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**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)**

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**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)**

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## KEYWORDS

Mental health, child and adolescent mental health services, transition, health services research, cluster randomised controlled trial, longitudinal cohort study, youth mental health, Europe

## ABSTRACT

**Introduction:** Disruption of care during transition from Child and Adolescent Mental Health (CAMHS) to Adult Mental Health Services (AMHS) may adversely affect the health and wellbeing of service users. The MILESTONE study aims to evaluate the longitudinal course and outcomes of adolescents approaching transition boundary (TB) of their CAMHS and to determine the effectiveness of the model of managed transition in improving outcomes, compared to usual care.

**Methods and analysis:** A cohort study with a nested cluster randomised controlled trial. Recruited CAMHS randomised to provide either i) managed transition underpinned by the Transition Readiness and Appropriateness Measure (TRAM) or ii) usual care for young people reaching the transition boundary. Participants are young people within one year of reaching the TB of their CAMHS in eight European countries; one parent/carer and a CAMHS clinician for each recruited young person; and adult mental health clinician or other community based care provider, if young person transitions. Primary outcome is Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA) at 15 months post-intervention. Secondary outcomes include mental health, social and adult functioning, quality-adjusted life years and health and social care resource utilisation assessed at 9, 15 and 24 months. With a mean cluster size of 21, a total of 840 participants will be randomised 1:2 intervention to control. This will provide 89% power to detect a difference in HoNOSCA score of 0.30 standard deviations. An additional 210 recruits for the cohort study will ensure sufficient power for studying predictors, resulting in 1050 participants and an approximate 1:3 randomisation.

**Ethics and dissemination:** The study protocol was approved by the UK National Research Ethics Service (15/WM/0052) and equivalent ethics boards in participating countries. Results will be reported at conferences, in peer-reviewed publications, and to all relevant stakeholder groups.

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3 Trial registration numbers: ISRCTN83240263; NCT03013595  
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6 **STRENGTHS AND LIMITATIONS OF THIS STUDY**  
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- 8
- 9 • This is the first ever methodologically robust trial to test whether a decision support and  
10 assessment tool can improve the mental health and social outcomes and functioning of  
11 transition age young people receiving care at Child and Adolescent Mental Health Services.  
12
  - 13 • Diverse health care settings in eight European countries are involved in the study.  
14
  - 15 • The cost-effectiveness of the intervention and research-related changes in health systems in  
16 terms of both expenditure and related health outcomes will be evaluated.  
17
  - 18 • A large, prospectively identified and robustly evaluated cohort of young people across  
19 several European countries is taking part in the study.  
20
  - 21 • There is a strong Patient and Public Involvement (PPI) embedded throughout the study.  
22
  - 23 • Due to the nature of the intervention it is not possible for clinicians or assessors to be blind  
24 to the allocation of clusters or of the service users within these clusters. To limit bias, several  
25 web-based service-user self-rated outcome measures will be used.  
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  - 27 • Transition boundaries vary between and within countries.  
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## INTRODUCTION

The MILESTONE (Managing the Link and Strengthening Transition from Child to Adult Mental Health Care) study focuses on the period when young people (YP) attending Child and Adolescent Mental Health Services (CAMHS) need to move on, or “transition” to, an adult mental health service (AMHS), if they still require ongoing care.

Adolescence is a high-risk period for psychological morbidity, and young adulthood is the period of onset of most of the serious mental disorders that disable or cause death in adult life.[1-4] The National Comorbidity Survey Replication in the USA found that 75% of people with a mental disorder have an age of onset younger than 24 years, 50% have an onset before 16.[1] However, only a small proportion of young people with mental health problems approaching adulthood, less than one in six, access services or receive appropriate care.[5 6]

There is international concern about young people who get ‘lost’ during their move from CAMHS to AMHS[7-15] and transition-related discontinuity of care is a major socioeconomic and societal challenge. In the UK, almost half of the service users reaching the transition boundary of their child and adolescent mental health service (CAMHS) do not go on to receive adult care.[7 16] The TRACK study found that less than 5% of patients undergoing CAMHS to AMHS transition experience continuity of care.[17] There is also a concern that despite recognition of ongoing mental health need, few young people are referred, with fewer than one third in one study.[18] Problems at the CAMHS-AMHS interface are accentuated by the fact that young people are simultaneously negotiating developmental and situational transitions, such as changes in housing and relationships and moving on to adult roles.[8 17] A lack of information about possible options, planning that takes too long and where no one professional takes charge to ensure decisions are acted upon, compound the problem.[19] Those who slip through the care net are likely to present to adult services at a subsequent time, with more severe and enduring mental health problems.[20-22] Disruption of care during transition adversely affects the health, wellbeing and potential of this vulnerable group,[23-



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3 28] and negative transition experiences adversely impact the young person's future engagement  
4 with mental health services.  
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8 Intervening at the level of transition represents one of the most important ways we can facilitate not  
9 only recovery but also mental health promotion and mental illness prevention in adulthood.  
10  
11 Ensuring sustained treatment through the transitional period is very likely to be cost-effective, since  
12 the presence of mental illness during childhood leads to ten times higher costs during  
13 adulthood.[29-31] However, there is currently no evidence for any effective model of transitional  
14 care or any interventions to reduce these individual and societal costs.[32]  
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### 20 21 **Transitional care**

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23 Ideally, transition to adult mental health services should be a planned, orderly, purposeful and  
24 patient-centred process that ensures continuity of care, optimises health, minimises adverse events  
25 and ensures that the young person attains his/her maximum potential.[33-37] Good transitional care  
26 starts with preparing a service user to leave the child-centred health care setting and ends when  
27 that person is received in, and properly engaged with, the adult provider or an appropriate  
28 alternative, or is discharged from care in a planned and managed fashion.[38 39].  
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37 European research on transition from CAMHS to AMHS is sparse, with little information available on  
38 the quality of transition and transition experiences in different EU countries in relation to long term  
39 mental health outcomes. The organisation of CAMHS in the member states vary, including the age at  
40 which young people are transitioned to adult services, size and complexity, sources of funding, and  
41 service provision and care. There is some evidence though that transition is a problem across all EU  
42 states.[40 41]  
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50 Barriers to good transition have been mapped,[16 17] but the evidence of interventions for  
51 improving transitional care is scant. A recent systematic review of CAMHS to AMHS transition  
52 identified only three initiatives, all in the USA,[42] including a case management model, a transition  
53 support model and an outpatient transition programme. Although all three programmes showed  
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3 improved clinical and social outcomes for those with facilitated transition, none of these was a  
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5 randomised trial and each model was deeply rooted within its own particular and specific healthcare  
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7 context. There is no consensus as to who can be discharged on reaching the CAMHS transitional  
8  
9 boundary, who should receive transitional care, and how this care should be delivered. Furthermore,  
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11 it is not clear what outcomes should be measured to assess clinical and cost effectiveness of the  
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13 model, what the outcomes of those who fall through the care gap are, and what the individual,  
14  
15 organisational and societal costs of poor, inadequate or inappropriate transition are. A recent NICE  
16  
17 review on transition from child to adult care across all specialities found that there was no robust  
18  
19 evidence on models of transitional care.[32]  
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22  
23 In the absence of a planned, purposeful and needs-based assessment of those who reach the  
24  
25 boundary, clinical judgment on transition can be influenced by misperceptions of other services,  
26  
27 time and resource constraints, poor communication between CAMHS-AMHS, and poor adherence to  
28  
29 existing policies. Research has confirmed several information gathering biases in unstructured  
30  
31 clinical judgements such as diagnostic biases, confirmation biases, ignoring conflicting information,  
32  
33 and assumptions based on patient and service background.[43] A recent study found that feeding  
34  
35 back structured assessment results to clinicians is leading to improved clinical decision making.[43]  
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38  
39 Ideally all young people who reach a transition boundary would be assessed in a structured and  
40  
41 standardised way to determine ongoing need for care. Those who need such care would make a  
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43 transition to adult services in a planned and managed manner ensuring continuity of care across all  
44  
45 domains. Those without ongoing need would be appropriately discharged. Despite the intuitive  
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47 simplicity and clinical importance of such a structured decision process, a transition model  
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49 incorporating this approach with regard to mentally ill patients has not been evaluated or reported  
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51 in research or health practice literature, although its need has been articulated.[11 14]  
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## The MILESTONE project

The five year MILESTONE project (February 2014 to January 2019) aims to improve the understanding of, and strengthen, CAMHS-AMHS transitional care across different healthcare systems in the EU. In a series of work packages, it will 1) map current services and transitional policies across EU; 2) develop and validate transition-specific outcomes measures; 3) conduct a longitudinal cohort study of transition process and outcomes across eight EU countries; 4) develop and test, in a cluster-randomised trial, the clinical and cost-effectiveness of an innovative transitional care model; 5) create clinical, organisational, policy and ethics guidelines for improving care and outcomes for transition age youth; and 6) develop and implement training packages for clinicians across EU. This paper presents the protocol for the work packages dealing with the longitudinal cohort study, the cluster randomised controlled trial and the economic evaluation of the trial, which combined constitute the MILESTONE study.

## 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. This 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), prior to reaching the transition boundary.
4. Feedback of TRAM results to relevant clinicians in both CAMHS and AMHS, users, and carers.

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3 5. Structured and regular follow-up of all young people using Transition Outcome Measure  
4 (TROM) to assess whether those who needed care were appropriately engaged with adult  
5 services and those who had been discharged or referred to other services have no unmet  
6 needs following cessation of care.  
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### 11 **Transition Readiness and Appropriateness Measure (TRAM) and the Transition** 12 **Related Outcome Measure (TROM)** 13

14 The Transition Readiness and Appropriateness Measure (TRAM) is a decision support and  
15 assessment tool using the HealthTracker™ platform. The Transition Related Outcome Measure  
16 (TROM) provides information on outcomes post-transition. The TRAM aims to identify a) high-risk,  
17 high-need cases for whom transition to AMHS is advisable and appropriate; b) those who can be  
18 appropriately discharged in a planned manner from CAMHS to a General Practitioner (GP); or c)  
19 transitioned to another community based service (such as social services, voluntary sector or other  
20 non-statutory agencies).  
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31 The TRAM and TROM were developed using existing literature, expert input and focus groups on  
32 developing and validating Patient Reported Outcome Measures (PROMS);[44] MILESTONE's group of  
33 young advisors also reviewed the scales and helped identify areas of duplication or unclear terms.  
34 These scales have been translated into Croatian, Dutch, Flemish, French, German, and Italian  
35 languages and provide a summary of all factors necessary to consider (including symptoms,  
36 functioning, risk and need for care) when making a transition decision and when assessing the  
37 outcomes of a transition. There are versions for young people pre-transition, young people post-  
38 transition, parents/carers and clinicians at CAMHS and AMHS which can be completed online, via the  
39 HealthTracker™ platform (<https://www.healthtracker.co.uk/index.php/our-platform/>), a web-based  
40 portal allowing measures to be completed remotely, which has been used in other EU FP7 projects  
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3 The construct validity, content validity, inter-rater validity, test-retest validity, and sensitivity to  
4 change of TRAM and TROM were assessed in a sub-study between June 2015 and April 2016.  
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8 The TRAM score summary report presents the scores from the young person, parent/carer and  
9 clinician for each item with graphs visualising differences or similarities in scoring. The report  
10 contains items that are relevant to the clinician's transition decision (symptoms, risk factors and  
11 disruption experienced by the young person) and those that can facilitate a smooth transition.  
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### 16 17 **AIMS AND OBJECTIVES**

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19 The overall aim of the nested cRCT is to determine the effectiveness and cost-effectiveness of the  
20 model of managed transition in improving the health and social outcomes of young people, and their  
21 transition to adult roles, as compared to treatment as usual, in eight participating EU countries. The  
22 specific objectives are  
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- 27  
28 1. To test the hypothesis that the implementation of the model of managed transition in  
29 CAMHS at the transition boundary improves the mental health and social outcomes of young  
30 people and their transition to adult roles when they move on from CAMHS, as compared to  
31 usual care.  
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- 34 2. To conduct an economic evaluation of the model of managed transition compared with  
35 usual care.  
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- 38 3. To explore the views and experiences of health professionals and young people concerning  
39 the intervention.  
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48 The prospective cohort study will delineate the transition journey of a large number of young people  
49 across eight EU countries. The aims are  
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53 4. To evaluate the mental health, quality of life, and functioning of young people who attend  
54 CAMHS and reach the CAMHS/AMHS transition boundary;  
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5. To evaluate the longitudinal course of mental health, social and adult functioning outcomes of young people who reach the CAMHS/AMHS transition boundary and transition into young adulthood;
6. To compare the outcomes in those CAMHS users who transition with those who do not transition to AMHS.

## METHODS AND ANALYSIS

### Study design and management

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,[46] by virtue of allocation to the intervention by cluster randomisation, with each distinct CAMHS comprising a cluster. MILESTONE is a superiority trial; the aim being to show that managed transition is superior to usual care in improving patient reported outcomes. The study flow diagram is presented in Figure 1. The trial has economic and qualitative components, addressing objectives 2 and 3, respectively.

### Figure 1 MILESTONE study flow diagram

The study is co-ordinated from the research office in the Mental Health and Wellbeing unit, Warwick Medical School, with Quality Assurance and Statistics from Warwick Clinical Trials Unit. The Study Co-ordinator is responsible for the day-to-day co-ordination and the Chief Investigator (CI) for clinical aspects. The study is managed by a trial management group (TMG), including work package leaders (i.e. country leads), and supported by MILESTONE research staff. The TMG speaks monthly by telephone conference chaired by the CI. The study conduct and progress is overseen by the MILESTONE Scientific Clinical and Ethical Advisory Board (SCEAB) comprising five international experts and four Patient and Public Involvement representatives. The SCEAB members are invited to the annual general meetings in order to monitor the progress of work, to assess the scientific quality

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3 and to give feed-back to the Consortium members, but without a right to vote. The SCEAB will also  
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5 review the main governance and any ethical issues which might require greater attention.  
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8 MILESTONE has strong Patient and Public Involvement (PPI) embedded throughout the project;  
9  
10 young advisors, some with experience of transition in mental health services provided feedback on  
11  
12 the protocol and study documents. Their ongoing role includes: attending and contributing to  
13  
14 project steering committee meetings, designing the intervention leaflet and other promotional  
15  
16 materials, and advising on recruitment and the engagement of young people. The first five PPI  
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18 representatives have been from the UK; in the third year service users from other participating  
19  
20 countries will be involved.  
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### 23 **Setting and site selection**

24  
25 The study is currently running in Belgium, Croatia, France, Germany, Italy, the Netherlands, Republic  
26  
27 of Ireland, and the United Kingdom. Recruitment of participants is underway in 52 CAMHS clusters  
28  
29 that fit the inclusion criteria below (October 2015 – December 2016, with last inclusions in January  
30  
31 2017). Face-to-face meetings with clinical and managerial leads were arranged at those sites that  
32  
33 expressed an interest and the study explained in detail. Signed site agreements or equivalent were  
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35 obtained from participating sites prior to the start of the study.  
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#### 39 **Cluster level eligibility criteria**

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41 For a CAMHS to be eligible, it had to be a service delivering medical and psycho-social interventions  
42  
43 for children and adolescents with mental health problems and disorders, and/or  
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45 neuropsychiatric/developmental disorders (e.g. emotional/neurotic disorders; eating disorders;  
46  
47 hyperkinetic disorder/ADHD; autism spectrum disorders); community-based, or provide outpatient  
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49 or inpatient care; publicly or privately funded; must have a formal upper *age limit* (the transition  
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51 boundary) for providing care to young people and; be responsible for transfer of care to an adult  
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53 service for those who reach the transition boundary. Forensic services and highly specialised  
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55 national services, which cater for rare/unusual disorders and/or serve a national population, such as  
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3 specialist clinics for rare metabolic disorders or long-term residential care for severe autism were  
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5 excluded. Eligible services could vary in size and complexity, ranging from single psychiatrists or  
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7 psychologists (e.g. Germany) or circumscribed teams to services with multiple teams and localities  
8  
9 offering multidisciplinary care (e.g. UK).

#### 10 11 12 Baseline service level data collection

13  
14 Baseline service data was collected from the CAMHS manager or leading CAMHS clinician at all  
15  
16 recruited CAMHS in the year preceding recruitment of study participants. The questionnaire  
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18 covered: 1) Size (number of staff), structure and function of CAMHS; 2) Transition boundary of the  
19  
20 service (i.e. age at expected transition); 3) The number and type of adult mental health services  
21  
22 (AMHS) that operate within the CAMHS catchment area; 4) Current transition policy and practice; 5)  
23  
24 Size of the catchment population. This information was used to establish the organisational  
25  
26 structure of CAMHS and identify potential cross-over and/or movement of staff between teams or  
27  
28 units so that distinct units (clusters) could be identified. If one or more CAMHS teams share the  
29  
30 same core clinicians, then these were classified as one cluster, becoming the unit of allocation.  
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33  
34 Upon leaving CAMHS care, young people may be referred on to AMHS or other another community  
35  
36 based service (e.g. social services, voluntary sector or other non-statutory agencies offering support  
37  
38 and therapeutic interventions for mental health needs), or discharged back to their GP. Community  
39  
40 based services will be invited to participate in the study, and service level data will be collected once  
41  
42 they are recruited.  
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#### 45 46 **Randomisation**

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48 As several countries only had three CAMHS clusters, this fixed the randomisation ratio at 1:2 and the  
49  
50 randomisation was conducted in a two stage process: First, randomly selected triplets of clusters  
51  
52 within each country were identified for inclusion in the cRCT. These three clusters were further  
53  
54 randomised in a 1:2 ratio between intervention and control arms. The excess clusters (those not  
55  
56 selected during the first stage for the cRCT) were used for the cohort study only to enhance  
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3 numbers. Overall, this two-stage process will equate approximately to a randomisation ratio of 1:3.

4  
5 All randomisation was conducted by the trial statistician using the statistical software Stata 14.[47]

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7  
8 The CAMHS were informed of their allocation after randomisation. The study personnel were also  
9 aware of the allocation as they are involved in delivering the intervention and assessing outcomes.

10  
11 The young people and their parents/carers, who are recruited after randomisation, will be informed  
12 of their allocation after they have consented to the study, yet only if they ask about this specifically  
13 [48].  
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### 18 19 **Participant eligibility and recruitment**

#### 20 21 **Young people**

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23 Individual recruitment targets were set for each CAMHS (cluster), based on local capacity, but with  
24 the constraint that in the cRCT there should be on average 21 participants per cluster. Databases of  
25 all participating CAMHS are scrutinised by CAMHS personnel to identify all young people  
26 approaching the service's transition boundary and meeting the inclusion criteria over a 15 month  
27 recruitment period (between October 2015 and December 2016).  
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36 Young people are eligible, if a) their age is within one year of reaching the transition boundary of  
37 their CAMHS during the trial recruitment period and, in exceptional cases, not more than 3 months  
38 older than the transition boundary, if a decision about transition has not yet been made; b) they  
39 have a mental disorder defined by DSM-IV-TR, DSM-5 or ICD 10/11, or they are under the regular  
40 care of CAMHS (if not yet diagnosed); c) they have an IQ  $\geq 70$  as ascertained by previous  
41 standardised assessment or diagnosed by clinician, or no indication of intellectual impairment; and  
42 d) they provide valid written informed consent, or assent, if below the legal age of consent. They will  
43 be ineligible if they a) are younger than a year before the transition boundary of their CAMHS; b)  
44 have a more severe intellectual impairment (IQ < 70) as ascertained by previous standardised  
45 assessment or diagnosed by clinician – if no data on intellectual functioning are available (because it  
46 has never been assessed) then care coordinators will be asked to make a clinical judgement on  
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3 intellectual impairment before baseline assessment takes place; c) are not able to (or expected not  
4 to be able to) complete the questionnaires due to severe physical disabilities or language problems,  
5 even with assistance from family members or a research assistant; d) are service users in a secure  
6 forensic institution; or e) don't provide valid written informed consent, or assent, if below the legal  
7 age of consent.  
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14 At each site, the clinicians of eligible young people will advise the research team of the  
15 ability/capacity of the young person to give informed, voluntary consent or assent. Young people will  
16 be introduced to the study (as appropriate, taking local ethical/legal conditions and best practice  
17 into consideration) either by a) a clinician or care coordinator, who will provide a study leaflet  
18 and/or briefing sheet and seek consent for the individual to be contacted by a MILESTONE  
19 researcher using a signed contact form; b) a letter signed by their care coordinator or clinician  
20 outlining the purpose of the study followed by a phone call by a CAMHS personnel if no response is  
21 received; or c) posters and/or leaflets displayed in the participating CAMHS sites, with contact  
22 details of the research team.  
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34 All young people who agree to be approached by a MILESTONE researcher will be individually  
35 contacted and provided with further information about the study; interested individuals are asked to  
36 sign a study consent form. Young people who are below the legal age of consent will be asked for  
37 their assent and signed consent is obtained from a parent/carer (or, in some countries,  
38 parents/carers, according to national medical ethics requirements).  
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#### 46 Parents/carers

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48 The information provided to young people will include separate information and consent forms for  
49 their parents/carers. After signing up to the study, the young person will be asked to name his/her  
50 primary care giver whom s/he would like to be involved. For young people under the legal age of  
51 consent, the parent/carer has to be the legal guardian of the young person. The aim will be to  
52 engage the same parent/carer throughout the whole study period. If the latter is not possible, then  
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3 the aim is to involve another parent/carer. If the young person doesn't live with his/her biological  
4 parent/s, then his/her carer will be involved. A carer may be the legal guardian or a partner or an  
5 older adult sibling, or another individual living with and/or providing regular support to the young  
6 person.  
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11 The parent/carer will be eligible if the young person consents to parent/carer participation and  
12 he/she provides a valid written informed consent. A parent/carer will be ineligible if he/she does not  
13 live with and/or provide regular support to the young person, and/or is not able to (or expected not  
14 to be able to) complete the questionnaires due to severe physical disabilities or language problems,  
15 even with assistance from family members or research assistant.  
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21 Young people who do not wish their parent/carer to be approached to participate in the study will  
22 have their wishes respected, regardless of their own capacity to consent. If a parent/carer is  
23 unwilling to participate, their wishes will be respected.  
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### 30 31 Clinicians/care providers

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33 Clinicians/care providers will be contacted and provided with separate information sheets and  
34 consent forms. They are eligible if they are responsible for the main care for the young person at  
35 CAMHS (and AMHS or other relevant service provider, if referral is made) and provide a valid written  
36 informed consent.  
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### 42 43 **Intervention**

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45 The CAMHS in the intervention arm will receive information on good quality managed transition and  
46 feedback the TRAM assessment in the form of a TRAM score summary report for each participating  
47 young person.  
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### 51 52 Information provision at CAMHS (AMHS)

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54 A special meeting will be held between MILESTONE personnel and participating CAMHS in the  
55 intervention arm prior to service user recruitment to establish clinicians' existing knowledge and  
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3 current practice of transition, and to discuss optimal transition, using TRAM as a decision support  
4 tool, and managed ending of care. Each meeting will follow a prescribed structure. Additionally,  
5 written information on good quality transitional care will be provided to all clinicians in the  
6 intervention arm CAMHS teams. This will consist of presentation handouts and a leaflet on good  
7 quality transition designed by our young project advisors.  
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12 The AMHS linked with the CAMHS will be provided with similar information once the service has  
13 been recruited into the study.  
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### 16 17 18 19 20 Feedback of TRAM results

21 TRAM findings (TRAM score summary report) will be fed back to clinicians soon after the young  
22 person, parent/carer and CAMHS clinician have completed the baseline assessments.  
23

- 24  
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27 1) The TRAM results will be communicated to the CAMHS clinician via an email, attaching the  
28 TRAM score summary report, and an offer made to explain the findings at a face-to-face  
29 meeting. If no response is received, the email will be followed up once only with a telephone  
30 call.  
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- 33  
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35 2) The CAMHS clinician is encouraged to communicate the TRAM findings to the young person  
36 and parent/carer.  
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- 39  
40 3) The CAMHS clinician will decide whether or not to refer the young person to adult services.  
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- 42  
43 4) If a referral is made, the CAMHS clinician should, if appropriate and with relevant  
44 permissions, send the TRAM score summary report along with the referral letter to the new  
45 adult service.  
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- 48  
49 5) The AMHS clinician or other care provider will be offered a chance to discuss the TRAM  
50 findings with an appropriate member of the MILESTONE research team.  
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53 The aim of the TRAM score summary report is to support clinicians in their decision making  
54 regarding transition, communication with stakeholders and planning of the transition process;  
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3 hence it supports and is the basis of managed transition. A flowchart of the study intervention is  
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5 depicted in Figure 2.  
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8 **Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up**  
9 **assessments with young person**  
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For peer review only

## The control arm

Young people, parent/carers and clinicians in the control arm complete the same baseline assessments but the latter do not receive any additional training or feedback of TRAM scores (i.e. will continue providing usual care).

## Outcome measures

### Primary outcome measure

The primary outcome measure is the clinician-rated Health of the Nation Outcome Scale for Child and Adolescents (HoNOSCA),[49] which has 15 items scored on scale of 0-4, and covers the severity of the behaviour, impairments, symptoms and social functioning of children and young people with mental health problems. The clinical usefulness of the HoNOSCA has been validated and its sensitivity to change confirmed.[50 51]

Although the HoNOSCA is intended as a measure that is completed by a clinician who is also responsible for treatment of the client, the measure can also be completed by a mental health care professional not involved in the treatment using semi-structured interview.[52] In our study the measure will be completed by a trained MILESTONE Research Assistant by interviewing the young person and taking into account all other available sources of information (parent/carer, relevant clinician and the medical records) to ensure accuracy of data.

