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Health Technology Agency

CADTH Health Technology Review

Early Intervention Programs for Adolescents and Young Adults with Eating Disorders – Project Protocol

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Questions or requests for information about this report can be directed to **Requests@CADTH.ca**

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Abbreviations

CI	confidence interval
DSM	Diagnostic and Statistical Manual of Mental Health
ECHTA	Equity Checklist for Health Technology Assessments
HTA	health technology assessment
MA	meta-analysis
PICO	Population, Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analyses
SR	systematic review
RCT	randomized controlled trial

Introduction and Rationale

People hospitalized due to eating disorders are reported to have mortality rates 5 to 7 times higher than the general population.[1] During the COVID-19 pandemic, the number of youth seeking treatment for eating disorders in Canada increased – with the Canadian Institute for Health Information (CIHI) reporting a more than 50% increase in hospitalizations for young women with eating disorders.[2,3] Those numbers are likely lower than the actual number of people with illness due to the underrepresentation of youth who may not be presenting to hospital because of issues with access to care or other cultural or social barriers to accessing treatment, in addition to the existence of access restrictions put in place during the COVID-19 pandemic. The increase of these hospitalizations underscores the importance of early intervention and prevention. Additionally, many people, even with severe illness, will not meet the criteria for medical admission. In Canada, there is currently limited ability for people outside of major urban centres to access care options for eating disorders, particularly inpatient care. Access to treatment is also impacted by access to diagnosis and other factors associated with marginalization (e.g., gender).[4] An additional barrier to mental health care, including eating disorders, is that it is often not publicly funded, making it financially out of reach for many to receive.

While there is currently no consensus on the definition of what 'early intervention' means in relation to eating disorder treatment, the general definition of early intervention is "the detection of illness at the earliest possible point during the course of a diagnosable disorder, followed by the initiation of stage-specific, tailored or targeted evidence-based treatment, which is adapted and sustained for as long as necessary and effective." (p. 321).[5] The authors of a systematic review determined that the average duration of untreated eating disorders before the first treatment ranges from 29.9 months for anorexia nervosa, 53.0 months for bulimia nervosa, and 67.4 months for binge eating disorder, where disease onset was determined through either self-reporting or clinician interview.[6] There is some uncertainty about the relationship between time to treatment initiation and patient outcomes, such as the likelihood of disease remission.[6] Earlier identification and treatment of adolescents and young adults with eating disorders can aid in the management of the eating disorder while it is relatively mild and aid in preventing negative medical outcomes before the condition becomes chronic. Preventing hospitalizations, morbidity, and mortality are some key goals of early intervention programs.

Early intervention programs may include components such as telehealth or virtual care, guided self-help applications or programs, digital tools for self-monitoring, and family-based interventions. Health care providers involved in the development and delivery of early intervention programs include but are not limited to general practitioners, nurse practitioners, nurses, occupational therapists, dieticians, social workers, counsellors, and clinical psychologists. These interventions may be delivered in various care settings, including outpatient hospital-based clinics, and primary or community care, out-of-hospital and without specialists.

Defined early intervention programs for adolescents and young adults with diagnosed eating disorders are not currently an established option for treatment in Canada. Some people may receive early intervention for eating disorders; however, it does not seem like these early interventions are delivered in a consistent way. There is some consensus in the clinical community that promoting earlier interventions for adolescents and young adults with eating disorders can significantly reduce health care and human resource costs and result in better patient outcomes, such as avoided hospitalizations.[5] Given the resourcing challenges associated with the provision of adequate and comprehensive care for adolescents and young adults with well-developed eating disorders, implementing early intervention programs represents an opportunity for health systems in Canada to reduce costs and improve health outcomes.

For clarity, CADTH has adopted the following definitions in this health technology assessment (HTA):

- an adolescent or young adult is any person between 10 and 25 years of age[5,7,8]
- early intervention includes any treatment or intervention that is provided within the first 3 years of diagnosable disorder[5]
- early Intervention programs are those delivered by community or health care-based organizations that offer interventions to treat adolescents living with eating disorders within the first 3 years of diagnosable disorder, which may include multidisciplinary approaches to care.[5]

Objective

The objective of this HTA is to determine clinical, economic, and social and ethical factors that decision-makers may consider when seeking whether to implement publicly funded early intervention programs for adolescents and young adults with eating disorders in Canada. In addition, this HTA aims to provide decision-makers with some insight on equity considerations for early intervention programming for adolescents and young adults with eating disorders and how they might be implemented equitably.

To do this, CADTH will conduct an HTA that:

- Engages people with lived experience of eating disorders, either as people with direct experience themselves or as caregivers, to understand what they consider to be key treatment priorities for early intervention programs and to identify potential challenges in meeting these priorities were early intervention programs to be publicly funded.
- Assesses the clinical evidence regarding the effectiveness, harms, and composition of early intervention programs for adolescents and young adults with eating disorders.
- Assesses the economic evidence regarding the cost-effectiveness of early intervention programs for adolescents and young adults with eating disorders.
- Describes the social and ethical value claims that characterize the conceptualization and practice of early intervention programming for adolescents and young adults with eating

disorders in order to help understand considerations relevant to the context of eating disorder care in Canada.

A final report will document all the analyses produced and patient engagement activities conducted as part of this project. In the Discussion section, the HTA project team will provide reflection on how the information collected across each of the above features relate to one another and may impact the potential implementation of early intervention programs for adolescents and young adults with eating disorders in Canada. What this means is that the role of the Discussion section is to provide a broad picture of the sorts of challenges decision-makers may need to navigate in order to equitably implement early intervention programs that are supportive of adolescents and young adults with eating disorders in their jurisdiction. This does not mean that the HTA is pointed toward the definite implementation of early intervention programs, but rather that the Discussion section will assume various jurisdictions may choose to implement early intervention programs regardless of the findings from any single domain of evidence assessed in this HTA (i.e., clinical effectiveness and safety, cost-effectiveness and resource requirements, or social and ethical dimensions). Given the variety of health care systems that may be interested in implementing early intervention programs, the Discussion section will focus on providing implementation considerations that have relevance across multiple jurisdictional settings.

Equity

This HTA draws on the conceptions of health equity articulated by Braveman et al.[9] in order to highlight equity considerations across all components of the final report. According to that definition, health equity means, "everyone has a fair and just opportunity to be as healthy as possible."(p.2)[9] Achieving this ideal, however, is not as straightforward as ensuring that there is an equal distribution of the most clinically effective health technologies. Instead, Braveman et al. suggest that successfully attaining health equity requires working toward "removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to good jobs with fair pay, quality education and housing, safe environments, and health care."(p.2)[9]

This broadened focus on the social determinants of health, and their impact on health equity, is relevant to this HTA given the longstanding archetype of the eating disordered patient as a thin, young, white, affluent, cisgender female.[10-12] While this archetype has been increasingly challenged by empirical data highlighting that anyone can be affected by an eating disorder,[13-16] new treatments and care approaches continue to be developed using this archetypal patient as the primary research participant.[17] Not only does this perpetuate the myth that eating disorders primarily affect thin, young, white, affluent, cisgender females, but it can also limit the relevance of novel treatments for people who do not fit the archetype.[10,12,18] For racialized, 2SLGBTQ+, or otherwise oppressed adolescents and young adults, this may be further compounded by well-intentioned overcorrections that conflate their personal experiences of discrimination and distress around food with those of a broader social identity (e.g., transgender) that

allows providers to assume a priori knowledge on where their disordered eating has emerged from and why.[19] Not only can this be disempowering, but it may also lead to these adolescents or young adults being misdiagnosed (or missed altogether) and referred onto ineffective or inappropriate treatment options.[19] This possibility is particularly pertinent in rural settings in Canada, where people who identify as 2SLGBTQ+, Indigenous, or from other minority cultural or ethnic origins, have been described as "alarmingly" under-resourced in eating disorder care.[20] For many, this may further compound the effects of the persistent and systemic discrimination they already experience in health care settings across Canada.[21-23]

With these challenges in mind, equity considerations highlighted throughout this HTA will focus on 2 overarching domains: equity of access and equity of outcomes.

