PROTOCOL: Characteristics and progression through care pathways of children and young people presenting for gender services care

Gender Services Living Systematic Reviews Group

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This protocol was prepared by members of the NIHR Bristol-UCL-King's Living Evidence Synthesis Group (BUcKLES), the London Alliance for Co-production and Evidence Synthesis (LACES) and the NIHR Bristol Evidence Synthesis Group (BESG).

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Protocol registration

This review will be registered on PROSPERO.

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Plain English summary

What is the problem?

Some people experience a mismatch between their gender identity and their biological sex - this is known as gender incongruence. For some, gender incongruence may be accompanied by feelings of discomfort or unease. When the feelings of unease are so intense that they lead to significant feelings of distress, or gender-related stress or lack of support leads to substantial impairment (such as disruption to academic performance or attendance, which would be a form of educational impairment), this is known as gender dysphoria. The number of children and young people presenting to healthcare services with gender dysphoria or gender incongruence has been increasing. However, we do not currently know the best way to support or treat these people. Various options are available for their management, but we are unsure how often they are used, how well they work, how people experience them, and how safe they are.

To address these uncertainties, we are carrying out a series of systematic reviews. Systematic reviews bring together all the available evidence on a particular topic, assess that evidence to determine its reliability, and attempt to make sense of what the evidence suggests. Our reviews will be 'living' systematic reviews, which means that we will update them as new evidence becomes available.

What are we trying to find out?

Our reviews will answer the following questions. How have the numbers of young people seeking help for their gender dysphoria or gender incongruence changed over time? Do the numbers seeking help vary by age and their gender recorded at birth? What sorts of young people are seen by gender identity

services? What types of care do they receive, and how long do they have to wait for services? Finally, what are the experiences of young people receiving care, their caregivers, and the people who work in gender identity services?

Scientific abstract

The number of children and young people presenting to healthcare services with gender incongruence or gender dysphoria has been increasing. There is a need to understand better the characteristics of these individuals and the pathways they follow within health care systems. This living systematic review aims to answer eight research questions, drawing from quantitative and qualitative evidence. Using quantitative evidence, we will examine how the numbers and characteristics of children and young people accessing gender services have changed over time, and identify the types of care provided and the waiting times associated with these services. We will also look at studies seeking to determine how the prevalence of gender dysphoria or gender incongruence in children and young people has changed in the general population over time. We will use qualitative evidence to explore the experiences of young people receiving care, and the perspectives of their caregivers and professionals working within gender identity services. Searches will be conducted in multiple bibliographic databases and preprint repositories for cross-sectional, longitudinal/cohort and qualitative studies. We will synthesize quantitative data graphically and, where appropriate, using meta-analyses. Qualitative evidence will be synthesized using thematic analysis. We will assess risk of bias using an interim version of RoB-Prev developed by PERSyst for quantitative studies, and for qualitative studies we will use the CASP tool. Certainty of the evidence will be assessed using the GRADE framework for quantitative evidence and GRADE-CERQual for qualitative evidence.

1 Background

1.1 Gender dysphoria and gender incongruence

The incidence of children and young people presenting to services with gender dysphoria or gender incongruence has been increasing globally [1–5]. Recent estimates from the UK indicate that diagnoses of gender dysphoria in 0–18-year-olds rose from 0.14 to 4.4 per 10,000 person years between 2011 and 2021 [2].

Although the terms *gender dysphoria* and *gender incongruence* are often used interchangeably, they have distinct meanings in the medical literature (See Appendix 1 for a glossary of key terms used in this document). Gender incongruence (a diagnostic category of the WHO's International Classification of Diseases (ICD-11)) refers to a marked and persistent incongruence between an individual's experienced gender and their gender/sex recorded at birth, without requiring the presence of distress or impairment (whether they be social, educational, occupational, or other). In contrast, gender dysphoria (a diagnostic category of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Illnesses (DSM-5)) emphasizes the psychological distress resulting from this incongruence [6]. Gender diversity incorporates a range of gender identities, expressions, and behaviours that do not conform to traditional, or typical, social norms. Transgender (or trans) people may be considered gender diverse. Trans is an umbrella term used to refer to people whose gender identity, expression, or behaviour does not conform to that typically associated with their sex registered at birth, encompassing transgender and gender nonconforming or gender variant individuals whose identity is not fully aligned with that gender/sex [7,8]. We note that gender non-conforming behaviour or expression is not exclusive to trans people and the terms are not interchangeable. We use the term young trans people to refer to children or young people whose gender identity differs from their sex recorded at birth, including non-binary.