To ensure consistency and comparability, HoNOSCA is used throughout (rather than switching to HoNOS at age 18 years). The primary outcome endpoint for the cRCT is 15 months.

### Secondary outcome measures

The secondary outcome measures are as indicated in Table 1. Two of them were developed specifically for the MIELSTONE study.

Table 1 Outcome measures

Study Instrument	Description
<b>Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA)[53]</b>	Used to assess the need for care based on a wide range of problems.
<b>Transition Related Outcome Measure (TROM)<sup>1</sup></b>	Informs on quality of transition and changes in symptoms, risk factors and impairment due to transition. It has been developed based on the TRAM.
<b>World Health Organization Quality of Life Brief Inventory (WHOQOL-BREF)[54 55]</b>	Assesses quality of life, covering physical and psychological health, social relationships and current environment.
<b>MILESTONE specific Client Service Receipt Inventory (CSRI)[56]</b>	Focuses on the use of health and social services.
<b>EuroQol health questionnaire (EQ-5D-5L)[57]</b>	Assesses health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).
<b>ASEBA: Youth Self Report (YSR)/Adult Self Report (ASR)/Child Behavior Checklist (CBCL)/Adult Behavior Checklist (ABCL)[58 59]</b>	Suite of measures assessing dimensions of emotional and behavioural problems.
<b>Ethics of Transitioning<sup>1</sup></b>	Assesses ethical challenges regarding the delivery of transitional care.
<b>Independent Behaviour During Consultation Scale (IBDCS)[60]</b>	Measures independent behaviour.
<b>Barriers to Care[61]</b>	Assesses practical (e.g. costs, time) and psychological barriers (e.g. fear to stigmatization) to care.
<b>Bullying – adapted from Retrospective Bullying and Friendship Interview Schedule[62 63]</b>	Assesses the experiences with bullying in different settings (e.g. school, at home, college).
<b>Life Events<sup>1</sup></b>	Assesses significant life events such as accidents, deaths in the family and separation of parents/carers.
<b>Brief Illness Perception Questionnaire (B-IPQ)[64 65]</b>	Assesses the cognitive and emotional representation of illness, including consequences. The term 'illness' has been replaced with the term 'condition'.
<b>On Your Own Feet: Transition Experience Scale (OYOF- TES)[66]</b>	Focuses on specific experiences with the transition process and has two versions: one for Young People who transition to AMHS (or other types of adult care) and one for Young People discharged from CAMHS.
<b>Specific Levels of Functioning Scale (SLOF)[67]</b>	Assesses adult functioning of the Young Person from the Parent/Carer's perspective.
<b>Clinical Global Impression Severity scale (CGI-S)[68]</b>	Assesses the severity of the patient's illness at the time of assessment, relative to the clinician's past experiences.

<sup>1</sup>Developed specifically for the MILESTONE study

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3 The Ethics of Transitioning questionnaire was developed based on the themes raised by a systematic  
4 literature review and focus groups and addresses the following research question: "What are the  
5 ethical challenges of ensuring delivery of transitional care to those who need it most against the risk  
6 of pathologising transient and self-limiting distress and dysfunction, which may be normal during  
7 adolescence?". It contains seven items rated on a five-point Likert scale, with one version to be  
8 completed prior to, and another after, transitioning.  
9

10  
11 The Life Events questionnaire is a dichotomous 13-item scale that is appropriate for both young  
12 people and adults, and focuses on significant life events, such as accidents, deaths in the family, and  
13 separation of parents/carers.  
14

### 15 **Data collection**

#### 16 **Baseline data**

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18 Table 2 highlights the number of contacts with the participants, the time points of the various  
19 assessments, and the type of data to be collected from the young person, parent/carer and clinician.  
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Table 2 Study assessments for participants (transition scenario)

Contact	1	2 (T1)	3 (T2)	4 (T3)	5 (T4)
<b>Contact Window</b> (No. months ± No. months)		<b>Within 6m before TB***</b>	<b>9m (± 1m) after T1</b>	<b>15m (± 1m) after T1</b>	<b>24m (± 1m) after T1</b>
Inclusion/exclusion criteria	YP P/C				
Informed consent	YP P/C	YP P/C C	(YP) (P/C) C	(YP) (P/C) (C)	(YP) (P/C) (C)
Contact details	YP P/C	YP P/C	YP P/C	YP P/C	YP P/C
Sociodemographic & personal information		YP P/C C	YP (C)	YP P/C (C)	YP P/C (C)
Need for Care (HoNOSCA – SR) (HoNOSCA – Clinician report)		YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)
Transition readiness / Transition outcome (TRAM/TROM)		YP P/C C	YP P/C C	YP P/C C	YP P/C C
Referral and Transition Status (CAMHS clinician only)			C	(C)	(C)
Quality of Life (WHOQOL-BREF)		YP		YP	YP
Cost-effectiveness (EQ-5D-5L)		YP	YP	YP	YP
Service use (CSRI)		YP	YP	YP	YP
Emotional/behavioural problems (YP: YSR/ASR P/C: CBCL/ABCL)		YP P/C	YP P/C	YP P/C	YP P/C
Ethics of transitioning		YP		YP	
Independent behaviour** (IBDCS)		YP	YP	YP	YP
Barriers to Care (BtC)**			YP	YP	YP
Bullying		YP			YP
Life events		YP	YP	YP	YP
Illness perception (B-IPQ)		YP			YP
Transition experience & readiness (OYOF-TES)*			YP P/C	(YP) (P/C)	
Functioning & Impairment (SLOF)		P/C		P/C	P/C
Illness severity (CGIS)		C	(C)	(C)	(C)
Psychopathology (YP: DAWBA 5-17/18+ SR) P/C: DAWBA 5-17/18+ PR) C: Clinical diagnosis		YP P/C C	(C)	(C)	YP P/C (C)

TB = Transition boundary of service; YP = young person; P/C = parent/carer

C = clinician. T1: CAMHS clinician; if YP is transitioned after T1, then at T2-T4 the clinician is based at AMHS. If there is a delay in transitioning, the clinician at T2-T4 will still be based at CAMHS. Consent and sociodemographic data will be sought from the clinician only once. (C) = if YP is a mental health service user, then clinician will be asked for information.

RA = Research Assistant

SR = Self-report

PR = Parent-report

\* = completed only once at the first assessment after transition

\*\* = if the YP is a service user the IBDCS will be administered, if the YP is not a current service user, the BtC will be administered.

\*\*\* = in exceptional cases, the assessment can take place up to 12 months before or 3 months after the TB (e.g. if transitions regularly happen earlier in a service or a decision about transition hasn't yet been made).

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3 The baseline assessment (T1) is undertaken after consent/assent has been given but before the  
4 delivery of the intervention, within 6 months before the transition boundary of the service or, in  
5 exceptional cases, within 12 months before or 3 months after the boundary (e.g. if transitions  
6 regularly happen earlier in a service or a decision about transition hasn't yet been made). Young  
7 people and their parents/carers are assessed at the clinic, or at an alternative location suitable for  
8 the young person, with both semi-structured interview (sociodemographic and personal  
9 information, and HoNOSCA) and online assessment. The sociodemographic and personal  
10 information questionnaire for young people and parent/carers collects general information about  
11 the young person and family, and the care the young person receives. The questionnaire covers also  
12 medical history and additional variables previously shown to contribute to continuity of mental  
13 health problems (for example, history of mental health problems and alcohol or drug abuse by  
14 parents). The last online assessment of T1 is the structured sections of the Development and Well-  
15 being Assessment (DAWBA),<sup>[69 70]</sup> which obtains information on mental health. Information from  
16 the assessment with the young person and parent/carer will be combined with a computer  
17 algorithm that provides an estimate of the probability of a certain individual diagnosis. Information  
18 on clinical diagnosis is obtained from clinician.

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38 The length of the baseline assessment (YP) is approximately 1.5 – 2 hours. The participant can take a  
39 short break in between the online measures, and if required, complete them over multiple sessions.  
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42 The research assistant is available to assist if there are any difficulties. The baseline assessment (T1)  
43 should be completed before the end of the recruitment period.  
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#### 47 Follow-up data

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49 Outcomes will be measured 9 months (T2), 15 months (T3) and 24 months (T4) after T1. The aim is  
50 to complete measures at T2 and T3 via telephone and online assessment, and at T4 via face-to-face  
51 contact with young people and their parents/carers, within a month ( $\pm$ ) of the calculated assessment  
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3 time point (Table 2). Assessments with CAMHS or AMHS clinicians (or other service provider), which  
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5 is dependent on transition status, follow the same schedule.  
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### 8 Evaluation of the study and intervention 9

10 The views and experiences of CAMHS clinicians in the intervention arm will be captured using a  
11  
12 semi-structured questionnaire. All clinicians will be approached and those willing to engage will be  
13  
14 interviewed over the telephone or face-to-face.  
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17 A sub-sample of young people taking part in the study will be invited to take part in focus groups at  
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19 T4 from three participating countries: Ireland, UK and Croatia. The purpose of the focus groups will  
20  
21 be to explore their experiences of leaving CAMHS, transition to AMHS if applicable, and views of  
22  
23 mental health services, the aim being to establish whether young people have better health,  
24  
25 educational and social outcomes, better quality of life and satisfaction with services if they: a) have  
26  
27 experienced a managed transition from child to adult services at the transitional boundary or b)  
28  
29 have experienced usual care (i.e. their transition to adult services, or their discharge from services, is  
30  
31 via the usual procedure of their CAMHS clinic). It is hoped that, as part of MILESTONE's patient and  
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33 public involvement activity, some of the young advisors, or other young people trained in facilitation  
34  
35 skills by some of the research sites, may co-facilitate these focus groups.  
36  
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38 Three audio-recorded focus groups will be held in each country with 9-12 young people in each  
39  
40 group. Recruitment will be from the study participants with purposive sampling to include some  
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42 young people who a) did not transition to adult services, b) who transitioned to adult services via  
43  
44 usual care and c) who experienced managed transition.  
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### 48 **Sample size** 49

50 Assuming an average cluster size of 15 participants, an allocation ratio of 2:1 (control : intervention),  
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52 a coefficient of variation of cluster size of 0.4 (cluster sizes ranging from approximately 5 to 30), and  
53  
54 an intracluster correlation coefficient of 0.01, with 600 participants (195 intervention arm (13  
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56 clusters), 405 control arm (27 clusters)), the cRCT will have 89% power to detect a difference of 0.30  
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3 standard deviations in the primary outcome measure (HoNOSCA). To allow for 30% dropout, 21  
4 participants will be recruited per cluster. Thus, for the cRCT the target sample size is 840 participants  
5 in total (273 intervention - 13 clusters of size 21; 567 control - 27 clusters of size 21). The  
6 randomisation will be stratified by country and the number and size of clusters dictated by local  
7 capacity. Excess clusters (those not required for the cRCT) will be allocated to the control arm and  
8 used in the analysis of the cohort study only to enhance numbers for sufficient power to study  
9 predictors for the longitudinal course and outcome of mental health during transition. Based on  
10 feasibility work to date we anticipate that there will be 10 such excess clusters (average size 21  
11 before drop outs). The recruitment target for the cohort study is therefore 777 participants (567  
12 from the control arm of the cRCT plus 210), and the total recruitment target is 1050 (840 plus 210).

### 23 24 25 **Retention of study participants**

26  
27 To ensure that contact is not lost with any members of the study population during the follow-up  
28 period and that data are as complete as possible, MILESTONE has paid considerable attention to its  
29 engagement and retention strategies, drawing extensively on the advice and experiences of its  
30 young advisors to create a special “Bonding Plan”. Participants may be contacted using several  
31 methods of communication (post/phone/email); contact details of all participants, including GP and  
32 CAMHS clinician details, will be recorded in a “keeping in touch” form; data will be collected in  
33 several different ways (face-to-face, online, phone); and each contact, or contact attempt, made  
34 with participants will be recorded in a bespoke contact log. There are multiple contact points  
35 between study assessments, where the participants can advise of any changes to their contact  
36 details. The Bonding plan activities vary by country taking local ethical and cultural requirements  
37 into consideration, and include items such as thank you cards and newsletters and small thank you  
38 gifts, such as multi retail gift vouchers or book tokens. Reasonable travel expenses will be  
39 reimbursed for young people and their parents/carers.  
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### Losses to follow up

Due to the characteristics of the study population group (young people, highly mobile, in the process of moving on to higher education, training or work), we have allowed for a 30% drop out rate.

### Withdrawal of young people from the study

All participants will remain in the study and follow-up data will be sought unless consent for participation in data collection is explicitly withdrawn.

### Data analysis

A detailed Statistical Analysis Plan, which will include specific methods of analysis for each outcome variable, will be drawn up by the study statisticians before any analysis is started, and will be reviewed and approved by the Trial Management Group.

A sensitivity analyses using multiple imputation will be conducted to explore the potential impact of missing data.

### Cohort study

Baseline, longitudinal course, and outcome data at T4 will be analysed. Trajectories of mental health, subjective need for care and quality of life will be determined using mixed growth models and related to whether transitions from CAMHS to AMHS took place.

Data will be analysed to predict and characterise those with better primary and secondary outcomes. Functional, clinical and quality of life outcomes will be assessed in those CAMHS users who transition with those who do not transition to AMHS.

### cRCT

Basic descriptive methods will be used to present the data on study participants, trial conduct, clinical outcomes and safety (in total and for each study group separately). The primary outcome will be HoNOSCA score at T3 and we will test the hypothesis that there is no difference in this between the managed transition and standard care arms over the study period using a multilevel model with

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3 random effects to account for clustering and repeated measures, and adjustment for design factors  
4 (country and size of service). Where appropriate, a similar approach will be applied to the analysis of  
5 secondary outcomes. All analyses will be on an intention to treat basis.  
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## 9 **Economic evaluation**

### 10 **Health economic data collection**

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12 To conduct the economic evaluation of the trial, information on health care usage, social care  
13 usage/social costs and intervention costs will be captured. Additionally, participant health-related  
14 quality of life, and HONOSCA score will be recorded.  
15  
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### 20 *Resource use data collection*

21  
22 Health and social care resource utilisation will be estimated using the MILESTONE specific Client  
23 Service Receipt Inventory (CSRI), which draws on a CSRI used previously to estimate mental health  
24 care costs in the UK,[56] but has been substantially revised for use in MILESTONE. It includes  
25 questions regarding not only health care usage, but also relating to social and judicial resource use,  
26 and these questions are tailored for each participating country to reflect local services. Young people  
27 complete the measure at all four time points. For the purpose of economic evaluation, interviews  
28 will also be conducted to ascertain the staff workload and additional resources required for patient  
29 care and decision-making related to service users passing through the transition boundary.  
30 CAMHS/AMHS in intervention sites will be asked, at end of the study, for specific details of the  
31 impact of the managed transition intervention in terms of the number of staff involved in transition,  
32 their workload, and additional service resources required. A sub-sample of members of staff will be  
33 involved in this part of the study.  
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51 The intervention costs associated with managed transition include the cost of implementing, as well  
52 as the delivery of the intervention. Questionnaires have been distributed to researchers in each  
53 country to ascertain the resources required to set up the intervention, whilst Excel logbooks capture  
54 the time spent by clinicians completing the TRAM. Likewise, the time spent by the University of  
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60

Warwick preparing the TRAM report is logged within an Excel database and clinician questionnaires will be used to capture the impact of the intervention on resource use.

#### *Outcomes for economic evaluation*

The two primary outcomes for the economic evaluation are quality adjusted life years (QALYs) and HONOSCA score.[49 50] Health-related quality of life (HRQL) will be measured using the EQ-5D-5L[57] and index scores[71] will be applied to calculate QALYs to determine the impact of the intervention on HRQL. Changes in QALYs and HONOSCA score between the two trial arms will be examined in conjunction with the costs to examine the cost-effectiveness of the intervention on mental health.

#### Economic evaluation: analysis

##### *General principles of the economic analysis*

**Intention to treat:** As recommended by best practice,[72] an intention to treat (ITT) framework will be adopted. That is, for each individual within the trial, the analysis will be conducted according to which arm they were randomised.

**Perspective:** The base-case analysis will adopt a healthcare and personal social services (PSS) perspective in accordance with NICE recommendations.[72] However, given the widespread acknowledgement of the wider costs of mental health, a societal perspective will be adopted as a secondary analysis.

**Time horizon:** The base-case analysis will be a trial based analysis and therefore consider just the years followed up within the trial. Given the complexity of the trial, the potential for long term decision modelling and extrapolation will be informed by a systematic review of the methods used within existing mental health literature. Long run extrapolation will therefore be considered in light of this.

1  
2  
3 **Discounting:** All costs and outcomes that occur after the first year of the trial will be discounted at  
4  
5 3.5%.  
6  
7

8 **Missing data:** Typically, within any economic evaluation of an RCT, there will be some missing data.  
9  
10 This may be for a number of reasons, and a certain degree of attrition is to be expected during  
11  
12 follow up. Should missing data be prevalent, the health economics analysis will address missing data  
13  
14 through the use of multiple imputation.  
15

16  
17 **Clustering:** The hierarchical nature of the data needs to be addressed within multiple imputation  
18  
19 procedures and within the analysis framework. To do this, random effects approaches will be used.  
20

21  
22 **Uncertainty:** The uncertainty around the results will be assessed through probabilistic sensitivity  
23  
24 analysis and the generation of cost-effectiveness acceptability curves (CEACs).  
25  
26

#### 27 *Calculating costs for economic evaluation*

28  
29 Data on staff time and other resources in the transition process will be obtained at each location,  
30  
31 and costed using appropriate sources of unit cost data (e.g. for the UK, standard unit cost sources  
32  
33 include the NHS reference costs and the Unit Costs of Health and Social Care report published  
34  
35 annually by the Personal Social Services Research Unit at the University of Kent). This will result in  
36  
37 location-specific estimates of the direct costs involved in implementing the managed transition  
38  
39 process.  
40  
41

#### 42 *Outcomes for economic evaluation*

43  
44 The primary economic analysis will be a cost utility analysis. The EQ-5D-5L measure allows the  
45  
46 calculation of QALYs. QALYs will be calculated for each child within the trial using the area under the  
47  
48 curve method. The trapezium rule will be used to calculate the area under the curve and thus  
49  
50 calculate QALYs. An underlying assumption of this methodology is that there is a linear line between  
51  
52 each utility value at each follow up. When analysing incremental QALYs between trial arms, it is  
53  
54 important to adjust for baseline differences in utility.[73] In addition to controlling for baseline  
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1  
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3 utility, it is important to account for the hierarchical nature the outcome data. The base-case  
4  
5 analysis of effectiveness will therefore use methods that incorporate a random-effects regression  
6  
7 model controlling for baseline health status and accounting for clustering. EQ-5D-5L tariffs for each  
8  
9 participating country, where available, will be used to allow for country-specific economic analyses.  
10  
11 The cost-effectiveness of the intervention over the duration of the trial will be examined, and  
12  
13 decision uncertainty assessed using probabilistic sensitivity analysis and scenario analysis.  
14

## 15 16 17 **Data management**

### 18 19 **Online data collection**

20  
21 All measures apart from DAWBA will be completed using HealthTracker™, which allows measures to  
22  
23 be completed remotely using developmentally appropriate interfaces and subjects to skip modules if  
24  
25 they do not score on screening questions for that module, thereby reducing the burden to  
26  
27 participants. Each questionnaire has been optimised for the screen, based on feedback from service  
28  
29 users and providers. HealthTracker™ automatically generates random participant (service user,  
30  
31 parent, and clinician) ID numbers and passwords when the participant is entered onto the system.  
32  
33 HealthTracker™ will store participant's month and year of birth. All other data will be anonymised.  
34  
35

36  
37 The DAWBA will be completed using the website <http://dawba.net> and anonymised scores  
38  
39 (identified and linked using the unique DAWBA ID) transferred to a centrally held secure database  
40  
41 that has been developed at Warwick Medical School to store information that is not collected by  
42  
43 HealthTracker™. This will include participant name, unique study ID, HealthTracker™ and DAWBA  
44  
45 IDs, contact details, information linking participants (for example, young person to CAMHS clinician)  
46  
47 and service level information. This database will be maintained locally at sites with access password  
48  
49 controlled and strictly limited to MILESTONE personnel to ensure confidentiality. No personally  
50  
51 identifiable information relating to participants will leave the local site. Only the unique identifiers,  
52  
53 linking information (using identifiers) and service level data will be shared with Warwick Medical  
54  
55 School.  
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Paper-copies of measures are only used as a last resort, or if preferred by the participant. All MILESTONE personnel will receive training on the HealthTracker™ platform and other systems for data collection prior to the study beginning.

#### Data transfer

All transfers of study data will be informed by and comply with the European Parliament and the Council of Europe's Directive 95/46/EC on protection of individuals with reference to the handling of personal data and on the free flow of such information between EU countries.

To ensure the security and integrity of data during such transfer an appropriate documented standard procedure will be established and followed without exception. Any study data that is to be transferred between research sites will be anonymised prior to transfer.

#### Data Storage

All essential documentation and trial records will be stored by Warwick Medical School and participating local sites in conformance with the applicable regulatory requirements with access to stored information restricted to authorised personnel.

#### Data access and quality assurance

In all partner countries, local research ethics committee requirements and national and EU law will underpin the collection, recording, sharing and secure storage of person identifiable data.

Personal information about potential and enrolled participants will be collected, shared, and maintained in a manner, which protects their confidentiality before, during and after the trial. All researchers working on the MILESTONE Study will be experienced in undertaking research in a way that maintains the privacy and confidentiality of study participants but which balances these demands against the needs to ensure that participants are not at risk. Names or addresses of participants will not be disclosed to anyone other than the staff involved in running the trial.

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3 Data will only be accessible by authorised personnel and made available to relevant bodies for audit  
4  
5 purposes only.  
6

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8 At the end of the MILESTONE project, analysis datasets will be made available following University of  
9  
10 Warwick's Research Data Management Policy which ensures that data produced through the  
11  
12 University's research activities is registered, stored, made accessible for use and reuse as  
13  
14 appropriate, managed over time and/or disposed of, according to legal, ethical, funder requirements  
15  
16 and good  
17  
18 practice. ([http://www2.warwick.ac.uk/services/rss/researchgovernance\\_ethics/research\\_code\\_of\\_practice/datacollection\\_retention/research\\_data\\_mgt\\_policy/](http://www2.warwick.ac.uk/services/rss/researchgovernance_ethics/research_code_of_practice/datacollection_retention/research_data_mgt_policy/))  
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#### 24 Archiving

25  
26 Data from this study will be retained intact in an appropriate format and storage facility for a  
27  
28 minimum of 10 years in the UK in line with the Medical Research Council's guidelines on Personal  
29  
30 Information in Medical Research; other countries will follow their relevant guidelines.  
31  
32 (<http://www.mrc.ac.uk/documents/pdf/personal-information-in-medical-research/>)  
33  
34

#### 35 Monitoring

36  
37 UK sites will be monitored by Warwick Medical School during the first few weeks after recruitment  
38  
39 of their first participant. Monitoring will include compliance to the protocol, quality of data  
40  
41 collection, storage of documentation and will require monitors to have access to relevant participant  
42  
43 notes/charts and trial documentation. Each overseas party will be responsible for monitoring their  
44  
45 sites according to local procedures.  
46  
47

#### 48 Adverse event management

49  
50 Adverse events as a direct consequence of the intervention are unlikely. At each study assessment,  
51  
52 participant will be asked whether any adverse events (bad or unfavourable medical occurrence)  
53  
54 have occurred since the last time point. This includes events from the first trial-related activity after  
55  
56 the participant has signed the consent form until the end point of the trial as defined in the protocol.  
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Any worsening of concomitant illness or new illness will be recorded as adverse events at each visit. If the event is classified as a Serious Adverse (SAE) event, an SAE form will be completed and the Principal Investigators (PIs) of each country will report all SAEs immediately to the trial coordinating centre at Warwick Medical School. The trial CI will determine whether SAEs require reporting to the trial sponsor or SCEAB.

## ETHICS AND DISSEMINATION

### Ethics and R&D governance

The study has been approved by the National Research Ethics Service in the UK (West Midlands: South Birmingham Research Ethics committee, Ref. no. 15/WM/0052) and by research ethics committees of all partaking countries. Regional and site-specific approvals have been obtained from NHS Research and Development offices in the UK and from other similar bodies in the other countries. The study is registered with the ISRCTN trial registry (ISRCTN83240263) (<http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21&page=1&pageSize=10&searchType=basic-search>) and ClinicalTrials.com (ADD REGISTRATION NUMBER).

The ethical conduct of the study will be monitored throughout by the MILESTONE Ethics work package.

### Service users

We are involving a potentially vulnerable population in research: adolescent mental health service users who, in the main, will be over the age of 16, but in areas where the transition boundary is 16 years they will be under the age of legal consent (i.e. 15 years old). In some countries the age of legal consent is 18.