Equity of access to early intervention programs will be split across 2 related, but distinct, components of access: potential and realized access.[24] Potential access is concerned with one's ability to engage with care services at "both the contextual (health policy, financing) and individual (regular source of care, health insurance, income) levels."(p.10)[24] Given the concerns highlighted above, we would add that the contextual level of potential access includes research and program development. Some examples of equity considerations around potential access may include those related to resource requirements for early intervention programs and their availability across various jurisdictions, or even which eating disorders are described as being treatable through these programs. *Realized access* concerns the actual use of services. This complements the notion of potential access and looks at how often people access health care services or who is accessing these services. An example of an equity consideration around realized access may be related to identifying the characteristics of people accessing early intervention programs and whether these are representative of the broader population of adolescents or young adults with eating disorders.

In addition to equity of access, this HTA will examine considerations related to equity of outcomes. Examples of equity considerations related to outcomes include those related to programmatic outcomes, such as dropout from early intervention programs (who and why?), and those related to health or well-being outcomes for adolescents or young adults with eating disorders, such as how successful health outcomes are defined across early intervention programs and whether there are disproportionate levels of attainment of these outcomes between different groups.

An equity perspective will be incorporated across all sections of this HTA and will be supported by the project team's engagement with the Equity Checklist for HTA (ECHTA).[25] ECHTA has been developed specifically for HTA practitioners from diverse disciplinary backgrounds and helps to prompt multidisciplinary reflection on how equity considerations may appear at various stages across the review process.

Patient Engagement

CADTH involves patients, families, and patient groups to improve the quality and relevance of our assessments, ensuring that those affected by the assessments have an opportunity to contribute to them. CADTH has adopted a Framework for Patient Engagement in HTA. The framework includes Standards for Patient Involvement in Individual HTAs and is used to support and guide our activities involving patients.

For this HTA on eating disorder programs, the belief that individuals who have experienced disordered eating have knowledge, perspectives, and experiences that are unique and contribute to essential evidence for HTA will guide our patient engagement activities.

Invitation to Participate and Consent

CADTH will engage individuals who have experience with treatment for eating disorders. They are not meant to represent all individuals in Canada who engage with eating disorder treatment; rather, we are interested in learning from a diversity of experiences and perspectives. Participants will receive an honorarium for their time.

Potential participants will be identified through CADTH connections with eating disorder patient groups and mental health groups. A CADTH Patient Engagement Officer will contact potential participants by email and phone to explore their interest to become involved. The preliminary request will include the purpose and scope of the project, the purpose of engagement, and the nature of engagement activities. The Patient Engagement Officer will obtain participants' informed consent to share their de-identified information and comments with CADTH staff.

Engagement Activities

People with direct experience of an eating disorder and caregivers will be engaged throughout the process by various methods. Upon completion of the final report, participants will be invited to provide feedback on the clarity of the writing and comment on the relevance of the findings to patients and families living in Canada. Additionally, conversations with participants around equity will be reflected on and considered as the team consults the ECHTA.[25] Participants will be asked if they feel their contributions to the project are reflected in the final draft of the report, and revisions will be made if needed.

Reporting

The final report will include the GRIPP2 Short Form reporting checklist[26] and include the outcomes, discussion, and reflection items, as suggested by that guidance, to outline the process of engagement and where and how participants' contributions were used in the assessment. The Patient Engagement

Officer will keep track of patient engagement activities and interactions in detailed notes and communications.

CADTH will provide reflections and critical perspectives on participant involvement for patients and families accessing eating disorder programs, as well as the research team, in the final report. A link to the final assessment will be shared.

Deliverables

A final report detailing all analyses conducted to achieve the objective will be published.

Research Questions

The HTA will explore the following research questions. Details on the specific interventions and outcomes for clinical effectiveness and harms are included in Table 1.

Clinical Effectiveness and Harms

What is the clinical effectiveness of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?

- What are the clinical components of early intervention programs?
- How are different patient populations affected by early intervention programs?
- What components of early intervention programs affect patient specific outcomes?

What are the clinical harms of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?

- What are the potential harms associated with early intervention programs?
- What are the risks involved in early intervention programs for different patient populations?

Health Economics

- What is the cost-effectiveness of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?
- What are the resources required for implementing an early intervention program for the treatment of adolescents and young adults living with an eating disorder?

Social and Ethical Dimensions

- How has early intervention for adolescents and young adults living with eating disorders) been conceptualized and practised as supportive of these adolescents, young adults, their families and the health care systems responsible for their care?
- What social and ethical considerations can be identified with regard to the ideals, goals, and values embedded in the conceptualization and practice of early intervention, or in the relationship between the 2, that are relevant to adolescent and young adult eating disorder care in Canada?

Methods

To inform the preparation of this protocol, a preliminary scoping review of the existing literature, including HTAs and systematic reviews was conducted. This protocol was written a priori, using appropriate reporting guidelines (e.g., the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols ([PRISMA-P]) for guidance on clarity and completeness, and will be followed throughout the study process. Any deviations from the protocol will be disclosed in the final report, and updates will be made to the PROSPERO submission accordingly (registration number: CRD42023431402).

Clinical Effectiveness and Harms

Research Questions

The following research questions will address the objective of the clinical systematic review:

1. What is the clinical effectiveness of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?
    a) What are the clinical components of early intervention programs?
    b) How are different patient populations affected by early intervention programs?
    c) What components of early intervention programs affect patient specific outcomes?
2. What are the clinical harms of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?
    a) What are the potential harms associated with early intervention programs?
    b) What are the risks involved in early intervention programs for different patient populations?

Study Design

A systematic review (SR) will be conducted to address research question 1 and 2. A predefined protocol (as described herein), which is guided by standard SR methodology, will be conducted for the review (refer to the Methods section).

This protocol for the SR was informed by an informal scoping search of existing literature conducted by 2 researchers with the goal of determining the feasibility of conducting a formal SR of relevant clinical literature. The results of the informal scoping search provided moderate confidence that enough primary literature related to the use of early intervention programs for the treatment of adolescents and young adults living with eating disorder would be available for review using a systematic method. Through the informal scoping search, it was determined that there is a high degree of heterogeneity across potential primary studies that may be included in the clinical review. Due to this heterogeneity, a quantitative synthesis of potential findings would likely be inappropriate, thus favouring a narrative synthesis approach for the data analysis of outcomes. Despite these findings from the informal scoping search, both quantitative and narrative synthesis methods will be considered depending on homogeneity of the literature search findings.

Based on the informal scoping search of existing literature, there is a lack of recent and relevant syntheses of evidence assessing the effectiveness and/or safety of formal early intervention programs for the treatment of adolescents and young adults living with an eating disorder. As a result, an overview of SRs or an update of existing SR would not be an appropriate or feasible method to inform the research questions of the current review due to the lack of relevant evidence syntheses. Therefore, a de novo SR of relevant primary studies examining the effectiveness and/or safety of formal early intervention programs for the treatment of adolescents and young adults living with an eating disorder would help address the objective of this report. This approach allows for the assessment of the population, intervention, comparator(s), and outcome(s) – PICO – elements in a manner suitable to address the research questions.

In an effort to capture equity considerations throughout this SR of clinical effectiveness and harms, the ECHTA checklist will be used as a prompt to help identify and reflect on equity consideration relevant to both the analysis of potential evidence and within the impact of the findings (i.e., how might the findings of this SR inform equity considerations for early intervention programs).[25] In addition, a special focus on the populations using early intervention programs will be considered using PROGRESS-Plus Factors[27] to include and assess which populations are accessing early intervention programs. The aim of addressing equity considerations within this SR is to assess and provide context related to both potential and realized access for early intervention programs, as highlighted above.

The purpose of this SR is to identify, gather, synthesize, and summarize relevant evidence to answer the research questions to support the objectives of this report with a focus on equity for early intervention programs.

Literature Search Methods

An information specialist will develop and conduct a literature search for clinical studies, using a peer-reviewed search strategy according to CADTH's *PRESS Peer Review of Electronic Search Strategies* checklist (McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. *J Clin Epidemiol*. 2016;75:40-46). The complete search strategy is presented in Appendix 1.

