

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cohort profile: demographic and clinical characteristics of the MILESTONE longitudinal cohort of young people approaching the upper age limit of their child mental health care service in Europe
<b>AUTHORS</b>	Gerritsen, Suzanne; Maras, Athanasios; van Bodegom, Larissa; Overbeek, Mathilde; Verhulst, Frank; Wolke, Dieter; Appleton, Rebecca; Bertani, Angelo; Cataldo, Maria; Conti, Patrizia; Da Fonseca, David; Davidović, Nikolina; Dodig-Ćurković, Katarina; Ferrari, Cecilia; Fiori, Federico; Franić, Tomislav; Gatherer, Charlotte; De Girolamo, Giovanni; Heaney, Natalie; Hendrickx, Gaëlle; Kolozsvari, Alfred; Levi, Flavia; Lievesley, Kate; Madan, Jason; Martinelli, Ottaviano; Mastroianni, Mathilde; Maurice, Virginie; McNicholas, Fiona; O'Hara, Lesley; Paul, Moli; Purper-Ouakil, Diane; de Roeck, Veronique; Russet, Frédérick; Saam, Melanie; Sagar-Ouriaghli, Ilyas; Santosh, Paramala; Sartor, Anne; Schandrin, Aurélie; Schulze, Ulrike; Signorini, Giulia; Singh, Swaran; Singh, Jatinder; Street, Cathy; Tah, Priya; Tanase, Elena; Tremmery, Sabine; Tuffrey, Amanda; Tuomainen, Helena; van Amelsvoort, T; Wilson, Anna; Walker, Leanne; Dieleman, Gwen

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Rickwood, Debra University of Canberra, Psychology
<b>REVIEW RETURNED</b>	14-Jul-2021

<b>GENERAL COMMENTS</b>	<p>The MILESTONE project is an exceptional and much-needed study that will substantially inform our understanding of the impact of transition from CAMHS to AMS. This paper describes the baseline profile of the cohort in terms of demographic and clinical characteristics. It also clearly presents the recruitment of participants and attrition and the measures used. A baseline description of participant characteristics is essential for this project, and this paper provides this.</p> <p>I have no substantive concerns with the paper - it provides appropriate information on the cohort in a clear manner.</p> <p>I have only the most minor editorial comments. There needs to be consistency in using numbers or text, including at the start of sentences.</p> <p>eg, 763 young people from 39 CAMHS in 8 European countries, their parents and CAMHS</p> <p>The mental health of young people reaching the upper age limit of their CAMHS in the MILESTONE cohort varied greatly in type and severity: 32.8% of young people reported clinical levels of self-reported problems; 18.6% were rated to be 'markedly ill', 'severely ill' or 'among the most extremely ill' by their clinician; and 57.0% of young people reported having used psychotropic medication in the</p>
-------------------------	---

	previous half year at baseline assessment.
<b>REVIEWER</b>	Rohleder, Cathrin The University of Sydney, Brain and Mind Centre
<b>REVIEW RETURNED</b>	14-Jul-2021

<b>GENERAL COMMENTS</b>	<p>Peer Review BMJ Open</p> <p>Cohort profile: demographic and clinical characteristics of the MILESTONE longitudinal cohort of young people approaching the upper age limit of their child mental health care service in Europe</p> <p>This well-written manuscript reports on an important prospective longitudinal cohort study, tracking young people in Europe approaching the upper age limit of the child and adolescent mental health care service to assess their service use and related mental health outcomes. However, as indicated by the chosen article type (cohort profile), this manuscript reports only the baseline characteristics of the cohort.</p> <p>Please find my mainly minor comments below:</p> <p>Page 9, line5/6: Although the service inclusion criteria may have been published previously, I suggest including at least a summary of the criteria in the current paper to facilitate the reader's understanding. Furthermore, I wonder if the authors could add some more details regarding the included CAMHS, e.g., how many centres were based in the different countries mentioned in the first line of page 9.</p> <p>Page 9, line 31: please add the in- and exclusion criteria in the text as well, as figure 1 may not comprises all criteria, as only those have to be listed that were not fulfilled by scanned participants. This information is in particular important as ~50% of the young people assessed for eligibility were found to be ineligible, as reported on page 14).</p> <p>Page 9/10: how many participants/parents/carers/clinicians completed all questionnaires/ assessments at the different follow-up time points?</p> <p>Page 10: I suggest changing the order of the PPI and the measures section, as the measures are part of the study procedures. Alternatively, the authors may refer to the measures section within the procedure section and indicate that the Health Tracker platform measures are described in more detail below. However, personally, I assume that readability and comprehension will improve if the procedure and the measures section are combined.</p> <p>Table 1: I understand that some data were only collected at the beginning and the end of the study (e.g., family characteristics). However, why were the young people only asked twice regarding their psychotic experience, illness perception, and bullying? Is there a reason why no specific questionnaire was included to assess psychotic symptoms and that other specific symptoms (depressive, anxious...) were not evaluated separately? And why were some assessments not done at the 9 months follow-up time point (e.g., quality of life, everyday functional skills)? It would be helpful if the authors could add some more explanatory information to the main text.</p>
-------------------------	---