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. The researchers in this study acknowledge these concerns and risks but also recognise the

1  
2  
3 importance of including individuals with enduring mental health difficulties in the study to better  
4 inform practice. The Council of Europe strongly promotes the participation of children in decisions  
5 affecting them. Young people will also have rights as service users, to expect appropriate and good  
6 quality services.  
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10  
11 The participant information sheets and consent/assent forms will make explicit the voluntary nature  
12 of young people's involvement. Even if the parent/carer gives consent but a young person refuses,  
13 that young person will not be included in the study. The young person's consent will be sought  
14 before follow-up assessments (verbal consent for telephone interviews), consent being implicit  
15 when they log on to give responses online. The forms will also seek permission to delay data  
16 collection until a later point should a young person become unwell or due to some other pressing  
17 circumstances, as long as transition doesn't take place in the meantime, and to liaise with a young  
18 person's clinician and parent/carer should such a delay be deemed necessary. The forms will explain  
19 the various safeguards in place, namely to liaise with a young person's clinician and/or family if  
20 required and the resulting impact on confidentiality.  
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34 In order to minimise any distress to young people taking part in face-to-face interviews, wherever  
35 possible these will be organised in venues that are known to the young person and will be scheduled  
36 at times when there will be familiar staff or family members or carers on hand to offer support  
37 should a young person become upset during any data collection processes.  
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44 In the event that during an interview or other data collection session, a MILESTONE researcher  
45 identifies any situation where a young person is thought to be at risk of abuse or neglect, or that  
46 young person discloses information that raises concern about the young person's safety, then a  
47 detailed risk management plan will be followed, which stipulates that the child protection policies  
48 and procedures applicable to that country will be adhered to. This is likely to involve close liaison by  
49 the researcher and the MILESTONE lead for that study site, with the young person's clinician and/or  
50 the nominated child protection leads within the mental health service attended by the young  
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3 person. Also, young people consenting to the study will be asked to nominate, and provide contact  
4  
5 details for, a health/care professional (for example, GP or CAMHS clinician) who we may contact  
6  
7 should any adverse event arise. This safeguard will be made explicit in the study information leaflets,  
8  
9 and at all data collection time points, so young people are aware of the impact on confidentiality  
10  
11 during the process of data collection.  
12

### 13 14 **Training**

15 All research assistants have participated in training sessions addressing Good Clinical Practice (GCP),  
16  
17 transition practices, rating procedures, compliance, TRAM feedback, and communication with young  
18  
19 people, families and clinicians. The study has been presented to all participating CAMHS teams and  
20  
21 additional meetings have been held to implement the specific transition procedures in the  
22  
23 intervention clusters.  
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### 27 28 **Dissemination**

29 The MILESTONE project has a work package that focuses on dissemination. Partnerships and  
30  
31 networks with target bodies will be strategically developed to support both short- and long-term  
32  
33 dissemination of the MILESTONE study and other project findings. External dissemination will target  
34  
35 the scientific community, but also the general public, lay and patients' associations, health care  
36  
37 authorities and care givers, scientific societies and professional boards, students, policy makers, and  
38  
39 the pharmaceutical industry. Particular attention will be paid to the information needs of the various  
40  
41 target audiences, and that they are addressed in the appropriate language and format.  
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45 The results of the MILESTONE study will be made available in the first instance to the clinicians of  
46  
47 CAMHS and AMHS partaking in the study, and then to the scientific community at large via  
48  
49 publications in scientific journals, presentations at meetings, the MILESTONE web site  
50  
51 (<http://milestone-transitionstudy.eu>), press releases, and leaflets.  
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## CONCLUSION

The continuity of adolescent psychopathology into adulthood means that transition to AMHS is necessary for many. However, there are real gaps in mental health care provision at this crucial stage, and those who experience transition frequently describe it as disruptive. The MILESTONE study is the first ever methodologically robust trial to test whether a decision support and assessment tool, the TRAM, can improve the mental health and social outcomes and functioning of transition age young people receiving CAMHS care. Young people in eight European countries are partaking in the trial; their longitudinal course of mental health, social and adult functioning outcomes are also evaluated as part of a longitudinal cohort study. The MILESTONE study has crucial input from young advisors, some with experience of transition in mental health services.

## MILESTONE CONSORTIUM – MEMBERS AND PARTNER INSTITUTIONS

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1  
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7

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## 28 **AUTHORS' CONTRIBUTIONS**

29  
30 SPS is the chief investigator who conceived the original study design and obtained funding, together  
31 with AM, GdG, PS, JM, FM, DPO, ST, US, TF, CS, MP, DW, FV, and GD. HT is the study coordinator  
32 who prepared the first draft of the protocol and this manuscript, and is joint first author with SPS.  
33 JW and AC contributed to the manuscript. JW is the senior trial statistician who led the calculation of  
34 the sample size; JG will undertake the statistical analysis under her direction. JM designed the health  
35 economic component and AC will undertake the health economics analysis under his direction. CD is  
36 the quality assurance manager. PT, SG, GS, LA, FR, SA, LOH, and ND are research assistants and  
37 helped set up the study in their countries and gain local ethical approvals. The UK young advisors,  
38 AT, AW, CG, and LW, reviewed the proposed study scales (including the likely time required for  
39 completion, to assess for possible burden on study participants), participated in the design of the  
40 intervention leaflet and reviewed all study information material before submission to ethics. All  
41 authors critically reviewed the protocol and the manuscript, and gave approval for the publication.  
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## COMPETING INTERESTS

Paramala Santosh is the director and shareholder of HealthTracker. Frank Verhulst publishes the Dutch translations of ASEBA from which he receives remuneration.

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**FIGURES**

Figure 1 MILESTONE study flow diagram

Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person

For peer review only

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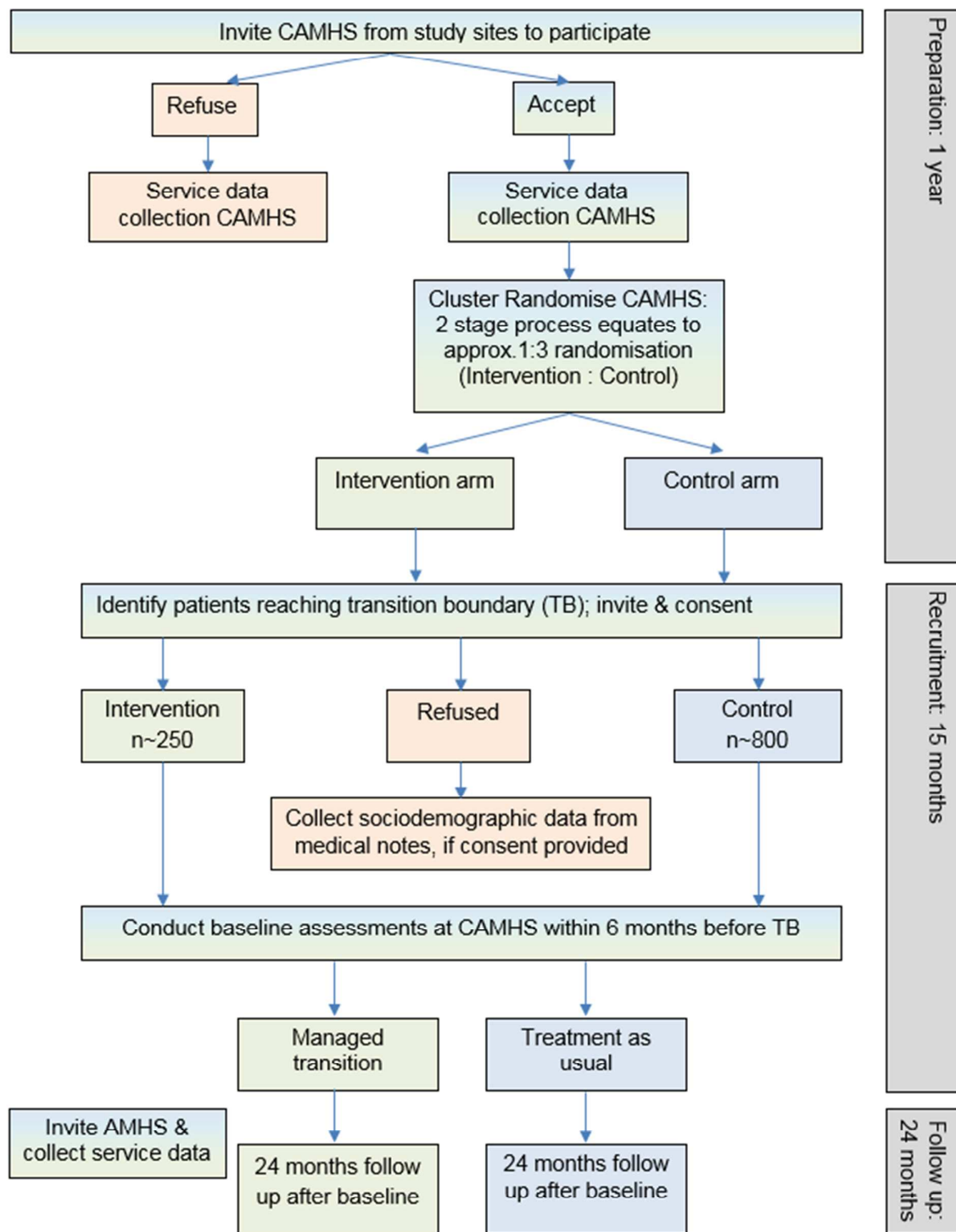


Figure 1 MILESTONE study flow diagram

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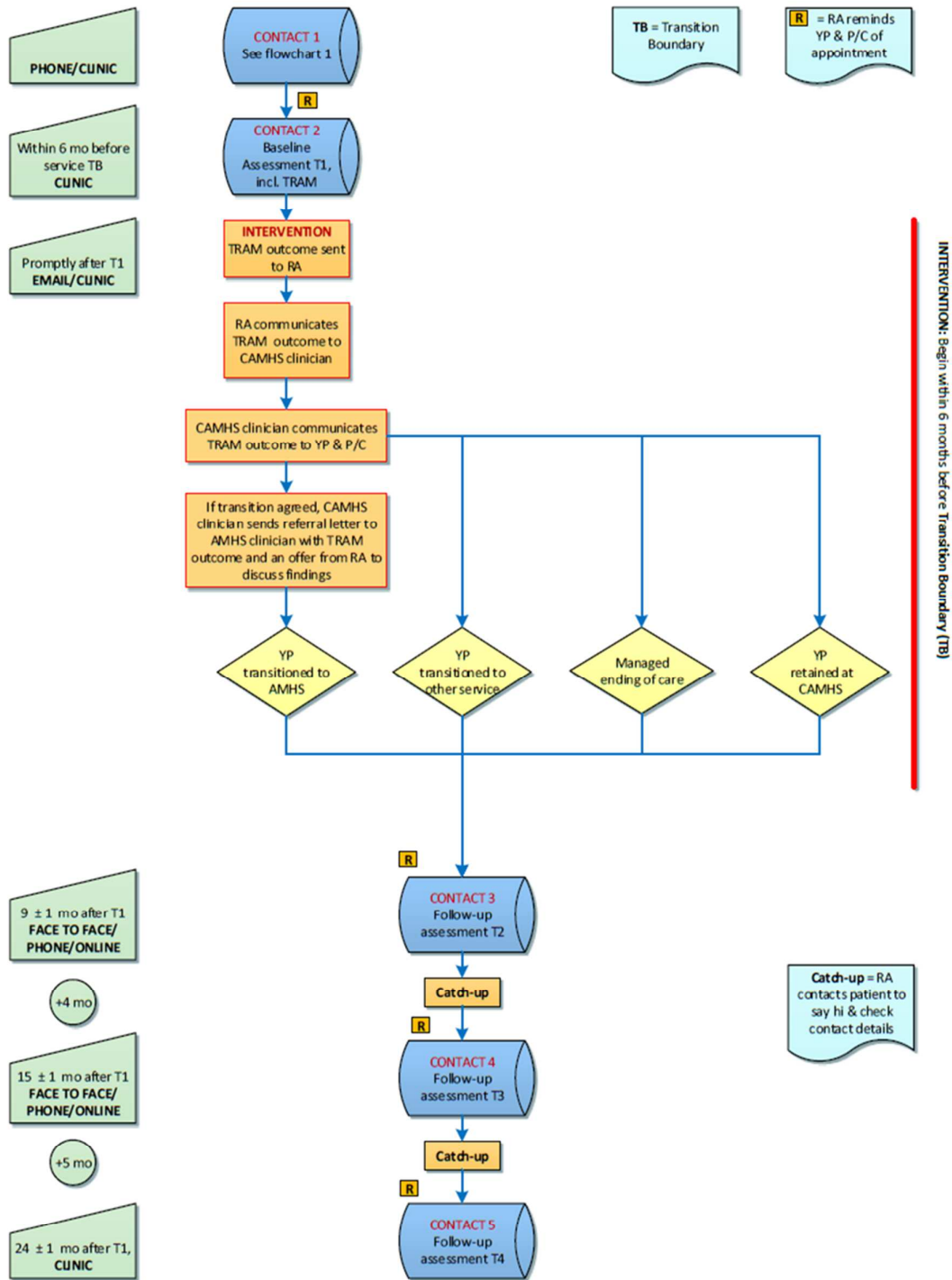


Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person



## CONSORT 2010 checklist of information to include when reporting a randomised trial\*

Section/Topic	Item No	Checklist item	Reported on page No
<b>Title and abstract</b>			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3
<b>Introduction</b>			
Background and objectives	2a	Scientific background and explanation of rationale	5 - 10
	2b	Specific objectives or hypotheses	10
<b>Methods</b>			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	11, 13
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a (protocol)
Participants	4a	Eligibility criteria for participants	14-16
	4b	Settings and locations where the data were collected	12-13
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	16-18
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	18-22
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a (protocol)
Sample size	7a	How sample size was determined	23-24
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
<b>Randomisation:</b>			
Sequence generation	8a	Method used to generate the random allocation sequence	13
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	13
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	n/a (cRCT)
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	13-15
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	13



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2		assessing outcomes) and how	
3			
4		11b If relevant, description of the similarity of interventions	n/a
5	Statistical methods	12a Statistical methods used to compare groups for primary and secondary outcomes	25-26
6		12b Methods for additional analyses, such as subgroup analyses and adjusted analyses	27-29
7			
8	<b>Results</b>		
9	Participant flow (a	13a For each group, the numbers of participants who were randomly assigned, received intended treatment, and	n/a (protocol)
10	diagram is strongly	were analysed for the primary outcome	
11	recommended)	13b For each group, losses and exclusions after randomisation, together with reasons	
12	Recruitment	14a Dates defining the periods of recruitment and follow-up	
13		14b Why the trial ended or was stopped	
14	Baseline data	15 A table showing baseline demographic and clinical characteristics for each group	
15	Numbers analysed	16 For each group, number of participants (denominator) included in each analysis and whether the analysis was	
16		by original assigned groups	
17	Outcomes and	17a For each primary and secondary outcome, results for each group, and the estimated effect size and its	
18	estimation	precision (such as 95% confidence interval)	
19		17b For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
20	Ancillary analyses	18 Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing	
21		pre-specified from exploratory	
22	Harms	19 All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
23			
24	<b>Discussion</b>		
25	Limitations	20 Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	n/a (protocol)
26	Generalisability	21 Generalisability (external validity, applicability) of the trial findings	
27	Interpretation	22 Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
28	<b>Other information</b>		
29	Registration	23 Registration number and name of trial registry	4
30	Protocol	24 Where the full trial protocol can be accessed, if available	
31	Funding	25 Sources of funding and other support (such as supply of drugs), role of funders	36

\*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see [www.consort-statement.org](http://www.consort-statement.org).

# BMJ Open

**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)**

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Keywords:	Child & adolescent psychiatry < PSYCHIATRY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

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**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)**

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## **WORDCOUNT**

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## KEYWORDS

Mental health, child and adolescent mental health services, transition, health services research, cluster randomised controlled trial, longitudinal cohort study, youth mental health, Europe

## ABSTRACT

**Introduction:** Disruption of care during transition from Child and Adolescent Mental Health (CAMHS) to Adult Mental Health Services (AMHS) may adversely affect the health and wellbeing of service users. The MILESTONE study aims to evaluate the longitudinal course and outcomes of adolescents approaching transition boundary (TB) of their CAMHS and to determine the effectiveness of the model of managed transition in improving outcomes, compared to usual care.

**Methods and analysis:** A cohort study with a nested cluster randomised controlled trial. Recruited CAMHS randomised to provide either i) managed transition underpinned by the Transition Readiness and Appropriateness Measure (TRAM) or ii) usual care for young people reaching the transition boundary. Participants are young people within one year of reaching the TB of their CAMHS in eight European countries; one parent/carer and a CAMHS clinician for each recruited young person; and adult mental health clinician or other community based care provider, if young person transitions. Primary outcome is Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA) measuring health and social functioning at 15 months post-intervention. Secondary outcomes include mental health, quality of life, transition experience, and health care usage assessed at 9, 15 and 24 months post-intervention. With a mean cluster size of 21, a total of 840 participants randomised 1:2 intervention to control is required. This provides 89% power to detect a difference in HoNOSCA score of 0.30 standard deviations. The addition of 210 recruits for the cohort study ensures sufficient power for studying predictors, resulting in 1050 participants and an approximate 1:3 randomisation.

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3 **Ethics and dissemination:** The study protocol was approved by the UK National Research Ethics  
4 Service (15/WM/0052) and equivalent ethics boards in participating countries. Results will be  
5 reported at conferences, in peer-reviewed publications, and to all relevant stakeholder groups.  
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10 **Trial registration numbers:** ISRCTN83240263; NCT03013595  
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## 12 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 13 • This is the first ever methodologically robust trial to test whether a decision support and  
14 assessment tool can improve the mental health and social outcomes and functioning of  
15 transition age young people receiving care at Child and Adolescent Mental Health Services.  
16
- 17 • A large, prospectively identified and robustly evaluated cohort of young people across  
18 several European countries with diverse health care systems is taking part in the study.  
19
- 20 • The cost-effectiveness of the intervention and research-related changes in health systems in  
21 terms of both expenditure and related health outcomes will be evaluated.  
22
- 23 • There is a strong Patient and Public Involvement (PPI) at all stages of the study.  
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- 25 • Due to the nature of the intervention it is not possible for clinicians or assessors to be blind  
26 to the allocation of clusters or of the service users within these clusters.  
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## INTRODUCTION

The MILESTONE (Managing the Link and Strengthening Transition from Child to Adult Mental Health Care) study focuses on the period when young people (YP) attending Child and Adolescent Mental Health Services (CAMHS) need to move on, or “transition” to, an adult mental health service (AMHS), if they still require ongoing care.

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.[1-4] The National Comorbidity Survey Replication in the USA found that 75% of people with a mental disorder have an age of onset younger than 24 years, 50% have an onset before 16.[1] However, only a small proportion of young people with mental health problems approaching adulthood, less than one in six, access services or receive appropriate care.[5 6]

There is international concern about young people who get ‘lost’ during their move from CAMHS to AMHS[7-15] and transition-related discontinuity of care is a major socioeconomic and societal challenge. In the UK, almost half of the service users reaching the transition boundary of their child and adolescent mental health service (CAMHS) do not go on to receive adult care.[7 16] The TRACK study found that less than 5% of patients undergoing CAMHS to AMHS transition experience continuity of care.[17] There is also a concern that despite recognition of ongoing mental health need, few young people are referred, with fewer than one third in one study.[18] 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



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3 adolescent and/or family resistance to transition.[19-21]. Furthermore, transition may differ widely  
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5 across different regions and countries due to lack of or different procedures.  
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8 Problems at the CAMHS-AMHS interface are accentuated by the fact that young people are  
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10 simultaneously negotiating developmental and situational transitions, such as changes in housing  
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12 and relationships and moving on to adult roles.[8 17] A lack of information about possible options,  
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14 planning that takes too long and where no one professional takes charge to ensure decisions are  
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16 acted upon, compound the problem.[22] Those who slip through the care net are likely to present to  
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18 adult services at a subsequent time, with more severe and enduring mental health problems.[23-25]  
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20 Disruption of care during transition adversely affects the health, wellbeing and potential of this  
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22 vulnerable group,[26-31] and negative transition experiences adversely impact the young person's  
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24 future engagement with mental health services.[32]  
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28 Intervening at the level of transition represents one of the most important ways we can facilitate not  
29  
30 only recovery but also mental health promotion and mental illness prevention in adulthood.  
31  
32 Ensuring sustained treatment through the transitional period is very likely to be cost-effective, since  
33  
34 the presence of mental illness during childhood leads to ten times higher costs during  
35  
36 adulthood.[33-35] However, there is currently no evidence for any effective model of appropriate  
37  
38 transitional mental health care or any interventions to reduce these individual and societal costs.[36]  
39  
40

#### 41 **Transitional care**

42  
43 Ideally, transition to adult mental health services should be a planned, orderly, purposeful and  
44  
45 patient-centred process that ensures continuity of care, optimises health, minimises adverse events  
46  
47 and ensures that the young person attains his/her maximum potential.[37-41] Good transitional care  
48  
49 starts with preparing a service user to leave the child-centred health care setting and ends when  
50  
51 that person is received in, and properly engaged with, the adult provider or an appropriate  
52  
53 alternative, or is discharged from care in a planned and managed fashion.[42 43].  
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3 European research on transition from CAMHS to AMHS is sparse, with little information available on  
4 the quality of transition and transition experiences in different EU countries in relation to long term  
5 mental health outcomes. The organisation of CAMHS in the member states vary, including the age at  
6 which young people are transitioned to adult services, size and complexity, sources of funding, and  
7 service provision and care. There is some evidence though that transition is a problem across all EU  
8 states.[44-46]  
9

10  
11 Barriers to good transition have been mapped,[16 17] but the evidence of interventions for  
12 improving transitional care is scant. A recent systematic review of CAMHS to AMHS transition  
13 identified only three initiatives, all in the USA,[20] including a case management model, a transition  
14 support model and an outpatient transition programme. Although all three programmes showed  
15 improved clinical and social outcomes for those with facilitated transition, none of these was a  
16 randomised trial and each model was deeply rooted within its own particular and specific healthcare  
17 context. There is no consensus as to who can be discharged on reaching the CAMHS transitional  
18 boundary, who should receive transitional care, and how this care should be delivered. Furthermore,  
19 it is not clear what outcomes should be measured to assess clinical and cost effectiveness of the  
20 model, what the outcomes of those who fall through the care gap are, and what the individual,  
21 organisational and societal costs of poor, inadequate or inappropriate transition are. A recent NICE  
22 review on transition from child to adult care across all specialities found that there was no robust  
23 evidence on models of transitional care.[36]  
24  
25

26  
27 In the absence of a planned, purposeful and needs-based assessment of those who reach the  
28 boundary, clinical judgment on transition can be influenced by misperceptions of other services,  
29 time and resource constraints, poor communication between CAMHS-AMHS, and poor adherence to  
30 existing policies.[19] Research has confirmed several information gathering biases in unstructured  
31 clinical judgements such as diagnostic biases, confirmation biases, ignoring conflicting information,  
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3 and assumptions based on patient and service background.[47] A recent study found that feeding  
4  
5 back structured assessment results to clinicians is leading to improved clinical decision making.[47]  
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8 Ideally all young people who reach a transition boundary would be assessed in a structured and  
9  
10 standardised way to determine ongoing need for care. Those who need such care would make a  
11  
12 transition to adult services in a planned and managed manner ensuring continuity of care across all  
13  
14 domains. Those without ongoing need would be appropriately discharged. Despite the intuitive  
15  
16 simplicity and clinical importance of such a structured decision process, a transition model  
17  
18 incorporating this approach with regard to mentally ill patients has not been evaluated or reported  
19  
20 in research or health practice literature, although its need has been articulated.[11 14]  
21  
22

### 23 **The MILESTONE project**

24  
25 The five year MILESTONE project (February 2014 to January 2019) aims to improve the  
26  
27 understanding of, and strengthen, CAMHS-AMHS transitional care across different healthcare  
28  
29 systems in the EU. In a series of work packages, it will 1) map current services and transitional  
30  
31 policies across the EU; 2) develop and validate transition-specific outcomes measures; 3) conduct a  
32  
33 longitudinal cohort study of transition process and outcomes across eight EU countries; 4) develop  
34  
35 and test, in a cluster-randomised trial, the clinical and cost-effectiveness of an innovative transitional  
36  
37 care model; 5) create clinical, organisational, policy and ethics guidelines for improving care and  
38  
39 outcomes for transition age youth; and 6) develop and implement training packages for clinicians  
40  
41 across the EU. This paper presents the protocol (v2.2) for the work packages dealing with the  
42  
43 longitudinal cohort study, the cluster randomised controlled trial and the economic evaluation of the  
44  
45 trial, which combined constitute the MILESTONE study.  
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### 49 **MILESTONE model of managed transition**

50  
51 The model of transitional care we have developed consists of an evidence-based decision-making  
52  
53 process and managed transition, incorporating key principles of continuity of care: adequate  
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55 information transfer, appropriate joint working, therapeutic and relational continuity, and  
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3 engagement with adult services.[48 49] The model of managed transition can be seen as one of the  
4  
5 cornerstones of a planned and purposeful transition process and can lead to more effective joint  
6  
7 working between services. It addresses the need to involve young people and parent/carers in the  
8  
9 planning process, tailor transition support to individual needs, identify barriers to smooth transition  
10  
11 and act on these, plan transition in a timely fashion, produce a succinct medical summary of the  
12  
13 service user, and improve information transfer and communication with adult providers.[36] The  
14  
15 model includes:  
16  
17

- 18  
19 1. The establishment and/or confirmation of shared understanding of criteria for good quality  
20  
21 transitional care at the CAMHS-AMHS interface, and managed ending of care, taking into  
22  
23 account clinicians' prior knowledge of good quality transition.  
24
- 25  
26 2. Systematic identification of all young people under CAMHS care who reach the transition  
27  
28 boundary for their service.  
29
- 30  
31 3. Structured and standardised assessment of their mental health and social care needs using a  
32  
33 bespoke Transition Readiness and Appropriateness Measure (TRAM), completed by the  
34  
35 young person, their parent/carer if available and CAMHS clinician prior to, ideally six months  
36  
37 before, the transition boundary.  
38
- 39  
40 4. Feedback of TRAM results from all parties in a short, clearly presented report to relevant  
41  
42 clinicians in CAMHS, allowing clinicians to identify areas in which attention should be  
43  
44 focused to ease a young person's path to transition.  
45
- 46  
47 5. Using the findings from the TRAM report to focus communication with service users and  
48  
49 carers on issues surrounding end of care at CAMHS and potential transition to AMHS or  
50  
51 other community based service.  
52
- 53  
54 6. Incorporation of critical information by clinician to young person's care or transition plan,  
55  
56 and designing goals for critical items that are achievable.  
57
- 58  
59 7. Sending the TRAM findings, along with a referral letter, to the new adult service, if a referral  
60  
to AMHS is made.

