outcome or if the intervention might be better for youth with certain diagnoses and severity of conditions. This model might work better for some groups of youth/young adults than others. The retention strategy did not have a protocol such as including who will do which of the strategies in what order so little will be learned as to which is best. As there was no discussion if the sites receive any of the funding, it is hard to evaluate the costs and therefore the feasibility of the implementation of the model. Lastly it was unclear how the social costs would be calculated and how the costs of utilization would be verified.

REVIEWER	Allan Colver,Professor of Community Child Health Institute of Health and Society Newcastle University Newcastle UK
REVIEW RETURNED	07-Apr-2017

GENERAL COMMENTS	1 It is always difficult to know how to assess a trial protocol for publication when the trial has already been funded, has ethics permission and has started. 2 One aspect is to look at the clarity of the documentation and I

	thought this was excellent. 3 Another aspect is the likelihood of generalisability of research findings and I also thought this was good. Being a trial and cohort study in many CAMHS services and in many countries will avoid niche local interventions which are rarely generalisable. 4 The authors introduce the concept of Transition Boundary which is the age at which young people in a given service leave CAMHS. This has two consequences which might make generalisability more difficult: • The Transition Boundary ages may vary much. We were not given information about them. Evaluation of the proposed intervention with a transition boundary of 15 years might produce very different results to a service where the boundary is age 20 years • Services which are more flexible without a fixed boundary are excluded from the study 5 Objective numbered 6 on page 11 in the cohort study is to compare the outcomes in those CAMHS users who transition with those that do not transition to AMHS. Surely these two groups are likely to be so different that comparison would not be very meaningful. Further those in the cluster trial are also part of the cohort study and so interpretation will be further complicated by the confounding effect of the intervention for some. 6 The study seemed to be anchored in CAMHS rather than in CAMHS and AMHS. Few, if any of the co-applicants were active in AMHS services. Primary consents for a service to take part in the cohort study and cluster trial are with CAMHS. AMHS are then asked to participate if they receive a referral. I would have been much more impressed if AMHS services had been involved from the outset in the planning of the research project, agreements about the intervention and prior agreement to take part. Communication between CAMS and AMHS is such an important part of good transition care that I think it should have been part of the research set up as well. 7 The TRAM Instrument Using the TRAM is the basis of the intervention in the cluster trial. The instrument is in the supplement protocol – but not in the paper at present – perhaps it should be? However, much more important, the TRAM has three versions (Young person, Parent, Clinician). And each has questions that relate to mental health symptoms and control, how mature the young person is in a variety of spheres of their life, risk factors, social factors, person factors, emotional factors and cognitive factors. I think the protocol needs a discussion of how the three questionnaires and the responses in each across so many aspects of life, are combined into a decision tool about whether to refer to AMHS. 8 I was not competent to assess the sample size calculations in relation to the variety of outcome measure being used.

REVIEWER	Kristin Cleverley University of Toronto; Canada
REVIEW RETURNED	18-Apr-2017

GENERAL COMMENTS	The authors are commended for their efforts in the development of this multi-site/multi-national cohort and embedded/cohort RCT. This will represent the first RCT of a CAMHS to AMHS transition intervention and respond to calls by stakeholders, including youth and their families, for interventions to improve continuity of care. Especially advantageous in this study is the recruitment of participants in 52 CAMHS clusters, representing diverse clinical settings and geographic locations. As well as the development of the TRAM intervention, which represents information collected via multiple informants and communicated with the YP. The TRAM intervention therefore provides the conduit to ensure informational continuity across transitions and an embedded RCT is an ideal methodology for evaluating the effectiveness of this intervention. There are a few areas that require more detail or referencing. Below I have outlined these suggested edits. Page 6, Line 3 – can you add a reference to this sentence “negative transition experiences adversely impact the young person’s future engagement with mental health services.” Page 6, Line 17 – would suggest adding ‘transitional mental health care’ to this sentence, as there is likely evidence from our physical health colleagues to support this “There is currently no evidence for any effective model of transitional care or any interventions to reduce these individual and societal costs.[32]” Page 7, Line 23 - suggest adding a reference to this sentence “…who reach the boundary, clinical judgment on transition…poor adherence to existing policies.” Page 13, Line 8 – are parents/carers involved in the patient and public engagement? If not, perhaps described in discussion/limitations section. Page 14, Line 43 – please provide more detail as to the inclusion criteria “under the regular care of CAMHS (if not yet diagnosed)”. What does ‘regular care’ refer to? Or is that decided by each CAMHS individually? For example, is there a lower limit to number of visits the YP may have had with the CAMHS to be considered eligible to participate? Page 15, Line 10 – what is the legal age of consent? Likely varies by country/region – perhaps just add that in so the reader can understand the complexity of this issue across sites/countries. NOTE: It is mentioned on Page 34, Line 44 – however, perhaps provide detail as to which Countries the age of consent is/is not 18 years of age. Page 15, Line23 & 34 – is it a MILESTONES researcher (i.e. PI/CO-Is) or is it a MILESTONES research assistant that is the approaching the YP/Carer? Page 17, Line 27 – suggest adding the work ‘secure’ to the line “a secure email” as the TRAM includes personal health information. Page 26, Line 49 – is the honorarium process too complicated across all countries to be described in detail? If so, that’s acceptable, but the lack of description about amount etc is a potential limitation. Section “Health Economics Evaluation Plan” – several analytical methods and statements would benefit from appropriate references. For example (Page 29, Line 40) “a societal perspective will be adopted as a secondary analysis”; and (Page 29, Line 45) “The base-case analysis will be a trial based analysis…” . The Missing

	Data, Clustering, and Uncertainty sub-sections may also benefit from referencing, where appropriate. Page 30, Line 3 – "Discounting: All costs and outcomes that occur after the first year of the trial will be discounted at 3.5%." Why? Perhaps reference accordingly for reader? Page 33, Line 49 – What is the basis for this statement "Adverse events as a direct consequence of the intervention are unlikely."? Page 34, Line 53 – while it is fairly agreed upon among researchers and advocacy groups, I think this line may benefit from references to relevant summaries/research "Despite best efforts, vulnerable people, either by virtue of being young and/or with mental health difficulties, are often omitted from research studies because of concerns regarding informed consent." As well, the following sentence could be referenced "The Council of Europe strongly promotes the participation of children in decisions affecting them."