There is a lack of consensus on the optimal care pathway and provision of treatment for children and young trans people who seek it. This review forms part of a suite of living systematic reviews that aim to identify and synthesize the available evidence on various aspects of healthcare for children and young people with gender dysphoria or gender incongruence. Living systematic reviews are warranted when a topic is a high priority for clinical or policy decision-making, an emerging health issue, or a rapidly evolving field but there is significant uncertainty in the existing evidence [9]. The suite of living reviews addresses a recommendation of the *Independent review of gender identity services for children and young people* (the Cass Review [10]). The reviews are being carried out independently of the systematic reviews that informed the Cass Review [11–16]. Our approach will: involve young trans people throughout; synthesize a broad range of evidence, including qualitative and quantitative research; use a wide range of research tools and methods; explore not only whether services are effective but also how they work and how they are experienced; keep the evidence up-to-date using a living approach; and ensure we are transparent about each piece of work by publishing an open access protocol for each review.

1.2 Service provision

To plan gender services, clinical commissioners and policymakers need to understand the people seeking these services and the likely care pathways they will take. The recent increase in numbers of children and young people seeking gender-affirming care brings a particular need to understand their characteristics, in order that clinical commissioners and policy makers can better plan gender services. Gender-affirming health care can include "any single or combination of a number of social, psychological, behavioural or medical (including hormonal treatment or surgery) interventions

designed to support and affirm an individual's gender identity" [17].Specialist services delivering gender-affirming care have evolved over time, partly as a consequence of recent developments in national policies regarding gender affirming care for young people around the world. Several nations have placed limitations on the availability of gender-affirming care for young people, while others have strengthened legal protections around access to care [18,19]. We therefore focus on recent evidence, specifically from the 10 years before initiation of our living systematic reviews.

Access to specialist gender care, including gender-affirming care, for trans and gender-diverse youth is unequal. Regional differences persist within countries, with rural youth often disadvantaged due to the concentration of specialist services in urban centres and long waiting lists [13,20]. Socioeconomic status also shapes access: families with greater financial means may seek private care or travel abroad, while low-income households are more likely to use public systems [21,22]. Intersectional barriers further exacerbate inequalities: ethnically minoritized and immigrant youth face discrimination and administrative exclusion, while neurodivergent or disabled youth often encounter heightened clinical scrutiny [23–25]. These barriers contribute to broader health inequalities. Long waiting times for access to specialist care are associated with worsening mental health outcomes [20,22,26], poorer health [20] and thoughts of suicide or self-harm [27].

1.3 The need for this review

Previous systematic reviews by Taylor et al. [13,14] and Thompson et al. [23] suggested that key characteristics of young people – including their recorded gender/sex at birth and age at time of referral to services – have changed over time. However, changing definitions of the population, diverse methods of collecting data, and ethical concerns associated with researching vulnerable young people present significant methodological challenges in this research area [24,28]. As such, the current evidence on the prevalence and characteristics of young people seeking gender affirming care is inconclusive.

The rapidly evolving political and social context in which young people are trying to access care underscores the importance of a living review of the research on the characteristics of these individuals and their progression through care pathways. In this review, we aim to collate and synthesize evidence on how the demand for gender services has changed (and is changing) over time, on the nature of children and young people currently seeking or accessing these services, and on the experiences of these people through the care pathway.

1.4 Review questions

In all of the following review questions (RQs), our primary interest is in children and young people up to 18 years of age (specifically, up to the day before their 18th birthday). However, we will include studies in the review if the participants are up to age 25 (see Section 2.3), and will undertake analyses separately for different age groups (see Section 2.7). For RQs 3 to 8, we are interested in recent evidence only, in order to inform decisions about care now and in the future. We made an a priori decision to look at evidence collected from 2015 onwards. Whilst, for example, the most recent *five* years would provide a stronger indication of recency, we decided to go further back because (i) data since 2020 may be impacted by the global COVID-19 pandemic; and (ii) the quantity of evidence will be more limited with a shorter period.

Questions about changes over time (quantitative evidence)

RQ 1. How have numbers (in total and by age and gender or sex recorded at birth) of children and young people (up to age 18) seeking/presenting to/referred to specialist gender services changed over time?

RQ 2 How has prevalence (overall and by age and gender or sex recorded at birth) of gender dysphoria or gender incongruence in children and young people in the general population changed over time?