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3 8. Structured and regular follow-up of all young people using Transition Outcome Measure  
4 (TROM) to assess whether those who needed care were appropriately engaged with adult  
5 services and those who had been discharged or referred to other services have no unmet  
6 needs following cessation of care.  
7  
8  
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### 10 11 **Transition Readiness and Appropriateness Measure (TRAM) and the Transition** 12 **Related Outcome Measure (TROM)** 13

14  
15 The Transition Readiness and Appropriateness Measure (TRAM), a decision support and assessment  
16 tool, uses the HealthTracker™ platform. The measure, together with the linked findings report, have  
17 been designed to help the clinician identify a) high-risk, high-need cases for whom transition to  
18 AMHS is advisable and appropriate; b) those who can be appropriately discharged in a planned  
19 manner from CAMHS to a General Practitioner (GP); or c) transitioned to another community based  
20 service (such as social services, voluntary sector or other non-statutory agencies). Obviously, the  
21 clinicians will need to take their local service provision into account when making the decisions. The  
22 Transition Related Outcome Measure (TROM) provides information on outcomes post-transition,  
23 and on the transition process and experience.  
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36 The TRAM and TROM were developed using existing literature, expert input and focus groups on  
37 developing and validating Patient Reported Outcome Measures (PROMS);[50 51] MILESTONE's  
38 group of young advisors also reviewed the scales and helped identify areas of duplication or unclear  
39 terms. These scales have been translated into Croatian, Dutch, Flemish, French, German, and Italian  
40 languages and provide a summary of all factors necessary to consider (including symptoms,  
41 functioning, risk and need for care) when making a transition decision and when assessing the  
42 outcomes of a transition. There are versions for young people pre-transition, young people post-  
43 transition, parents/carers and clinicians at CAMHS and AMHS which can be completed online, via the  
44 HealthTracker™ platform (<https://www.healthtracker.co.uk/index.php/our-platform/>), a web-based  
45 portal allowing measures to be completed remotely, which has been used in other EU FP7 projects  
46 [52].  
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3 TRAM and TROM contain 20 questions common to both scales for all participants; further eight  
4  
5 questions are relevant only to the clinician versions and nine only to the young person and  
6  
7 parent/carer. All participant versions of TRAM contain 15 additional questions that are not in TROM,  
8  
9 yet to allow comparison of results over time, most of the domains present in TRAM are also present  
10  
11 in TROM, with versions for AMHS and CAMHS clinicians and different follow-up time points.  
12

13  
14 The construct validity, content validity, inter-rater validity, test-retest validity, and sensitivity to  
15  
16 change of TRAM and TROM were assessed in a sub-study between June 2015 and April 2016.  
17

18  
19 The “TRAM score summary report” presents the scores from the young person, parent/carer and  
20  
21 clinician for each item, with graphs visualising differences or similarities in scoring. The report  
22  
23 contains items that are relevant to the clinician’s transition decision (symptoms, risk factors and  
24  
25 disruption experienced by the young person) and those that can facilitate a smooth transition. It  
26  
27 displays all information in a user-friendly, relevant and accessible format, helping identify young  
28  
29 people requiring further care and allowing key facts to be easily transferred to care plans and  
30  
31 referrals. It should complement a much more comprehensive evaluation, with the ultimate decision  
32  
33 about transition being the outcome of a process involving key stakeholders.  
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36  
37 HealthTracker Ltd will optimize the TRAM on the HealthTracker™ platform based on decision  
38  
39 making algorithms derived from the study. If appropriately funded, this will be made available to  
40  
41 serve as the platform for optimization of transitions to adult mental health in the EU.  
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#### 44 45 **AIMS AND OBJECTIVES**

46  
47 The overall aim of the nested cRCT is to determine the effectiveness and cost-effectiveness of the  
48  
49 model of managed transition in improving the health and social outcomes of young people, and their  
50  
51 transition to adult roles, as compared to treatment as usual, in eight participating EU countries. The  
52  
53 specific objectives are  
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- 3 1. To test the hypothesis that the implementation of the model of managed transition in
- 4 CAMHS at the transition boundary improves the mental health and social outcomes of young
- 5 people and their transition to adult roles when they move on from CAMHS, as compared to
- 6 usual care.
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- 12 2. To conduct an economic evaluation of the model of managed transition compared with
- 13 usual care.
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- 17 3. To explore the views and experiences of health professionals and young people concerning
- 18 the intervention.
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22 The prospective cohort study will delineate the transition journey of a large number of young people  
23 across eight EU countries. The aims are

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- 27 4. To evaluate the mental health, quality of life, and functioning of young people who attend
- 28 CAMHS and reach the CAMHS/AMHS transition boundary;
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- 32 5. To evaluate the longitudinal course of mental health, social and adult functioning outcomes
- 33 of young people who reach the CAMHS/AMHS transition boundary and transition into young
- 34 adulthood;
- 35
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- 37 6. To compare the outcomes in those young people who transition with those who do not
- 38 transition to AMHS (i.e. remain in CAMHS, are discharged or referred to other care).
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## 45 **METHODS AND ANALYSIS**

### 46 **Study design and management**

47 A large cohort of young people approaching the CAMHS-AMHS transition boundary in eight EU  
48 countries will be recruited and a nested cluster randomised controlled trial (cRCT) in a randomly  
49 selected subset of clusters (CAMHS services) will be implemented. The study design is a modification  
50 of the Cohort Multiple Randomised Controlled Trial,[53] by virtue of allocation to the intervention by  
51 cluster randomisation, with each distinct CAMHS comprising a cluster. The control arm clusters from  
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3 the cRCT together with additional excess clusters form the longitudinal cohort study, with a follow-  
4 up period of 24 months. The cRCT is a superiority trial; the aim is to show that managed transition is  
5 superior to usual care in improving patient reported outcomes. Usual care varies by CAMHS and may  
6 or may not include transitioning planning. The primary outcome endpoint is 15 months. The study  
7 flow diagram is presented in Figure 1. All arms of the study undergo the same data collection. The  
8 trial has economic and qualitative components, addressing objectives 2 and 3, respectively. Detailed  
9 Statistical Analysis Plans have been developed for both the cRCT and longitudinal cohort study. Final  
10 versions will be signed off prior to commencement of the analysis and made available on the study  
11 website.

### 22 23 **Figure 1 MILESTONE study flow diagram**

24  
25  
26 The study is sponsored by the University of Warwick and co-ordinated from the research office in  
27 the Mental Health and Wellbeing unit, Warwick Medical School, with Quality Assurance and  
28 Statistics from Warwick Clinical Trials Unit. The Study Coordinator is responsible for the day-to-day  
29 coordination and the Chief Investigator (CI) for clinical aspects. The study is managed by a trial  
30 management group (TMG), including work package leaders (i.e. country leads), and supported by  
31 MILESTONE research staff. The TMG speaks monthly by telephone conference chaired by the CI. The  
32 study conduct and progress is overseen by the independent MILESTONE Scientific, Clinical and  
33 Ethical Advisory Board (SCEAB) comprising five international experts and four Patient and Public  
34 Involvement representatives. The SCEAB members are invited to the annual general meetings in  
35 order to monitor the progress of work, to assess the scientific quality and to give feed-back to the  
36 Consortium members, but without a right to vote. The SCEAB will also review the main governance  
37 and any ethical issues which might require greater attention.

38  
39  
40 MILESTONE has strong Patient and Public Involvement (PPI) embedded throughout the project;  
41 young advisors, some with experience of transition in mental health services provided feedback on  
42 the protocol and study documents. Their ongoing role includes: attending and contributing to



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2  
3 project steering committee meetings, designing the intervention leaflet and other promotional  
4 materials, and advising on recruitment and the engagement of young people. The first five PPI  
5 representatives have been from the UK; in the third year service users from other participating  
6 countries will be involved.  
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### 10 11 **Setting and site selection**

12 The study is currently running in Belgium, Croatia, France, Germany, Italy, the Netherlands, Republic  
13 of Ireland, and the United Kingdom. Recruitment of participants is underway in 52 CAMHS clusters  
14 that fit the inclusion criteria below (October 2015 – December 2016, with last inclusions in January  
15 2017). Face-to-face meetings with clinical and managerial leads were arranged at those sites that  
16 expressed an interest and the study explained in detail. Signed site agreements or equivalent were  
17 obtained from participating sites prior to the start of the study. The majority of sites received no  
18 funding from the EU grant (no 602442) for taking part in the study. However, two German recruiting  
19 sites received payments under subcontract to facilitate recruitment.  
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32 In most countries, other than the UK, there is no umbrella organisation to facilitate collaboration  
33 between AMHS and CAMHS. Furthermore, a single CAMHS may be linked with numerous AMHS  
34 (inpatient services, clinics, teams and individuals), making it difficult for AMHS clinicians to be  
35 engaged from the start, particularly given our limited resources. Also, we were not able to predict  
36 which AMHS would be involved, as this is dependent on transition decisions.  
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### 44 **Cluster level eligibility criteria**

45 For a CAMHS to be eligible, it had to be a service delivering medical and psycho-social interventions  
46 for children and adolescents with mental health problems and disorders, and/or  
47 neuropsychiatric/developmental disorders (e.g. emotional/neurotic disorders; eating disorders;  
48 hyperkinetic disorder/ADHD; autism spectrum disorders); community-based, or provide outpatient  
49 or inpatient care; publicly or privately funded; must have a formal upper *age limit* (the transition  
50 boundary) for providing care to young people and; be responsible for transfer of care to an adult  
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3 service for those who reach the transition boundary. Forensic services and highly specialised  
4 national services, which cater for rare/unusual disorders and/or serve a national population, such as  
5 specialist clinics for rare metabolic disorders or long-term residential care for severe autism were  
6 excluded. Eligible services could vary in size and complexity, ranging from single psychiatrists or  
7 psychologists (e.g. Germany) or circumscribed teams to services with multiple teams and localities  
8 offering multidisciplinary care (e.g. UK).  
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#### 16 Baseline service level data collection

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18 Baseline service data was collected from the CAMHS manager or leading CAMHS clinician at all  
19 recruited CAMHS in the year preceding recruitment of study participants. The questionnaire  
20 covered: 1) Size (number of staff), structure and function of CAMHS; 2) Transition boundary of the  
21 service (i.e. age at expected transition); 3) The number and type of adult mental health services  
22 (AMHS) that operate within the CAMHS catchment area; 4) Current transition policy and practice; 5)  
23 Size of the catchment population. This information was used to establish the organisational  
24 structure of CAMHS and identify potential cross-over and/or movement of staff between teams or  
25 units so that distinct units (clusters) could be identified. If one or more CAMHS teams share the  
26 same core clinicians, then these were classified as one cluster, becoming the unit of allocation.  
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39 The data revealed that the CAMHS-AMHS transition boundary for most countries was 18 years, i.e.  
40 the age of majority. In the UK, Belgium and France there was more variation, the boundary ranging  
41 from 15 to 18 years. We also discovered that some services in Belgium, France, the Netherlands and  
42 Germany adopt a more flexible approach to the boundary, and in these situations we agreed a  
43 nominal boundary (18 years), which reflects the age at which transitions most commonly occur and,  
44 in most instances, is also the official TB.  
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52 Upon leaving CAMHS care, young people may be referred on to AMHS or another community based  
53 service (e.g. social services, voluntary sector or other non-statutory agencies offering support and  
54 therapeutic interventions for mental health needs), or discharged back to their GP. AMHS and  
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3 community based services will be invited to participate in the study, and service level data will be  
4  
5 collected once they are recruited.  
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### 8 **Randomisation**

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10 As several countries only had three CAMHS clusters, this fixed the randomisation ratio at 1:2 and the  
11  
12 randomisation was conducted in a two stage process: First, randomly selected triplets of clusters  
13  
14 within each country were identified for inclusion in the cRCT. These three clusters were further  
15  
16 randomised in a 1:2 ratio between intervention and control arms. The excess clusters (those not  
17  
18 selected during the first stage for the cRCT) were used for the cohort study only to enhance  
19  
20 numbers. Overall, this two-stage process equates approximately to a randomisation ratio of 1:3. All  
21  
22 randomisation was conducted by the trial statistician using the statistical software Stata 14.[54]  
23

24  
25 The CAMHS were informed of their allocation after randomisation. The study personnel were also  
26  
27 aware of the allocation as they are involved in delivering the intervention and assessing outcomes.  
28

29  
30 The young people and their parents/carers, who are recruited after randomisation, are informed of  
31  
32 their allocation after they have consented to the study, yet only if they ask about this specifically  
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34 [55].  
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36

### 37 **Participant eligibility and recruitment**

#### 38 **Young people**

39  
40 Individual recruitment targets were set for each CAMHS (cluster), based on local capacity, but with  
41  
42 the constraint that in the cRCT there should be on average 21 participants per cluster. Databases of  
43  
44 all participating CAMHS are scrutinised by CAMHS personnel to identify all young people  
45  
46 approaching the service's transition boundary and meeting the inclusion criteria over a 15 month  
47  
48 recruitment period (between October 2015 and December 2016).  
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51  
52 Young people are eligible, if a) their age is within one year of reaching the transition boundary of  
53  
54 their CAMHS during the trial recruitment period and, in exceptional cases, not more than 3 months  
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56 older than the transition boundary, if a decision about transition has not yet been made; b) they  
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3 have a mental disorder defined by DSM-IV-TR, DSM-5 or ICD 10/11, or they are under the regular  
4 care of CAMHS (attended at least one appointment, if not yet diagnosed); c) they have an IQ  $\geq$  70 as  
5 ascertained by previous standardised assessment or diagnosed by clinician, or no indication of  
6 intellectual impairment; and d) they provide valid written informed consent, or assent, if below the  
7 legal age of consent (in England this age is 16, in all other participating countries 18). They are  
8 ineligible if they a) are younger than a year before the transition boundary of their CAMHS; b) have a  
9 more severe intellectual impairment (IQ < 70) as ascertained by previous standardised assessment  
10 or diagnosed by clinician – if no data on intellectual functioning are available (because it has never  
11 been assessed) then care coordinators are asked to make a clinical judgement on intellectual  
12 impairment before baseline assessment takes place; c) are not able to (or expected not to be able  
13 to) complete the questionnaires due to severe physical disabilities or language problems, even with  
14 assistance from family members or a research assistant; d) are service users in a secure forensic  
15 institution; or e) don't provide valid written informed consent, or assent, if below the legal age of  
16 consent.

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34 At each site, the clinicians of eligible young people advise the research team of the ability/capacity  
35 of the young person to give informed, voluntary consent or assent. Young people are introduced to  
36 the study (as appropriate, taking local ethical/legal conditions and best practice into consideration)  
37 either by a) a clinician or care coordinator, who provide a study leaflet and/or briefing sheet and  
38 seek consent for the individual to be contacted by a MILESTONE research assistant using a signed  
39 contact form; b) a letter signed by their care coordinator or clinician outlining the purpose of the  
40 study followed by a phone call by a CAMHS personnel if no response is received; or c) posters and/or  
41 leaflets displayed in the participating CAMHS sites, with contact details of the research team.

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52 All young people who agree to be approached by a MILESTONE researcher are individually contacted  
53 and provided with further information about the study; interested individuals are asked to sign a  
54 study consent form. Young people who are below the legal age of consent are asked for their assent  
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3 and signed consent is obtained from a parent/carer (or, in some countries, parents/carers, according  
4  
5 to national medical ethics requirements).  
6  
7

8 A compensatory inclusion process has been factored in; if one country is unable to meet its  
9  
10 recruitment target, another country is allowed to over-recruit.  
11  
12

### 13 14 15 16 Parents/carers

17  
18 The information provided to young people include separate information and consent forms for their  
19  
20 parents/carers. After signing up to the study, the young person is asked to name his/her primary  
21  
22 care giver whom s/he would like to be involved. For young people under the legal age of consent,  
23  
24 the parent/carer has to be the legal guardian of the young person. The aim is to engage the same  
25  
26 parent/carer throughout the whole study period. If the latter is not possible, then the aim is to  
27  
28 involve another parent/carer. If the young person doesn't live with his/her biological parent/s, then  
29  
30 his/her carer is involved. A carer may be the legal guardian or a partner or an older adult sibling, or  
31  
32 another individual living with and/or providing regular support to the young person.  
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36 The parent/carer is eligible if the young person consents to parent/carer participation and he/she  
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38 provides a valid written informed consent. A parent/carer is ineligible if he/she does not live with  
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40 and/or provide regular support to the young person, and/or is not able to (or expected not to be  
41  
42 able to) complete the questionnaires due to severe physical disabilities or language problems, even  
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44 with assistance from family members or research assistant.  
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48 Young people who do not wish their parent/carer to be approached to participate in the study have  
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50 their wishes respected, regardless of their own capacity to consent. If a parent/carer is unwilling to  
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52 participate, their wishes are respected.  
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### Clinicians/care providers

Clinicians/care providers are contacted and provided with separate information sheets and consent forms. They are eligible if they are responsible for the main care for the young person at CAMHS (and AMHS or other relevant service provider, if referral is made) and provide a valid written informed consent.

### Intervention

The CAMHS in the intervention arm receive information on good quality managed transition and feedback from the TRAM assessment in the form of a TRAM score summary report for each participating young person.

### Information provision at CAMHS

A special meeting is held between MILESTONE personnel and participating CAMHS in the intervention arm prior to service user recruitment to establish clinicians' existing knowledge and current practice of transition, and to discuss optimal transition, using TRAM as a decision support tool, and managed ending of care. Each meeting follows a prescribed structure. Additionally, written information on good quality transitional care is provided to all clinicians in the intervention arm CAMHS teams. This consists of presentation handouts and a leaflet on good quality transition designed by our young project advisors.

### Feedback of TRAM results

The aim is to conduct the TRAM assessment approximately six months prior to the transition boundary. The TRAM findings (TRAM score summary report) are fed back to clinicians soon after the young person, parent/carer and CAMHS clinician have completed the baseline assessments.

- 1) 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 is 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.

- 2) The CAMHS clinician is encouraged to communicate the TRAM findings to the young person and parent/carer, and incorporate critical information to young person's care or transition plan, and design goals for critical items that are achievable.
- 3) The CAMHS clinician decides whether or not to refer the young person to adult services.
- 4) If a referral is made, the CAMHS clinician is asked, if appropriate and with relevant permissions, to send the TRAM score summary report along with the referral letter to the new adult service.
- 5) The AMHS clinician or other care provider is offered a chance to discuss the TRAM findings with an appropriate member of the MILESTONE research team.

The aim of the TRAM score summary report is to support clinicians in their decision making regarding transition, communication with stakeholders and planning of the transition process. A flowchart of the study intervention is depicted in Figure 2.

**Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person**

## The control arm

Young people, parent/carers and clinicians in the control arm complete the same baseline assessments but the latter do not receive any additional training or feedback of TRAM scores, i.e. continue providing usual care, which may or may not include transition planning.

## Outcome measures

### Primary outcome measure

The primary outcome measure is the clinician-rated Health of the Nation Outcome Scale for Child and Adolescents (HoNOSCA),[56] which has 15 items scored on scale of 0-4, and covers the severity of the behaviour, impairments, symptoms and social functioning of children and young people with mental health problems. The clinical usefulness of the HoNOSCA has been validated and its sensitivity to change confirmed.[57 58]

Although the HoNOSCA is intended as a measure that is completed by a clinician who is also responsible for treatment of the client, the measure can also be completed by a mental health care professional not involved in the treatment using semi-structured interview.[59] In our study the measure is completed by a trained MILESTONE Research Assistant by interviewing the young person and taking into account all other available sources of information (parent/carer, relevant clinician and the medical records) to ensure accuracy of data.

To ensure consistency and comparability, HoNOSCA is used throughout (rather than switching to HoNOS at age 18 years). The primary outcome endpoint for the cRCT is 15 months.

### Secondary outcome measures

The secondary outcome measures are as indicated in Table 1. Apart from the TROM, two others were developed specifically for the MILESTONE study.



Table 1 Outcome measures

Study Instrument	Description
<b>Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA)[60]</b>	Used to assess the need for care based on a wide range of problems (behaviour, impairment, symptoms and social functioning).
<b>Transition Related Outcome Measure (TROM)<sup>1</sup></b>	Informs on quality of transition and changes in symptoms, risk factors and impairment due to transition. It has been developed based on the TRAM.
<b>World Health Organization Quality of Life Brief Inventory (WHOQOL-BREF)[61 62]</b>	Assesses quality of life, covering physical and psychological health, social relationships and current environment.
<b>MILESTONE specific Client Service Receipt Inventory (CSRI)[63]</b>	Focuses on the use of health and social services, and medication use.
<b>EuroQol health questionnaire (EQ-5D-5L)[64]</b>	Assesses health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).
<b>ASEBA: Youth Self Report (YSR)/Adult Self Report (ASR)/Child Behavior Checklist (CBCL)/Adult Behavior Checklist (ABCL)[65 66]</b>	Suite of measures assessing dimensions of emotional and behavioural problems.
<b>Ethics of Transitioning<sup>1</sup></b>	Assesses ethical challenges regarding the delivery of transitional care.
<b>Independent Behaviour During Consultation Scale (IBDCS)[67]</b>	Measures independent behaviour.
<b>Barriers to Care[68]</b>	Assesses practical (e.g. costs, time) and psychological barriers (e.g. fear to stigmatization) to care.
<b>Bullying – adapted from Retrospective Bullying and Friendship Interview Schedule[69 70]</b>	Assesses the experiences with bullying in different settings (e.g. school, at home, college).
<b>Life Events<sup>1</sup></b>	Assesses significant life events such as accidents, deaths in the family, separation of parents/carers, and parent/carer losing jobs.
<b>Brief Illness Perception Questionnaire (B-IPQ)[71 72]</b>	Assesses the cognitive and emotional representation of illness, including consequences. The term 'illness' has been replaced with the term 'condition'.
<b>On Your Own Feet: Transition Experience Scale (OYOF- TES)[73]</b>	Focuses on specific experiences with the transition process and has two versions: one for Young People who transition to AMHS (or other types of adult care) and one for Young People discharged from CAMHS.
<b>Specific Levels of Functioning Scale (SLOF)[74]</b>	Assesses adult functioning of the Young Person from the Parent/Carer's perspective.
<b>Clinical Global Impression Severity scale (CGI-S)[75]</b>	Assesses the severity of the patient's illness at the time of assessment, relative to the clinician's past experiences.

<sup>1</sup>Developed specifically for the MILESTONE study

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2  
3 The Ethics of Transitioning questionnaire was developed based on the themes raised by a systematic  
4 literature review and focus groups and addresses the following research question: "What are the  
5 ethical challenges of ensuring delivery of transitional care to those who need it most against the risk  
6 of pathologising transient and self-limiting distress and dysfunction, which may be normal during  
7 adolescence?". It contains seven items rated on a five-point Likert scale, with one version to be  
8 completed prior to, and another after, transitioning.  
9

10  
11 The Life Events questionnaire is a dichotomous 13-item scale that is appropriate for both young  
12 people and adults, and focuses on significant life events, such as accidents, deaths in the family, and  
13 separation of parents/carers.  
14

### 15 **Data collection**

16 Data collection is the same in the intervention, control and cohort arms of the study.  
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### 18 **Baseline data**

19 Table 2 highlights the number of contacts with the participants, the time points of the various  
20 assessments, and the type of data to be collected from the young person, parent/carer and clinician.  
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Table 2 Study assessments for participants (transition scenario)

Contact	1	2 (T1)	3 (T2)	4 (T3)	5 (T4)
<b>Contact Window</b> (No. months ± No. months)		<b>Within 6m before TB***</b>	<b>9m (± 1m) after T1</b>	<b>15m (± 1m) after T1</b>	<b>24m (± 1m) after T1</b>
Inclusion/exclusion criteria	YP P/C				
Informed consent	YP P/C	YP P/C C	(YP) (P/C) C	(YP) (P/C) (C)	(YP) (P/C) (C)
Contact details	YP P/C	YP P/C	YP P/C	YP P/C	YP P/C
Sociodemographic & personal information		YP P/C C	YP (C)	YP P/C (C)	YP P/C (C)
Need for Care (HoNOSCA – SR) (HoNOSCA – Clinician report)		YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)
Transition readiness / Transition outcome (TRAM/TROM)		YP P/C C	YP P/C C	YP P/C C	YP P/C C
Referral and Transition Status (CAMHS clinician only)			C	(C)	(C)
Quality of Life (WHOQOL-BREF)		YP		YP	YP
Cost-effectiveness (EQ-5D-5L)		YP	YP	YP	YP
Service use (CSRI)		YP	YP	YP	YP
Emotional/behavioural problems (YP: YSR/ASR P/C: CBCL/ABCL)		YP P/C	YP P/C	YP P/C	YP P/C
Ethics of transitioning		YP		YP	
Independent behaviour** (IBDCS)		YP	YP	YP	YP
Barriers to Care (BtC)**			YP	YP	YP
Bullying		YP			YP
Life events		YP	YP	YP	YP
Illness perception (B-IPQ)		YP			YP
Transition experience & readiness (OYOF-TES)*			YP P/C	(YP) (P/C)	(YP) (P/C)
Functioning & Impairment (SLOF)		P/C		P/C	P/C
Illness severity (CGIS)		C	(C)	(C)	(C)
Psychopathology (YP: DAWBA 5-17/18+ SR) P/C: DAWBA 5-17/18+ PR) C: Clinical diagnosis		YP P/C C	(C)	(C)	YP P/C (C)

TB = Transition boundary of service; YP = young person; P/C = parent/carer

C = clinician. T1: CAMHS clinician; if YP is transitioned after T1, then at T2-T4 the clinician is based at AMHS. If there is a delay in transitioning, the clinician at T2-T4 will still be based at CAMHS. Consent and sociodemographic data is sought from the clinician only once. (C) = if YP is a mental health service user, then clinician is asked for information.