	<p>Page 14, lines 56+: only 51.3% of the eligible subjects were invited to participate in the study. 17.2% of them were considered to be unwell or unable to consent. Was ability/inability to provide informed consent not an inclusion/exclusion criterion of the cohort study? Is there any information on why 31.5% of the eligible young people who were considered to be able to consent were not invited to participate?</p> <p>Findings to date: Although 715 young people have already been assessed at all time points, the paper reports the baseline assessments only. This should be highlighted more clearly in the abstract, introduction, and current findings section, although the authors have chosen the article type "cohort profile".</p>
--	---

### VERSION 1 – AUTHOR RESPONSE

**Reviewer: 1, Dr. Debra Rickwood, University of Canberra**

**The MILESTONE project is an exceptional and much-needed study that will substantially inform our understanding of the impact of transition from CAMHS to AMS. This paper describes the baseline profile of the cohort in terms of demographic and clinical characteristics. It also clearly presents the recruitment of participants and attrition and the measures used. A baseline description of participant characteristics is essential for this project, and this paper provides this.**

**I have no substantive concerns with the paper - it provides appropriate information on the cohort in a clear manner.**

**I have only the most minor editorial comments. There needs to be consistency in using numbers or text, including at the start of sentences.**

**eg,**

**763 young people from 39 CAMHS in 8 European countries, their parents and CAMHS**

**The mental health of young people reaching the upper age limit of their CAMHS in the MILESTONE cohort varied greatly in type and severity: 32.8% of young people reported clinical levels of self-reported problems; 18.6% were rated to be ‘markedly ill’, ‘severely ill’ or ‘among the most extremely ill’ by their clinician; and 57.0% of young people reported having used psychotropic medication in the previous half year at baseline assessment.**

Thank you for notifying us of this inconsistency. Sentences that started with a number were rewritten to start with text. Any numbers below 10 that were expressed with numerals were rewritten with words according according to the guidelines from the American Psychological Association.

*“Seven hundred sixty-three young people from 39 CAMHS in eight European countries, their parents and CAMHS clinicians ...” Abstract, p. 3.*

*“The mental health of young people varied greatly in type and severity: 32.8% of young people reported clinical levels of self-reported problems and 18.6% were rated to be ‘markedly ill’, ‘severely ill’ or ‘among the most extremely ill’ by their clinician.” Abstract, p. 3.*

*“Thirteen CAMHS were excluded as they were in the trial intervention arm in which ‘managed transition’ was implemented.” Cohort description, p. 6.*

*(Not all numbers rewritten in words were included here. Please see the manuscript for all changes tracked)*

---

**Reviewer: 2, Dr. Cathrin Rohleder, The University of Sydney**

**This well-written manuscript reports on an important prospective longitudinal cohort study, tracking young people in Europe approaching the upper age limit of the child and adolescent mental health care service to assess their service use and related mental health outcomes. However, as indicated by the chosen article type (cohort profile), this manuscript reports only the baseline characteristics of the cohort.**

**Please find my mainly minor comments below:**

**Page 9, line5/6: Although the service inclusion criteria may have been published previously, I suggest including at least a summary of the criteria in the current paper to facilitate the reader’s understanding. Furthermore, I wonder if the authors could add some more details regarding the included CAMHS, e.g., how many centres were based in the different countries mentioned in the first line of page 9.**

Additional information on the services included was added, including the service inclusion criteria and the number of centres per country.