Published literature will be identified by searching the following bibliographic databases: MEDLINE via Ovid, Embase via Ovid, and the Cochrane Central Register of Controlled Trials (CENTRAL) via Ovid and PsycInfo via Ovid. All Ovid searches will be run simultaneously as a multifile search. Duplicates will be removed using Ovid deduplication for multifile searches, followed by manual deduplication in EndNote. The search strategy will be comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts will be developed based on the elements of the patient/population, intervention, comparison and outcomes (PICOS) framework and research questions. The main search concepts will be eating disorders, adolescents or young adults, and early intervention programs. The eating disorder concept was developed based on clinical definitions and keywords related to a variety of eating disorder conditions. Clinical trials registries will be searched: the US National Institutes of Health's clinicaltrials.gov, World Health Organization's International Clinical Trials Registry Platform (ICTRP) search portal, the European Union Clinical Trials Register and the European Union Clinical Trials Information System (CTIS).

No filters will be applied to limit the retrieval by study type. Retrieval will be limited to documents published between January 1, 2008 and December 31, 2023 and to the English or French language. Conference abstracts will be excluded from the search results.

The initial search will be completed in April, 2023. Regular alerts will update the database literature searches until the publication of the final report. The clinical trials registries search will be updated prior to the completion of the stakeholder feedback period.

Grey literature (literature that is not commercially published) will be identified by searching sources listed in relevant sections of CADTH's Grey Matters: A Practical Tool For Searching Health-Related Grey Literature, which includes the websites of regulatory agencies, HTA agencies, clinical guideline repositories, SR repositories, patient-related groups, and professional associations. Google will be used to search for additional internet-based materials. These searches will be supplemented by reviewing bibliographies of key papers and through contacts with experts and industry, as appropriate. The grey

literature search will be updated prior to the completion of the stakeholder feedback period. See Appendix 1 for more information on the grey literature search strategy.

Selection and Eligibility Criteria

The study eligibility criteria for the SR can be found in the following table.

Table 1: Selection Criteria for SR

Inclusion	Exclusion
Population	
Adolescents and young adults (between 10 and 25 years of age) who have been diagnosed or self-identified with any eating disorder Subgroups of interest: • Age • PROGRESS-Plus Factors[27] including but not limited to place of residence, race, ethnicity, culture, language, gender and sex, disability status, and socioeconomic status • Type of eating disorder • Stage of eating disorder (e.g., subclinical eating disorder, disease onset, late-stage disease) • Type of early intervention program	• Age < 10 year or > 25 years • Patient populations where eating disorder conditions are not the primary concern or reason for delivering or accessing an early intervention program
Intervention	
Any formal early intervention program for eating disorder(s)[a]	Intervention programs for eating disorders that do not fulfill the definition (e.g., not offered in a formal programmatic manner, not delivered at the early phase of illness)
Comparators	
Any alternative interventions for eating disorder treatment; no intervention (including waitlist); no comparator	Not applicable
Outcomes	
Question 1: Any outcomes in the following domains, irrespective of the follow-up duration and outcome ascertainment method: • personal recovery (e.g., self-efficacy, health-related quality of life measures, patient goal achievement,	Not applicable

Inclusion	Exclusion
patient functioning measures, recovery duration and sustainability) • clinical effectiveness (e.g., weight recovery, body mass index, change in symptoms, relapse prevention) • health care resource utilization (e.g., hospitalizations, emergency department visits, hospital length of stay, wait times, duration of untreated eating disorder and time to treatment) • program outcomes (e.g., treatment fidelity[b], user dropout, program end points) • social outcomes (e.g., social support, social isolation, impact on activities of daily living) **Question 2:** Any outcome in the following domains, irrespective of follow-up duration and ascertainment method: • program appropriateness (e.g., patient compliance to treatment, population or cultural competency) • treatment emergent adverse events (e.g., worsening of symptoms, emergency room visits, hospitalizations) • program withdrawal or discontinuation • personal harms (e.g., stigmatization)	
Study designs	
Comparative and noncomparative study designs, including: • randomized controlled trials • nonrandomized controlled clinical trials • cohort studies (controlled or uncontrolled) • case-control studies • before-and-after studies (controlled and uncontrolled)	• Cross-sectional studies • Case reports/series • Qualitative studies and qualitative evidence from mixed-methods studies • Evidence syntheses • Protocols and trial registers • Editorials, letters, and commentaries • Studies of any designs published as conference abstracts, presentations, thesis documents, or preprints
Time frame	
2008 to present[c]	Before 2008[c]

[a] Formal early intervention programs are those delivered by community or health care-based organizations that offer interventions to treat adolescents and young adults living with eating disorders within the first 3 years of diagnosable disorder, which may include multidisciplinary approaches to care.

[b] Treatment fidelity refers to the reliability of the administration of a treatment intervention.[28]

[c] Time frame is based on expert consensus with the knowledge of literature landscape and confirmation that a 15-year literature would be sufficient for this report.

Screening and Selecting Studies for Inclusion

The following will be considered when selecting studies for inclusion:

- all studies must meet the eligibility criteria outlined in Table 1
- for this review, adolescents and young adults are defined as individuals between 10 and 25 years of age
- there are no restrictions placed on sex or gender, ethnicity, comorbidities, setting, or severity of symptoms
- studies with wider populations (i.e., including children and/or adults) will be considered if any of the following are met:
    - findings for adolescents and young adults can be isolated (e.g., subgroup analyses)
    - greater than or equal to 80% of the sample consists of adolescents and young adults
    - the mean age plus or minus 1.5 standard deviation falls between 10 and 25 years
    - the interquartile range falls between 10 and 25 years.
- Eating disorders conditions refer to those that are either self-identified or formally diagnosed, and includes but is not limited to anorexia nervosa, atypical anorexia nervosa, bulimia nervosa, avoidant and restrictive food intake disorder, binge eating disorder, and other specified and nonspecified eating disorders.
- Diagnostic criteria for eating disorders may not be consistent throughout publication dates (i.e., earlier publications may rely of DSM-IV diagnostic criteria rather than DSM-5 diagnostic criteria); however, any diagnostic criteria used to determine a specified eating disorder will be considered in the context of the publication.
- Formal early intervention programs are delivered by community or health-based organizations which include trained workers specialized in eating disorder treatment.
- Early intervention programs must be delivered within the first 3 years of diagnosable disorder.
- Early intervention programs can be offered on a 1:1 or group basis, can be in person or virtual, and can be synchronous (i.e., where a trained provider engages a patient at the same time of delivering the intervention) or asynchronous (e.g., where a patient can use materials for intervention prerecorded by a trained provider but without requiring the provider to be present at the same time). Studies that have a larger scope than only adolescents and young adults living with eating disorders (e.g., studies with adolescents and young adults living with additional mental health concerns and/or substance use disorders) will be included if relevant findings related to early intervention programs primarily for eating disorders are reported in isolation.
- Adolescents and young adults living with eating disorder can receive concurrent interventions (e.g., early intervention therapy program and pharmacotherapy).

- For outcomes, all instruments used to collect clinical information and all time points during patient treatment are eligible for inclusion.

Exclusion criteria:

- Studies not meeting the eligibility criteria outlined in Table 1, duplicate publications or papers published in a language other than English or French.

This review will be limited to studies published in English or French. While there is evidence that suggests excluding non-English publications from evidence synthesis does not bias conclusions,[29,30] publications in French will also be included as CADTH has the capacity for reviewing in both official languages. In the event that multiple publications are identified for the same study, they will all be included and cited; however, only unique data will be extracted without duplication and the publications will be considered as a single study in the analysis. The first publication of the study will be considered the primary publication, while subsequent publications will be considered as associated publications.

Study Selection

The SR management software DistillerSR (Evidence Partners, Ottawa) will be used to facilitate study selection. We will use the DistillerSR's continuous reprioritization feature (DAISY) to expedite screening but not to automatically exclude any records. Two reviewers will conduct the study selection, beginning with a pilot round to independently screen 100 randomly selected articles in duplicate, after which they meet to resolve disagreements. Additional pilot rounds will be run as needed, for example, if there are major disagreements or changes to the selection criteria.