RA = Research Assistant

SR = Self-report

PR = Parent-report

\* = completed only once at the first assessment after transition

\*\* = if the YP is a service user the IBDCS is administered, if the YP is not a current service user, the BtC is administered.

\*\*\* = in exceptional cases, the assessment can take place up to 12 months before or 3 months after the TB (e.g. if transitions regularly happen earlier in a service or a decision about transition hasn't yet been made).

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3 The baseline assessment (T1) is undertaken after consent/assent has been given but before the  
4 delivery of the intervention, within 6 months before the transition boundary of the service or, in  
5 exceptional cases, within 12 months before or 3 months after the boundary (e.g. if transitions  
6 regularly happen earlier in a service or a decision about transition hasn't yet been made). Young  
7 people and their parents/carers are assessed at the clinic, or at an alternative location suitable for  
8 the young person, with both semi-structured interview (sociodemographic and personal  
9 information, and HoNOSCA) and online assessment. The sociodemographic and personal  
10 information questionnaire for young people and parent/carers collects general information about  
11 the young person and family, and the care the young person receives. The questionnaire covers also  
12 medical history and additional variables previously shown to contribute to continuity of mental  
13 health problems (for example, history of mental health problems and alcohol or drug abuse by  
14 parents). The last online assessment of T1 is the structured sections of the Development and Well-  
15 being Assessment (DAWBA),<sup>[76 77]</sup> which obtains information on mental health. Information from  
16 the assessment with the young person and parent/carer will be combined with a computer  
17 algorithm that provides an estimate of the probability of a certain individual diagnosis. Information  
18 on clinical diagnosis is obtained from the clinician.

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38 The length of the baseline assessment (YP) is approximately 1.5 – 2 hours. The participant can take a  
39 short break in between the online measures, and if required, complete them over multiple sessions.  
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41  
42 The research assistant is available to assist if there are any difficulties. The baseline assessment (T1)  
43 should be completed before the end of the recruitment period.  
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#### 47 Follow-up data

48  
49 Outcomes are measured 9 months (T2), 15 months (T3) and 24 months (T4) after T1. The aim is to  
50 complete measures at T2 and T3 via telephone and online assessment, and at T4 via face-to-face  
51 contact with young people and their parents/carers, within a month ( $\pm$ ) of the calculated assessment  
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3 time point (Table 2). Assessments with CAMHS or AMHS clinicians (or other service provider), which  
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5 is dependent on transition status, follow the same schedule.  
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### 8 Evaluation of the intervention and experiences of young people regarding services

9  
10 The views and experiences of CAMHS clinicians in the intervention arm are captured using a semi-  
11  
12 structured questionnaire. All clinicians are approached and those willing to engage are interviewed  
13  
14 over the telephone or face-to-face.  
15  
16

17  
18 A sub-sample of young people taking part in the study will be invited to take part in focus groups at  
19  
20 T4 from three participating countries: Ireland, UK and Croatia. The purpose of the focus groups will  
21  
22 be to explore their experiences of leaving CAMHS, transition to AMHS if applicable, and views of  
23  
24 mental health services, the aim being to establish whether young people have better health,  
25  
26 educational and social outcomes, better quality of life and satisfaction with services if they: a) have  
27  
28 experienced a managed transition from child to adult services at the transitional boundary or b)  
29  
30 have experienced usual care (i.e. their transition to adult services, or their discharge from services, is  
31  
32 via the usual procedure of their CAMHS clinic). It is hoped that, as part of MILESTONE's patient and  
33  
34 public involvement activity, some of the young advisors, or other young people trained in facilitation  
35  
36 skills by some of the research sites, may co-facilitate these focus groups.  
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40 Three audio-recorded focus groups will be held in each country with 9-12 young people in each  
41  
42 group. Recruitment will be from the study participants with purposive sampling to include some  
43  
44 young people who a) did not transition to adult services, b) who transitioned to adult services via  
45  
46 usual care and c) who experienced managed transition.  
47  
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### 49 **Sample size**

50  
51 Assuming an average cluster size of 15 participants, an allocation ratio of 2:1 (control : intervention),  
52  
53 a coefficient of variation of cluster size of 0.4 (cluster sizes ranging from approximately 5 to 30), and  
54  
55 an intracluster correlation coefficient of 0.01, with 600 participants (195 intervention arm [13  
56  
57 clusters], 405 control arm [27 clusters]), the cRCT has 89% power to detect a difference of 0.30  
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standard deviations in the primary outcome measure (HoNOSCA). To allow for 30% dropout, the required average cluster size is 21 participants. Thus, for the cRCT the target sample size is 840 participants in total (273 intervention - 13 clusters of size 21; 567 control - 27 clusters of size 21). The randomisation was stratified by country, with the number and size of clusters dictated by local capacity. Excess clusters (those not required for the cRCT) were allocated to the control arm and will be used in the analysis of the cohort study only to enhance numbers for sufficient power to study predictors for the longitudinal course and outcome of mental health during transition. There are 10 such excess clusters (average size 21 before drop outs). The recruitment target for the cohort study is therefore 777 participants (567 from the control arm of the cRCT plus 210), and the total recruitment target is 1050 (840 plus 210).

### **Retention of study participants**

To ensure that contact is not lost with any members of the study population during the follow-up period and that data are as complete as possible, MILESTONE has paid considerable attention to its engagement and retention strategies, drawing extensively on the advice and experiences of its young advisors to create a special “Bonding Plan”. Participants may be contacted using several methods of communication (post/phone/email); contact details of all participants, including GP and CAMHS clinician details, are recorded in a “keeping in touch” form; data is collected in several different ways (face-to-face, online, phone); and each contact, or contact attempt, made with participants is recorded in a bespoke contact log. There are multiple contact points between study assessments, where the participants can advise of any changes to their contact details. 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.

### Losses to follow up

Due to the characteristics of the study population group (young people, highly mobile, in the process of moving on to higher education, training or work), we have allowed for a 30% drop out rate.

### Withdrawal of young people from the study

All participants remain in the study and follow-up data is sought unless consent for participation in data collection is explicitly withdrawn.

### Data analysis

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/>).

A sensitivity analyses using multiple imputation will be conducted to explore the potential impact of missing data.

### cRCT

Basic descriptive methods will be used to present the data on study participants, trial conduct, clinical outcomes and safety (in total and for each study group separately). The primary outcome will be HoNOSCA score at T3 and we will test the hypothesis that there is no difference in this between the managed transition and standard care arms over the study period using a multilevel model with random effects to account for clustering and repeated measures, and adjustment for design factors (country and size of service). Where appropriate, a similar approach will be applied to the analysis of secondary outcomes. All analyses will be on an intention to treat basis.

### Cohort study

Baseline, longitudinal course, and outcome data at T4 will be analysed. Trajectories of mental health, subjective need for care and quality of life will be determined using mixed growth models and related to whether transitions from CAMHS to AMHS took place.

**Data will be analysed to predict and characterise those with higher primary and secondary outcome scores. Functional, clinical and quality of life outcomes will be assessed in those CAMHS users who transition with those who do not transition to AMHS.****Economic evaluation**

#### Health economic data collection

To conduct the economic evaluation of the trial, information on health care usage, social care usage/social costs and intervention costs will be captured. Additionally, participant health-related quality of life, and HONOSCA score will be recorded.

#### *Resource use data collection*

Health and social care resource utilisation for both trial arms will be estimated using the MILESTONE specific Client Service Receipt Inventory (CSRI), which draws on a CSRI used previously to estimate mental health care costs in the UK,[63] but has been substantially revised for use in MILESTONE. It includes questions regarding not only health care usage, but also relating to social and judicial resource use, and these questions are tailored for each participating country to reflect local services. Young people complete the measure at all four time points. For the purpose of economic evaluation, a questionnaire on the burden and impact of TRAM will be completed by all clinicians within the cRCT. This will assess how much extra burden is placed upon staff involved within the transition process due to the intervention compared to usual care.

The intervention costs associated with managed transition include the cost of implementing, as well as the delivery of the intervention. Questionnaires have been distributed to researchers in each country to ascertain the resources required to set up the intervention, whilst Excel logbooks capture



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2  
3 the time spent by clinicians completing the TRAM. Likewise, the time spent by the University of  
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5 Warwick preparing the TRAM report is logged within an Excel database and clinician questionnaires  
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7 will be used to capture the impact of the intervention on resource use.  
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#### 10 *Outcomes for economic evaluation*

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12 The two primary outcomes for the economic evaluation are quality adjusted life years (QALYs) and  
13  
14 HONOSCA score.[56 57] Health-related quality of life (HRQL) will be measured using the EQ-5D-  
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16 5L[64] and index scores[78] will be applied to calculate QALYs to determine the impact of the  
17  
18 intervention on HRQL. Changes in QALYs and HONOSCA score between the two trial arms will be  
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20 examined in conjunction with the costs to examine the cost-effectiveness of the intervention on  
21  
22 mental health.  
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#### 25 26 Economic evaluation: analysis

##### 27 28 *General principles of the economic analysis*

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30 **Intention to treat:** As recommended by best practice,[79] an intention to treat (ITT) framework will  
31  
32 be adopted. That is, for each individual within the trial, the analysis will be conducted according to  
33  
34 which arm they were randomised.  
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38 **Perspective:** The base-case analysis will adopt a healthcare and personal social services (PSS)  
39  
40 perspective in accordance with NICE recommendations.[79] However, given the widespread  
41  
42 acknowledgement of the wider costs of mental health,[80] a societal perspective will be adopted as  
43  
44 a secondary analysis. Societal costs will include: social care, productivity, and criminal justice system  
45  
46 contacts.  
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50 **Time horizon:** The base-case analysis will be a trial based analysis and therefore consider just the  
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52 years followed up within the trial. Given the complexity of the trial, the potential for long term  
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54 decision modelling and extrapolation will be informed by a systematic review of the methods used  
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56 within existing mental health literature. Long run extrapolation will therefore be considered in light  
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58 of this.  
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3 **Discounting:** As recommended by NICE,[79] all costs and outcomes that occur after the first year of  
4 the trial will be discounted at 3.5%.

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8 **Missing data:** Typically, within any economic evaluation of an RCT, there will be some missing  
9 data.[81] This may be for a number of reasons, and a certain degree of attrition is to be expected  
10 during follow up. Should missing data be prevalent, the health economics analysis will address  
11 missing data through the use of multiple imputation.[81]

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17 **Clustering:** The hierarchical nature of the data needs to be addressed within multiple imputation  
18 procedures and within the analysis framework. To do this, random effects approaches will be  
19 used.[82]

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24 **Uncertainty:** The uncertainty around the results will be assessed through sensitivity analyses and the  
25 generation of cost-effectiveness acceptability curves (CEACs).[83]

#### 26 27 28 29 *Calculating costs for economic evaluation*

30  
31 Data on staff time and other resources in the transition process will be obtained at each location,  
32 and costed using appropriate sources of unit cost data (e.g. for the UK, standard unit cost sources  
33 include the NHS reference costs and the Unit Costs of Health and Social Care report published  
34 annually by the Personal Social Services Research Unit at the University of Kent). This will result in  
35 location-specific estimates of the direct costs involved in implementing the managed transition  
36 process.

#### 37 38 39 40 41 42 43 44 45 *Outcomes for economic evaluation*

46  
47 The primary economic analysis will be a cost utility analysis. The EQ-5D-5L measure allows the  
48 calculation of QALYs. QALYs will be calculated for each child within the trial using the area under the  
49 curve method. The trapezium rule will be used to calculate the area under the curve and thus  
50 calculate QALYs. An underlying assumption of this methodology is that there is a linear line between  
51 each utility value at each follow up. When analysing incremental QALYs between trial arms, it is  
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3 important to adjust for baseline differences in utility.[84] In addition to controlling for baseline  
4 utility, it is important to account for the hierarchical nature the outcome data.[82] The base-case  
5 analysis of effectiveness will therefore use methods that incorporate a random-effects regression  
6 model controlling for baseline health status and accounting for clustering.[82] EQ-5D-5L tariffs for  
7 each participating country, where available, will be used to allow for country-specific economic  
8 analyses. The cost-effectiveness of the intervention over the duration of the trial will be examined,  
9 and decision uncertainty assessed using probabilistic sensitivity analysis and scenario analysis.

### 18 **Data management**

#### 21 Online data collection

22 All measures apart from DAWBA are completed using HealthTracker™, which allows measures to be  
23 completed remotely using developmentally appropriate interfaces and subjects to skip modules if  
24 they do not score on screening questions for that module, thereby reducing the burden to  
25 participants. Each questionnaire has been optimised for the screen, based on feedback from service  
26 users and providers. HealthTracker™ automatically generates random participant (service user,  
27 parent, and clinician) ID numbers and passwords when the participant is entered onto the system.  
28 HealthTracker™ stores participant's month and year of birth. All other data is anonymised.

29 The DAWBA is completed using the website <http://dawba.net> and anonymised scores (identified  
30 and linked using the unique DAWBA ID) transferred to a bespoke form on the HealthTracker™  
31 system. A secure database developed at Warwick Medical School stores information that is not  
32 collected by HealthTracker™. This includes participant name, unique study ID, HealthTracker™ and  
33 DAWBA IDs, contact details, information linking participants (for example, young person to CAMHS  
34 clinician) and service level information. This database is maintained locally at sites with access  
35 password controlled and strictly limited to MILESTONE personnel to ensure confidentiality. No  
36 personally identifiable information relating to participants leaves the local site. Only the unique  
37

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3 identifiers, linking information (using identifiers) and service level data is shared with Warwick  
4  
5 Medical School.

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8 Paper-copies of measures are only used as a last resort, or if preferred by the participant. All  
9  
10 MILESTONE researchers have received training on the HealthTracker™ platform and other systems  
11  
12 for data collection prior to the study beginning.

#### 13 14 15 Data transfer

16  
17 All transfers of study data are informed by and comply with the European Parliament and the  
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19 Council of Europe's Directive 95/46/EC on protection of individuals with reference to the handling of  
20  
21 personal data and on the free flow of such information between EU countries.

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24 To ensure the security and integrity of data during such transfer an appropriate documented  
25  
26 standard procedure has been established and is followed without exception. Any study data that is  
27  
28 to be transferred between research sites is anonymised prior to transfer.

#### 29 30 31 Data Storage

32  
33 All essential documentation and trial records is stored by Warwick Medical School and participating  
34  
35 local sites in conformance with the applicable regulatory requirements with access to stored  
36  
37 information restricted to authorised personnel.

#### 38 39 40 Data access and quality assurance

41  
42 In all partner countries, local research ethics committee requirements and national and EU law  
43  
44 underpin the collection, recording, sharing and secure storage of person identifiable data.

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46  
47 Personal information about potential and enrolled participants are collected, shared, and  
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49 maintained in a manner, which protects their confidentiality before, during and after the trial. All  
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51 researchers working on the MILESTONE Study are experienced in undertaking research in a way that  
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53 maintains the privacy and confidentiality of study participants but which balances these demands  
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3 against the needs to ensure that participants are not at risk. Names or addresses of participants are  
4  
5 not disclosed to anyone other than the staff involved in running the trial.  
6

7  
8 Data is only accessible by authorised personnel and made available to relevant bodies for audit  
9  
10 purposes only.

11  
12 At the end of the MILESTONE project, analysis datasets will be made available following University of  
13  
14 Warwick's Research Data Management Policy which ensures that data produced through the  
15  
16 University's research activities is registered, stored, made accessible for use and reuse as  
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18 appropriate, managed over time and/or disposed of, according to legal, ethical, funder requirements  
19  
20 and  
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22 good  
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24 practice. ([http://www2.warwick.ac.uk/services/rss/researchgovernance\\_ethics/research\\_code\\_of\\_practice/datacollection\\_retention/research\\_data\\_mgt\\_policy/](http://www2.warwick.ac.uk/services/rss/researchgovernance_ethics/research_code_of_practice/datacollection_retention/research_data_mgt_policy/))  
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### 28 Archiving

29  
30 Data from this study will be retained intact in an appropriate format and storage facility for a  
31  
32 minimum of 10 years in the UK in line with the Medical Research Council's guidelines on Personal  
33  
34 Information in Medical Research; other countries will follow their relevant guidelines.  
35  
36 (<http://www.mrc.ac.uk/documents/pdf/personal-information-in-medical-research/>)  
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### 40 Monitoring

41  
42 UK sites are monitored by Warwick Medical School. Monitoring includes compliance to the protocol,  
43  
44 quality of data collection, storage of documentation and requires monitors to have access to  
45  
46 relevant participant notes/charts and trial documentation. Each overseas party is responsible for  
47  
48 monitoring their sites according to local procedures.  
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### 51 Adverse event management

52  
53 A young person experiencing adverse events as a direct consequence of the intervention are  
54  
55 unlikely, as the intervention is as aimed at the clinician. At each study assessment, the young person  
56  
57 is asked whether any adverse events (bad or unfavourable medical occurrence) have occurred since  
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3 the last time point. This includes events from the first trial-related activity after the participant has  
4 signed the consent form until the end point of the trial as defined in the protocol. Any worsening of  
5 concomitant illness or new illness is recorded as adverse events at each visit. If the event is classified  
6 as a Serious Adverse (SAE) event, an SAE form is completed and the Principal Investigators (PIs) of  
7 each country report all SAEs immediately to the trial coordinating centre at Warwick Medical School.  
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9 The trial CI determines whether SAEs require reporting to the trial sponsor or SCEAB.  
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## 17 **ETHICS AND DISSEMINATION**

### 18 **Ethics and R&D governance**

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20 The study has been approved by the National Research Ethics Service in the UK (West Midlands:  
21 South Birmingham Research Ethics committee, Ref. no. 15/WM/0052) and by research ethics  
22 committees of all partaking countries. Regional and site-specific approvals have been obtained from  
23 NHS Research and Development offices in the UK and from other similar bodies in the other  
24 countries. The study is registered with the ISRCTN trial registry (ISRCTN83240263)  
25 ([http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21](http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21&page=1&pageSize=10&searchType=basic-search)  
26 [27 &page=1&pageSize=10&searchType=basic-search](http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21&page=1&pageSize=10&searchType=basic-search)) and ClinicalTrials.com (NCT03013595)  
28 (<https://clinicaltrials.gov/ct2/show/NCT03013595?term=NCT03013595&rank=1>).  
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39 The ethical conduct of the study is monitored throughout by the MILESTONE Ethics work package.

### 40 **Service users**

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42 We are involving a potentially vulnerable population in research: adolescent mental health service  
43 users who, in the main, are over the age of 16, but in areas where the transition boundary is 16  
44 years (some parts of England) or 16.5 years (some parts of France) they are 15 years. In England, the  
45 legal age of consent is 16, in all other participating countries it is 18.  
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53 Despite best efforts, vulnerable people, either by virtue of being young and/or with mental health  
54 difficulties, are often omitted from research studies because of concerns regarding informed  
55 consent.[85 86] The researchers in this study acknowledge these concerns and risks but also  
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2  
3 recognise the importance of including individuals with enduring mental health difficulties in the  
4  
5 study to better inform practice. The Council of Europe strongly promotes the participation of  
6  
7 children in decisions affecting them.[87] Young people will also have rights as service users, to  
8  
9 expect appropriate and good quality services.

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11  
12 The participant information sheets and consent/assent forms make explicit the voluntary nature of  
13  
14 young people's involvement. Even if the parent/carer gives consent but a young person refuses, that  
15  
16 young person is not included in the study. The young person's consent is sought before follow-up  
17  
18 assessments (verbal consent for telephone interviews), consent being implicit when they log on to  
19  
20 give responses online. The forms also seek permission to delay data collection until a later point  
21  
22 should a young person become unwell or due to some other pressing circumstances, as long as  
23  
24 transition doesn't take place in the meantime, and to liaise with a young person's clinician and  
25  
26 parent/carer should such a delay be deemed necessary. The forms explain the various safeguards in  
27  
28 place, namely to liaise with a young person's clinician and/or family if required and the resulting  
29  
30 impact on confidentiality.  
31  
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34  
35 In order to minimise any distress to young people taking part in face-to-face interviews, wherever  
36  
37 possible these are organised in venues that are known to the young person and are scheduled at  
38  
39 times when there are familiar staff or family members or carers on hand to offer support should a  
40  
41 young person become upset during any data collection processes.  
42

43  
44 In the event that during an interview or other data collection session, a MILESTONE researcher  
45  
46 identifies any situation where a young person is thought to be at risk of abuse or neglect, or that  
47  
48 young person discloses information that raises concern about the young person's safety, then a  
49  
50 detailed risk management plan is followed, which stipulates that the child protection policies and  
51  
52 procedures applicable to that country are adhered to. This is likely to involve close liaison by the  
53  
54 researcher and the MILESTONE lead for that study site, with the young person's clinician and/or the  
55  
56 nominated child protection leads within the mental health service attended by the young person.  
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Also, young people consenting to the study are asked to nominate, and provide contact details for, a health/care professional (for example, GP or CAMHS clinician) who we may contact should any adverse event arise. This safeguard is made explicit in the study information leaflets, and at all data collection time points, so young people are aware of the impact on confidentiality during the process of data collection.

### **Training**

All research assistants have participated in training sessions addressing Good Clinical Practice (GCP), transition practices, rating procedures, compliance, TRAM feedback, and communication with young people, families and clinicians. 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.[88] The study has been presented to all participating CAMHS teams and additional meetings have been held to implement the specific transition procedures in the intervention clusters.

### **Dissemination**

The MILESTONE project has a work package that focuses on dissemination. Partnerships and networks with target bodies will be strategically developed to support both short- and long-term dissemination of the MILESTONE study and other project findings. External dissemination will target the scientific community, but also the general public, lay and patients' associations, health care authorities and care givers, scientific societies and professional boards, students, policy makers, and the pharmaceutical industry. Particular attention will be paid to the information needs of the various target audiences, and that they are addressed in the appropriate language and format.

The results of the MILESTONE study will be made available in the first instance to the clinicians of CAMHS and AMHS partaking in the study, and then to the scientific community at large via publications in scientific journals, presentations at meetings, the MILESTONE web site (<http://milestone-transitionstudy.eu>), press releases, and leaflets.



## CONCLUSION

The continuity of adolescent psychopathology into adulthood means that transition to AMHS is necessary for many. However, there are real gaps in mental health care provision at this crucial stage, and those who experience transition frequently describe it as disruptive. The MILESTONE study is the first ever methodologically robust trial to test whether a decision support and assessment tool, the TRAM, can improve the mental health and social outcomes and functioning of transition age young people receiving CAMHS care. Young people in eight European countries are partaking in the trial; their longitudinal course of mental health, social and adult functioning outcomes are also evaluated as part of a longitudinal cohort study. The MILESTONE study has crucial input from young advisors, some with experience of transition in mental health services.

## MILESTONE CONSORTIUM – CURRENT MEMBERS AND PARTNER INSTITUTIONS

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## AUTHORS' CONTRIBUTIONS

SPS is the chief investigator who conceived the original study design and obtained funding, together with AM, GdG, PS, JM, FM, DPO, ST, US, TF, CS, MP, DW, FV, and GD. HT is the study coordinator who prepared the first draft and subsequent versions of the protocol and this manuscript, and is joint first author with SPS. JW and AC contributed to the manuscript. JW is the senior trial statistician who led the calculation of the sample size; JG will undertake the statistical analysis under her direction. JM designed the health economic component and AC will undertake the health economics analysis under his direction. CD is the quality assurance manager. PT, SG, GS, LA, FR, SA, LOH, and ND are research assistants and helped set up the study in their countries and gain local ethical approvals. The UK young advisors, AT, AW, CG, and LW, reviewed the proposed study scales (including the likely time required for completion, to assess for possible burden on study participants), participated in the design of the intervention leaflet and reviewed all study information material before submission to ethics. All authors critically reviewed the protocol and the manuscript, and gave approval for the publication.

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## COMPETING INTERESTS

Paramala Santosh is the director and shareholder of HealthTracker Ltd. Frank Verhulst publishes the Dutch translations of ASEBA from which he receives remuneration.