*“A total of 52 CAMHS in eight countries (Belgium, Croatia, France, Germany, Ireland, Italy, the Netherlands, and the United Kingdom) agreed to participate and fitted the service inclusion criteria: a service delivering medical and psychosocial interventions for children and adolescents with mental health problems or disorders and/or neuropsychiatric/developmental disorders, with a formal upper age limit for providing care and responsible for transfer of care to adult services. Highly specialised services for rare disorders and forensic services were excluded[14]. Thirty-nine CAMHS were included in this cohort study (four in Belgium, two in Croatia, four in France, two in Germany, two in Ireland, eight in Italy, six in the Netherlands and 11 in the UK; see supplementary Table 1 for the number of participants recruited per country), which varied in size and types of services offered, including services run by a single psychiatrist/psychologist and services with multiple locations and teams.” Cohort description, study design and participants, p. 6.*

**Page 9, line 31: please add the in- and exclusion criteria in the text as well, as figure 1 may not comprises all criteria, as only those have to be listed that were not fulfilled by scanned participants. This information is in particular important as ~50% of the young people assessed for eligibility were found to be ineligible, as reported on page 14).**

Figure 1 happens to comprise all inclusion criteria, but this was not stated anywhere. The inclusion criteria were added to the text under 'study design and participants':

*"In addition to the age criterion, the following inclusion criteria were applied: eligible young people had a mental disorder or were regular CAMHS service users, had an IQ over 70 or no indication of intellectual impairment and were able to complete questionnaires and interviews (also see Figure 1)." Cohort description, study design and participants, young people, p. 6.*

**Page 9/10: how many participants/parents/carers/clinicians completed all questionnaires/assessments at the different follow-up time points?**

Whether or not a specific questionnaire had to be completed at a specific timepoint was dependent on factors such as service use: young people who were using services completed a slightly different set of questionnaires than young people who did not use services. Clinician participation at a particular assessment was entirely dependent on the young person's service use. This complicates calculating the number of participants/parents/clinicians who completed all questionnaires. As this was not stated clearly in this version of the manuscript and because we completely agree that it is important to be transparent about the proportion of missing data at baseline as well as follow-up assessments, we added the following information:

*"Whether specific measures were administered to participants was dependent on whether or not the young person was using services at the time of assessment, and which type of services. Additionally, clinician participation at a particular assessment was entirely dependent on the young person's service use. Due to an increasing proportion of young people no longer using services at follow-up assessments, the proportion of missing data at follow-up for measures such as clinician-rated severity of psychopathology (CGI-S) increased from 16.1% at T1, to 50.5% at T2, 76.9% at T3 and 81.1% at T4. Important outcome measures such as self-reported emotional and behavioural problems (YSR/ASR), parent-reported emotional and behavioural problems (CBCL/ABCL) and mental health problems assessed with HoNOSCA were administered at every time-point. For these measures, the proportions of missing data per timepoint were: 10.5% at T1, 26.9% at T2, 33.2% at T3 and 37.4% at T4 for Y/ASR; 25.0% at T1, 37.5% at T2, 46.0% at T3 and 50.6% at T4 for C/ABCL and; 3.9% at T1, 18.7% at T2, 28.3% at T3 and 31.1% at T4 for HoNOSCA." Cohort description, missing data, p. 12.*

**Page 10: I suggest changing the order of the PPI and the measures section, as the measures are part of the study procedures. Alternatively, the authors may refer to the measures section within the procedure section and indicate that the Health Tracker platform measures are described in more detail below. However, personally, I assume that readability and comprehension will improve if the procedure and the measures section are combined.**

Thank you for these suggestions, which certainly improve readability of the manuscript. The paragraph on PPI was moved to p. 12 to follow the paragraph describing measures. The sections 'measures' and 'procedure' were combined to form 'measures and procedure', starting page 7. The structure was changed slightly to improve readability and redundant sentences were removed.

**Table 1: I understand that some data were only collected at the beginning and the end of the study (e.g., family characteristics). However, why were the young people only asked twice regarding their psychotic experience, illness perception, and bullying? Is there a reason why no specific questionnaire was included to assess psychotic symptoms and that other specific symptoms (depressive, anxious...) were not evaluated separately?**

**And why were some assessments not done at the 9 months follow-up time point (e.g., quality of life, everyday functional skills)? It would be helpful if the authors could add some more explanatory information to the main text.**

The MILESTONE assessment battery is very comprehensive, resulting in a baseline assessment that required 1.5 to 2 hours for young people to complete. We carefully chose a number of instruments that covered the most important domains, but did not want to put too much burden on participants. We chose to include measures such as the DAWBA and the Y/ASR and C/ABCL as they are generic and provide categorical and continuous information on mental health problems, but also allow separate evaluation of specific mental health problems, for example by using the psychotic experiences domain in the DAWBA, or the anxious/depressed scale in the Y/ASR and C/ABCL. These sub-scales will be used in studies with research questions on these specific types of mental health problems, but were not presented in this manuscript in order to keep it comprehensive and readable.