Once the reviewers are satisfied with their understanding of the selection criteria, they will independently screen titles and abstracts of all retrieved citations for relevance to the SR research questions following a liberal-accelerated approach, whereby selection by a single reviewer is required to include a study and exclusion by both reviewers is needed to exclude a study. Full texts of titles and abstracts that are judged to be potentially relevant by a single reviewer will be retrieved and independently assessed for possible inclusion based on the predetermined selection criteria outlined in Table 1. Discrepancies between reviewers at the full-text level will be discussed until consensus is reached, involving a third reviewer if required. One reviewer will screen the reference lists of the included studies and relevant SRs identified by the search for potentially relevant titles, and screen full-text publications of such titles for inclusion. If any potentially relevant studies published as summaries (e.g., conference abstracts, presentations) or in trial registries are identified, or further information is needed to determine the relevance of any study, authors will be contacted to confirm whether a full-text publication is available or for clarification. Authors will be contacted by email twice, one week apart, before abandoning attempts at retrieving further information.

The study selection process will be presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart. A list of studies selected for inclusion in the SR will be posted to the CADTH website for stakeholder review for 10 business days. Studies identified through stakeholder feedback on the draft list of included studies will be reviewed and considered for inclusion if appropriate. Studies identified through alerts before the period assigned for the stakeholder feedback on a draft report ends will be reviewed and incorporated into the analysis if they meet the selection criteria for the review. Relevant publications identified after the stakeholder feedback period for the draft report will be described in the discussion, with a focus on comparing their results with those obtained from the synthesis of earlier reports included in the review. Studies excluded after full-text review will be documented along with the reason for their exclusion.

Data Extraction

Data will be extracted directly into a review-specific Microsoft Excel workbook. The form will be piloted prior to beginning full data extraction to ensure that it is usable and that it completely and reliably captures the items of interest, while avoiding redundancies. In the pilot round, reviewers will independently extract data from 2 included studies, then meet to resolve disagreements through discussion. Additional pilot rounds will be run in the event of major changes and as needed until reviewers are satisfied with the contents and usability of the form. Formal data extraction will then be performed by one reviewer, and independently checked for accuracy and completeness by a second reviewer. Disagreements will be resolved through discussion until consensus is reached or through involvement of a third reviewer, if required. Relevant information to be extracted will include details of the study characteristics, methodology (e.g., study design), population, intervention, comparator, results, and the subgroups of interest listed in Table 1.

Attempts will be made to contact corresponding authors to obtain or clarify relevant data, if those data are needed for data synthesis, or to clarify conflicting relevant data in the included studies. Authors will be contacted twice over a period of 2 weeks, after which attempts to obtain further information will be abandoned. Relevant data will be deemed missing if numerical data supporting qualitative statements or findings presented in figures are absent. Furthermore, if data are not reported for an outcome, no assumptions will be made about its presence or absence. Relevant data will be deemed conflicting if there are discrepancies within the study (e.g., between the abstract and the main text of a publication) or between different publications of the same study. If the authors do not provide clarifications for the conflicting information, all data will be reported and the most conservative data available will be incorporated into data synthesis.

Critical Appraisal

Two reviewers involved in risk-of-bias appraisal will independently pilot the selected tools across 2 included studies of varying study designs if possible and meet to resolve disagreements, to ensure a mutual understanding of the tool and methodological intricacies across studies. After piloting, risk of bias will be assessed in duplicate by 2 independent reviewers. Any disagreements in the risk of bias for the domain-level and overall assessments will be resolved through discussion, with involvement of a third reviewer if consensus cannot be reached. In evaluating the risk of bias in the included studies, the risk-of-bias tools will be considered as guides and additional insight beyond the instruments' signalling items (e.g., other concerns about design or conduct) will be applied if necessary. Studies will not be excluded from the review based on the results of the risk-of-bias appraisal. However, the risk-of-bias appraisal results and how they affect the overall interpretation of study findings will be discussed for each potential outcome-comparison.

Outcome-level risk of bias of relevant randomized controlled trials (RCTs), based on the effect of assignment to the intervention (i.e., intention-to-treat effect), will be evaluated using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2).[31] The RoB 2 assessment tool facilitates the evaluation of potential biases across 5 domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. A judgment of low risk of bias, high risk of bias, or some concerns will be assigned for each domain. The overall risk of bias of each trial will be rated and designated as low risk of bias, some concerns, or high risk of bias based on the domain-level determinations. If a study is judged to have "some concerns" about risk of bias for multiple domains, its overall risk of bias might be judged as high. Where possible, we will attempt to predict the direction of the potential bias. A rationale will be provided for decisions about the risk of bias for both the domain-level and overall assessments.

Outcome-level risk of bias in nonrandomized studies will be assessed using the Risk of Bias In Nonrandomized Studies – Interventions (ROBINS-I).[32] This tool was chosen for ease of comparison to assessments of risk of bias in the included RCTs. ROBINS-I facilitates the assessment of risk of bias across 34 potential items in 7 domains: confounding, selection bias, measurement of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results. Each item is answered "yes," "probably yes," "probably no," "no," and "no information," with "yes" indicating low concern of a risk of bias, and "no" indicating significant concern. Risk of bias per domain per study will be assessed and used to assign an overall judgment of "low," "moderate," "serious," "critical," or "no information" to each study.[32] Where possible, we will attempt to predict the direction of the potential bias. A rationale will be provided for decisions about the risk of bias for both the domain-level and overall assessments.

Attempts will be made to contact corresponding authors to obtain or clarify missing or unclear information relevant to the risk-of-bias appraisal. Authors will be contacted twice over a period of 2 weeks, after which attempts to obtain further information will be abandoned.

Data Analysis and Synthesis

A narrative summary of study characteristics from studies identified through database and grey literature searches will be provided in tables, together with detailed descriptions in the main text for clarity. The study and patient characteristics will be considered in the analysis of the effectiveness and safety measures within and across the studies to determine the likelihood of clinical benefits (i.e., clinical effectiveness) or harm.

A narrative summary of the results of the risk-of-bias appraisals for each included study will be provided. Specifically, tables will be developed to present the answers to the questions within the risk-of-bias appraisal tools and a narrative description of the strengths and limitations of the included studies will be provided within the main text of the report to give the reader an overview of the methodological quality of the literature.

Narrative Synthesis

A narrative synthesis will be conducted as per existing guidance by Popay et al.[33] The within- and between-study relationships will be evaluated, and the findings about the direction and magnitude of any observed effects, trends, and deviations will be discussed by outcome-comparison. When possible, we will standardize the outcome measures used across the studies for ease of comparison. When this is not possible, outcomes will be reported in the measurement units used by the study authors. Findings will be interpreted with due consideration for the differences in the instruments of assessment across the studies. Data from different populations or different time points will not be combined (unless deemed appropriate) but rather described separately and compared. Data on specific subgroups of interest reported within studies will be narratively described and compared if appropriate. If relevant, visual displays will also be used to present the findings.

Quantitative Synthesis

In the event that data are sufficiently homogenous in clinical and methodological characteristics, an attempt will be made to pool outcome data of the included studies in a meta-analysis (MA). If deemed appropriate, MAs will be conducted for each outcome-comparison of interest reported across multiple studies via pairwise analysis using Der Simonian and Laird random effects model[34] in ReviewManager (v.5.3, the Cochrane Collaboration, Copenhagen, Denmark). The findings will be presented in forest plots. If data from certain studies cannot be entered into MA, they will be presented narratively alongside the MA and compared descriptively to the findings of corresponding MAs. Results from randomized and

nonrandomized studies will not be pooled together in the analysis. Instead, separate MAs will be conducted for these 2 types of study designs.