Questions about characteristics at presentation and progression through care pathways (quantitative evidence)

RQ 3. What are the characteristics of children and young people recently seeking or attending specialist services for gender dysphoria or gender incongruence (since 2015) in terms of (but not limited to):

- Demographic/personal characteristics
    - age (at referral and/or at assessment of other characteristics)
    - ethnicity
    - geographical location (including country, urban vs rural)
    - sexual orientation
    - socio-economic status
- Gender-related characteristics
    - age at onset/progression/diagnosis of gender dysphoria/gender incongruence
    - diagnosis of gender dysphoria (DSM)/gender incongruence (ICD)
    - gender identity
    - sex recorded at birth
    - extent of social transitioning
- Mental health characteristics
    - anxiety and depression
    - eating disorders
    - neurodevelopmental conditions (including attention deficit hyperactivity disorder (ADHD), autism)
    - resilience, self confidence and self esteem
    - self-harm, suicide attempt(s) and suicidal ideation
- Other contextual characteristics
    - adverse childhood experiences (ACEs) and protective factors. ACEs are "stressful experiences during childhood which may harm a child or negatively affect their living environment; they include: physical, sexual or emotional abuse; neglect; domestic violence in the home; homelessness or living in care; parental mental health problems or substance abuse; and parents who are absent through imprisonment, separation or death" [29]. Protective factors include communication skills and problem-solving skills [30].
    - being a victim of bullying, discrimination, minority stress factors, stigma, micro-aggressions, or related concepts
    - supportive school culture
    - family context not covered under ACEs, such as family constitution and supportiveness of transitioning

RQ 4. What are the numbers and proportions of children and young people recently seeking or attending specialist services for gender dysphoria or gender incongruence (since 2015) who:

- are assessed;
- are diagnosed with gender dysphoria or gender incongruence;

- are considered eligible for medical intervention;
- receive medical intervention;
- are provided with psychological care while under the care of a specialist gender service;
- are provided with fertility preservation options;
- access "DIY" (do-it-yourself) medical treatments, which are most commonly hormonal treatments without direct involvement or supervision from medical professionals;
- stop or reverse treatment (with reasons); and
- re-transition?

RQ 5. What are the patterns of wait times and time intervals between referral, assessment, diagnosis, and initiation of medical or psychological care?

Questions about views and experiences of the care pathway (qualitative evidence)

RQ 6. What are the views and experiences of children and young people recently seeking specialist services for gender dysphoria or gender incongruence, their caregivers, and service providers (since 2015) in terms of:

- the referral process;
- the assessment process;
- receiving a diagnosis of gender dysphoria or gender incongruence;
- eligibility criteria for medical intervention and how these are applied;
- accessing DIY medical treatments;
- stop or reverse treatment (including reasons why individuals leave the service pathway or cease assessment and/or medical intervention);
- re-transitioning (including reasons why)?

RQ 7: What are the similarities and differences between children and young people recently seeking specialist services for gender dysphoria or gender incongruence, their caregivers, and service providers in their views and experiences (since 2015)?

RQ 8: What are the barriers and facilitators to accessing care at different points of the care pathway for children and young people recently seeking specialist services for gender dysphoria or gender incongruence (since 2015)?

2 Methods

The systematic review will follow general, accepted principles as reflected in guidance from the Cochrane Collaboration [31] and in evolving guidance from the *Prevalence Estimates Reviews – Systematic Review Methodology Group* (PERSyst). We will report in line with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and the extension for living systematic reviews [32,33].

2.1 Public involvement

We are involving members of the public with lived experience of gender dysphoria or gender incongruence in all stages of the review process, from conceptualization, through refining research questions, to interpretation and dissemination of the findings. Our approach is guided by the principles of Patient and Public Involvement (PPI) in co-production [34]. This means that decisions about the review are made collaboratively between researchers, practitioners, and public contributors, including young people, families, and carers. The approach ensures inclusivity, valuing all perspectives and

recognizing diverse forms of expertise, including lived experience. We emphasize the importance of building and maintaining relationships, open dialogue, trust, and adaptability throughout the review process. Reflection and ongoing evaluation will be integrated into our processes, ensuring continuous learning and assessment of impact. This approach should enhance the rigour, relevance, and applicability of the systematic review [34].

2.2 Inequity considerations

We have considered issues of inequity in formulating the research questions, and will further address inequity in data extraction, analysis, interpretation and dissemination of the review, using structured guidance developed by the NIHR Bristol Evidence Synthesis Group. The guidance is rooted in the PROGRESS-Plus framework [35,36], which maps inequity-relevant characteristics that should be addressed in evidence synthesis, including Place of residence, Race/ethnicity/culture/language, (parent) Occupation, Gender/sex, Religion, (parent) Education, Socioeconomic status, Social capital, Plus other equity-related characteristics (e.g., age, sexual orientation, disability) or circumstances (young carers, looked-after children/care leavers and those in contact with the justice system). [35,36]

2.3 Eligibility criteria

Eligibility criteria for quantitative evidence (RQ 1-RQ 5)