Before finalizing the assessment battery, MILESTONE young advisors tested the assessment battery and its burden. The 1.5 to 2 hours it took to complete the assessment was considered an absolute maximum, and young advisors advised against including additional measures which would lead to questions being repeated across different questionnaires. We therefore decided not to include additional questionnaires assessing specific mental health problems/disorders. As the baseline and final (24-months) assessments were considered most important, and retention of young people in the cohort was crucial, we decided to minimize the burden at 9 and 15 months by cutting specific questionnaires from the assessment battery at those timepoints. This was especially important as some questionnaires on transition and the care received were added to the assessments at 9, 15 and 24 months, while the total time to complete the assessment battery could not increase relative to the assessment at baseline. The Y/ASR and C/ABCL are administered at every time-point, but the DAWBA, which can take up to an hour to complete, was only administered at baseline and 24-months follow-up.

We included the following in the manuscript:

*“To limit the burden on participants, the most important interviews and questionnaires were repeated*

at 9 and 15 months, most interviews were conducted by phone (some face-to-face) and questionnaires were completed online.” Cohort description, measures and procedure, p. 7.

**Page 14, lines 56+: only 51.3% of the eligible subjects were invited to participate in the study. 17.2% of them were considered to be unwell or unable to consent. Was ability/inability to provide informed consent not an inclusion/exclusion criterion of the cohort study? Is there any information on why 31.5% of the eligible young people who were considered to be able to consent were not invited to participate?**

The ability/inability to consent was considered a state that could change over time, and therefore not strictly an in/exclusion criterion. We did exclude young people who were expected not to be able to complete questionnaires, due to an intellectual impairment, disabilities or language issues. After assessing inclusion criteria, clinicians were asked to advise the research team of the ability/capacity of the eligible young person to give informed, voluntary consent or assent at the time of recruitment. At this time, some young people were considered so unwell, that this consent could not be requested. According to study procedures, young people that were previously considered unwell, could be recruited at a later time during the inclusion period, providing they were no longer considered unwell and they still met the age criterion. If this was the case, they were not included in the number of young people reported as ‘too unwell or unable to consent’ as reported in the manuscript. Young people that were excluded because they were ‘too unwell or unable to consent’, were too unwell during the entire period in which they were eligible and young people were being recruited.

Most eligible young people who were well enough and able to consent were introduced to the study by care coordinators or clinicians. These young people then indicated whether they consented to being contacted by the research team. Due to medical ethical reasons, our research team was not allowed to contact young people who did not consent to being contacted. For 31.5% of eligible young people, we did not have confirmation from the care coordinator or clinician that the study was introduced and/or whether the young person consented to be contacted. Therefore, the research team was not allowed to contact the young person. In the manuscript, this is stated as follows: “For 1,037 (31.5% of all eligible) young people, the research assistant did not have evidence that the study had been introduced and therefore could not contact the young person.” (Findings to date, p. 13). As this is a limitation of our study, this is also reflected on in the section ‘Strengths and limitations’: “The dependency on medical records and clinicians for determining eligibility, approaching and informing participants, and for gaining consent is known to make the screening and recruitment process ethically, legally and technically challenging[37]. This dependency also complicated registration of the recruitment, resulting in missing information.” (Strengths and limitations, p. 18).

While working on this revision, we found a mistake in the calculation of the response rate reported: 45.7%. The correct response rate is 45.1%. This was corrected at three points in the manuscript:

*“Of all young people to whom the study was introduced, 763 young people (45.1%) consented to participate and completed in the first assessment (before the first assessment, 23 young people*

*withdrew).” Findings to date, p. 13.*

*“The second indication of a potential selection bias relates to the response rate of 45.1%.” Strengths and limitations, p. 18.*

*“Ultimately, the response rate of 45.1% in the MILESTONE cohort is similar to response rates in other cohort studies on adolescents with mental health problems[38-40].” Strengths and limitations, p. 19.*

**Findings to date: Although 715 young people have already been assessed at all time points, the paper reports the baseline assessments only. This should be highlighted more clearly in the abstract, introduction, and current findings section, although the authors have chosen the article type "cohort profile".**

This was addressed as follows:

*“This cohort profile describes the baseline characteristics of the MILESTONE cohort.” Abstract, p. 3.*

*“This cohort profile describes demographic and clinical characteristics of young people at baseline only.” Introduction, p. 5.*

*“This cohort profile describes the demographic and clinical characteristics of young people in the MILESTONE cohort as they reach the upper age limit of their CAMHS (i.e. results from young people’s baseline assessments only).” Findings to date, p. 13.*

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Rohleder, Cathrin The University of Sydney, Brain and Mind Centre
<b>REVIEW RETURNED</b>	01-Nov-2021
<b>GENERAL COMMENTS</b>	Thank you for addressing all my comments and your detailed explanations.