If available, dichotomous data will be summarized as risk ratios or odds ratios with corresponding 95% confidence intervals (CI). When the event rate in at least one study is zero, we will instead present the risk difference and 95% CI. Continuous data will be analyzed using either mean differences or standardized mean differences with 95% CIs. If both unadjusted and adjusted effects are reported, the unadjusted effects will be used in MAs of RCTs, and adjusted effects for nonrandomized studies. If multiple adjusted estimates of effects are reported, the one that is judged to minimize the risk of bias due to confounding will be used in MAs. Statistical heterogeneity will be assessed using graphical presentations (e.g., forest plots) and the I^2 statistic, which quantifies the variability in effect estimates due to reasons other than chance (i.e., sampling error).[35] A sensitivity analysis may be used to understand the robustness of the synthesized findings by removing studies (e.g., those at high risk of bias), or exploring the impact of different outcomes that may have been affected through decisions made during the review process. If there is substantial heterogeneity as a result of subgroup or sensitivity analysis in the pooled effect, findings may be presented narratively instead. As appropriate, the potential for reporting bias will be assessed visually using funnel plots and objectively using Egger's regression test and/or Begg's rank correlation test.[36-41]

Reporting of Findings

The SR will be prepared in consideration of relevant reporting guidelines (e.g., PRISMA,[38] PRISMA-HARMS,[42] PRISMA-Equity,[43] or Synthesis Without Meta-analysis [SWiM][44]) and will aim to meet criteria outlined in the A Measurement Tool to Assess Systematic Reviews 2 checklist.[45]

Health Economics

Review of Economic Literature

A review of the economic literature will be undertaken to provide evidence to address the following economic research question.

- What is the cost-effectiveness of early intervention programs for the treatment of adolescents and young adults living with an eating disorder?

Literature Search Methods

An information specialist will conduct a focused, peer-reviewed literature search for economic studies using the following bibliographic databases: MEDLINE via Ovid, Embase via Ovid, and the NHS Economic Evaluation Database (NHS EED) via Ovid. The main search concepts will be eating disorders, adolescents or young adults, and early intervention programs. CADTH-developed search filters will be

applied to limit retrieval to economic studies. Grey literature (literature that is not commercially published) will be identified by searching sources listed in relevant sections of CADTH's Grey Matters: A Practical Tool For Searching Health-Related Grey Literature. The search will be limited to English or French language documents published from January 1, 2008 to December 31, 2023. The initial search will be completed in April 2023. Regular alerts will update the search until project completion.

Any relevant studies identified will be described and referenced in the Summary of Results section. Studies excluded by full text will be documented, along with the reason for their exclusion.

Selection and Eligibility Criteria

Studies published in English or French that conducted a cost-effectiveness analysis will be eligible for this review. Studies must be in a population of adolescents and young adults between the ages of 10 years and 25 years engaging in a formal early intervention program for eating disorders. Where a formal early intervention program is defined as programs delivered by community or health care-based organizations that offer interventions to treat adolescents and young adults living with eating disorders within the first 3 years of diagnosable disorder, which may include multidisciplinary approaches to care. Intervention programs may include family-based treatment, cognitive behavioural therapy, psychotherapy, nutrition rehabilitation or peer support. Outcomes of interest should be measured in the domain of cost-effectiveness, such as costs and quality-adjusted life years, or other measures of health benefit as they become apparent. The following types of publications will be excluded: theses and dissertations, data presented in abstract form only, commentaries, case reports, and editorials. In addition, the following elements will render a study ineligible for inclusion: prevention programs, health promotion programs, and other exclusions as they become apparent.

Screening and Selecting Studies for Inclusion

A single reviewer will screen titles and abstracts for relevance to the economic research question. Microsoft Excel will be used to facilitate study selection and track screening. Full texts of potentially relevant articles will be retrieved and assessed for possible inclusion based on the predetermined selection and eligibility criteria. The study selection process and results will be presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.

The ECHTA checklist will be used to guide our consideration of equity throughout the HTA.[25] The checklist will provide prompts for ongoing reflections during the review of the economic literature to capture equity considerations both within the analysis of available evidence and the impact of findings (i.e., how might the findings of this review inform equity considerations for early intervention programs). The aim of addressing equity considerations within this review is to assess and provide context related to both potential and realized access for early intervention programs, as mentioned before.

Data Extraction

A single reviewer will extract relevant data using a predrafted data extraction form in Excel. We will extract relevant data on the following:

- publication source (i.e., author's name, location, publication year)
- study design and perspective
- study population
- interventions and comparators
- outcomes (e.g., health outcomes, costs, and incremental cost-effectiveness ratio).

Evidence Synthesis

The available evidence will be summarized by intervention and/or outcome. A narrative summary of study characteristics will be provided in tables, together with detailed descriptions in the main text for clarity. Each study's applicability to the research question will be described narratively in the main text by comparing the modelled population, adopted perspective, adopted interventions and any other study characteristics that may become apparent.

Cost-Effectiveness Analysis

Based on an informal scoping search of the existing clinical and economic literature, it was determined there is a high degree of heterogeneity across potential primary clinical studies. As such, it is likely that a quantitative synthesis of clinical outcomes will not be conducted, and therefore a de novo cost-effectiveness analysis cannot be conducted. In the event sufficient data are found, a protocol adjustment will be made, and CADTH will proceed with an economic evaluation.

Health Care Resource Inventory

In place of a cost-effectiveness analysis, an analysis will be conducted to address the following economic research question.

- What are the resources required for implementing an early intervention program for the treatment of adolescents and young adults living with an eating disorder?

Analytical Framework

To help inform decision-makers on implementation feasibility, a narrative summary of resource requirements for implementing and running an early intervention program will be described (e.g., number and type of health care worker, medical equipment, and so forth.). Program administrators and clinical experts will be consulted as a means of accounting for required health care resources needed for a program with a duration of more than 1 year in clinical practice in Canada. The resources captured will

be specific to the program, including all resources covered by the publicly funded health care system. Early intervention programs assessed will be specific to the expertise of surveyed experts, and existing programs available in Canada.

Social and Ethical Dimensions

Research Questions:

1. How has early intervention for adolescents and young adults living with eating disorders been conceptualized and practised as supportive of these adolescents, young adults, their families, and the health care systems responsible for their care?
2. What social and ethical considerations can be identified with regard to the ideals, goals, and values embedded in the conceptualization and practice of early intervention, or in the relationship between the 2, that are relevant to adolescent and young adult eating disorder care in Canada?

Study Approach

We will conduct an analysis of social and ethical dimensions related to the development and use of early intervention programs for adolescents and young adults with eating disorders. This work aims to support decision-makers when considering whether to implement early intervention programs despite the presently unsettled nature of what qualifies as an early intervention program in eating disorder care.[5] While there are some more established early intervention programs available for review (e.g., FREED programming from the UK), early intervention has also been described by content experts as an abstract ideal focused on "rapid access to care" rather than in reference to well-defined programmatic features or interventions. This lack of consensus around the features of early intervention programs can make it challenging for decision-makers to understand what, exactly, they are appraising and how these programs come to matter (or not) in their jurisdictions.

In light of this ambiguity, our review is meant to provide details about the variety of ways in which early intervention is conceptualized and currently practised, as well as to highlight social and ethical considerations decision-makers may face if seeking to implement early intervention programs. In particular, we will provide decision-makers with some clarity around:

- which actors frame, define, and shape early intervention for eating disorders
- how these actors frame, define, and shape early intervention for eating disorders (i.e., what is and what is not early intervention for eating disorders), and what values, ideals and meanings are embedded within the conceptualization and practice of early intervention for eating disorders (e.g., what a successful program looks like)

- which actors are excluded from that framing, defining and shaping of early intervention for eating disorders and how this might affect who does or does not benefit from the resulting forms of early intervention
- and how early intervention for eating disorders may (or may not) help address disparities in care (e.g., diagnosis, treatment, therapeutic relationships) and care outcomes, or other related inequities and injustices experienced by young adults and adolescents with eating disorders.