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**FIGURES**

Figure 1 MILESTONE study flow diagram

Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person

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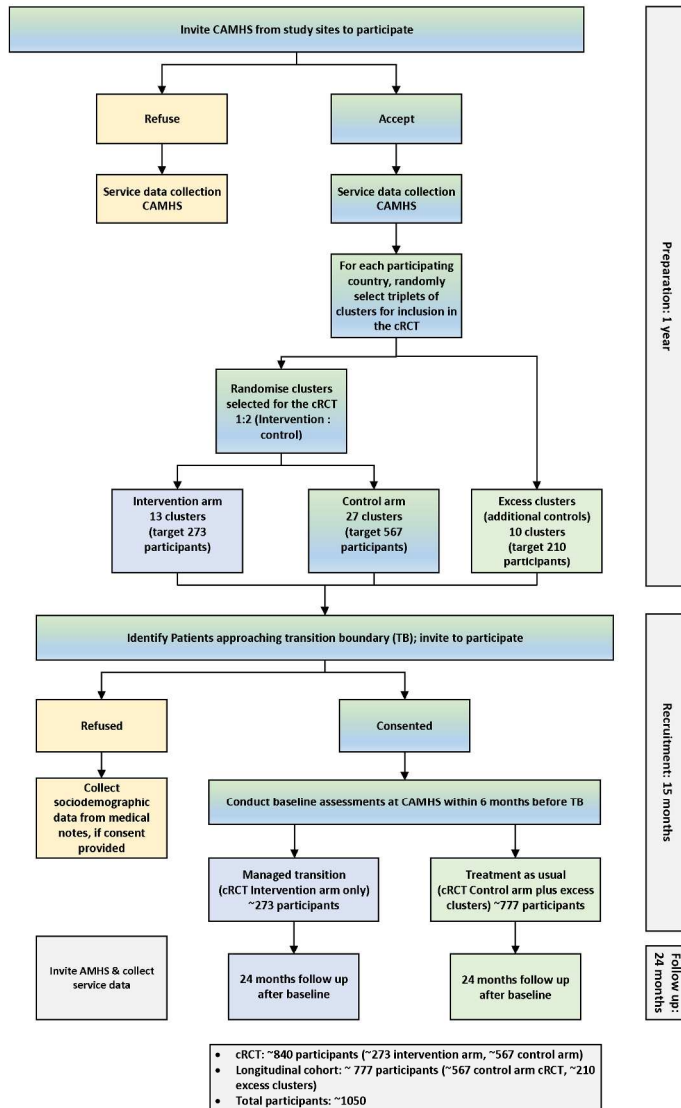


Figure 1 MILESTONE study flow diagram

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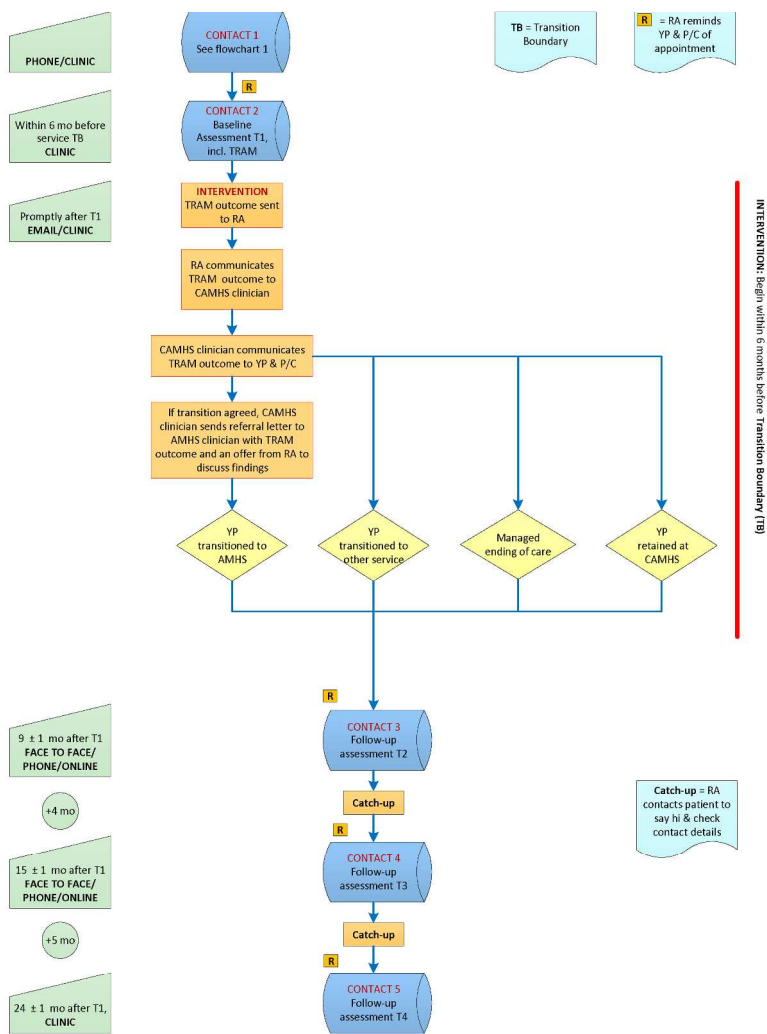


Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Addressed on page number
<b>Administrative information</b>			Protocol paper in track changes: PP Main protocol: MP v2.2 03.03.2017
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1 (PP) _____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 4 (PP)_____
	2b	All items from the World Health Organization Trial Registration Data Set	_____
Protocol version	3	Date and version identifier	p. 1 (MP)_
Funding	4	Sources and types of financial, material, and other support	p. 41 (PP)_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	p. 1-2 (PP)_____
	5b	Name and contact information for the trial sponsor	p. 2 (MP)_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	p. 41 (PP) _____

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	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	p. 13-14 (PP)_____
<b>Introduction</b>			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	p. 5-12 (PP)_____
	6b	Explanation for choice of comparators	p. 13 (PP)_____
Objectives	7	Specific objectives or hypotheses	p. 12 (PP)_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	p. 13 (PP)_____
<b>Methods: Participants, interventions, and outcomes</b>			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	p. 14 (PP)_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	p. 17-19 (PP)____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	p. 19-22_(PP)____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	_n/a_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	_n/a_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	_n/a_____

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Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	p. 22-23, 25_(PP)
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	p. 23_(PP) & Fig 1__
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	p. 27-28 (PP)___
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	p. 17-19 (PP)___

**Methods: Assignment of interventions (for controlled trials)**

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	p. 16 (PP)
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_n/a (cluster randomised)____ —
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_n/a_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	p. 16 (PP)_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_n/a_____

**Methods: Data collection, management, and analysis**

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3	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related	p. 22-23, 24-27,
4	methods		processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of	38-39_(PP)_____
5			study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known.	
6			Reference to where data collection forms can be found, if not in the protocol.	
7				
8		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be	p. 28-29
9			collected for participants who discontinue or deviate from intervention protocols	(PP)_____
10				
11	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality	p. 33-36
12			(eg, double data entry; range checks for data values). Reference to where details of data management	(PP)_____
13			procedures can be found, if not in the protocol	
14				
15	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the	p. 29-30
16			statistical analysis plan can be found, if not in the protocol	(PP)_____
17				
18		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	p. 30 (PP)_____
19				
20		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any	
21			statistical methods to handle missing data (eg, multiple imputation)	p. 30 (PP)
22				
23				
24	<b>Methods: Monitoring</b>			
25				
26	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of	p. 13-14 (PP)
27			whether it is independent from the sponsor and competing interests; and reference to where further details	p. 10, 58-59
28			about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not	(MP)_____
29			needed	
30				
31		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim	_n/a_____
32			results and make the final decision to terminate the trial	–
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35	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse	p. 36 (PP)_____
36			events and other unintended effects of trial interventions or trial conduct	
37				
38	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent	p. 59 (MP)_____
39			from investigators and the sponsor	
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42	<b>Ethics and dissemination</b>			
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Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 4, 36_(PP)___
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p. 57 (MP)_____
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p. 18 (PP)_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	_n/a_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 34-35 (PP)___
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 42 (PP)_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 35 (PP)_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_n/a_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 39-40 (PP)___
	31b	Authorship eligibility guidelines and any intended use of professional writers	p. 61 (MP)___
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	p. 35-36 (PP)___
<b>Appendices</b>			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available upon request___

Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_n/a_____
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

For peer review only



# BMJ Open

## 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)

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<b>Primary Subject Heading</b>:	Mental health
Secondary Subject Heading:	Health services research
Keywords:	Child & adolescent psychiatry < PSYCHIATRY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

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**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)**

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46 **for the MILESTONE Consortium**

#### 47 48 49 **WORDCOUNT**

50 10906 (excludes references)

## KEYWORDS

Mental health, child and adolescent mental health services, transition, health services research, cluster randomised controlled trial, longitudinal cohort study, youth mental health, Europe

## ABSTRACT

**Introduction:** Disruption of care during transition from Child and Adolescent Mental Health (CAMHS) to Adult Mental Health Services (AMHS) may adversely affect the health and wellbeing of service users. The MILESTONE study evaluates the longitudinal course and outcomes of adolescents approaching the transition boundary (TB) of their CAMHS and determines the effectiveness of the model of managed transition in improving outcomes, compared to usual care.

**Methods and analysis:** A cohort study with a nested cluster randomised controlled trial. Recruited CAMHS randomised to provide either i) managed transition using the Transition Readiness and Appropriateness Measure (TRAM) score summary as a decision aid or ii) usual care for young people reaching the TB. Participants are young people within one year of reaching the TB of their CAMHS in eight European countries; one parent/carer and a CAMHS clinician for each recruited young person; and adult mental health clinician or other community based care provider, if young person transitions. Primary outcome is Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA) measuring health and social functioning at 15 months post-intervention. Secondary outcomes include mental health, quality of life, transition experience, and health care usage assessed at 9, 15 and 24 months post-intervention. With a mean cluster size of 21, a total of 840 participants randomised 1:2 intervention to control is required, providing 89% power to detect a difference in HoNOSCA score of 0.30 standard deviations. The addition of 210 recruits for the cohort study ensures sufficient power for studying predictors, resulting in 1050 participants and an approximate 1:3 randomisation.

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3 **Ethics and dissemination:** The study protocol was approved by the UK National Research Ethics  
4 Service (15/WM/0052) and equivalent ethics boards in participating countries. Results will be  
5 reported at conferences, in peer-reviewed publications, and to all relevant stakeholder groups.  
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10 **Trial registration numbers:** ISRCTN83240263; NCT03013595  
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## 12 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 13 • This is the first ever methodologically robust trial to test whether a decision support and  
14 assessment tool can improve the mental health and social outcomes and functioning of  
15 transition age young people receiving care at Child and Adolescent Mental Health Services.  
16
- 17 • A large, prospectively identified and robustly evaluated cohort of young people across  
18 several European countries with diverse health care systems is taking part in the study.  
19
- 20 • The cost-effectiveness of the intervention and research-related changes in health systems in  
21 terms of both expenditure and related health outcomes will be evaluated.  
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- 23 • There is a strong Patient and Public Involvement (PPI) at all stages of the study.  
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- 25 • Due to the nature of the intervention it is not possible for clinicians or assessors to be blind  
26 to the allocation of clusters or of the service users within these clusters.  
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## INTRODUCTION

The MILESTONE (Managing the Link and Strengthening Transition from Child to Adult Mental Health Care) study focuses on the period when young people (YP) attending Child and Adolescent Mental Health Services (CAMHS) need to move on, or “transition” to, an adult mental health service (AMHS), if they still require ongoing care.

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.[1-4] The National Comorbidity Survey Replication in the USA found that 75% of people with a mental disorder have an age of onset younger than 24 years, 50% have an onset before 16.[1] However, only a small proportion of young people with mental health problems approaching adulthood, less than one in six, access services or receive appropriate care.[5 6]

There is international concern about young people who get ‘lost’ during their move from CAMHS to AMHS[7-15] and transition-related discontinuity of care is a major socioeconomic and societal challenge. In the UK, almost half of the service users reaching the transition boundary of their child and adolescent mental health service (CAMHS) do not go on to receive adult care.[7 16] The TRACK study found that less than 5% of patients undergoing CAMHS to AMHS transition experience continuity of care.[17] There is also a concern that despite recognition of ongoing mental health need, few young people are referred, with fewer than one third in one study.[18] 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

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3 adolescent and/or family resistance to transition.[19-21]. Furthermore, transition may differ widely  
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5 across different regions and countries due to lack of or different procedures.  
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8 Problems at the CAMHS-AMHS interface are accentuated by the fact that young people are  
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10 simultaneously negotiating developmental and situational transitions, such as changes in housing  
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12 and relationships and moving on to adult roles.[8 17] A lack of information about possible options,  
13  
14 planning that takes too long and where no one professional takes charge to ensure decisions are  
15  
16 acted upon, compound the problem.[22] Those who slip through the care net are likely to present to  
17  
18 adult services at a subsequent time, with more severe and enduring mental health problems.[23-25]  
19  
20 Disruption of care during transition adversely affects the health, wellbeing and potential of this  
21  
22 vulnerable group,[26-31] and negative transition experiences adversely impact the young person's  
23  
24 future engagement with mental health services.[32]  
25  
26

27  
28 Intervening at the level of transition represents one of the most important ways we can facilitate not  
29  
30 only recovery but also mental health promotion and mental illness prevention in adulthood.  
31  
32 Ensuring sustained treatment through the transitional period is very likely to be cost-effective, since  
33  
34 the presence of mental illness during childhood leads to ten times higher costs during  
35  
36 adulthood.[33-35] However, there is currently no evidence for any effective model of appropriate  
37  
38 transitional mental health care or any interventions to reduce these individual and societal costs.[36]  
39  
40

#### 41 **Transitional care**

42  
43 Ideally, transition to adult mental health services should be a planned, orderly, purposeful and  
44  
45 patient-centred process that ensures continuity of care, optimises health, minimises adverse events  
46  
47 and ensures that the young person attains his/her maximum potential.[37-41] Good transitional care  
48  
49 starts with preparing a service user to leave the child-centred health care setting and ends when  
50  
51 that person is received in, and properly engaged with, the adult provider or an appropriate  
52  
53 alternative, or is discharged from care in a planned and managed fashion.[42 43]  
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3 European research on transition from CAMHS to AMHS is sparse, with little information available on  
4 the quality of transition and transition experiences in different EU countries in relation to long term  
5 mental health outcomes. The organisation of CAMHS in the member states vary, including the age at  
6 which young people are transitioned to adult services, size and complexity, sources of funding, and  
7 service provision and care. There is some evidence though that transition is a problem across all EU  
8 states.[44-46]  
9

10  
11 Barriers to good transition have been mapped,[16 17] but the evidence of interventions for  
12 improving transitional care is scant. A recent systematic review of CAMHS to AMHS transition  
13 identified only three initiatives, all in the USA,[20] including a case management model, a transition  
14 support model and an outpatient transition programme. Although all three programmes showed  
15 improved clinical and social outcomes for those with facilitated transition, none of these was a  
16 randomised trial and each model was deeply rooted within its own particular and specific healthcare  
17 context. There is no consensus as to who can be discharged on reaching the CAMHS transitional  
18 boundary, who should receive transitional care, and how this care should be delivered. Furthermore,  
19 it is not clear what outcomes should be measured to assess clinical and cost effectiveness of the  
20 model, what the outcomes of those who fall through the care gap are, and what the individual,  
21 organisational and societal costs of poor, inadequate or inappropriate transition are. A recent NICE  
22 review on transition from child to adult care across all specialities found that there was no robust  
23 evidence on models of transitional care.[36]  
24  
25

26  
27 In the absence of a planned, purposeful and needs-based assessment of those who reach the  
28 boundary, clinical judgment on transition can be influenced by misperceptions of other services,  
29 time and resource constraints, poor communication between CAMHS-AMHS, and poor adherence to  
30 existing policies.[19] Research has confirmed several information gathering biases in unstructured  
31 clinical judgements such as diagnostic biases, confirmation biases, ignoring conflicting information,  
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3 and assumptions based on patient and service background.[47] A recent study found that feeding  
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5 back structured assessment results to clinicians is leading to improved clinical decision making.[47]  
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8 Ideally all young people who reach a transition boundary would be assessed in a structured and  
9  
10 standardised way to determine ongoing need for care. Those who need such care would make a  
11  
12 transition to adult services in a planned and managed manner ensuring continuity of care across all  
13  
14 domains. Those without ongoing need would be appropriately discharged. Despite the intuitive  
15  
16 simplicity and clinical importance of such a structured decision process, a transition model  
17  
18 incorporating this approach with regard to mentally ill patients has not been evaluated or reported  
19  
20 in research or health practice literature, although its need has been articulated.[11 14]  
21  
22

### 23 **The MILESTONE project**

24  
25 The five year MILESTONE project (February 2014 to January 2019) aims to improve the  
26  
27 understanding of, and strengthen, CAMHS-AMHS transitional care across different healthcare  
28  
29 systems in the EU. In a series of work packages, it will 1) map current services and transitional  
30  
31 policies across the EU; 2) develop and validate transition-specific outcomes measures; 3) conduct a  
32  
33 longitudinal cohort study of transition process and outcomes across eight EU countries; 4) develop  
34  
35 and test, in a cluster-randomised trial, the clinical and cost-effectiveness of an innovative transitional  
36  
37 care model; 5) create clinical, organisational, policy and ethics guidelines for improving care and  
38  
39 outcomes for transition age youth; and 6) develop and implement training packages for clinicians  
40  
41 across the EU. This paper presents the protocol (v2.2) for the work packages dealing with the  
42  
43 longitudinal cohort study, the cluster randomised controlled trial and the economic evaluation of the  
44  
45 trial, which combined constitute the MILESTONE study.  
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### 50 **MILESTONE model of managed transition**

51  
52 The model of transitional care we have developed consists of an evidence-based decision-making  
53  
54 process and managed transition, incorporating key principles of continuity of care: adequate  
55  
56 information transfer, appropriate joint working, therapeutic and relational continuity, and  
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3 engagement with adult services.[48 49] The model of managed transition can be seen as one of the  
4  
5 cornerstones of a planned and purposeful transition process and can lead to more effective joint  
6  
7 working between services. It addresses the need to involve young people and parent/carers in the  
8  
9 planning process, tailor transition support to individual needs, identify barriers to smooth transition  
10  
11 and act on these, plan transition in a timely fashion, produce a succinct medical summary of the  
12  
13 service user, and improve information transfer and communication with adult providers.[36] The  
14  
15 model includes:  
16  
17

- 18  
19 1. The establishment and/or confirmation of shared understanding of criteria for good quality  
20  
21 transitional care at the CAMHS-AMHS interface, and managed ending of care, taking into  
22  
23 account clinicians' prior knowledge of good quality transition.  
24
- 25  
26 2. Systematic identification of all young people under CAMHS care who reach the transition  
27  
28 boundary for their service.  
29
- 30  
31 3. Structured and standardised assessment of their mental health and social care needs using a  
32  
33 bespoke Transition Readiness and Appropriateness Measure (TRAM), completed by the  
34  
35 young person, their parent/carer if available and CAMHS clinician prior to, ideally six months  
36  
37 before, the transition boundary.  
38
- 39  
40 4. Feedback of TRAM results from all parties in a short, clearly presented report to relevant  
41  
42 clinicians in CAMHS, allowing clinicians to identify areas in which attention should be  
43  
44 focused to ease a young person's path to transition.  
45
- 46  
47 5. Using the findings from the TRAM report to focus communication with service users and  
48  
49 carers on issues surrounding end of care at CAMHS and potential transition to AMHS or  
50  
51 other community based service.  
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- 53  
54 6. Incorporation of critical information by clinician to young person's care or transition plan,  
55  
56 and designing goals for critical items that are achievable.  
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- 58  
59 7. Sending the TRAM findings, along with a referral letter, to the new adult service, if a referral  
60  
to AMHS is made.

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3 8. Structured and regular follow-up of all young people using Transition Outcome Measure  
4 (TROM) to assess whether those who needed care were appropriately engaged with adult  
5 services and those who had been discharged or referred to other services have no unmet  
6 needs following cessation of care.  
7  
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### 10 11 **Transition Readiness and Appropriateness Measure (TRAM) and the Transition** 12 **Related Outcome Measure (TROM)** 13

14  
15 The Transition Readiness and Appropriateness Measure (TRAM), a decision support and assessment  
16 tool, uses the HealthTracker™ platform. The measure, together with the linked findings report, have  
17 been designed to help the clinician identify a) high-risk, high-need cases for whom transition to  
18 AMHS is advisable and appropriate; b) those who can be appropriately discharged in a planned  
19 manner from CAMHS to a General Practitioner (GP); or c) transitioned to another community based  
20 service (such as social services, voluntary sector or other non-statutory agencies). Obviously, the  
21 clinicians will need to take their local service provision into account when making the decisions. The  
22 Transition Related Outcome Measure (TROM) provides information on outcomes post-transition,  
23 and on the transition process and experience.  
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36 The TRAM and TROM were developed using existing literature, expert input and focus groups on  
37 developing and validating Patient Reported Outcome Measures (PROMS);[50 51] MILESTONE's  
38 group of young advisors also reviewed the scales and helped identify areas of duplication or unclear  
39 terms. These scales have been translated into Croatian, Dutch, Flemish, French, German, and Italian  
40 languages and provide a summary of all factors necessary to consider (including symptoms,  
41 functioning, risk and need for care) when making a transition decision and when assessing the  
42 outcomes of a transition. There are versions for young people pre-transition, young people post-  
43 transition, parents/carers and clinicians at CAMHS and AMHS which can be completed online, via the  
44 HealthTracker™ platform (<https://www.healthtracker.co.uk/index.php/our-platform/>), a web-based  
45 portal allowing measures to be completed remotely, which has been used in other EU FP7 projects  
46 [52].  
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3 TRAM and TROM contain 20 questions common to both scales for all participants; further eight  
4 questions are relevant only to the clinician versions and nine only to the young person and  
5 parent/carer. All participant versions of TRAM contain 15 additional questions that are not in TROM,  
6 yet to allow comparison of results over time, most of the domains present in TRAM are also present  
7 in TROM, with versions for AMHS and CAMHS clinicians and different follow-up time points  
8 (available from the corresponding author, upon request).  
9

10  
11  
12 The construct validity, content validity, inter-rater validity, test-retest validity, and sensitivity to  
13 change of TRAM and TROM were assessed in a sub-study between June 2015 and April 2016.  
14

15  
16 The “TRAM score summary report” presents the scores from the young person, parent/carer and  
17 clinician for each item, with graphs visualising differences or similarities in scoring. The report  
18 contains items that are relevant to the clinician’s transition decision (symptoms, risk factors and  
19 disruption experienced by the young person) and those that can facilitate a smooth transition. It  
20 displays all information in a user-friendly, relevant and accessible format, helping identify young  
21 people requiring further care and allowing key facts to be easily transferred to care plans and  
22 referrals. It should complement a much more comprehensive evaluation, with the ultimate decision  
23 about transition being the outcome of a process involving key stakeholders.  
24  
25

26  
27 HealthTracker Ltd will optimize the TRAM on the HealthTracker™ platform based on decision  
28 making algorithms derived from the study. If appropriately funded, this will be made available to  
29 serve as the platform for optimization of transitions to adult mental health in the EU.  
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### 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 **AIMS AND OBJECTIVES**

48 The overall aim of the nested cRCT is to determine the effectiveness and cost-effectiveness of the  
49 model of managed transition in improving the health and social outcomes of young people, and their  
50 transition to adult roles, as compared to treatment as usual, in eight participating EU countries. The  
51 specific objectives are  
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- 3 1. To test the hypothesis that the implementation of the model of managed transition in
- 4 CAMHS at the transition boundary improves the mental health and social outcomes of young
- 5 people and their transition to adult roles when they move on from CAMHS, as compared to
- 6 usual care.
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- 12 2. To conduct an economic evaluation of the model of managed transition compared with
- 13 usual care.
- 14
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- 17 3. To explore the views and experiences of health professionals and young people concerning
- 18 the intervention.
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22 The prospective cohort study will delineate the transition journey of a large number of young people  
23 across eight EU countries. The aims are

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- 27 4. To evaluate the mental health, quality of life, and functioning of young people who attend
- 28 CAMHS and reach the CAMHS/AMHS transition boundary;
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- 32 5. To evaluate the longitudinal course of mental health, social and adult functioning outcomes
- 33 of young people who reach the CAMHS/AMHS transition boundary and transition into young
- 34 adulthood;
- 35
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- 37 6. To compare the outcomes in those young people who transition with those who do not
- 38 transition to AMHS (i.e. remain in CAMHS, are discharged or referred to other care).
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## 45 **METHODS AND ANALYSIS**

### 46 **Study design and management**

47 A large cohort of young people approaching the CAMHS-AMHS transition boundary in eight EU  
48 countries will be recruited and a nested cluster randomised controlled trial (cRCT) in a randomly  
49 selected subset of clusters (CAMHS services) will be implemented. The study design is a modification  
50 of the Cohort Multiple Randomised Controlled Trial,[53] by virtue of allocation to the intervention by  
51 cluster randomisation, with each distinct CAMHS comprising a cluster. The control arm clusters from  
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3 the cRCT together with additional excess clusters form the longitudinal cohort study, with a follow-  
4  
5 up period of 24 months. The cRCT is a superiority trial; the aim is to show that managed transition is  
6  
7 superior to usual care in improving patient reported outcomes. Usual care varies by CAMHS and may  
8  
9 or may not include transitioning planning. The primary outcome endpoint is 15 months. The study  
10  
11 flow diagram is presented in Figure 1. All arms of the study undergo the same data collection. The  
12  
13 trial has economic and qualitative components, addressing objectives 2 and 3, respectively. Detailed  
14  
15 Statistical Analysis Plans have been developed for both the cRCT and longitudinal cohort study. Final  
16  
17 versions will be signed off prior to commencement of the analysis and made available on the study  
18  
19 website.  
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21

### 22 23 **Figure 1 MILESTONE study flow diagram**

24  
25  
26 The study is sponsored by the University of Warwick and co-ordinated from the research office in  
27  
28 the Mental Health and Wellbeing unit, Warwick Medical School, with Quality Assurance and  
29  
30 Statistics from Warwick Clinical Trials Unit. The Study Coordinator is responsible for the day-to-day  
31  
32 coordination and the Chief Investigator (CI) for clinical aspects. The study is managed by a trial  
33  
34 management group (TMG), including work package leaders (i.e. country leads), and supported by  
35  
36 MILESTONE research staff. The TMG speaks monthly by telephone conference chaired by the CI. The  
37  
38 study conduct and progress is overseen by the independent MILESTONE Scientific, Clinical and  
39  
40 Ethical Advisory Board (SCEAB) comprising five international experts and four Patient and Public  
41  
42 Involvement representatives. The SCEAB members are invited to the annual general meetings in  
43  
44 order to monitor the progress of work, to assess the scientific quality and to give feed-back to the  
45  
46 Consortium members, but without a right to vote. The SCEAB will also review the main governance  
47  
48 and any ethical issues which might require greater attention.  
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51  
52 MILESTONE has strong Patient and Public Involvement (PPI) embedded throughout the project;  
53  
54 young advisors, some with experience of transition in mental health services provided feedback on  
55  
56 the protocol and study documents. Their ongoing role includes: attending and contributing to  
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3 project steering committee meetings, designing the intervention leaflet and other promotional  
4 materials, and advising on recruitment and the engagement of young people. The first five PPI  
5 representatives have been from the UK; in the third year service users from other participating  
6 countries will be involved.  
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### 10 11 **Setting and site selection**