REVIEWER	Astrid Janssens University of Exeter Medical School Exeter, UK
REVIEW RETURNED	28-Apr-2017

GENERAL COMMENTS	My sincere apologies for the delay in reviewing this protocol. Once I got to it, it was a pleasure reading this protocol. The study addresses a very pressing problem: transition between children's services and adult services. Although national guidelines exist, they don't seem to be implemented in services. I assume this protocol has been scrutinised by many peer review processes. I have very few comments. I have a few questions for the authors related to the study, which shouldn't stop this manuscript from being accepted. I would like to wish the authors good luck with this study and look forward to read about the findings. Small comments: Pg 5 – line 16 – please check this sentence. Pg 9 – line 34 – is this the correct reference (44) – this paper does not report on focus groups or the development of TRAM / TROM. Pg 11 – line 10 – this is not entirely clear ("in those CAMHS users …"). Could this be rephrased? The following questions should not withhold the manuscript from being accepted, as I assume it will not be possible to address the questions as the study has already started. Pg 9 – line 25: Role of GP: discharge in a planned manner from CAMHS to a GP – how will / does the TRAM take into account that the role and tasks of a GP might be different in different countries? Taken the example of ADHD – some GPs are allowed to prescribe medication, some are not. Hence, discharging to a GP might lead to an unsuccessful transition or deprive the young person from the necessary care. Pg 23 – 39: baseline assessment for young people: 1.5 – 2 hours. This is very long for young people (with or without mental health issues). Is there an option to take out some measures? Could some outcome measures be replaced with routinely collected data? Pg 26 – line 7: 30% drop out margin is very high, even for this group. With all the support in place it should be feasible to decrease drop-out to 20-25%?

	Pg 27 – line 51: costs of the intervention: would you not assume that by using the TRAM – you might have more people going through transition (and thus accessing adult services) or less (or being referred to GP) than expected? If that is the case, should these costs not be taken into account?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comment:
It would be better to publish this model when there is some data to guide the readers if it is worthy of utilization.

Response:
There is no data in the paper as it is a protocol paper, outlining the methodology linked with the cohort study and trial.

Reviewer:
There are some fundamental issues with the model that need to be addressed to better understand the model and the analysis. Transition is about planning, transfer and then integration into the new adult system/practice. This model discussed some of the planning components that include shared understanding, systematic identification and a readiness assessment(TRAM), but no discussion of what would be offered to the youth/young adults to address the issues found in the TRAM, for example, a plan of care and/or educational process to improve the skills the youth needs to handle their illness and care in the adult system.

Response:
To address the reviewer's concern about limited information or discussion linked with the model of managed transition, we have now provided a more comprehensive outline of the model on p.8-10, adding information about the ideal timing and three new steps to make the model less ambiguous and more explicit. Similar changes have been made in the section describing Feedback of TRAM results, on p. 19-20. We have also added a paragraph on p. 9-10 clarifying how the model of managed transition addresses important aspects of good quality transition, which have been identified in the literature.

REVISED SECTION:

MILESTONE model of managed transition
The model of transitional care we have developed consists of an evidence-based decision-making process and managed transition, incorporating key principles of continuity of care: adequate information transfer, appropriate joint working, therapeutic and relational continuity, and engagement with adult services.[1 2] The model of managed transition can be seen as one of the cornerstones of a planned and purposeful transition process and can lead to more effective joint working between services. It addresses the need to involve young people and parent/carers in the planning process, tailor transition support to individual needs, identify barriers to smooth transition and act on these, plan transition in a timely fashion, produce a succinct medical summary of the service user, and improve information transfer and communication with adult providers.[3] The model includes:

1. The establishment and/or confirmation of shared understanding of criteria for good quality transitional care at the CAMHS-AMHS interface, and managed ending of care, taking into account clinicians' prior knowledge of good quality transition.
2. Systematic identification of all young people under CAMHS care who reach the transition boundary for their service.
3. Structured and standardised assessment of their mental health and social care needs using a bespoke Transition Readiness and Appropriateness Measure (TRAM), completed by the young person, their parent/carer if available and CAMHS clinician prior to, ideally six months before, the transition boundary.
4. Feedback of TRAM results from all parties in a short, clearly presented report to relevant clinicians in CAMHS, allowing clinicians to identify areas in which attention should be focused to ease a young person's path to transition.
5. Using the findings from the TRAM report to focus communication with service users and carers on issues surrounding end of care at CAMHS and potential transition to AMHS or other community based service.
6. Incorporation of critical information by clinician to young person's care or transition plan, and designing goals for critical items that are achievable.
7. Sending the TRAM findings, along with a referral letter, to the new adult service, if a referral to AMHS is made.
8. Structured and regular follow-up of all young people using Transition Outcome Measure (TROM) to assess whether those who needed care were appropriately engaged with adult services and those who had been discharged or referred to other services have no unmet needs following cessation of care.

Comment:
For the transfer component there is mention that adult and pediatric providers "have a common understanding " with appropriate information transfer. This should be spelled out knowing that one of the key barriers in the literature for adult providers (especially generalist physicians) in accepting young adults is not receiving the appropriate information such as a medical summary, care plan and information about the condition and ability to consult back with the pediatric providers if needed. This was not articulated in this proposal and thus makes this proposal difficult to reproduce.

Response:
We entirely agree that lack of appropriate information transfer is a key barrier to transition. We have added this in the introduction about barriers to continuity of care (p. 5; see paragraph below). In our managed transition model, clinicians are encouraged to include the completed TRAM assessment in their referral letter, thus ensuring that all transition-related information that helped the CAMHS clinician make a transition decision is also available to the adult provider.
p. 5: "Continuity of care is hampered by a multitude of reasons, including differences between adult and child models of care; differing referral criteria; lack of a planned, purposeful and needs-based assessment of those who reach the boundary; communication and information transfer problems between services caused partly by different beliefs, attitudes, mutual misperceptions and lack of understanding of different service structures; lack of shared protocols/manuals for transition; lack of shared client planning between child and adult systems; young people's level of maturity and understanding; and adolescent and/or family resistance to transition.[19-21]"

Comment:
Lastly, in the literature the careful integration into the adult system is as important as the planning component. There is no mention of the process of integration into the adult system and the timing to that first appointment that may be critical to the success of the integration. Thus, the model proposed

is one that is not complete and should be further flushed out given the recent medical transition literature.

Response:
Our trial is designed to assess whether a decision-making tool (TRAM developed with the input of all stakeholders, can facilitate appropriate transition for those who need it. We do not claim to solve all the problems of transition, since no single intervention can possibly solve a problem of this complexity and one that is rooted in organisational history, culture, development and boundaries. The reviewer asserts that “timing of first assessment is crucial”. This is an interesting observation, which lends itself to a randomised trial. However that would be a different study with a different aim and methodology. In the development of our managed transition model, we were driven by two imperatives: first our well-cited and internationally acknowledged research has shown that the biggest barrier to successful transition was lack of shared understanding of who needs transition, and that there was no robustly tested model that could be prescribed to services. We wanted to create an intervention that was clinically meaningful and could be implemented in routine practice; hence we did not insist on clinicians following a prescriptive set of guidelines. However, given the reviewer’s concern, we will certainly test whether in our model, the time to first assessment is related to transition outcomes.

Comment:
Also, there was no explanation as to what “usual care “entails to help the reader understand what the real difference is between this approach and usual care.

Response:
We have clarified on p. 13 under ‘Study design and management’ that ‘usual care’ varies according to service and may or may not include transition planning. We can establish this through the CAMHS baseline service level survey.