	RQ 1	RQ 2	RQ 3	RQ 4	RQ 5
Participants	Children and young people aged 0 to 25 years of age at presentation/ referral/ first measurement at a health service from which specialist gender services may be accessed.	Any general population sample (e.g. country or region).	Children and young people aged 0 to 25 years of age seeking or attending specialist services for gender dysphoria or gender incongruence.		
Condition of interest	Must report numbers presenting to health services with concerns about gender identity or referral to specialist gender services (or information sufficient to calculate these).	Must report proportions with a measure/diagnosis of GD/GI in people under 25 (or information sufficient to calculate these).	Must report numbers/proportions with at least one characteristic from the specified list.	Must report numbers/proportions progressing to at least one event in the specified list.	Must report quantitative information on timing of events in the specified list for RQ 4.
Study design	Repeated cross-sectional studies with measurements at least two distinct time points at least a year part.		Cross-sectional study or longitudinal/cohort study.		
Dates of interest	No date restrictions.		The review will be restricted to data collected since 2015.		
Publication status	Peer-reviewed research articles and research preprints only.				

Note. Where people enter the study, both under and over 25 years of age, we will include the study (with limitations noted) if at least half of the participants are under 25 (or, if that information is not available, if the mean age is under 25).

Eligibility criteria for qualitative evidence (RQ 6 – RQ 8)

	RQ 6 – RQ 8
Participants	People who have sought access, have accessed, or have been referred to a child or young persons' health service (typically children and young people aged 0 to 25 years of age) from which specialist gender services may be accessed, their parents or carers, or providers of such services.
Phenomenon of interest	Must report views and experiences of care pathways, including: • the referral process, including failing to get referred • the assessment process • receiving a diagnosis of gender dysphoria or gender incongruence • being eligible for medical intervention • seeking or obtaining hormone treatments without direct involvement or supervision from medical professionals ('DIY') • desisting (i.e., leaving the service pathway or ceasing assessment and/or medical intervention) • de-transitioning • re-transitioning • barriers and facilitators to accessing care at different points of the care pathway
Study design	Any form of qualitative or mixed methods study reporting on the views or experiences of care pathways for the population of interest. Exclude single case reports.
Context	Any general population. Eligible data may be reported for entire countries, regions, or individual centres. There will be no restrictions on geographical location.
Dates of interest	The review will be restricted to data collected since 2015.
Publication status	Full research articles and research preprints only. Exclude short reports, letters, and conference abstracts.

Note. Where people enter the study, both under and over 25 years of age, we will include the study (with limitations noted) if at least half of the participants are under 25 (or, if that information is not available, if the mean age is under 25). For study design, any quantitative survey studies reporting on views or experiences may be considered in the background or discussion section, but would not be included in the thematic synthesis.

2.4 Study identification and selection

2.4.1 Bibliographic database searches for the baseline review

Bibliographic database searches for the baseline review will be undertaken in two stages. All searches will use relevant subject headings (controlled vocabularies), text-words, and search syntax appropriate to the resource, and will be unrestricted by date. All search strategies will be developed by one information specialist and peer reviewed by a second. They will also be reviewed by our public contributors to ensure inclusion of relevant terms.

First, we will search for literature relating to gender dysphoria/gender incongruence across the following bibliographic databases:

- MEDLINE (via Ovid)
- Embase (via Ovid)
- PsycINFO (via Ovid)
- CINAHL (via EBSCO)
- Social Sciences Citation Index (via Web of Science)
- Emerging Sources Citation Index (via Web of Science)
- MedRxiv
- PsyArXiv

The Ovid MEDLINE search strategy for this first search is included in Appendix 2. This stage will be used to identify studies potentially relevant for any of the four living systematic reviews in the programme of work. We will add to the search all records of the 213 articles included in the six previously published systematic reviews on gender identity conducted by researchers based at the University of York. The retrieved titles and abstracts will be screened by two reviewers independently (by members of the teams undertaking all four review) as described in Section 2.4.3. Those considered to be potentially relevant to the current review will be retained for a second round of screening by the team dedicated to this review.

Second, we will undertake searches specific to the current review. The searches be run in the same databases as listed above. One review-specific search will address RQs 2 to 5, focussing on young people accessing gender services. A second review-specific search, addressing RQ 1, will incorporate a search filter for studies of prevalence. A third review-specific search, addressing RQs 6 to 8 (qualitative evidence) will incorporate a search filter for qualitative evidence and will be run in three additional databases: the Health Management Information Consortium (HMIC), Social Policy & Practice database and Emcare (all via Ovid).