12 The study is currently running in Belgium, Croatia, France, Germany, Italy, the Netherlands, Republic  
13 of Ireland, and the United Kingdom. Recruitment of participants is underway in 52 CAMHS clusters  
14 that fit the inclusion criteria below (October 2015 – December 2016, with last inclusions in January  
15 2017). Face-to-face meetings with clinical and managerial leads were arranged at those sites that  
16 expressed an interest and the study explained in detail. Signed site agreements or equivalent were  
17 obtained from participating sites prior to the start of the study. The majority of sites received no  
18 funding from the EU grant (no 602442) for taking part in the study. However, two German recruiting  
19 sites received payments under subcontract to facilitate recruitment.  
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32 In most countries, other than the UK, there is no umbrella organisation to facilitate collaboration  
33 between AMHS and CAMHS. Furthermore, a single CAMHS may be linked with numerous AMHS  
34 (inpatient services, clinics, teams and individuals), making it difficult for AMHS clinicians to be  
35 engaged from the start, particularly given our limited resources. Also, we were not able to predict  
36 which AMHS would be involved, as this is dependent on transition decisions.  
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### 44 **Cluster level eligibility criteria**

45 For a CAMHS to be eligible, it had to be a service delivering medical and psycho-social interventions  
46 for children and adolescents with mental health problems and disorders, and/or  
47 neuropsychiatric/developmental disorders (e.g. emotional/neurotic disorders; eating disorders;  
48 hyperkinetic disorder/ADHD; autism spectrum disorders); community-based, or provide outpatient  
49 or inpatient care; publicly or privately funded; must have a formal upper *age limit* (the transition  
50 boundary) for providing care to young people and; be responsible for transfer of care to an adult  
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3 service for those who reach the transition boundary. Forensic services and highly specialised  
4 national services, which cater for rare/unusual disorders and/or serve a national population, such as  
5 specialist clinics for rare metabolic disorders or long-term residential care for severe autism were  
6 excluded. Eligible services could vary in size and complexity, ranging from single psychiatrists or  
7 psychologists (e.g. Germany) or circumscribed teams to services with multiple teams and localities  
8 offering multidisciplinary care (e.g. UK).  
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#### 16 Baseline service level data collection

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18 Baseline service data was collected from the CAMHS manager or leading CAMHS clinician at all  
19 recruited CAMHS in the year preceding recruitment of study participants. The questionnaire  
20 covered: 1) Size (number of staff), structure and function of CAMHS; 2) Transition boundary of the  
21 service (i.e. age at expected transition); 3) The number and type of adult mental health services  
22 (AMHS) that operate within the CAMHS catchment area; 4) Current transition policy and practice; 5)  
23 Size of the catchment population. This information was used to establish the organisational  
24 structure of CAMHS and identify potential cross-over and/or movement of staff between teams or  
25 units so that distinct units (clusters) could be identified. If one or more CAMHS teams share the  
26 same core clinicians, then these were classified as one cluster, becoming the unit of allocation.  
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39 The data revealed that the CAMHS-AMHS transition boundary for most countries was 18 years, i.e.  
40 the age of majority. In the UK, Belgium and France there was more variation, the boundary ranging  
41 from 15 to 18 years. We also discovered that some services in Belgium, France, the Netherlands and  
42 Germany adopt a more flexible approach to the boundary, and in these situations we agreed a  
43 nominal boundary (18 years), which reflects the age at which transitions most commonly occur and,  
44 in most instances, is also the official TB.  
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52 Upon leaving CAMHS care, young people may be referred on to AMHS or another community based  
53 service (e.g. social services, voluntary sector or other non-statutory agencies offering support and  
54 therapeutic interventions for mental health needs), or discharged back to their GP. AMHS and  
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3 community based services will be invited to participate in the study, and service level data will be  
4  
5 collected once they are recruited.  
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### 8 **Randomisation**

9  
10 As several countries only had three CAMHS clusters, this fixed the randomisation ratio at 1:2 and the  
11  
12 randomisation was conducted in a two stage process: First, randomly selected triplets of clusters  
13  
14 within each country were identified for inclusion in the cRCT. These three clusters were further  
15  
16 randomised in a 1:2 ratio between intervention and control arms. The excess clusters (those not  
17  
18 selected during the first stage for the cRCT) were used for the cohort study only to enhance  
19  
20 numbers. Overall, this two-stage process equates approximately to a randomisation ratio of 1:3. All  
21  
22 randomisation was conducted by the trial statistician using the statistical software Stata 14.[54]  
23

24  
25  
26 The CAMHS were informed of their allocation after randomisation. The study personnel were also  
27  
28 aware of the allocation as they are involved in delivering the intervention and assessing outcomes.

29  
30 The young people and their parents/carers, who are recruited after randomisation, are informed of  
31  
32 their allocation after they have consented to the study, yet only if they ask about this specifically  
33  
34 [55].  
35  
36

### 37 **Participant eligibility and recruitment**

#### 38 **Young people**

39  
40 Individual recruitment targets were set for each CAMHS (cluster), based on local capacity, but with  
41  
42 the constraint that in the cRCT there should be on average 21 participants per cluster. Databases of  
43  
44 all participating CAMHS are scrutinised by CAMHS personnel to identify all young people  
45  
46 approaching the service's transition boundary and meeting the inclusion criteria over a 15 month  
47  
48 recruitment period (between October 2015 and December 2016).  
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54 Young people are eligible, if a) their age is within one year of reaching the transition boundary of  
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56 their CAMHS during the trial recruitment period and, in exceptional cases, not more than 3 months  
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58 older than the transition boundary, if a decision about transition has not yet been made; b) they  
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3 have a mental disorder defined by DSM-IV-TR, DSM-5 or ICD 10/11, or they are under the regular  
4 care of CAMHS (attended at least one appointment, if not yet diagnosed); c) they have an IQ  $\geq$  70 as  
5 ascertained by previous standardised assessment or diagnosed by clinician, or no indication of  
6 intellectual impairment; and d) they provide valid written informed consent, or assent, if below the  
7 legal age of consent (in England this age is 16, in all other participating countries 18). They are  
8 ineligible if they a) are younger than a year before the transition boundary of their CAMHS; b) have a  
9 more severe intellectual impairment (IQ < 70) as ascertained by previous standardised assessment  
10 or diagnosed by clinician – if no data on intellectual functioning are available (because it has never  
11 been assessed) then care coordinators are asked to make a clinical judgement on intellectual  
12 impairment before baseline assessment takes place; c) are not able to (or expected not to be able  
13 to) complete the questionnaires due to severe physical disabilities or language problems, even with  
14 assistance from family members or a research assistant; d) are service users in a secure forensic  
15 institution; or e) don't provide valid written informed consent, or assent, if below the legal age of  
16 consent.

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34 At each site, the clinicians of eligible young people advise the research team of the ability/capacity  
35 of the young person to give informed, voluntary consent or assent. Young people are introduced to  
36 the study (as appropriate, taking local ethical/legal conditions and best practice into consideration)  
37 either by a) a clinician or care coordinator, who provide a study leaflet and/or briefing sheet and  
38 seek consent for the individual to be contacted by a MILESTONE research assistant using a signed  
39 contact form; b) a letter signed by their care coordinator or clinician outlining the purpose of the  
40 study followed by a phone call by a CAMHS personnel if no response is received; or c) posters and/or  
41 leaflets displayed in the participating CAMHS sites, with contact details of the research team.

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52 All young people who agree to be approached by a MILESTONE researcher are individually contacted  
53 and provided with further information about the study; interested individuals are asked to sign a  
54 study consent form. Young people who are below the legal age of consent are asked for their assent  
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3 and signed consent is obtained from a parent/carer (or, in some countries, parents/carers, according  
4  
5 to national medical ethics requirements).  
6

7  
8 A compensatory inclusion process has been factored in; if one country is unable to meet its  
9  
10 recruitment target, another country is allowed to over-recruit.  
11

### 12 13 Parents/carers

14  
15 The information provided to young people include separate information and consent forms for their  
16  
17 parents/carers. After signing up to the study, the young person is asked to name his/her primary  
18  
19 care giver whom s/he would like to be involved. For young people under the legal age of consent,  
20  
21 the parent/carer has to be the legal guardian of the young person. The aim is to engage the same  
22  
23 parent/carer throughout the whole study period. If the latter is not possible, then the aim is to  
24  
25 involve another parent/carer. If the young person doesn't live with his/her biological parent/s, then  
26  
27 his/her carer is involved. A carer may be the legal guardian or a partner or an older adult sibling, or  
28  
29 another individual living with and/or providing regular support to the young person.  
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33 The parent/carer is eligible if the young person consents to parent/carer participation and he/she  
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35 provides a valid written informed consent. A parent/carer is ineligible if he/she does not live with  
36  
37 and/or provide regular support to the young person, and/or is not able to (or expected not to be  
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39 able to) complete the questionnaires due to severe physical disabilities or language problems, even  
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41 with assistance from family members or research assistant.  
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45 Young people who do not wish their parent/carer to be approached to participate in the study have  
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47 their wishes respected, regardless of their own capacity to consent. If a parent/carer is unwilling to  
48  
49 participate, their wishes are respected.  
50

### 51 52 Clinicians/care providers

53  
54 Clinicians/care providers are contacted and provided with separate information sheets and consent  
55  
56 forms. They are eligible if they are responsible for the main care for the young person at CAMHS  
57  
58  
59  
60

(and AMHS or other relevant service provider, if referral is made) and provide a valid written informed consent.

### **Intervention**

The CAMHS in the intervention arm receive information on good quality managed transition and feedback from the TRAM assessment in the form of a TRAM score summary report for each participating young person.

#### **Information provision at CAMHS**

A special meeting is held between MILESTONE personnel and participating CAMHS in the intervention arm prior to service user recruitment to establish clinicians' existing knowledge and current practice of transition, and to discuss optimal transition, using TRAM as a decision support tool, and managed ending of care. Each meeting follows a prescribed structure. Additionally, written information on good quality transitional care is provided to all clinicians in the intervention arm CAMHS teams. This consists of presentation handouts and a leaflet on good quality transition designed by our young project advisors.

#### **Feedback of TRAM results**

The aim is to conduct the TRAM assessment approximately six months prior to the transition boundary. The TRAM findings (TRAM score summary report) are fed back to clinicians soon after the young person, parent/carer and CAMHS clinician have completed the baseline assessments.

- 1) 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 is 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.
- 2) The CAMHS clinician is encouraged to communicate the TRAM findings to the young person and parent/carer, and incorporate critical information to young person's care or transition plan, and design goals for critical items that are achievable.

- 3) The CAMHS clinician decides whether or not to refer the young person to adult services.
- 4) If a referral is made, the CAMHS clinician is asked, if appropriate and with relevant permissions, to send the TRAM score summary report along with the referral letter to the new adult service.
- 5) The AMHS clinician or other care provider is offered a chance to discuss the TRAM findings with an appropriate member of the MILESTONE research team.

The aim of the TRAM score summary report is to support clinicians in their decision making regarding transition, communication with stakeholders and planning of the transition process. A flowchart of the study intervention is depicted in Figure 2.

**Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person**

## The control arm

Young people, parent/carers and clinicians in the control arm complete the same baseline assessments but the latter do not receive any additional training or feedback of TRAM scores, i.e. continue providing usual care, which may or may not include transition planning.

## Outcome measures

### Primary outcome measure

The primary outcome measure is the clinician-rated Health of the Nation Outcome Scale for Child and Adolescents (HoNOSCA),[56] which has 15 items scored on scale of 0-4, and covers the severity of the behaviour, impairments, symptoms and social functioning of children and young people with mental health problems. The clinical usefulness of the HoNOSCA has been validated and its sensitivity to change confirmed.[57 58]

Although the HoNOSCA is intended as a measure that is completed by a clinician who is also responsible for treatment of the client, the measure can also be completed by a mental health care professional not involved in the treatment using semi-structured interview.[59] In our study the measure is completed by a trained MILESTONE Research Assistant by interviewing the young person and taking into account all other available sources of information (parent/carer, relevant clinician and the medical records) to ensure accuracy of data.

To ensure consistency and comparability, HoNOSCA is used throughout (rather than switching to HoNOS at age 18 years). The primary outcome endpoint for the cRCT is 15 months.

### Secondary outcome measures

The secondary outcome measures are as indicated in Table 1. Apart from the TROM, two others were developed specifically for the MILESTONE study.

Table 1 Outcome measures

Study Instrument	Description
<b>Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA)[60]</b>	Used to assess the need for care based on a wide range of problems (behaviour, impairment, symptoms and social functioning).
<b>Transition Related Outcome Measure (TROM)<sup>1</sup></b>	Informs on quality of transition and changes in symptoms, risk factors and impairment due to transition. It has been developed based on the TRAM.
<b>World Health Organization Quality of Life Brief Inventory (WHOQOL-BREF)[61 62]</b>	Assesses quality of life, covering physical and psychological health, social relationships and current environment.
<b>MILESTONE specific Client Service Receipt Inventory (CSRI)[63]</b>	Focuses on the use of health and social services, and medication use.
<b>EuroQol health questionnaire (EQ-5D-5L)[64]</b>	Assesses health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).
<b>ASEBA: Youth Self Report (YSR)/Adult Self Report (ASR)/Child Behavior Checklist (CBCL)/Adult Behavior Checklist (ABCL)[65 66]</b>	Suite of measures assessing dimensions of emotional and behavioural problems.
<b>Ethics of Transitioning<sup>1</sup></b>	Assesses ethical challenges regarding the delivery of transitional care.
<b>Independent Behaviour During Consultation Scale (IBDCS)[67]</b>	Measures independent behaviour.
<b>Barriers to Care[68]</b>	Assesses practical (e.g. costs, time) and psychological barriers (e.g. fear to stigmatization) to care.
<b>Bullying – adapted from Retrospective Bullying and Friendship Interview Schedule[69 70]</b>	Assesses the experiences with bullying in different settings (e.g. school, at home, college).
<b>Life Events<sup>1</sup></b>	Assesses significant life events such as accidents, deaths in the family, separation of parents/carers, and parent/carer losing jobs.
<b>Brief Illness Perception Questionnaire (B-IPQ)[71 72]</b>	Assesses the cognitive and emotional representation of illness, including consequences. The term 'illness' has been replaced with the term 'condition'.
<b>On Your Own Feet: Transition Experience Scale (OYOF- TES)[73]</b>	Focuses on specific experiences with the transition process and has two versions: one for Young People who transition to AMHS (or other types of adult care) and one for Young People discharged from CAMHS.
<b>Specific Levels of Functioning Scale (SLOF)[74]</b>	Assesses adult functioning of the Young Person from the Parent/Carer's perspective.
<b>Clinical Global Impression Severity scale (CGI-S)[75]</b>	Assesses the severity of the patient's illness at the time of assessment, relative to the clinician's past experiences.

<sup>1</sup>Developed specifically for the MILESTONE study



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2  
3 The Ethics of Transitioning questionnaire was developed based on the themes raised by a systematic  
4 literature review and focus groups and addresses the following research question: "What are the  
5 ethical challenges of ensuring delivery of transitional care to those who need it most against the risk  
6 of pathologising transient and self-limiting distress and dysfunction, which may be normal during  
7 adolescence?". It contains seven items rated on a five-point Likert scale, with one version to be  
8 completed prior to, and another after, transitioning.  
9

10  
11 The Life Events questionnaire is a dichotomous 13-item scale that is appropriate for both young  
12 people and adults, and focuses on significant life events, such as accidents, deaths in the family, and  
13 separation of parents/carers.  
14

### 15 **Data collection**

16 Data collection is the same in the intervention, control and cohort arms of the study.  
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### 18 **Baseline data**

19 Table 2 highlights the number of contacts with the participants, the time points of the various  
20 assessments, and the type of data to be collected from the young person, parent/carer and clinician.  
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Table 2 Study assessments for participants (transition scenario)

Contact	1	2 (T1)	3 (T2)	4 (T3)	5 (T4)
<b>Contact Window</b> (No. months ± No. months)		<b>Within 6m before TB***</b>	<b>9m (± 1m) after T1</b>	<b>15m (± 1m) after T1</b>	<b>24m (± 1m) after T1</b>
Inclusion/exclusion criteria	YP P/C				
Informed consent	YP P/C	YP P/C C	(YP) (P/C) C	(YP) (P/C) (C)	(YP) (P/C) (C)
Contact details	YP P/C	YP P/C	YP P/C	YP P/C	YP P/C
Sociodemographic & personal information		YP P/C C	YP (C)	YP P/C (C)	YP P/C (C)
Need for Care (HoNOSCA – SR) (HoNOSCA – Clinician report)		YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)	YP RA (C;YP;P/C)
Transition readiness / Transition outcome (TRAM/TROM)		YP P/C C	YP P/C C	YP P/C C	YP P/C C
Referral and Transition Status (CAMHS clinician only)			C	(C)	(C)
Quality of Life (WHOQOL-BREF)		YP		YP	YP
Cost-effectiveness (EQ-5D-5L)		YP	YP	YP	YP
Service use (CSRI)		YP	YP	YP	YP
Emotional/behavioural problems (YP: YSR/ASR P/C: CBCL/ABCL)		YP P/C	YP P/C	YP P/C	YP P/C
Ethics of transitioning		YP		YP	
Independent behaviour** (IBDCS)		YP	YP	YP	YP
Barriers to Care (BtC)**			YP	YP	YP
Bullying		YP			YP
Life events		YP	YP	YP	YP
Illness perception (B-IPQ)		YP			YP
Transition experience & readiness (OYOF-TES)*			YP P/C	(YP) (P/C)	(YP) (P/C)
Functioning & Impairment (SLOF)		P/C		P/C	P/C
Illness severity (CGIS)		C	(C)	(C)	(C)
Psychopathology (YP: DAWBA 5-17/18+ SR) P/C: DAWBA 5-17/18+ PR) C: Clinical diagnosis		YP P/C C	(C)	(C)	YP P/C (C)

TB = Transition boundary of service; YP = young person; P/C = parent/carer

C = clinician. T1: CAMHS clinician; if YP is transitioned after T1, then at T2-T4 the clinician is based at AMHS. If there is a delay in transitioning, the clinician at T2-T4 will still be based at CAMHS. Consent and sociodemographic data is sought from the clinician only once. (C) = if YP is a mental health service user, then clinician is asked for information.

RA = Research Assistant

SR = Self-report

PR = Parent-report

\* = completed only once at the first assessment after transition

\*\* = if the YP is a service user the IBDCS is administered, if the YP is not a current service user, the BtC is administered.

\*\*\* = in exceptional cases, the assessment can take place up to 12 months before or 3 months after the TB (e.g. if transitions regularly happen earlier in a service or a decision about transition hasn't yet been made).

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3 The baseline assessment (T1) is undertaken after consent/assent has been given but before the  
4 delivery of the intervention, within 6 months before the transition boundary of the service or, in  
5 exceptional cases, within 12 months before or 3 months after the boundary (e.g. if transitions  
6 regularly happen earlier in a service or a decision about transition hasn't yet been made). Young  
7 people and their parents/carers are assessed at the clinic, or at an alternative location suitable for  
8 the young person, with both semi-structured interview (sociodemographic and personal  
9 information, and HoNOSCA) and online assessment. The sociodemographic and personal  
10 information questionnaire for young people and parent/carers collects general information about  
11 the young person and family, and the care the young person receives. The questionnaire covers also  
12 medical history and additional variables previously shown to contribute to continuity of mental  
13 health problems (for example, history of mental health problems and alcohol or drug abuse by  
14 parents). The last online assessment of T1 is the structured sections of the Development and Well-  
15 being Assessment (DAWBA),<sup>[76 77]</sup> which obtains information on mental health. Information from  
16 the assessment with the young person and parent/carer will be combined with a computer  
17 algorithm that provides an estimate of the probability of a certain individual diagnosis. Information  
18 on clinical diagnosis is obtained from the clinician.

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38 The length of the baseline assessment (YP) is approximately 1.5 – 2 hours. The participant can take a  
39 short break in between the online measures, and if required, complete them over multiple sessions.  
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41  
42 The research assistant is available to assist if there are any difficulties. The baseline assessment (T1)  
43 should be completed before the end of the recruitment period.  
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#### 47 Follow-up data

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49 Outcomes are measured 9 months (T2), 15 months (T3) and 24 months (T4) after T1. The aim is to  
50 complete measures at T2 and T3 via telephone and online assessment, and at T4 via face-to-face  
51 contact with young people and their parents/carers, within a month ( $\pm$ ) of the calculated assessment  
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3 time point (Table 2). Assessments with CAMHS or AMHS clinicians (or other service provider), which  
4  
5 is dependent on transition status, follow the same schedule.  
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### 8 Evaluation of the intervention and experiences of young people regarding services

9  
10 The views and experiences of CAMHS clinicians in the intervention arm are captured using a semi-  
11  
12 structured questionnaire. All clinicians are approached and those willing to engage are interviewed  
13  
14 over the telephone or face-to-face.  
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16

17  
18 A sub-sample of young people taking part in the study will be invited to take part in focus groups at  
19  
20 T4 from three participating countries: Ireland, UK and Croatia. The purpose of the focus groups will  
21  
22 be to explore their experiences of leaving CAMHS, transition to AMHS if applicable, and views of  
23  
24 mental health services, the aim being to establish whether young people have better health,  
25  
26 educational and social outcomes, better quality of life and satisfaction with services if they: a) have  
27  
28 experienced a managed transition from child to adult services at the transitional boundary or b)  
29  
30 have experienced usual care (i.e. their transition to adult services, or their discharge from services, is  
31  
32 via the usual procedure of their CAMHS clinic). It is hoped that, as part of MILESTONE's patient and  
33  
34 public involvement activity, some of the young advisors, or other young people trained in facilitation  
35  
36 skills by some of the research sites, may co-facilitate these focus groups.  
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40 Three audio-recorded focus groups will be held in each country with 9-12 young people in each  
41  
42 group. Recruitment will be from the study participants with purposive sampling to include some  
43  
44 young people who a) did not transition to adult services, b) who transitioned to adult services via  
45  
46 usual care and c) who experienced managed transition.  
47  
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### 49 **Sample size**

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51 Assuming an average cluster size of 15 participants, an allocation ratio of 2:1 (control : intervention),  
52  
53 a coefficient of variation of cluster size of 0.4 (cluster sizes ranging from approximately 5 to 30), and  
54  
55 an intracluster correlation coefficient of 0.01, with 600 participants (195 intervention arm [13  
56  
57 clusters], 405 control arm [27 clusters]), the cRCT has 89% power to detect a difference of 0.30  
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standard deviations in the primary outcome measure (HoNOSCA). To allow for 30% dropout, the required average cluster size is 21 participants. Thus, for the cRCT the target sample size is 840 participants in total (273 intervention - 13 clusters of size 21; 567 control - 27 clusters of size 21). The randomisation was stratified by country, with the number and size of clusters dictated by local capacity. Excess clusters (those not required for the cRCT) were allocated to the control arm and will be used in the analysis of the cohort study only to enhance numbers for sufficient power to study predictors for the longitudinal course and outcome of mental health during transition. There are 10 such excess clusters (average size 21 before drop outs). The recruitment target for the cohort study is therefore 777 participants (567 from the control arm of the cRCT plus 210), and the total recruitment target is 1050 (840 plus 210).

### **Retention of study participants**

To ensure that contact is not lost with any members of the study population during the follow-up period and that data are as complete as possible, MILESTONE has paid considerable attention to its engagement and retention strategies, drawing extensively on the advice and experiences of its young advisors to create a special “Bonding Plan”. Participants may be contacted using several methods of communication (post/phone/email); contact details of all participants, including GP and CAMHS clinician details, are recorded in a “keeping in touch” form; data is collected in several different ways (face-to-face, online, phone); and each contact, or contact attempt, made with participants is recorded in a bespoke contact log. There are multiple contact points between study assessments, where the participants can advise of any changes to their contact details. 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.

### Losses to follow up

Due to the characteristics of the study population group (young people, highly mobile, in the process of moving on to higher education, training or work), we have allowed for a 30% drop out rate.

### Withdrawal of young people from the study

All participants remain in the study and follow-up data is sought unless consent for participation in data collection is explicitly withdrawn.

### Data analysis

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/>).

A sensitivity analyses using multiple imputation will be conducted to explore the potential impact of missing data.

### cRCT

Basic descriptive methods will be used to present the data on study participants, trial conduct, clinical outcomes and safety (in total and for each study group separately). The primary outcome will be HoNOSCA score at T3 and we will test the hypothesis that there is no difference in this between the managed transition and standard care arms over the study period using a multilevel model with random effects to account for clustering and repeated measures, and adjustment for design factors (country and size of service). Where appropriate, a similar approach will be applied to the analysis of secondary outcomes. All analyses will be on an intention to treat basis.

## Cohort study

Baseline, longitudinal course, and outcome data at T4 will be analysed. Trajectories of mental health, subjective need for care and quality of life will be determined using mixed growth models and related to whether transitions from CAMHS to AMHS took place.

Data will be analysed to predict and characterise those with higher primary and secondary outcome scores. Functional, clinical and quality of life outcomes will be assessed in those CAMHS users who transition with those who do not transition to AMHS.