We approach this work with an understanding that health technologies, and the forms of care they are oriented toward, are neither value-free nor immutable. In other words, we understand the conceptualization and practice of any given technology as social and ethical. Practically speaking then, our work considers what is at stake in early intervention programs by exploring who is involved in their development and use, what outcomes are prioritized, who is (and is not) intended as an end-user and potential beneficiary, and how these intended end users might understand their need for, and intended outcomes of, early intervention. This work can provide insight into social and ethical considerations to inform decision-making around early intervention programs, including about who is likely to benefit, who is not, how benefit is defined, and how adolescents or young adults with eating disorders, or their families and caregivers, might value (or not) these ideals.

To better understand the stakes outlined above, we will also explore how concepts, practices, desired outcomes and intended end users respond to and change by the context in which early interventions are being practised. To do so, we will explore how factors like the sociopolitical conditions (e.g., racism, ongoing colonialism, eating disorder-specific legislation, and policy landscape) or resource and capacity challenges currently facing eating disorder care might impact, or be impacted by, the implementation of early intervention. Detailing the social and ethical dimensions associated with these external factors can provide decision-makers with some added clarity around existing injustices and inequities that they may need to navigate if seeking to implement early intervention programs.

Our review will complement the work being done across the larger HTA report, which will also include a literature review of the clinical effectiveness of existing early intervention programs and a review of their resource requirements.

Based on an initial conversation with eating disorder clinical and community health experts, there is a clear need for early intervention, but how that translates into a concrete program remains poorly defined. As a result, our work will remain open to the variety of ways that early intervention may be conceptualized and practised in eating disorder care. By acknowledging and engaging with the ongoing indeterminacy of early intervention, the goals, ideals, and values embedded within, and emerging from, early intervention programming will be clarified for decision-makers.

As both qualitative and ethical analyses are concerned with identifying, and providing insight into, the normative consequences of implementing health technologies, this review integrates the 2 forms of

analysis to provide a more comprehensive representation of the social and ethical considerations related to early intervention programs. Dimensions that we will be considering as "social" are those that are concerned with, but not limited to, the relationships between: people living with eating disorders and those involved in their care (e.g., family members or guardians, health care providers, and so forth.), knowledge claims or practices related to eating disorder care, social identities (e.g., 2SLGBTQ+, racialized, and differently abled peoples), social conditions (e.g., racism, colonialism, sexism, health care access, and food security), and conceptualizations of the value of early intervention programming. Examples of ethical dimensions include, but are not restricted to, claims related to: potential harms and benefits, vulnerability, equity (and considerations of who benefits or not), distributive justice (e.g., the fair distribution of benefits and burdens), relational justice (e.g., fair, nondiscriminatory relationships, recognizing dynamics of power, stigmatization, and marginalization), procedural justice (e.g., fair decision-making processes), priority setting, resource allocation, privacy, understandings of acceptable levels of risk, goals of care and treatment, respect for persons and communities, and ethical issues in the evidentiary basis for an intervention, including ethical consequences of choices in research design or conduct.

This protocol provides a general overview of methods to be used at each stage of the review. Keeping with the iterative nature of qualitative and ethics research, protocol refinement and amendment will occur at several stages as the review team responds to the set of eligible studies and available data for analysis. The potential for refinements and amendments are identified in each of the sections that follow. This iterative approach to protocol development and execution is not only consistent with the inductive principles of qualitative and ethics research, but also allows further reflection on the relationship between the available studies, broader project inputs, and decisions being made on study selection and analysis within the broader HTA. Any subsequent refinements or amendments will be documented along with their rationale.

Data Collection and Project Inputs

Data to inform this report will be drawn from consultations with clinical content experts, engagement with various other stakeholders (e.g., adolescents or young adults in recovery, family members, and allied health professionals), and a complementary review of published and grey literature. Ongoing collaboration and communication with the project team will also be used to assist in the clarification and identification of social and ethical considerations raised in other components of this HTA. Data sought from these inputs will focus on the identification of social and ethical dimensions of early intervention programs for adolescents and young adults with eating disorders.

Literature Search Methods

An information specialist will conduct a literature search on key resources including MEDLINE via Ovid, Philosopher's Index via Ovid, PsycInfo via Ovid, the Cumulative Index to Nursing and Allied Health

Literature (CINAHL) via EBSCO, and Scopus. The search strategy will be comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. CADTH-developed search filters will be applied to limit retrieval to citations related to ethical considerations or qualitative studies. The main search concepts will be eating disorders, adolescents or young adults, and early intervention programs.

Duplicates will be removed by manual deduplication in EndNote. Retrieval will be limited to the English or French language. The search will be completed in April 2023. The search strategy will be available on request.

Grey literature (literature that is not commercially published) will be identified by searching sources listed in the relevant section of CADTH's Grey Matters: A Practical Tool For Searching Health-Related Grey Literature. The grey literature search for social and ethical considerations will be conducted in May 2023. All search results will be limited to English or French language documents. Google will be used to search for additional internet-based materials. These searches will be supplemented by reviewing bibliographies of key papers and through contacts with experts and industry, as appropriate. Refer to Appendix 1 or more information on the grey literature search strategy.

Literature Selection and Screening

Literature will be screened by a single reviewer for relevance to the context of social and ethical dimensions of early intervention programming for adolescents with eating disorder based on our description of what qualifies as a social and ethical dimension above. As with the rest of the HTA, we will also focus on equity considerations as raised in Braveman et al.'s definition and using the Equity Checklist for HTA (ECHTA) and CADTH's rapid custom report of access and inclusion in adolescent eating disorder care as guideposts.

The selection of relevant literature will proceed in 2 broad stages. In the first stage, titles and abstracts of citations will be screened for relevance by the primary author and marked as either retrieve, unsure, or exclude. Publications will be marked retrieve if they identify social and ethical considerations related to:

- the emergence of early intervention programs as a possibility in the care of adolescents and young adults with eating disorders
- the purpose of early intervention programs and the unmet needs early intervention programs are meant to address
- the sorts of eating disorders early intervention programs are meant to address and for whom (e.g., are there populations of particular interest)
- determinations of eligibility for early intervention programs (e.g., diagnostic criteria, assessment tools)

- how motivation for care is conceptualized in early intervention and how decisions to proceed with treatment (or not) are navigated for those adolescents or young adults determined to be unmotivated
- how early intervention programs have been designed and by whom
- the practice (e.g., through clinical practice, health policy and organizational funding decisions) of early intervention programs with adolescents or young adults with eating disorders.

Publications marked unsure will be shared with additional reviewers for discussion on whether they should be retrieved for full-text review.

In the second stage, the primary author will read and assess the eligibility of all publications retrieved for full-text review. Publications meeting the above criteria will be included in the social and ethical dimensions report and those that do not will be excluded. If, at this time, there are more than 35 texts eligible for inclusion, the primary author and additional reviewers will discuss the adoption of a sampling strategy and document this strategy in the final report.

As a parallel process, grey literature, and other sources drawn from relevant bibliographies or in consultation with experts or other CADTH reviewers will be retrieved and reviewed following the selection criteria listed above. Both published and grey literature screening and selection will be iterative and remain open for adjustment throughout this review.

Data Analysis and Synthesis

Research Question 1

To address our first question we will map social and ethical dimensions of the conceptualization and practice of early intervention programs through qualitative description.[46] The goal of the work involved in addressing question 1 is to provide the foundation to conduct the comparative analysis of question 2, and to begin articulating a series of social and ethical considerations that may be relevant for decision-makers to consider in their appraisals of early intervention programs. To guide this mapping, we will pay particular attention to the following sensitizing questions:

- How has the concept of “early intervention” emerged within the care space of eating disorders and how is early intervention imagined as fitting into the larger eating disorder landscape?
    - And what actors (e.g., providers, policy-makers, people with eating disorders, caregivers, and so forth.) have been involved (or excluded) in the conceptualization, and practice, of early intervention and development of programs for eating disorders?
- Which eating disorders are identified as being treatable through early intervention programs and what are the goals of treatment?