Comment:
There are some concerns about a potential bias in the results by having the clinician and the TRAM be the deciding factor as to who will transfer. For example, perhaps only those youths that are “easier’ to transfer will be recommended to transfer. This has been shown to be the case in transition clinic experiences that are being evaluated in studies for efficacy.

Response:
In this study, we are testing in an RCT whether implementing the TRAM score summary report as a decision aid impacts the transition and its outcomes on the mental health, wellbeing and functioning of young people. In the control arm, the clinician makes the decision as per normal practice; in the intervention arm, the clinician makes the decision with the added information from the TRAM score summary report. Thus, any difference between the control and intervention arms of the trial can be attributed to the TRAM report. We will compare those who transition with those who do not, to ascertain whether the systematic bias, to which the reviewer alludes, exists.

Comment:
Similarly, the analytic approach is not well described.

Response:
We have clarified our analytic approach by being more explicit about our study design on p. 13, by providing a better flowchart in Figure 1, and also on p. 22. We have a detailed analytical approach for both studies which we have not presented for the sake of brevity, but have clarified this also on p. 28.
Amended paragraph on p. 13:
"A large cohort of young people approaching the CAMHS-AMHS transition boundary in eight EU countries will be recruited and a nested cluster randomised controlled trial (cRCT) in a randomly selected subset of clusters (CAMHS services) will be implemented. The study design is a modification of the Cohort Multiple Randomised Controlled Trial,[52] by virtue of allocation to the intervention by cluster randomisation, with each distinct CAMHS comprising a cluster. The control arm clusters from the cRCT together with additional excess clusters form the longitudinal cohort study, with a follow-up period of 24 months. The cRCT is a superiority trial; the aim is to show that managed transition is superior to usual care in improving patient reported outcomes. Usual care varies by CAMHS and may or may not include transitioning planning. The primary outcome endpoint is 15 months. The study flow diagram is presented in Figure 1. All arms of the study undergo the same data collection. The trial has economic and qualitative components, addressing objectives 2 and 3, respectively. Detailed Statistical Analysis Plans have been developed for both the cRCT and longitudinal cohort study. Final versions will be signed off prior to commencement of the analysis and made available on the study website."
Amended paragraph on p. 28:
"Detailed Statistical Analysis Plans, which include specific methods of analysis for each outcome variable, have been developed individually for both studies, and final versions will be reviewed and approved by the Trial Management Group and made available on the study website (http://www.milestone-transitionstudy.eu/)."

Comment:
Many of the assessments are over lapping in what they are asking and practically will take too long to be useful in replication in busy practices.

Response:
TRAM and TROM were developed, piloted and tested with clinicians and service users, including MILESTONE's young project advisors for ease of use, relevance of areas covered, resources needed and generalizability. In our health economic analysis, we are specifically looking at the time taken to complete these tools and costing this against benefits. We also plan to conduct qualitative interviews with clinicians in the intervention arm to understand whether the tool will be useful in busy clinical practice or what modifications might be needed in order for it to become routinely used in the future. The reviewer is asking us to reject something before it has been tested. We would rather test it first and let the data guide us.
Since the longitudinal cohort study is intertwined with the clinical trial, the number of assessments or questionnaires at baseline and follow-up time points are far more numerous than if it were a trial only. The key trial assessments are the TRAM and the TROM, and they will be available for use in practice after the end of the study, provided the platform is funded appropriately. The following sentence about this has been added to the section on TRAM and TROM (p. 11):
"HealthTracker Ltd will optimize the TRAM on the HealthTrackerTM platform based on decision making algorithms derived from the study. If appropriately funded, this will be made available to serve as the platform for optimization of transitions to adult mental health in the EU."

Comment:
There was no mention if the data could be used to determine if one assessment tool was better than another in predicting transition outcome.

Response:

It was not our primary goal to test if any of the instruments were useful as predicting tools. We are not comparing TRAM with anything else on predicting transition outcomes. The TROM is an instrument that is measuring multiple outcome domains from the service user, parent/carer and clinician perspectives.

Comment:
The assessments seemed more about the global health and well-being than about the transition process and experience.

Response::
The TROM contains questions about the transition process and experience. We have added this to the section on TRAM and TROM on p. 10. Another measure “On Your Own Feet: Transition Experience Scale (OYOF-TES)” also specifically assesses transition experience.

Comment:
It has been shown that the transition could be successful by all quantitative measures but if an unrelated to transition event occurs, such as a parent losing their job, the measured quality of life for the youth would be registered as poor.

Response:
Our life events questionnaire collects information about significant life events, such as a parent losing their job. We have added this to the description of the instrument in Table 1, p. 22.

Comment:
Considering the questions in HoNOSCA, the reviewer wondered if the results gathered by a research assistant and the youth would be reliable.

Response:
All MILESTONE research assistants have been trained as per the guidelines training for the HoNOSCA and related measures and only started collecting data after they were considered well qualified and trained to undertake the HoNOSCA interview with the young person. The fact that RAs are trained has been mentioned in the section on the primary outcome (p. 20) but we have added further clarification to the section on Training, including a reference (p. 37; see below added sentence).
p. 37: “A special focus of the training has been the primary outcome measure, the clinician-rated HoNOSCA, completed by research assistants. The training has included ratings and discussions of clinical vignettes and how to conduct the HoNOSCA interview.”[85]

Comment:
More quantitative outcomes that are well reported in the literature such as adherence with medications, appointments, etc. should be considered.

Response:
The MILESTONE specific Client Service Receipt Inventory (CSRI) and the Sociodemographic questionnaire contain questions about medication use and appointments with various service providers. The TRAM contains a question about whether the young person takes medication as prescribed in the correct dose. We have added clarification in Table 1 (p. 22) that the CSRI also asks about medication use.

Comment:

There was no mention in the analysis to understand if some components of the model are better than others in relationship to the outcome or if the intervention might be better for youth with certain diagnoses and severity of conditions. This model might work better for some groups of youth/young adults than others.

Response:
The reviewer correctly points out that we have not considered in the paper whether some components of the model of managed transition may be better than others in relationship to the outcome; or that the intervention may work better for youth with certain diagnoses & severity of conditions. The intervention is aimed at the clinician who ultimately decides, ideally together with key stakeholders, whether the young person should transition to adult services and also whether they will address any of the barriers for smooth transition. We will undertake sub-group analyses based on diagnosis and other factors that may influence the decision to transition. Hence we will be able to test whether the nature or severity of a condition is related to the decision to transition.
We will also capture some of that decision making in the follow-up communication with the clinician, and will be able to report on it. This has been described in the section on 'Evaluation of the intervention and experiences of young people regarding services' (section heading changed to reflect content better) on p. 26.

Commment:
The retention strategy did not have a protocol such as including who will do which of the strategies in what order so little will be learned as to which is best.

Response:
We are collecting information about the various retention strategies used, and who is doing what, so will be able to report about this when writing up the findings and also contemplate the effectiveness of the various strategies.