In addition, we will undertake a ‘network graph’ search of the OpenAlex dataset using EPPI Reviewer [37]. OpenAlex is a large, open-access repository and dataset comprising approximately 250 million bibliographic records of research articles from across science, connected in a large network graph [38]. The network graph search will retrieve all records that are connected, in the OpenAlex dataset, to specified ‘seed’ records by either a forwards citation relationship (i.e. all articles that cite the seed records) and or a related publications relationship (i.e. up to 20 articles 'recommended’ by the seed record based on a composite metric that combines all the various network graph relationships available within the dataset). For the initial broad search for these baseline reviews, ‘seed’ records will be the 213 unique reports included in one or more of six previously published systematic reviews on gender identity conducted by researchers based at the University of York.

2.4.2 Searching other sources

To help identify further studies, we will scan the reference lists of included studies and any relevant reviews or systematic reviews we encounter.

2.4.3 Deduplication and title/abstract screening methods

Records identified by searches of bibliographic databases and other sources will be imported into EPPI Reviewer. Records imported from OpenAlex will be filtered to remove specific types of records that are not relevant for these systematic reviews (e.g. preprints except those from MedRxiv and PsyArXiv, peer reviews, e-books, magazine articles). Duplicate records will be identified and removed within EPPI Reviewer. Two reviewers will independently screen each title and abstract for relevance to the review. Reviewers involved in screening will meet regularly to discuss disagreements, to reduce variation in screening decisions amongst the team. The title/abstract screening process will allow records to be directed to other systematic reviews in our programme, where appropriate. Correspondingly, records identified through work on other reviews in the programme that are relevant to this review may be identified and added to the full-text screening step.

2.4.4 Full text screening and inclusion decisions

We will obtain full copies of all reports considered potentially relevant to the review by at least one reviewer. Two reviewers will independently assess these for inclusion. Any disagreements will be resolved by consensus or discussion with a third reviewer. If the full text of a potentially eligible record cannot be retrieved, we will contact the corresponding author.

We will use a PRISMA flowchart to report the study selection process and we will report all studies that were excluded at full-text stage along with justification for their exclusion [32,33]. We will check for any relevant retraction statements or errata of included studies. We will not extract data from retracted articles and will exclude any studies whose primary publications have been retracted.

2.5 Data collection

We will extract data into standardized forms developed in EPPI Reviewer. These data extraction forms will be piloted by at least two reviewers on a small sample of papers and adapted as necessary. Descriptive data and results of the studies will be extracted by two reviewers independently, with any disagreements resolved by consensus or discussion with a third reviewer.

We will collect the following information:

- Country and setting
- Study design
- Description of the service
- Years during which data were collected
- Inclusion/exclusion criteria for participants
- Numbers referred
- Numbers assessed
- Demographic characteristics - age (at referral and/or at assessment of other characteristics); ethnicity; socio-economic status; other PROGRESS-plus factors
- Gender-related characteristics - gender identity; gender/sex recorded at birth; diagnosis of gender dysphoria (DSM)/gender incongruence (ICD); age at onset of gender dysphoria/gender incongruence; social transitioning
- Health characteristics – depression; anxiety; suicidality; self-harm; eating disorder; autism; attention deficit hyperactivity disorder (ADHD)

- Other contextual characteristics – including adverse childhood experiences, victim status and family context
- General population reference comparator data for demographic, gender-related and health and other contextual characteristics – where contemporaneous comparative data for the characteristic is presented in the study report (either through primary research or by quoting an external source) for the same country/region.
- Numbers who were:
    - considered eligible for medical intervention
    - received medical intervention (by intervention type)
    - received psychological care while under the care of a specialist gender service
    - provided with fertility preservation options
    - desisted
    - de-transitioned
    - re-transitioned
- Average waiting times
- Time interval(s) between referral, assessment, diagnosis.

We will collect data relating to the 0 to <18 age group at the start of the study separately from data relating to the 18-25 age group at the start of the study, where available. We will collect data throughout the subsequent care pathway with no upper limit on follow-up.

2.6 Assessment of risk of bias or methodological limitations

We will assess risk of bias in the main quantitative results. We prefer to assess risk of bias in specific study results rather than methodological quality of the study for several reasons. We regard risk of bias as more relevant than quality because results of well-conducted studies can be biased for reasons beyond the control of the investigators. Furthermore, not all aspects of high-quality research introduce biases (e.g. conducting a sample size calculation or obtaining ethical approval). Furthermore, different results from the same study can be at different risks of bias, for example if they have different degrees of missing data or use different methods of ascertaining presence of the condition of interest.

The evidence sought by this review is descriptive and non-comparative and will mainly be in the form of proportions. We will assess risk of bias in proportions (including prevalences) using a tool developed by PERSyst - a progression from the earlier RoB-PrevMH tool [39]. When assessing risk of bias for repeated cross-sectional studies, the key question is whether measurement or population definitions have changed over time. As such, for RQ 1 and RQ 2, changes over time will be misleading only if there are differences over time in how the denominator is defined (i.e. changes to the target population or sample selection methods) or how the numerator is defined (i.e. changes in the condition of interest or ways of measuring/diagnosing it); sources of bias that are unchanging over time will not affect patterns of change. Assessment will be performed in duplicate by two reviewers independently, with disagreements resolved by consensus, or with recourse to a third reviewer.