## Economic evaluation

### Health economic data collection

To conduct the economic evaluation of the trial, information on health care usage, social care usage/social costs and intervention costs will be captured. Additionally, participant health-related quality of life, and HONOSCA score will be recorded.

### *Resource use data collection*

Health and social care resource utilisation for both trial arms will be estimated using the MILESTONE specific Client Service Receipt Inventory (CSRI), which draws on a CSRI used previously to estimate mental health care costs in the UK,[63] but has been substantially revised for use in MILESTONE. It includes questions regarding not only health care usage, but also relating to social and judicial resource use, and these questions are tailored for each participating country to reflect local services. Young people complete the measure at all four time points. For the purpose of economic evaluation, a questionnaire on the burden and impact of TRAM will be completed by all clinicians within the cRCT. This will assess how much extra burden is placed upon staff involved within the transition process due to the intervention compared to usual care.

The intervention costs associated with managed transition include the cost of implementing, as well as the delivery of the intervention. Questionnaires have been distributed to researchers in each country to ascertain the resources required to set up the intervention, whilst Excel logbooks capture

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2  
3 the time spent by clinicians completing the TRAM. Likewise, the time spent by the University of  
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5 Warwick preparing the TRAM report is logged within an Excel database and clinician questionnaires  
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7 will be used to capture the impact of the intervention on resource use.  
8  
9

#### 10 *Outcomes for economic evaluation*

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12 The two primary outcomes for the economic evaluation are quality adjusted life years (QALYs) and  
13  
14 HONOSCA score.[56 57] Health-related quality of life (HRQL) will be measured using the EQ-5D-  
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16 5L[64] and index scores[78] will be applied to calculate QALYs to determine the impact of the  
17  
18 intervention on HRQL. Changes in QALYs and HONOSCA score between the two trial arms will be  
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20 examined in conjunction with the costs to examine the cost-effectiveness of the intervention on  
21  
22 mental health.  
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#### 25 26 Economic evaluation: analysis

##### 27 28 *General principles of the economic analysis*

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30 **Intention to treat:** As recommended by best practice,[79] an intention to treat (ITT) framework will  
31  
32 be adopted. That is, for each individual within the trial, the analysis will be conducted according to  
33  
34 which arm they were randomised.  
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36

37  
38 **Perspective:** The base-case analysis will adopt a healthcare and personal social services (PSS)  
39  
40 perspective in accordance with NICE recommendations.[79] However, given the widespread  
41  
42 acknowledgement of the wider costs of mental health,[80] a societal perspective will be adopted as  
43  
44 a secondary analysis. Societal costs will include: social care, productivity, and criminal justice system  
45  
46 contacts.  
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50 **Time horizon:** The base-case analysis will be a trial based analysis and therefore consider just the  
51  
52 years followed up within the trial. Given the complexity of the trial, the potential for long term  
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54 decision modelling and extrapolation will be informed by a systematic review of the methods used  
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56 within existing mental health literature. Long run extrapolation will therefore be considered in light  
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58 of this.  
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3 **Discounting:** As recommended by NICE,[79] all costs and outcomes that occur after the first year of  
4 the trial will be discounted at 3.5%.

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8 **Missing data:** Typically, within any economic evaluation of an RCT, there will be some missing  
9 data.[81] This may be for a number of reasons, and a certain degree of attrition is to be expected  
10 during follow up. Should missing data be prevalent, the health economics analysis will address  
11 missing data through the use of multiple imputation.[81]

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17 **Clustering:** The hierarchical nature of the data needs to be addressed within multiple imputation  
18 procedures and within the analysis framework. To do this, random effects approaches will be  
19 used.[82]

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23  
24 **Uncertainty:** The uncertainty around the results will be assessed through sensitivity analyses and the  
25 generation of cost-effectiveness acceptability curves (CEACs).[83]

#### 26 27 28 29 *Calculating costs for economic evaluation*

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31 Data on staff time and other resources in the transition process will be obtained at each location,  
32 and costed using appropriate sources of unit cost data (e.g. for the UK, standard unit cost sources  
33 include the NHS reference costs and the Unit Costs of Health and Social Care report published  
34 annually by the Personal Social Services Research Unit at the University of Kent). This will result in  
35 location-specific estimates of the direct costs involved in implementing the managed transition  
36 process.

#### 37 38 39 40 41 42 43 44 *Outcomes for economic evaluation*

45  
46 The primary economic analysis will be a cost utility analysis. The EQ-5D-5L measure allows the  
47 calculation of QALYs. QALYs will be calculated for each child within the trial using the area under the  
48 curve method. The trapezium rule will be used to calculate the area under the curve and thus  
49 calculate QALYs. An underlying assumption of this methodology is that there is a linear line between  
50 each utility value at each follow up. When analysing incremental QALYs between trial arms, it is  
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3 important to adjust for baseline differences in utility.[84] In addition to controlling for baseline  
4 utility, it is important to account for the hierarchical nature the outcome data.[82] The base-case  
5 analysis of effectiveness will therefore use methods that incorporate a random-effects regression  
6 model controlling for baseline health status and accounting for clustering.[82] EQ-5D-5L tariffs for  
7 each participating country, where available, will be used to allow for country-specific economic  
8 analyses. The cost-effectiveness of the intervention over the duration of the trial will be examined,  
9 and decision uncertainty assessed using probabilistic sensitivity analysis and scenario analysis.

### 18 **Data management**

#### 21 Online data collection

22 All measures apart from DAWBA are completed using HealthTracker™, which allows measures to be  
23 completed remotely using developmentally appropriate interfaces and subjects to skip modules if  
24 they do not score on screening questions for that module, thereby reducing the burden to  
25 participants. Each questionnaire has been optimised for the screen, based on feedback from service  
26 users and providers. HealthTracker™ automatically generates random participant (service user,  
27 parent, and clinician) ID numbers and passwords when the participant is entered onto the system.  
28 HealthTracker™ stores participant's month and year of birth. All other data is anonymised.

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40 The DAWBA is completed using the website <http://dawba.net> and anonymised scores (identified  
41 and linked using the unique DAWBA ID) transferred to a bespoke form on the HealthTracker™  
42 system. A secure database developed at Warwick Medical School stores information that is not  
43 collected by HealthTracker™. This includes participant name, unique study ID, HealthTracker™ and  
44 DAWBA IDs, contact details, information linking participants (for example, young person to CAMHS  
45 clinician) and service level information. This database is maintained locally at sites with access  
46 password controlled and strictly limited to MILESTONE personnel to ensure confidentiality. No  
47 personally identifiable information relating to participants leaves the local site. Only the unique  
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3 identifiers, linking information (using identifiers) and service level data is shared with Warwick  
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5 Medical School.  
6

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8 Paper-copies of measures are only used as a last resort, or if preferred by the participant. All  
9  
10 MILESTONE researchers have received training on the HealthTracker™ platform and other systems  
11  
12 for data collection prior to the study beginning.  
13

#### 14 15 Data transfer

16  
17 All transfers of study data are informed by and comply with the European Parliament and the  
18  
19 Council of Europe's Directive 95/46/EC on protection of individuals with reference to the handling of  
20  
21 personal data and on the free flow of such information between EU countries.  
22

23  
24 To ensure the security and integrity of data during such transfer an appropriate documented  
25  
26 standard procedure has been established and is followed without exception. Any study data that is  
27  
28 to be transferred between research sites is anonymised prior to transfer.  
29

#### 30 31 Data Storage

32  
33 All essential documentation and trial records is stored by Warwick Medical School and participating  
34  
35 local sites in conformance with the applicable regulatory requirements with access to stored  
36  
37 information restricted to authorised personnel.  
38

#### 39 40 Data access and quality assurance

41  
42 In all partner countries, local research ethics committee requirements and national and EU law  
43  
44 underpin the collection, recording, sharing and secure storage of person identifiable data.  
45

46  
47 Personal information about potential and enrolled participants are collected, shared, and  
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49 maintained in a manner, which protects their confidentiality before, during and after the trial. All  
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51 researchers working on the MILESTONE Study are experienced in undertaking research in a way that  
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53 maintains the privacy and confidentiality of study participants but which balances these demands  
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3 against the needs to ensure that participants are not at risk. Names or addresses of participants are  
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5 not disclosed to anyone other than the staff involved in running the trial.  
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8 Data is only accessible by authorised personnel and made available to relevant bodies for audit  
9  
10 purposes only.  
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12  
13 At the end of the MILESTONE project, analysis datasets will be made available following University of  
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15 Warwick's Research Data Management Policy which ensures that data produced through the  
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17 University's research activities is registered, stored, made accessible for use and reuse as  
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19 appropriate, managed over time and/or disposed of, according to legal, ethical, funder requirements  
20  
21 and good  
22  
23 practice. ([http://www2.warwick.ac.uk/services/rss/researchgovernance\\_ethics/research\\_code\\_of\\_practice/datacollection\\_retention/research\\_data\\_mgt\\_policy/](http://www2.warwick.ac.uk/services/rss/researchgovernance_ethics/research_code_of_practice/datacollection_retention/research_data_mgt_policy/))  
24  
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27

### 28 29 Archiving

30  
31 Data from this study will be retained intact in an appropriate format and storage facility for a  
32  
33 minimum of 10 years in the UK in line with the Medical Research Council's guidelines on Personal  
34  
35 Information in Medical Research; other countries will follow their relevant guidelines.  
36  
37 (<http://www.mrc.ac.uk/documents/pdf/personal-information-in-medical-research/>)  
38  
39

### 40 41 **Monitoring**

42  
43 UK sites are monitored by Warwick Medical School. Monitoring includes compliance to the protocol,  
44  
45 quality of data collection, storage of documentation and requires monitors to have access to  
46  
47 relevant participant notes/charts and trial documentation. Each overseas party is responsible for  
48  
49 monitoring their sites according to local procedures.  
50

### 51 52 **Adverse event management**

53  
54 A young person experiencing adverse events as a direct consequence of the intervention are  
55  
56 unlikely, as the intervention is as aimed at the clinician. At each study assessment, the young person  
57  
58 is asked whether any adverse events (bad or unfavourable medical occurrence) have occurred since  
59  
60

1  
2  
3 the last time point. This includes events from the first trial-related activity after the participant has  
4 signed the consent form until the end point of the trial as defined in the protocol. Any worsening of  
5 concomitant illness or new illness is recorded as adverse events at each visit. If the event is classified  
6 as a Serious Adverse (SAE) event, an SAE form is completed and the Principal Investigators (PIs) of  
7 each country report all SAEs immediately to the trial coordinating centre at Warwick Medical School.  
8  
9 The trial CI determines whether SAEs require reporting to the trial sponsor or SCEAB.  
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16

## 17 **ETHICS AND DISSEMINATION**

### 18 **Ethics and R&D governance**

19  
20 The study has been approved by the National Research Ethics Service in the UK (West Midlands:  
21 South Birmingham Research Ethics committee, Ref. no. 15/WM/0052) and by research ethics  
22 committees of all partaking countries. Regional and site-specific approvals have been obtained from  
23 NHS Research and Development offices in the UK and from other similar bodies in the other  
24 countries. The study is registered with the ISRCTN trial registry (ISRCTN83240263)  
25 ([http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21](http://www.isrctn.com/ISRCTN83240263?q=MILESTONE&filters=&sort=&offset=3&totalResults=21&page=1&pageSize=10&searchType=basic-search)  
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The ethical conduct of the study is monitored throughout by the MILESTONE Ethics work package.

### 41 **Service users**

42 We are involving a potentially vulnerable population in research: adolescent mental health service  
43 users who, in the main, are over the age of 16, but in areas where the transition boundary is 16  
44 years (some parts of England) or 16.5 years (some parts of France) they are 15 years. In England, the  
45 legal age of consent is 16, in all other participating countries it is 18.  
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53 Despite best efforts, vulnerable people, either by virtue of being young and/or with mental health  
54 difficulties, are often omitted from research studies because of concerns regarding informed  
55 consent.[85 86] The researchers in this study acknowledge these concerns and risks but also  
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2  
3 recognise the importance of including individuals with enduring mental health difficulties in the  
4  
5 study to better inform practice. The Council of Europe strongly promotes the participation of  
6  
7 children in decisions affecting them.[87] Young people will also have rights as service users, to  
8  
9 expect appropriate and good quality services.

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11  
12 The participant information sheets and consent/assent forms make explicit the voluntary nature of  
13  
14 young people's involvement. Even if the parent/carer gives consent but a young person refuses, that  
15  
16 young person is not included in the study. The young person's consent is sought before follow-up  
17  
18 assessments (verbal consent for telephone interviews), consent being implicit when they log on to  
19  
20 give responses online. The forms also seek permission to delay data collection until a later point  
21  
22 should a young person become unwell or due to some other pressing circumstances, as long as  
23  
24 transition doesn't take place in the meantime, and to liaise with a young person's clinician and  
25  
26 parent/carer should such a delay be deemed necessary. The forms explain the various safeguards in  
27  
28 place, namely to liaise with a young person's clinician and/or family if required and the resulting  
29  
30 impact on confidentiality.  
31  
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34  
35 In order to minimise any distress to young people taking part in face-to-face interviews, wherever  
36  
37 possible these are organised in venues that are known to the young person and are scheduled at  
38  
39 times when there are familiar staff or family members or carers on hand to offer support should a  
40  
41 young person become upset during any data collection processes.  
42

43  
44 In the event that during an interview or other data collection session, a MILESTONE researcher  
45  
46 identifies any situation where a young person is thought to be at risk of abuse or neglect, or that  
47  
48 young person discloses information that raises concern about the young person's safety, then a  
49  
50 detailed risk management plan is followed, which stipulates that the child protection policies and  
51  
52 procedures applicable to that country are adhered to. This is likely to involve close liaison by the  
53  
54 researcher and the MILESTONE lead for that study site, with the young person's clinician and/or the  
55  
56 nominated child protection leads within the mental health service attended by the young person.  
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Also, young people consenting to the study are asked to nominate, and provide contact details for, a health/care professional (for example, GP or CAMHS clinician) who we may contact should any adverse event arise. This safeguard is made explicit in the study information leaflets, and at all data collection time points, so young people are aware of the impact on confidentiality during the process of data collection.

### Training

All research assistants have participated in training sessions addressing Good Clinical Practice (GCP), transition practices, rating procedures, compliance, TRAM feedback, and communication with young people, families and clinicians. 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.[88] The study has been presented to all participating CAMHS teams and additional meetings have been held to implement the specific transition procedures in the intervention clusters.

### Dissemination

The MILESTONE project has a work package that focuses on dissemination. Partnerships and networks with target bodies will be strategically developed to support both short- and long-term dissemination of the MILESTONE study and other project findings. External dissemination will target the scientific community, but also the general public, lay and patients' associations, health care authorities and care givers, scientific societies and professional boards, students, policy makers, and the pharmaceutical industry. Particular attention will be paid to the information needs of the various target audiences, and that they are addressed in the appropriate language and format.

The results of the MILESTONE study will be made available in the first instance to the clinicians of CAMHS and AMHS partaking in the study, and then to the scientific community at large via publications in scientific journals, presentations at meetings, the MILESTONE web site (<http://milestone-transitionstudy.eu>), press releases, and leaflets.

## CONCLUSION

The continuity of adolescent psychopathology into adulthood means that transition to AMHS is necessary for many. However, there are real gaps in mental health care provision at this crucial stage, and those who experience transition frequently describe it as disruptive. The MILESTONE study is the first ever methodologically robust trial to test whether a decision support and assessment tool, the TRAM, can improve the mental health and social outcomes and functioning of transition age young people receiving CAMHS care. Young people in eight European countries are partaking in the trial; their longitudinal course of mental health, social and adult functioning outcomes are also evaluated as part of a longitudinal cohort study. The MILESTONE study has crucial input from young advisors, some with experience of transition in mental health services.

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## AUTHORS' CONTRIBUTIONS

SPS is the chief investigator who conceived the original study design and obtained funding, together with AM, GdG, PS, JM, FM, DPO, ST, US, TF, CS, MP, DW, FV, and GD. HT is the study coordinator who prepared the first draft and subsequent versions of the protocol and this manuscript, and is joint first author with SPS. JW and AC contributed to the manuscript. JW is the senior trial statistician who led the calculation of the sample size; JG will undertake the statistical analysis under her direction. JM designed the health economic component and AC will undertake the health economics analysis under his direction. CD is the quality assurance manager. PT, SG, GS, LA, FR, SA, LOH, and ND are research assistants and helped set up the study in their countries and gain local ethical approvals. The UK young advisors, AT, AW, CG, and LW, reviewed the proposed study scales (including the likely time required for completion, to assess for possible burden on study participants), participated in the design of the intervention leaflet and reviewed all study information material before submission to ethics. All authors critically reviewed the protocol and the manuscript, and gave approval for the publication.

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## COMPETING INTERESTS

Paramala Santosh is the director and shareholder of HealthTracker Ltd. Frank Verhulst publishes the Dutch translations of ASEBA from which he receives remuneration.

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**FIGURES**

Figure 1 MILESTONE study flow diagram

Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person

For peer review only

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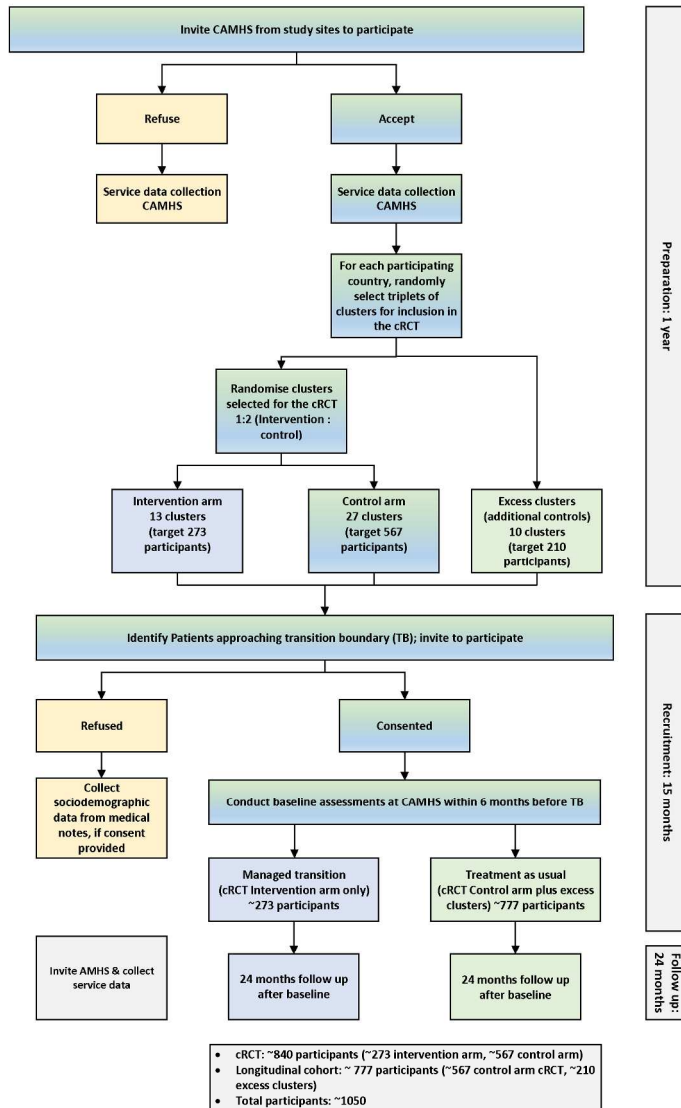


Figure 1 MILESTONE study flow diagram

210x297mm (300 x 300 DPI)



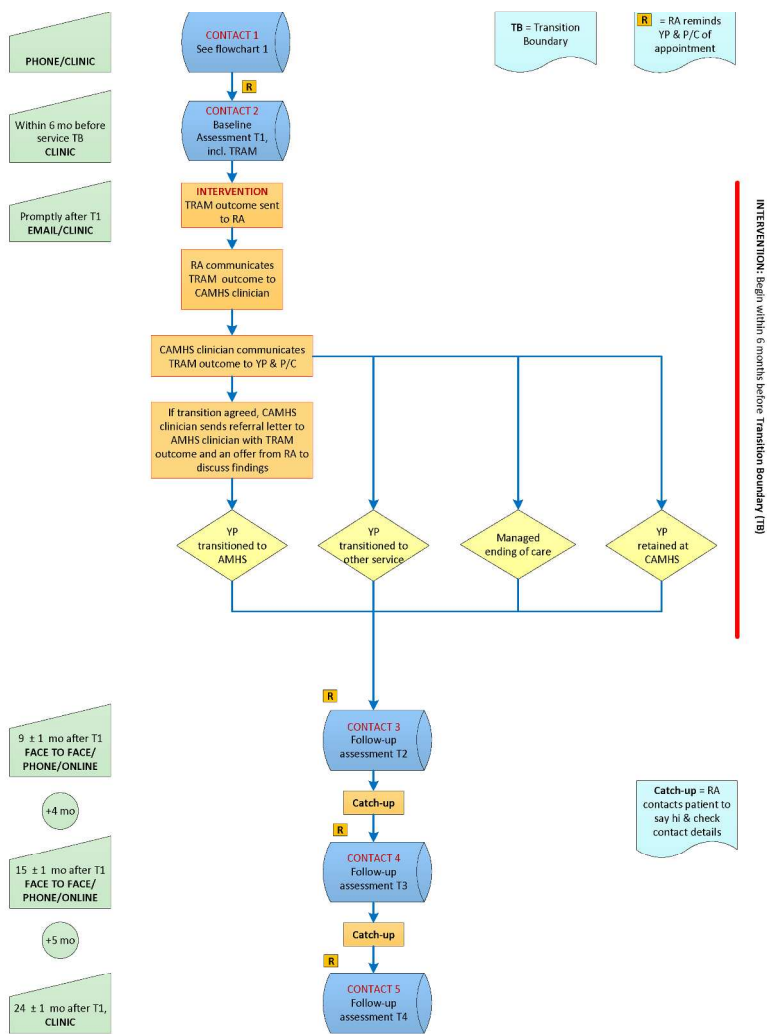


Figure 2 Flowchart of study intervention (Feedback of TRAM results) and follow-up assessments with young person

210x297mm (300 x 300 DPI)



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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Addressed on page number
<b>Administrative information</b>			Protocol paper in track changes: PP Main protocol: MP v2.2 03.03.2017
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1 (PP) _____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 4 (PP)_____
	2b	All items from the World Health Organization Trial Registration Data Set	_____
Protocol version	3	Date and version identifier	p. 1 (MP)_
Funding	4	Sources and types of financial, material, and other support	p. 41 (PP)_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	p. 1-2 (PP)_____
	5b	Name and contact information for the trial sponsor	p. 2 (MP)_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	p. 41 (PP) _____

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3		5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint
4			adjudication committee, data management team, and other individuals or groups overseeing the trial, if
5			applicable (see Item 21a for data monitoring committee)
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11	<b>Introduction</b>		
12			
13	Background and	6a	Description of research question and justification for undertaking the trial, including summary of relevant
14	rationale		studies (published and unpublished) examining benefits and harms for each intervention
15			
16		6b	Explanation for choice of comparators
17			
18	Objectives	7	Specific objectives or hypotheses
19			
20	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group),
21			allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
22			
23			
24	<b>Methods: Participants, interventions, and outcomes</b>		
25			
26	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will
27			be collected. Reference to where list of study sites can be obtained
28			
29	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and
30			individuals who will perform the interventions (eg, surgeons, psychotherapists)
31			
32	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be
33			administered
34			
35		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose
36			change in response to harms, participant request, or improving/worsening disease)
37			
38		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence
39			(eg, drug tablet return, laboratory tests)
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41		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial
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Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	p. 22-23, 25_(PP)
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	p. 23_(PP) & Fig 1__
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	p. 27-28 (PP)___
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	p. 17-19 (PP)___

**Methods: Assignment of interventions (for controlled trials)**

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	p. 16 (PP)
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	_n/a (cluster randomised)____ —
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_n/a_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	p. 16 (PP)_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_n/a_____

**Methods: Data collection, management, and analysis**

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3	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related	p. 22-23, 24-27,
4	methods		processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of	38-39_(PP)_____
5			study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known.	
6			Reference to where data collection forms can be found, if not in the protocol.	
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8		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be	p. 28-29
9			collected for participants who discontinue or deviate from intervention protocols	(PP)_____
10				
11	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality	p. 33-36
12			(eg, double data entry; range checks for data values). Reference to where details of data management	(PP)_____
13			procedures can be found, if not in the protocol	
14				
15	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the	p. 29-30
16			statistical analysis plan can be found, if not in the protocol	(PP)_____
17				
18		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	p. 30 (PP)_____
19				
20		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any	
21			statistical methods to handle missing data (eg, multiple imputation)	p. 30 (PP)
22				
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24	<b>Methods: Monitoring</b>			
25				
26	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of	p. 13-14 (PP)
27			whether it is independent from the sponsor and competing interests; and reference to where further details	p. 10, 58-59
28			about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not	(MP)_____
29			needed	
30				
31		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim	_n/a_____
32			results and make the final decision to terminate the trial	–
33				
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35	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse	p. 36 (PP)_____
36			events and other unintended effects of trial interventions or trial conduct	
37				
38	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent	p. 59 (MP)_____
39			from investigators and the sponsor	
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42	<b>Ethics and dissemination</b>			
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Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 4, 36_(PP)___
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p. 57 (MP)_____
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p. 18 (PP)_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	_n/a_____
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 34-35 (PP)___
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 42 (PP)_____
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 35 (PP)_____
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_n/a_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 39-40 (PP)___
	31b	Authorship eligibility guidelines and any intended use of professional writers	p. 61 (MP)___
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	p. 35-36 (PP)___
<b>Appendices</b>			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available upon request___

Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_n/a_____
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

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