Comment:
As there was no discussion if the sites receive any of the funding, it is hard to evaluate the costs and therefore the feasibility of the implementation of the model.

Response:
Apart from two German sites, sites received no funding from the EU grant for taking part in the study. We have added the following sentence to the section on Setting and site selection (p. 14):
"The majority of sites received no funding from the EU grant (no 602442) for taking part in the study. However, two German recruiting sites received payments under subcontract to facilitate recruitment."

Comment:
Lastly it was unclear how the social costs would be calculated and how the costs of utilization would be verified.

Response:
The economic evaluation considers the costs of implementing the new transition model by capturing the impact of the intervention on decision making. A clinician questionnaire is being used to assess the impact of the TRAM on clinician's time. The feasibility of introducing such an intervention will be informed by data on additional burden placed on clinicians, as well as impact on health care resource use more generally. Regarding societal costs, within health economics, the scope of a societal perspective has to be balanced with what is pragmatically achievable. In this instance, we will gather information on the following resource use beyond healthcare: social care, productivity (employment

status) and criminal justice system contacts. Resource use for these wider costs is being captured through the CSRI. For each type of resource use, unit costs will be identified from relevant sources (e.g. PSSRU, reference costs, existing micro-costing studies). Unit costs will be combined with the resource use information to calculate the total costs. To add clarity within the protocol paper, a sentence on the scope of societal costs has been added (p. 31). “Societal costs will include: social care, productivity, and criminal justice system contacts.”
In terms of validation, we are relying on self-report data and thus there is no external verification. This is typical for such a study and it is a known limitation which would be highlighted within the discussion of any health economic papers following the study.

Reviewer: 2

2) One aspect is to look at the clarity of the documentation and I thought this was excellent.

Response:
We are pleased to hear this. Thank you.

4) The authors introduce the concept of Transition Boundary which is the age at which young people in a given service leave CAMHS. This has two consequences which might make generalisability more difficult:
• The Transition Boundary ages may vary much. We were not given information about them. Evaluation of the proposed intervention with a transition boundary of 15 years might produce very different results to a service where the boundary is age 20 years

Response:
We have added information (paragraph below) about transition boundaries (ages) in the protocol (p. 15). The intervention is directed at the clinician and not the young person. We therefore do not believe that the intervention will work markedly differently in different age groups, especially as outcome data is collected using age appropriate scales. However, we will analyse whether age of transition boundary is associated with transition outcomes.
p. 15: “The data revealed that the CAMHS-AMHS transition boundary for most countries was 18 years, i.e. the age of majority. In the UK, Belgium and France there was more variation, the boundary ranging from 15 to 18 years. We also discovered that that some services in Belgium, France, the Netherlands and Germany adopt a more flexible approach to the boundary, and in these situations we agreed a nominal boundary (18 years), which reflects the age at which transitions most commonly occur and, in most instances, is also the official TB.”
• Services which are more flexible without a fixed boundary are excluded from the study

Response:
When we embarked on the study we thought that boundaries would be fixed. We soon realised that some countries and/or services adopt a flexible approach to transition age. In such situations we have agreed a nominal boundary which reflects the age at which transitions most commonly occur in that particular service, discussed and agreed this with CAMHS clinicians from that service, and used that age boundary to determine eligibility to entry into study. See added paragraph above.

5) Objective numbered 6 on page 11 in the cohort study is to compare the outcomes in those CAMHS users who transition with those that do not transition to AMHS. Surely these two groups are likely to be so different that comparison would not be very meaningful. Further those in the cluster trial are also part of the cohort study and so interpretation will be further complicated by the confounding effect of the intervention for some.

Response:
We agree that those who transition might generally be very different to those who do not. This is one of the questions we will answer. Our previous work and international literature shows that transition is sometimes determined by capacity rather than clinical need (in addition to other factors such as patient engagement, the strength of pre-existing therapeutic relationships, etc.). We also know that a significant number of CAMHS users will not transition but then reappear in AMHS some years later (i.e. disengage for a few years). We are therefore planning analysis using propensity score matching (and will explore other methodology, as appropriate), to ensure that when making any comparisons we are comparing "like with like". This is of course dependent upon there being sufficient numbers in the group of CAMHS users who do not transition to AMHS but perhaps ought to, an empirical question to which our study will be the first to provide an answer. We do not believe that there will be confounding since this is a cluster randomized trial and young people in the intervention arm will be excluded from the cohort study. We have clarified this, modified Figure 1 and been more explicit in the text.

6) The study seemed to be anchored in CAMHS rather than in CAMHS and AMHS. Few, if any of the co-applicants were active in AMHS services. Primary consents for a service to take part in the cohort study and cluster trial are with CAMHS. AMHS are then asked to participate if they receive a referral. I would have been much more impressed if AMHS services had been involved from the outset in the planning of the research project, agreements about the intervention and prior agreement to take part. Communication between CAMS and AMHS is such an important part of good transition care that I think it should have been part of the research set up as well.

Response:
We agree that prior engagement of AMHS would have been beneficial. Our intention was to engage AMHS more from the beginning but realised soon that this would be a very difficult task in the international context and with limited researcher capacity. Nevertheless, SS, GdG, and AM are AMHS psychiatrists and all MILESTONE clinicians have maintained ongoing to engagement with adult mental health services.
We could not find one specific AMHS clinician to engage in each service or site. Unlike in the UK and the Netherlands, in most of the participating countries AMHS do not work under the same umbrella organisation as the CAMHS. Furthermore, in all countries the number of AMHS linked with CAMHS are numerous and we were unable to predict which services young people may be referred to. We have added the following sentence in the paper to clarify this matter (p. 14):
"In most countries, other than the UK, there is no umbrella organisation to facilitate collaboration between AMHS and CAMHS. Furthermore, a single CAMHS may be linked with numerous AMHS (inpatient services, clinics, teams and individuals), making it difficult for AMHS clinicians to be engaged from the start, particularly given our limited resources. Also, we were not able to predict which AMHS would be involved, as this is dependent on transition decisions."
Nevertheless, the TRAM summary score report is intended to aid communication between CAMHS and AMHS, and our discussion will address the potential of the TRAM tool as a communication aid.

7) The TRAM Instrument
Using the TRAM is the basis of the intervention in the cluster trial. The instrument is in the supplement protocol – but not in the paper at present – perhaps it should be?

Response:
We cannot add the instruments as an appendix, as it will impact the submission of a separate manuscript specifically about the development and validation of the TRAM and TROM. We would rather make the TRAM available on specific request from a reader than put it out in its current form in this paper.

Comment:
However, much more important, the TRAM has three versions (Young person, Parent, Clinician). And each has questions that relate to mental health symptoms and control, how mature the young person is in a variety of spheres of their life, risk factors, social factors, person factors, emotional factors and cognitive factors.
I think the protocol needs a discussion of how the three questionnaires and the responses in each across so many aspects of life, are combined into a decision tool about whether to refer to AMHS.