We will assess qualitative studies using the CASP tool, which is a widely used and validated tool [40]. To support consistent application of the tool within the team and across studies, we will develop and pilot detailed internal guidance. To support the use of the GRADE-CERQual tool in assessing the overall certainty of evidence [41], we will specify our level of concern (significant, moderate, minor, or none) in the methodology and provide reasons for any concerns in the appraisal summary. Any disagreements regarding the CASP appraisal will be resolved by discussion or by consultation with a third reviewer.

2.7 Synthesis methods

2.7.1 Quantitative synthesis

Our intended primary analysis will exclude results considered to be at high or serious risk of bias and results not from peer-reviewed publications. This will be supplemented by sensitivity analyses including all relevant results, although our strategy may depend on the amount of evidence available for the intended primary analysis. Our focus in RQ 1 and RQ 2 is on changes (in prevalence of gender dysphoria or numbers presenting for gender services) over time. Our primary synthesis for these RQs will be graphical: we will plot data points with a horizontal time axis, connecting points from the same study. Prevalences will be presented on the natural scale. Numbers of presentations will be scaled to allow superimposition on the same plot; such scaling will not impact on the visual impression of trends over time.

We will consider whether it is appropriate to provide summary estimates of levels, prevalences and proportions for RQs 3 and 4, depending on the similarities among included studies. Where multiple studies have measured the same condition or characteristic, fixed-effect and random-effects meta-analyses will be performed. We will transform proportions to the logit scale prior to synthesis. For random-effects meta-analyses, we will estimate between-study variance using restricted maximum likelihood and we will adjust the confidence intervals using the Hartung-Knapp method [42]. We will present and interpret meta-analysis results using 95% confidence intervals and will not use thresholds for statistical significance. Heterogeneity across studies will be quantified statistically using the between-study standard deviation and may be expressed in results of random-effects meta-analyses using prediction intervals. If it is not appropriate or possible to conduct a meta-analysis then we will summarize the results using alternative methods, following ideas described in the *Cochrane Handbook for Systematic Reviews of Interventions* [43].

For all RQs, our primary interest is in children and young people up to 18 years of age (specifically, up to the day before their 18th birthday). Where data allow, we will undertake subgroup analyses for questions about characteristics at presentation and progression through care pathways, according to the following participant-level characteristics:

- gender identity
- sex recorded at birth;
- age at presentation (particularly for a comparison of 0-<18 years versus 18-25 years);
- co-occurring mental health issues;
- family context; and
- type of clinical service/healthcare provider (including private vs public when both are available in the same country; and DIY).

2.7.2 Qualitative synthesis

The qualitative evidence will be synthesized through thematic synthesis [44]. In this approach, the researchers take a largely inductive approach to identifying and labelling themes that occur across the studies. The nature of the likely source material of interest (a mixture of descriptions of actual experiences, views and interpretations of these experiences, and wider social and cultural influences on those experiences) is well-suited to thematic synthesis.

Thematic synthesis will be used to explore the perspectives and experiences of individuals, carers, and healthcare professionals, as reported in the results, findings, and/or conclusions sections of the studies. This method is widely used for synthesizing qualitative evidence [44,45] and involves three key stages:

- *Coding*: We will closely engage with each study through line-by-line reading and initial coding based on themes identified through discussions with our young trans collaborators. We will also draw on the NHS England 'Interim service specification for specialist gender incongruence services for children and young people' [46] to identify initial organizing themes relating to care pathways. New insights will be captured with additional codes, including both original participant quotes (first-order data) and authors' interpretations (second-order data), although the method does not typically differentiate between the two orders of data in the actual synthesis process.
- *Descriptive themes*: Codes may be grouped based on similarities and differences, to form higher-level descriptive themes.
- *Analytical themes*: These will be developed by critically examining the descriptive themes in relation to the review question and ensuring interpretations align with the original studies.

At least two reviewers will conduct coding and theme development, with discussions with the broader team including our young trans collaborators to check interpretations.

Conceptual closeness to the data can be lost when dealing with large numbers of studies in a qualitative evidence synthesis. Therefore, if we identify a large number of studies, we may need to invoke a richness/thickness approach [45]. A richness / thickness approach entails including only those studies with conceptually rich and contextually thick data [45], thereby providing the most information to the synthesis. Criteria for determining richness and thickness would be set before the synthesis stage.