- What criteria and tools are used to determine which adolescents and young adults (living with which eating disorders) are most likely to benefit (or not) from early intervention? How has "most likely to benefit" been defined to date and by whom?
- How do adolescents, young adults, their families, and their care providers navigate challenges related to motivation and consent for participating in an early intervention program? Are there distinctions based on eating disorder, stage of eating disorder, or age of the adolescent/young adult with an eating disorder? What other aims beyond treatment might early intervention be oriented toward (e.g., health care expenditure, safeguarding hospital resources, forth.)?
- What resources are involved in providing early intervention programs and how is their availability and distribution described?
- What are the characteristics of the adolescents and young adults included in the data from early intervention programs identified for assessment in this HTA's Clinical Effectiveness and Harms, and Health Economics reviews? Which adolescents and young adults have been able to access early intervention to date?
    - Are there early intervention programs, or conceptualizations of early intervention, that are not captured by the clinical and health economics reviews? If so, what are the features of these programs or conceptualizations and who is accessing them?

To do this work, we will conduct a qualitative content analysis, which focuses on providing a descriptive, rather than interpretive, summary of the information that has been collected. The analysis will be iterative and proceed in 3 overarching stages. The first stage will consist of several close reads of all data sources (i.e., included published and grey literature, clinical expert input, and other stakeholder input) and involve highlighting, marginal notes, and broader memos articulating first impressions, thoughts, and any insights relevant to the research question. The second stage will consist of translating these initial reflections and marginal notes into a series of descriptive codes. These codes will be considered for relevance to the research question and form a foundational coding scheme to be applied on subsequent reads through data inputs. If, in these subsequent reads, the author identifies relevant data not being covered by the initial codes, the initial scheme will be modified as necessary to incorporate this new information. The final stage will be the completion of a narrative summary of these descriptive codes.

Research Question 2

To address our second research question, we will draw on the narrative summary produced in response to our first research question as well as project inputs detailed throughout this protocol (i.e., clinical expert input, stakeholder engagement, published and grey literature). Using these inputs, we will develop a series of social and ethical considerations that may be relevant to decision-makers positioned around adolescent and young adult eating disorder care in Canada. These considerations will be developed over

2 stages by a single reviewer. While we describe the work in 2 linear stages below, depending on what we are identifying, we may need to take an iterative approach that involves moving back and forth between these stages.

In the first stage, the reviewer will draw on components of the constant comparative method[47] to develop a series of analytic connections and distinctions across the descriptive themes identified in the narrative summary. If necessary, they will return to the raw data in the project inputs to clarify how these descriptive themes from the narrative summary relate to one another. To help identify these analytic connections and distinctions, the reviewer will interrogate the data using a series of sensitizing questions informed by the EUnetHTA Core Model, ECHTA, and the CADTH rapid review on access and inclusion in eating disorder care broadly. Some of these questions may include:

- Is the symbolic value of the program of any moral relevance?[48]
- How does the implementation or withdrawal of the program affect the distribution of health care resources?[48]
- Are there factors that could prevent a group, or person, from gaining access to the program?[48]
- Is there a need for any specific interventions or supportive actions concerning information in order to respect patient autonomy associated with this program?[48]
- Are there structural or organizational realties that may disadvantage certain groups? [25]
- Do the assessment tools and procedures that are used to determine eligibility for this program perpetuate exclusions for adolescents outside of the young, white, affluent, cisgender, female archetype? If so, how? [19]

Throughout this process, the reviewer will write descriptive and analytic memos detailing their thoughts on how the descriptive themes from the narrative summary (or data from other project inputs) respond to these sensitizing questions and where they might relate (or not) to one another. The initial analytic connections and distinctions identified in these memos will serve as an orienting frame to be refined into a series of social and ethical considerations in the following stage.

The second stage will consist of iterative refinement and development of analytic findings. The goal of this stage is to detail social and ethical considerations associated with early intervention in eating disorder care. To do so, the reviewer will draw on their growing familiarity with the dataset as built through iterative readings and the memos described above. Throughout, the primary reviewer will share the nascent considerations with the broader HTA project team and ask for their reflections on how these considerations relate to the work being produced in their respective sections.

At the same time, the primary reviewer will lead conversations with other section leads on potential policy implications of the social and ethical considerations identified in this review as well as any implications identified from the findings of other reviews in this HTA. While these conversations will be

oriented toward developing a strong and cohesive Discussion section for the larger HTA report, these conversations may also highlight existing gaps in the considerations detailed in our review that should be addressed prior to project completion. This will help keep our work oriented toward identifying the normative considerations of the unsettled nature of what qualifies as early intervention in eating disorder care and how this comes to matter for decision-makers when determining whether to implement early intervention programs in the context of eating disorder care in Canada.

Opportunities for Stakeholder Feedback

All stakeholders will be given the opportunity to provide feedback on the draft list of included studies, and draft report. Unpublished data identified as part of the feedback process may only be included if the source of data is in the public domain.

Protocol Amendments

If amendments are required at any time during the study, reasons for changes will be recorded in a study file and subsequently reported within the final study report. If necessary, a rescreening of the previous literature search or an updated literature search will be performed to capture additional data, according to the amendments. Updates to the PROSPERO submission (registration number CRD42023431402) and the project protocol on the CADTH website will be made, as appropriate.

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Appendix 1: Literature Search Strategy

Clinical Database Search

Overview

Interface: Ovid

Databases:

- MEDLINE All (1946-present)
- Embase (1974-present)
- Cochrane Central Register of Controlled Trials (CCTR)
- APA PsycInfo

Note: Subject headings and search fields have been customized for each database. Duplicates between databases were removed in Ovid.

Date of search: May 24, 2023
Alerts: Monthly search updates until project completion
Search filters applied: No filters were applied to limit the retrieval by study type.

Limits:

- Publication date limit: 2008-present
- Language limit: English and French language
- Conference abstracts: excluded

Table 2: Syntax Guide

Syntax	Description
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
.fs	Floating subheading
exp	Explode a subject heading
*****	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
#	Truncation symbol for one character
?	Truncation symbol for one or no characters only
adj#	Requires terms to be adjacent to each other within # number of words (in any order)
.ti	Title
.ot	Original title
.ab	Abstract

Syntax	Description
.hw	Heading word; usually includes subject headings and controlled vocabulary
.kf	Keyword heading word
.dq	Candidate term word (Embase)
.pt	Publication type
.mp	Mapped term
.rn	Registry number
.nm	Name of substance word (MEDLINE)
.yr	Publication year
.jw	Journal title word (MEDLINE)
.jx	Journal title word (Embase)
freq=#	Requires terms to occur # number of times in the specified fields
medall	Ovid database code: MEDLINE All, 1946 to present, updated daily
oemezd	Ovid database code; Embase, 1974 to present, updated daily
cctr	Ovid database code; Cochrane Central Register of Controlled Trials
psyh	Ovid database code; APA PsychInfo

Multidatabase Strategy

1. exp "feeding and eating disorders"/ or compulsive exercise/ or anorexia/ or Bulimia/
2. Body Dysmorphic Disorders/
3. ((eating or food or feeding or body dysmorph*) adj3 (disorder* or addict* or compulsi*)).ti,kf.
4. ((eating or food or feeding or body dysmorph*) adj3 (disorder* or addict* or compulsi*)).ab. /freq=2
5. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic* or ARFID or orthorexia or orthorexic* or orthorectic* or compulsive exercis* or exercis* addict* or diabulimi* or rumination disorder* or rumination syndrome* or merycism or night eating syndrome or EDNOS or OSFED or UFED).ti,kf.
6. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic* or ARFID or orthorexia or orthorexic* or orthorectic* or compulsive exercis* or exercis* addict* or diabulimi* or rumination disorder* or rumination syndrome* or merycism or night eating syndrome or EDNOS or OSFED or UFED).ab. /freq=2
7. ((binge or binging or bingeing or purge or purging) adj3 (disorder* or syndrome*)).ti,kf.
8. ((binge or binging or bingeing or purge or purging) adj3 (disorder* or syndrome*)).ab. /freq=2
9. (bing* adj2 (purg* or eat*)).ti,kf.
10. (bing* adj2 (purg* or eat*)).ab. /freq=2
11. (pica and (eat* or food*)).ti,kf.
12. (pica and (eat* or food*)).ab. /freq=2
13 or/1-12