Response:
The following paragraph has been added to the section describing TRAM and TROM (p. 11), to address this matter:
"TRAM and TROM contain 20 questions common to both scales for all participants; further eight questions are relevant only to the clinician versions and nine only to the young person and parent/carer versions. All participant versions of TRAM contain 15 additional questions that are not in TROM, yet to allow comparison of results over time, most of the domains present in TRAM are also present in TROM, with versions for AMHS and CAMHS clinicians and different follow-up time points."
Based on the discussions with the various stakeholders during the development of the TRAM and TROM, it was agreed that ratings may vary between raters, based on the type of disorder, for example, in a patient with florid psychosis with limited insight, the service user's response may not be the most accurate one; as opposed to that in anxiety disorders, where the service user may be better than carers/parents to accurately give the information. We will examine data from those with different disorders and explore whether different weightings need to be incorporated into the scoring scheme, for different disorders when using information from different sources. We will specifically model this once we have the data from the study.

Reviewer: 3

Comment:
Page 6, Line 3 – can you add a reference to this sentence "negative transition experiences adversely impact the young person's future engagement with mental health services."

Response:
This has been done (Singh SP. Transition of care from child to adult mental health services: the great divide. Current opinion in psychiatry 2009;22(4):386-90.)

Comment:

Page 6, Line 17 – would suggest adding ‘transitional mental health care’ to this sentence, as there is likely evidence from our physical health colleagues to support this “There is currently no evidence for any effective model of transitional care or any interventions to reduce these individual and societal costs.[32]”

Response:
We have added ‘mental health’ to the sentence.

Comment:
Page 7, Line 23 - suggest adding a reference to this sentence “…who reach the boundary, clinical judgment on transition…poor adherence to existing policies.”

Response:
This has been done (McLaren S, Belling R, Paul M, et al. ‘Talking a different language’: an exploration of the influence of organizational cultures and working practices on transition from child to adult mental health services. BMC Health Serv Res 2013;13(1):254.)

Comment:
Page 13, Line 8 – are parents/carers involved in the patient and public engagement? If not, perhaps described in discussion/limitations section.

Response:
We have no parents/carers as Patient and Public Involvement representatives, as we decided to prioritise Young people due to limited PPI budget. However, parents/carers took part in the focus group research that preceded the development of the TRAM and TROM and we hope in the later stages of the study to involve some parent carer groups (as well as a wider range of young people’s groups) as the findings emerge and begin work on drawing out the implications of these data.

Comment:
Page 14, Line 43 – please provide more detail as to the inclusion criteria “under the regular care of CAMHS (if not yet diagnosed)”. What does ‘regular care’ refer to? Or is that decided by each CAMHS individually? For example, is there a lower limit to number of visits the YP may have had with the CAMHS to be considered eligible to participate?

Response:
Different CAMHS will have different referral criteria. With regular care we mean that the young person should have attended at least one appointment at CAMHS. We have added clarification to the paper (p. 16): (“b) they have a mental disorder defined by DSM-IV-TR, DSM-5 or ICD 10/11, or they are under the regular care of CAMHS (attended at least one appointment, if not yet diagnosed);”

Comment:
Page 15, Line 10 – what is the legal age of consent? Likely varies by country/region – perhaps just add that in so the reader can understand the complexity of this issue across sites/countries. NOTE: It is mentioned on Page 34, Line 44 – however, perhaps provide detail as to which Countries the age of consent is/is not 18 years of age.

Response:
We have added clarification regarding the legal age of consent to the relevant sentences (p. 16 & 36). P. 16: “d) they provide valid written informed consent, or assent, if below the legal age of consent (in England this age is 16, in all other participating countries 18).”

P. 36: “We are involving a potentially vulnerable population in research: adolescent mental health service users who, in the main, are over the age of 16, but in areas where the transition boundary is 16 years (some parts of England) or 16.5 years (some parts of France) they are 15 years. In England, the legal age of consent is 16, in all other participating countries it is 18.”

Comment:
Page 15, Line23 & 34 – is it a MILESTONES researcher (i.e. PI/CO-Is) or is it a MILESTONES research assistant that is the approaching the YP/Carer?

Response:
It is the research assistant, and we have clarified this (p. 17)

Page 17, Line 27 – suggest adding the work ‘secure’ to the line “a secure email” as the TRAM includes personal health information.

Response:
We have amended the sentence on p. 19 to the following: “The TRAM results are communicated to the CAMHS clinician in a secure fashion via an email, attaching the TRAM score summary report (which contains no identifiable information), and an offer made to explain the findings at a face-to-face meeting. If no response is received, the email is followed up once only with a telephone call.”

Comment:
Page 26, Line 49 – is the honorarium process too complicated across all countries to be described in detail? If so, that’s acceptable, but the lack of description about amount etc is a potential limitation.

Response:
We have amended text on p. 27 in the following fashion to include some more detail about the honorarium process. “The Bonding plan activities vary by country taking local ethical and cultural requirements into consideration. Items include thank you cards, newsletters, gift vouchers and a chance to win a prize in a lottery. The value of gift vouchers provided after assessments range from £10-£20 or similar equivalent in Euros. In Italy and Croatia, the research ethics committees did not allow providing any gifts after the individual assessment time points. Reasonable travel expenses are reimbursed for young people and their parents/carers.” We will present more detail about retention activities in relevant findings papers.

Comment:
Section “Health Economics Evaluation Plan” – several analytical methods and statements would benefit from appropriate references. For example (Page 29, Line 40) “a societal perspective will be adopted as a secondary analysis”; and (Page 29, Line 45) “The base-case analysis will be a trial based analysis…” . The Missing Data, Clustering, and Uncertainty sub-sections may also benefit from referencing, where appropriate.

Response:
Appropriate references have been added throughout this section for the missing data, clustering, societal perspective, and uncertainty subsections. In terms of ‘the base case being a trial based analysis’, this has been left unchanged as it is a statement of fact, that is, we are relying on the trial data, not modelling from the literature.

Comment:
Page 30, Line 3 – “Discounting: All costs and outcomes that occur after the first year of the trial will be discounted at 3.5%.” Why? Perhaps reference accordingly for reader?

Response:
Words have been added along with a reference to highlight that this is the discount recommended by the NICE reference case. . (p. 31): “As recommended by NICE,[75] all costs and outcomes that occur after the first year of the trial will be discounted at 3.5%.”

Comment:
Page 33, Line 49 – What is the basis for this statement “Adverse events as a direct consequence of the intervention are unlikely.”?

Response:
Our intervention is directed at the clinician. We have clarified this in the sentence on p. 35:
“A young person experiencing adverse events as a direct consequence of the intervention are unlikely, as the intervention is as aimed at the clinician.”