2.8 Certainty of the evidence

Our certainty in the body of evidence for each synthesis result will be assessed using the five considerations proposed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group. For quantitative evidence, we will judge the domains of imprecision, inconsistency, indirectness, risk of bias, and (non)reporting bias. Each domain will be rated as 'no concerns', 'serious concerns' or 'very serious concerns' by one reviewer and checked by a second reviewer. If any domains are rated serious or very serious concerns, we will report reasons for this. Based on these domain-level assessments, we will present our overall certainty or confidence in the body of evidence for each synthesis result as high, moderate, low or very low.

For syntheses of qualitative research, we will use the GRADE-CERQual tool [41] to assess our confidence in the body of evidence synthesis findings. We will consider methodological limitations in the included studies, adequacy of the data, coherence across the body of evidence, and relevance of the findings. For GRADE-CERQual, the levels of concern are 'no or very minor concerns', 'minor concerns', 'moderate concerns', or 'serious concerns'.

3 Updating the living systematic review

We plan to repeat searches of MEDLINE, PsycInfo, CINAHL, medRxiv and PsyArXiv every three months to identify new eligible studies. If the search string changes, we will report this. The OpenAlex network graph search will also be repeated every three months on the same cycle, except that we will progress to using OpenAlex records sourced or matched from the growing corpus of reports of studies included in this suite of four living systematic reviews as the seed records. We will also add an auto-update search of the OpenAlex dataset using the same set of seed records. In this auto-update search, seed records are subscribed to a machine learning 'recommender' model implemented in EPPI Reviewer

[47]. The model will automatically score all new records prospectively added to the OpenAlex dataset in each monthly snapshot and recommend those most similar to the seed records, ordered by a similarity score. The top 250 ranked records will be imported from auto-update searches of each monthly OpenAlex snapshot on a three-month cycle to coincide with the repeated searches of bibliographic databases and preprint repositories.

We will also consider the feasibility of adding a third kind of OpenAlex search known as a 'custom search'. OpenAlex custom searches are essentially the same as conventional Boolean searches of bibliographic databases, using a combination of OpenAlex concepts and keywords, except with a (currently) more limited set of Boolean operators available, compared with searches of bibliographic databases such as MEDLINE. Common and unique yields from each resource searched for updating these living systematic reviews will be investigated using a Study Within A Review (SWAR) framework. If the range of resources used in the search changes based on the results of the SWAR, or for any other reason, we will report this. Duplicate records will be identified and removed using the same two-stage process already described in methods for the baseline reviews.

The same processes as used in the baseline review will be implemented to screen newly identified records for eligibility at each update. If new evidence relevant to the review is identified, we will assess its potential to change the findings of the previous iteration of the review substantially. Criteria for consideration of full incorporation of the evidence into the review will be: identification of evidence that has the potential to modify existing synthesis findings; identification of a new intervention type; and identification of a substantially new outcome type. If the studies merely corroborate what is already in the synthesis, this would not trigger a full update. If, after a 12-month period (i.e., after 4 surveillance cycles), no updated synthesis has been triggered, we would consider whether to integrate any new findings and generate an updated version of the report. This would allow for updates to the precision of the findings, even if the conclusions themselves have not changed.

A versioning system will be used to report each update, to indicate any added evidence and to record when each update has been performed. After the first iteration of the review, suitability and efficiency of the methods used will be considered and if necessary, approaches of data extraction and/or synthesis may be adapted accordingly and documented. Any deviations from this protocol will be reported along with justifications. When the review is in living mode, the potential of using machine learning (including large language models) to automate study selection and data extraction will be examined. Should these technologies be able to save manual effort without reducing the reliability of the review, we may integrate these into our overall workflows.

3.1 Ending the living mode of the review

Updates to each specific review question in the living mode may be discontinued if one or more of the following circumstances occur:

- Sufficiently certain/confident answer to the research question (e.g. contributing quantitative syntheses are judged at least as moderate certainty or qualitative syntheses as moderate confidence)
- The research question ceases to be relevant
- Funding ends

4 Dissemination of information

The findings of the review will be published open access in peer reviewed journals and promoted on our Evidence Synthesis Groups' websites. An evidence review will be provided to NHS England. Further dissemination options will be developed with our public contributors and with an expert advisory group. A plain language summary will accompany the review.

5 Data availability

Quantitative data extracted during the review will be available in a GitHub repository. Should a quantitative synthesis be conducted, R code for the analysis will also be uploaded. The repository will be updated for each iteration of the review with any new data clearly highlighted.

6 Software

We will use EPPI-Reviewer Systematic Review Software for study selection and data extraction. Available at: https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=2914

Quantitative data synthesis will be conducted in R statistical software.