14. Early Medical Intervention/ or Early Intervention, Educational/
15. (early adj5 (intervention* or treatment? or therapy or therapies or prevention*)).ti,ab,kf.
16. early onset.ti,ab,kf.
17. or/14-16
18. Pediatrics/ or Hospitals, Pediatric/ or Intensive Care Units, Pediatric/ or Adolescent/ or exp Child/ or Pediatric Nursing/ or Child, Hospitalized/ or Adolescent, Hospitalized/ or (child* or infant* or paediatric* or pediatric* or girl? or boy? or kid? or teen or teens or teenage* or youngster? or youth* or preteen* or adolescent* or adolescence or school age? or preadolescen* or juvenile* or prepubescen* or prepubert* or pre-pubescen* or pre-pubert* or pre-adolescen* or young adult* or young people* or young person* or student* or early adult* or emerging adult* or college* or universit* or high school* or post secondary or postsecondary or classmate* or class mate*).ti,ab,kf. or (pediat* or paediat* or child* or adolescen* or juvenile*).jw.
19. 13 and 17 and 18
20. program development/ or program evaluation/ or health promotion/ or pilot projects/
21. (program* or service model?).ti,ab,kf.
22. (project or projects or campaign* or promotion* or service*).ti,kf.
23. (project or projects or campaign* or promotion* or service*).ab. /freq=2
24. or/20-23
25. 13 and 18 and 24
26. 19 or 25
27. 26 use medall,cctr
28. exp eating disorder/ or exercise addiction/
29. ((eating or food or feeding or body dysmorph*) adj3 (disorder* or addict* or compulsi*)).ti,kf.
30. ((eating or food or feeding or body dysmorph*) adj3 (disorder* or addict* or compulsi*)).ab. /freq=2
31. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic* or ARFID or orthorexia or orthorexic* or orthorectic* or compulsive exercis* or exercis* addict* or diabulimi* or rumination disorder* or rumination syndrome* or merycism or night eating syndrome or EDNOS or OSFED or UFED).ti,kf.
32. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic* or ARFID or orthorexia or orthorexic* or orthorectic* or compulsive exercis* or exercis* addict* or diabulimi* or rumination disorder* or rumination syndrome* or merycism or night eating syndrome or EDNOS or OSFED or UFED).ab. /freq=2
33. ((binge or binging or bingeing or purge or purging) adj3 (disorder* or syndrome*)).ti,kf.
34. ((binge or binging or bingeing or purge or purging) adj3 (disorder* or syndrome*)).ab. /freq=2
35. (bing* adj2 (purg* or eat*)).ti,kf.
36. (bing* adj2 (purg* or eat*)).ab. /freq=2
37. (pica and (eat* or food*)).ti,kf.
38. (pica and (eat* or food*)).ab. /freq=2

39. or/28-38
40. early intervention/ or early childhood intervention/
41. (early adj5 (intervention* or treatment? or therapy or therapies or prevention*)).ti,ab,kf.
42. early onset.ti,ab,kf.
43. or/40-42
44. exp pediatrics/ or pediatric hospital/ or pediatric intensive care unit/ or exp adolescent/ or exp child/ or exp pediatric nursing/ or exp Young adult/ or exp Juvenile/ or (child* or paediatric* or pediatric* or girl? or boy? or kid? or teen or teens or teenage* or youngster? or youth* or preteen* or adolescent* or adolescence or school age? or preadolescen* or juvenile* or prepubescen* or prepubert* or pre-pubescen* or pre-pubert* or pre-adolescen* or young adult* or young people* or young person* or student* or early adult* or emerging adult* or college* or universit* or high school* or post secondary or postsecondary or classmate* or class mate*).ti,ab,kf. or (pediat* or paediat* or child* or adolescen* or juvenile*).jx.
45. 39 and 43 and 44
46. program development/ or program evaluation/ or health promotion/ or health program/
47. (program* or service model?).ti,ab,kf.
48. (project or projects or campaign* or promotion* or service*).ti,kf.
49. (project or projects or campaign* or promotion* or service*).ab. /freq=2
50. or/46-49
51. 39 and 44 and 50
52. 45 or 51
53. 52 use oemezd
54. 53 not (conference review or conference abstract).pt.
55. exp eating disorders/
56. ((eating or food or feeding) adj3 (disorder* or addict* or compulsi*)).ti,ab,id.
57. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic* or ARFID or orthorexia or orthorexic* or orthorectic* or compulsive exercis* or exercis* addict* or diabulimi* or rumination disorder* or rumination syndrome* or merycism or night eating syndrome or EDNOS or OSFED or UFED).ti,ab,id.
58. (eating disturbance* or anorexia or anorexic* or anorectic* or bulimia or bulimic*).ti,ab,id.
59. ((binge or binging or bingeing or purge or purging) adj3 (disorder* or syndrome*)).ti,ab,id.
60. (bing* adj2 (purg* or eat*)).ti,ab,id.
61. (pica and (eat* or food*)).ti,ab,id.
62. or/55-61
63. early intervention/
64. (early adj5 (intervention* or treatment? or therapy or therapies or prevention*)).ti,ab,id.
65. early onset.ti,ab,id.

66. or/63-65
67. pediatrics/
68. (child* or paediatric* or pediatric* or girl? or boy? or kid? or teen or teens or teenage* or youngster? or youth* or preteen* or adolescent* or adolescence or school age? or preadolescen* or juvenile* or prepubescen* or prepubert* or pre-pubescen* or pre-pubert* or pre-adolescen* or young adult* or young people* or young person* or student* or early adult* or emerging adult* or college* or universit* or high school* or post secondary or postsecondary or classmate* or class mate*).ti,ab,id.
69. (pediat* or paediat* or child* or adolescen* or juvenile*).jx.
70. or/67-69
71. 62 and 66 and 70
72. program*.hw.
73. (program* or service model?).ti,ab,id.
74. (project or projects or campaign* or promotion* or service*).ti,ab,id.
75. or/72-74
76. 62 and 70 and 75
77. 71 or 76
78. 77 use psyh
79. 27 or 54 or 78
80. limit 79 to (english or french)
81. limit 80 to yr="2008 - 2018"
82. remove duplicates from 81
83. limit 80 to yr="2019 -Current"
84. remove duplicates from 83
85. 82 or 84
86. ("First Episode Rapid Early Intervention" or FREED-4-All or "Operation EAT" or "Operation Early Action and Treatment" or "EQUIP ONLINE" or ((FREED-Up or "Nip it in the bud" or Orygen*) and eating disorder*)).ti,ab,kf,id.
87. limit 86 to (english or french)
88. limit 87 to yr="2008 -Current"
89. 85 or 88
90. remove duplicates from 89

Clinical Trials Registries

ClinicalTrials.gov

Produced by the US National Library of Medicine. Targeted search used to capture registered clinical trials.

[Search -- Studies with results | eating disorders AND adolescents AND early interventions OR programs]

WHO ICTRP

International Clinical Trials Registry Platform, produced by the World Health Organization. Targeted search used to capture registered clinical trials.

[Search -- Studies with results | eating disorders AND adolescents AND early interventions OR programs]

EU Clinical Trials Register

European Union Clinical Trials Register, produced by the European Union. Targeted search used to capture registered clinical trials.

[Search -- Studies with results | eating disorders AND adolescents AND early interventions OR programs]

EU Clinical Trials Information System (CTIS)

European Union Clinical Trials Information System, produced by the European Union. Targeted search used to capture registered clinical trials.

[Search -- Studies with results | eating disorders AND adolescents AND early interventions OR programs]

Clinical Grey Literature

Search dates: May/June 2023

Keywords: eating disorders AND adolescents AND early interventions OR programs

Limits: Publication years: 2008-present

Updated: Search updated prior to the completion of stakeholder feedback period

Relevant websites from the following sections of the CADTH grey literature checklist *Grey Matters: A Practical Tool for Searching Health-Related Grey Literature* were searched:

- Health Technology Assessment Agencies
- Health Economics
- Clinical Practice Guidelines
- Clinical Trials Registries

- Databases (free)
- Health Statistics
- Internet Search.

The complete search archive of sites consulted for this report is available on request.