Comment:
Page 34, Line 53 – while it is fairly agreed upon among researchers and advocacy groups, I think this line may benefit from references to relevant summaries/research “Despite best efforts, vulnerable people, either by virtue of being young and/or with mental health difficulties, are often omitted from research studies because of concerns regarding informed consent.” As well, the following sentence could be referenced “The Council of Europe strongly promotes the participation of children in decisions affecting them.”

Response:
We have added relevant references to the section on p. 36-7 (highlighted):
Yan EG, Munir KM. Regulatory and ethical principles in research involving children and individuals with developmental disabilities. Ethics & behavior 2004;14(1):31-49.
Medical Research Council. MRC Ethics Guide: Medical research involving children. London: Medical Research Council, 2004.
Parliamentary Assembly. Promoting the participation by children in decisions affecting them. Recommendation 1864; Doc. 12080: Council of Europe, 2009

Reviewer: 4

Pg 5 – line 16 – please check this sentence.

Response:
We have reworded the sentence for clarity (p. 5): “Adolescence is a high-risk period for psychological morbidity, and young adulthood is the period during which most of the serious mental disorders that disable or cause death in adult life have their onset.”

Comment:
Pg 9 – line 34 – is this the correct reference (44) – this paper does not report on focus groups or the development of TRAM / TROM.

Response:
The following references have been added, to clarify PROMS:
Nelson EC, Eftimovska E, Lind C, et al. Patient reported outcome measures in practice. Bmj 2015;350:g7818.
Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Silver Spring: U.S. Department of Health and Human Services Food and Drug Administration, 2009.

Comment:
Pg 11 – line 10 – this is not entirely clear ("in those CAMHS users …"). Could this be rephrased?

Response:
We have amended the sentence to: "To compare the outcomes in those young people who transition with those who do not transition to AMHS (i.e. remain in CAMHS, are discharged or referred to other care)." (p. 12)
Our more detailed statistical analysis plan linked with the cohort study provides more detail linked with this objective, outlining the plan how we will differentiate between the various groups and pathways.

Comment:
Pg 9 – line 25: Role of GP: discharge in a planned manner from CAMHS to a GP – how will / does the TRAM take into account that the role and tasks of a GP might be different in different countries? Taken the example of ADHD – some GPs are allowed to prescribe medication, some are not. Hence, discharging to a GP might lead to an unsuccessful transition or deprive the young person from the necessary care.

Response:
As already clarified above, the TRAM itself will not be able to identify cases needing transition or discharge to GP, instead it is designed to aid the clinician, who can take the local country context into consideration when making transition decisions. We have clarified the paragraph accordingly (p. 10): "The Transition Readiness and Appropriateness Measure (TRAM), a decision support and assessment tool, uses the HealthTrackerTM platform. The measure, together with the linked findings report, have been designed to help the clinician identify a) high-risk, high-need cases for whom transition to AMHS is advisable and appropriate; b) those who can be appropriately discharged in a planned manner from CAMHS to a General Practitioner (GP); or c) transitioned to another community based service (such as social services, voluntary sector or other non-statutory agencies). Obviously, the clinicians will need to take their local service provision into account when making the decisions. The Transition Related Outcome Measure (TROM) provides information on outcomes post-transition, and on the transition process and experience."

Comment:
Pg 23 – 39: baseline assessment for young people: 1.5 – 2 hours. This is very long for young people (with or without mental health issues). Is there an option to take out some measures? Could some outcome measures be replaced with routinely collected data?

Response:
We have stated in the paper (p. 24) that the young person does not have to complete all scales in one session, but can have a break in between individual scales or complete the scales over multiple sessions. Whenever this has not been possible, they have completed them over two or more sessions within a restricted timeframe. Our experience with baseline data collection has shown that the majority of participants tend to complete all scales in one session. Participants are willing to complete all scales within the entire assessment, with over 80% of recruited young people completing all specified scales.

Comment:
Pg 26 – line 7: 30% drop out margin is very high, even for this group. With all the support in place it should be feasible to decrease drop-out to 20-25%?

Response:
We are putting in all effort to reduce drop-out, and hope that it will less than 20%.

Comment:
Pg 27 – line 51: costs of the intervention: would you not assume that by using the TRAM – you might have more people going through transition (and thus accessing adult services) or less (or being referred to GP) than expected? If that is the case, should these costs not be taken into account?

Response:
The reviewer is correct. It may well be the case that as a result of the TRAM, more individuals receive the care they require, and thus healthcare costs will be greater for the intervention group. This is typical within economic evaluations where costs associated with intervention arm are greater than the control arm. Regardless of this, all costs related to health care utilisation (including GP visits, hospital visits, CAMHS, and AMHS) are being captured through the CSRI and consequently the scenarios suggested by the reviewer will be accounted for. To clarify we have added 'for both trial arms' on p. 30 to ensure the reader understands data is being collected for both arms, not just intervention participants.

VERSION 2 – REVIEW

REVIEWER	Patience H. White, MD, MA Got Transition: Center for Health Care Transition Improvement Professor of Medicine and Pediatrics George Washington University School of Medicine and Health Sciences
REVIEW RETURNED	28-Jun-2017

GENERAL COMMENTS	The authors did an excellent job in addressing the majority of the concerns raised. The only issue is to be more explicit in the abstract that is protocol is (in their words) "... testing in an RCT manner whether implementing the TRAM score summary as a decision aid impacts the transition and its outcomes on the mental health, well-being and functioning of young people". As this is the key component of this model of managed transition, this reviewer recommend they add it to the abstract. It would clarify the central role of the TRAMS in this study. This would make the study" objective more clearly defined" and the "abstract more accurate and complete".

REVIEWER	Allan Colver Newcastle University UK
REVIEW RETURNED	16-Jun-2017

The reviewer completed the checklist but made no further comments.

REVIEWER	Kristin Cleverley University of Toronto; Canada
REVIEW RETURNED	20-Jun-2017

GENERAL COMMENTS	All comments and suggestions that I raised to the authors have been adequately addressed. This is an timely study that will make important contributions to the field.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
The authors did an excellent job in addressing the majority of the concerns raised. The only issue is to be more explicit in the abstract that is protocol is (in their words) "... testing in an RCT manner whether implementing the TRAM score summary as a decision aid impacts the transition and its outcomes on the mental health, well-being and functioning of young people". As this is the key component of this model of managed transition, this reviewer recommend they add it to the abstract. It would clarify the central role of the TRAMS in this study. This would make the study" objective more clearly defined" and the "abstract more accurate and complete".

Response:
We are grateful for the positive remarks of the reviewer. We have clarified the text of the abstract.

Reviewer: 2
This response is my second review of the manuscript, now taking account of the authors' responses to the first round of reviews. I have concerns about the authors' responses to one of reviewer 1's comments. And concerns about authors' responses to some of my comments (reviewer2).

Response:
We note that Reviewer 1 is entirely happy with our responses to their comments

Reviewer 1 had written:
For the transfer component there is mention that adult and pediatric providers “have a common understanding “ with appropriate information transfer. This should be spelled out knowing that one of the key barriers in the literature for adult providers (especially generalist physicians) in accepting young adults is not receiving the appropriate information such as a medical summary, care plan and information about the condition and ability to consult back with the pediatric providers if needed. This was not articulated in this proposal and thus makes this proposal difficult to reproduce.