7 Competing interests of authors

None of the authors declare a competing interest.

8 Acknowledgements

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Appendix 1: glossary of key terms as used in this document

'DIY' ('do-it-yourself') Interventions	Medical treatments (most commonly hormonal treatments) which are accessed without direct involvement or supervision from medical professionals.
Gender-affirming (or gender-affirmative) care	Any single or combination of a number of social, psychological, behavioural or medical (including hormonal treatment or surgery) interventions designed to support and affirm an individual's gender identity [1].
Gender dysphoria	The discomfort or distress experienced by a person whose gender identity does not align with their sex recorded at birth. The term can also refer to a clinical diagnosis included in the DSM-5-TR [2].
Gender identity	A person's innate sense of their own gender, whether male, female, or something else, which may or may not correspond to their sex assigned at birth [3].
Gender Incongruence of childhood	Gender incongruence of childhood is characterized by a marked incongruence between an individual's experienced/expressed gender and the sex recorded at birth in pre-pubertal children. It includes a strong desire to be a different gender than the registered sex; a strong dislike on the child's part of his or her sexual anatomy or anticipated secondary sex characteristics and/or a strong desire for the primary and/or anticipated secondary sex characteristics that match the experienced gender; and make-believe or fantasy play, toys, games, or activities and playmates that are typical of the experienced gender rather than the assigned sex. The incongruence must have persisted for about 2 years. Gender variant behaviour and preferences alone are not a basis for assigning the diagnosis [3]. The term 'gender incongruence' can also be used to refer to a clinical diagnosis for someone who is trans [4].
Gender incongruence of adolescence or adulthood	Gender incongruence of adolescence and adulthood is characterized by a marked and persistent incongruence between an individual's experienced gender and the assigned sex, which often leads to a desire to 'transition', in order to live and be accepted as a person of the experienced gender, through hormonal treatment, surgery or other health care services to make the individual's body align, as much as desired and to the extent possible, with the experienced gender. The diagnosis cannot be assigned prior the onset of puberty. Gender variant behaviour and preferences alone are not a basis for assigning the diagnosis [5]. The term 'gender incongruence' can also be used to refer to a clinical diagnosis for someone who is trans [4].
Gender non-conforming	A person whose gender expression doesn't align with societal expectations of gender. Both cis and trans people can be gender non-conforming [4].

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Appendix 2: search strategy for Ovid MEDLINE

Ovid MEDLINE(R) ALL <1946 to October 08, 2025>

1 GENDER DYSPHORIA/ 1203

2 (gender* adj3 dysphori*).mp. 2890

3 (gender* adj3 incongruen*).mp. 666

4 (gender* identit* and (dysphori* or incongruen*)).mp. 1564

5 (sex* adj3 dysphori*).mp. 102

6 (discordance and gender* and sex*).mp. 220

7 (gender* adj3 identit* adj3 disorder*).mp. 675

8 gender* disorder*.mp. 183

9 (Gender Identity/ and Child Behavior Disorders/) or ((gender* identit* and (behavi* adj3 disorder*)) or gender* disturb*).mp. 308

10 or/1-9 4349

11 exp Child/ or Child Behavior/ or Child Health/ or Child Welfare/ or Psychology, Child/ or Child Psychiatry/ or Child Health Services/ or Child Development/ 2313782

12 Minors/ 2935

13 (infant* or child* or minors or boys or boyhood* or girls or girlhood* or juvenil*).mp,jw. 3774591

14 pediatrics/ 60399

15 (pediatric* or paediatric* or peadiatric*).mp,jw. 1043975

16 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ or Psychology, Adolescent/ or Adolescent Psychiatry/ or Adolescent Health Services/ or Adolescent Medicine/ or Adolescent Development/ 2358622

17 exp Puberty/ 19899

18 (adolescent* or adolescence or preadolescen* or pubescen* or prepubescen* or postpubescen* or pubert* or prepubert* or postpubert* or teens or teenage* or tween* or preteen* or juvenile* or youth or youths).mp,jw. 2653744

19 (gonadarch* or menarch* or (menstruat* adj2 (onset or start*)) or pubarch* or spermarch* or semenarch*).mp. 13597

20 (young* adj (people* or persons or adult* or men or "men's" or women* or male* or female*)).mp. 1365463

21 emerging adult*.mp. 5557

22 (transinfant* or transchild* or transminor* or transboy* or transgirl* or transyoung* or transyouth* or transteen* or transtween* or transadoles* or transjuvenil*).mp. 17

23	or/11-22	5791863
24	10 and 23	2328
25	exp animals/ not humans/	5382439
26	24 not 25	2323
27	(editorial or news or comment or case reports).pt. or case report.ti.	4333605
28	26 not 27	2035