Response:
We entirely agree that lack of appropriate information transfer is a key barrier to transition. We have added this in the introduction about barriers to continuity of care (p. 5; see paragraph below). In our managed transition model, clinicians are encouraged to include the completed TRAM assessment in their referral letter, thus ensuring that all transition-related information that helped the CAMHS clinician make a transition decision is also available to the adult provider.
p. 5: “Continuity of care is hampered by a multitude of reasons, including differences between adult and child models of care; differing referral criteria; lack of a planned, purposeful and needs-based assessment of those who reach the boundary; communication and information transfer problems between services caused partly by different beliefs, attitudes, mutual misperceptions and lack of understanding of different service structures; lack of shared protocols/manuals for transition; lack of shared client planning between child and adult systems; young people’s level of maturity and understanding; and adolescent and/or family resistance to transition.[19-21]”

My observation at second review
I think this remains a substantial weakness. Although the protocol is about a trial, on many occasions the authors have to explain that they cannot standardise, only encourage. This is because, as they state themselves:
1 Models and systems vary between countries

2 Other than in the UK, there is no overarching body for CAMHS and AMHS
3 They were not able to engage adult services in design of the study because of the multiplicity of referral pathways – thus they have to rely on the hope that an adult service will engage when a transfer is recommended; and the hope that the adult service will follow the protocol.
4 “Usual care varies between centres

Response:
We respectfully disagree with the reviewer that our trial has substantial weaknesses. We believe we have done the best we can within the constraints of this difficult setting. Considering the complexity of transition pathways and service provision within and between the different European countries, we designed an intervention approach which is in line with modern concepts of shared-decision making and self-determination of service users. This approach is facilitated by the provision of transition-relevant clinical information, collected and summarized in the standardized, newly developed instrument, TRAM. It is a clinicians’ decision-aid, not a prescriptive decision making tool. Our intervention is predicated on the idea that child and adult mental health services have different thresholds for service entry and our TRAM model is designed to give both sides a shared understanding of the needs of the young person. Apart from providing and encouraging the use of the TRAM summary score report, we will monitor its real use in clinical practice both in CAMHS and AMHS and take this into account in sub-analyses.
We would also like to emphasise that this is a complex study that went through two external EU review processes before being funded, received ethical approval in eight countries, and the design and associated challenges were discussed extensively and at different stages of development with our independent Scientific, Clinical and Ethical Advisory Board members, young service user advisers, clinicians and academics. No one considered this trial to be fundamentally flawed or having substantial weaknesses. When we publish the results, all limitations will be presented and findings interpreted in light of these limitations.

Reviewer 2 (ie me) had written
The Transition Boundary ages may vary much. We were not given information about them. Evaluation of the proposed intervention with a transition boundary of 15 years might produce very different results to a service where the boundary is age 20 years.

Response:
We have added information (paragraph below) about transition boundaries (ages) in the protocol (p. 15). The intervention is directed at the clinician and not the young person. We therefore do not believe that the intervention will work markedly differently in different age groups, especially as outcome data is collected using age appropriate scales. However, we will analyse whether age of transition boundary is associated with transition outcomes.

My observation at second review
I still do not agree. I think the transition boundary is likely to influence results. The nature and requirements of transfer of a 20 year old are likely to be different to those of a 16 year old. In terms of developmentally appropriate health care, which I agree is not entirely determined by age, will in this study of those with mental health problems be determined to a significant extent by age.

Response:
We wish to reiterate that the TRAM summary currently (i.e. in its beta version) highlights the discrepancies between the three views and flags up rows where problems or issues are identified in any one of the three views, so that the clinician knows where to focus their decision making with the young person. Thus, it is an age independent tool and there is no reason to assume that it will be more effective in some age groups than others.

Reviewer 2 (ie me) had written
Services which are more flexible without a fixed boundary are excluded from the study

Response:
When we embarked on the study we thought that boundaries would be fixed. We soon realised that some countries and/or services adopt a flexible approach to transition age. In such situations we have agreed a nominal boundary which reflects the age at which transitions most commonly occur in that particular service, discussed and agreed this with CAMHS clinicians from that service, and used that age boundary to determine eligibility to entry into study. See added paragraph above.

My observation at second review
I find this confusing. I do not understand what a nominal boundary is. I do not see how you can assign a nominal boundary to a country which is transferring children at different ages.
The authors cannot have it both ways. Using a fixed boundary, they disagreed with me that a boundary of 16 would be likely to have different implication for transition of a boundary at 20 (see earlier point). But if that is the case and the boundary is not critical, then they could allow every country to have a variable boundary.

Response:
Re: transition boundaries being different in some countries and/or nominal, we wish to make the following points:
1) Nominal boundary: In all countries involved in MILESTONE services have an official service boundary which is typically 18. However, there are local and/or service specific variations. Furthermore, as we investigated more deeply during the set-up of the study it became apparent that in some countries and services this boundary is not strictly adhered to. Yet, we needed to identify YP of an appropriate age approaching transition prior to clinician making their decision. Were we to recruit YP aged 17.5 in a service which actually transitions YP at 16, we would have missed them. Furthermore, if we were to allow each clinician to choose their own flexible age boundary, we would not have been able to select a representative cohort, since recall bias and selective memory would have influenced who the clinicians considered as eligible. So in clusters where clinicians had flexibility in choosing a transition boundary, we agreed with the service leads what the ‘commonest’ age boundary was. Thus, the nominal boundary, may be the same as the official one or differ.
2) The nominal boundary is used to set the eligibility criteria so that the majority of YP who we recruit will undergo transition within the time limits of our study, i.e. it is a tool or means to identify YP who are most likely to transition. Our statistical analyses will take into account the age of YP at transition; hence we will test whether it is a moderating factor regarding transition decision and outcome.

Reviewer 2 (ie me) had written
Objective numbered 6 on page 11 in the cohort study is to compare the outcomes in those CAMHS users who transition with those that do not transition to AMHS. Surely these two groups are likely to be so different that comparison would not be very meaningful.

Response:
We agree that those who transition might generally be very different to those who do not. This is one of the questions we will answer. Our previous work and international literature shows that transition is sometimes determined by capacity rather than clinical need (in addition to other factors such as patient engagement, the strength of pre-existing therapeutic relationships, etc.). We also know that a significant number of CAMHS users will not transition but then reappear in AMHS some years later (i.e. disengage for a few years). We are therefore planning analysis using propensity score matching (and will explore other methodology, as appropriate), to ensure that when making any comparisons we are comparing "like with like". This is of course dependent upon there being sufficient numbers in the group of CAMHS users who do not transition to AMHS but perhaps ought to, an empirical question to which our study will be the first to provide an answer.

Comment:
My observation at second review
I still do not see that the Objective number 6 is interesting. The authors state themselves that the two groups are likely to be very different.

Response:
In our more detailed statistical analysis plans, which will be published on the MILESTONE website before any final data analysis, we provide further detail regarding Objective 6, with secondary objectives as follows:
o To establish differences between groups with different transitional trajectories and outcome in terms of mental health, quality of life, functioning, illness severity, socio-demographic variables, and service use;
o Determine predictors for 'membership' of different transitional trajectory groups, such as barriers to care, illness perception, and diagnosis.

Comment:
For example, we do not yet know the size of the group who do not transition, or the degree of overlap as regards YP characteristics. Nevertheless, based on our previous research (TRACK) it is clear that there will be a large group of YP who should transition but do not and it is this group that we wish to compare to the group who do transition as regards outcomes. We do not agree that such an analysis would not be interesting.

Reviewer 2 (ie me) had written
The study seemed to be anchored in CAMHS rather than in CAMHS and AMHS. Few, if any of the co-applicants were active in AMHS services. Primary consents for a service to take part in the cohort study and cluster trial are with CAMHS. AMHS are then asked to participate if they receive a referral. I would have been much more impressed if AMHS services had been involved from the outset in the planning of the research project, agreements about the intervention and prior agreement to take part. Communication between CAMS and AMHS is such an important part of good transition care that I think it should have been part of the research set up as well.

Response:
We agree that prior engagement of AMHS would have been beneficial. Our intention was to engage AMHS more from the beginning but realised soon that this would be a very difficult task in the international context and with limited researcher capacity. Nevertheless, SS, GdG, and AM are AMHS

psychiatrists and all MILESTONE clinicians have maintained ongoing to engagement with adult mental health services.
We could not find one specific AMHS clinician to engage in each service or site. Unlike in the UK and the Netherlands, in most of the participating countries AMHS do not work under the same umbrella organisation as the CAMHS. Furthermore, in all countries the number of AMHS linked with CAMHS are numerous and we were unable to predict which services young people may be referred to. We have added the following sentence in the paper to clarify this matter (p. 14):
"In most countries, other than the UK, there is no umbrella organisation to facilitate collaboration between AMHS and CAMHS. Furthermore, a single CAMHS may be linked with numerous AMHS (inpatient services, clinics, teams and individuals), making it difficult for AMHS clinicians to be engaged from the start, particularly given our limited resources. Also, we were not able to predict which AMHS would be involved, as this is dependent on transition decisions."
Nevertheless, the TRAM summary score report is intended to aid communication between CAMHS and AMHS, and our discussion will address the potential of the TRAM tool as a communication aid.

Comment:
My observation at second review
I think the authors are admitting above that, by virtue of their limited resources and the complexity of services, their design has significant weaknesses. This should be stated more explicitly. It should also be included in the Strengths and Limitations section at the start of the study.

Response:
As already stated, we cannot know in advance which adult services the young person will transition to. So we have no feasible way to engage adult services till the trial has started and the CAMHS have made a decision to transition. This is the point at which we can realistically engage adult services. And this is what we have done.
- Whilst agreeing that more input from AMHS would have been helpful, especially in the early stages of delivering this study, we do not agree that the lack of it necessarily undermines the science. Our protocol reflects very strongly the current situation at the service interface; we believe the TRAM summary report will enhance transition in at least two ways: by highlighting to the CAMHS clinician the areas on which to focus discussion and decision making, and by providing the AMHS with an easily readable and interpretable document that can enhance their decision to accept or reject a referral. By engaging too closely with AMHS, we may have changed current behaviour and therefore undermined the trial.
- Furthermore, AMHS clinicians will be involved in the interpretation of results and recommendations for clinical practice and policy.
- MILESTONE is the first study worldwide to deliver true insight into this real life problem, and at the same time offer an intervention for improving transition. Our view is that it is a pragmatic and pioneering study.

Reviewer 2 (ie me) had written
7 The TRAM Instrument
Using the TRAM as the basis of the intervention in the cluster trial. The instrument is in the supplement protocol – but not in the paper at present – perhaps it should be?

Response:
We cannot add the instruments as an appendix, as it will impact the submission of a separate manuscript specifically about the development and validation of the TRAM and TROM. We would

rather make the TRAM available on specific request from a reader than put it out in its current form in this paper.

Comment:
My observation at second review
I think this should be explained in the text – and explicitly stated that an interested reader could request it from the authors.

Response:
We agree and have added this to the text in the section on TRAM and TROM (p. 11).

Reviewer 2 (ie me) had written
The TRAM has three versions (Young person, Parent, Clinician). And each has questions that relate to mental health symptoms and control, how mature the young person is in a variety of spheres of their life, risk factors, social factors, person factors, emotional factors and cognitive factors.
I think the protocol needs a discussion of how the three questionnaires and the responses in each across so many aspects of life, are combined into a decision tool about whether to refer to AMHS.

Response:
The following paragraph has been added to the section describing TRAM and TROM (p. 11), to address this matter:
"TRAM and TROM contain 20 questions common to both scales for all participants; further eight questions are relevant only to the clinician versions and nine only to the young person and parent/carer versions. All participant versions of TRAM contain 15 additional questions that are not in TROM, yet to allow comparison of results over time, most of the domains present in TRAM are also present in TROM, with versions for AMHS and CAMHS clinicians and different follow-up time points."
Based on the discussions with the various stakeholders during the development of the TRAM and TROM, it was agreed that ratings may vary between raters, based on the type of disorder, for example, in a patient with florid psychosis with limited insight, the service user's response may not be the most accurate one; as opposed to that in anxiety disorders, where the service user may be better than carers/parents to accurately give the information. We will examine data from those with different disorders and explore whether different weightings need to be incorporated into the scoring scheme, for different disorders when using information from different sources. We will specifically model this once we have the data from the study.

Comment:
My observation at second review
As the basis of the RCT is the TRAM, I think the protocol has to have an explicit decision making algorithm based on the data collected by the TRAM. Otherwise it will be impossible to draw any conclusions becasue we will have no idea how it has been used.

Response:
We reiterate our points above that the current version of the tool does not advise the clinician what decision to make. We have an algorithm for creating the TRAM summary but as emphasised above, this only highlights particularly significant scores (i.e. areas for focus). In future, when the full data from MILESTONE becomes available, we would like to develop the tool further, to possibly be more prescriptive and/or give definite advice as to whether or not the YP should transition but this is not one of our immediate or main MILESTONE aims as it seems unlikely, based on the discussions we have had and are continuing to have with clinicians, that a single instrument or algorithm will tackle all the different issues that influence transition decisions (e.g. compliance of YP with therapy, dependency

on parents [financially and care], executive functioning of YP, delinquency, etc.) i.e. To develop such tools would clearly be a major piece of work and is outside the scope of MILESTONE.

Reviewer: 3

All comments and suggestions that I raised to the authors have been adequately addressed. This is an timely study that will make important contributions to the field.