Evidence-based Practice Center Systematic Review Protocol

Project Title: ***Implementation of Recommended Screening and Counseling Interventions to Prevent Mental Health Disorders in Children and Adolescents***

I. Background

Mental health disorders, including substance use disorders, are common among children and adolescents in the United States, with nearly 20 percent experiencing a mental health disorder in a given year. The prevalence of mental health disorders[1] among children and adolescents is increasing,[2, 3] with the number of children and adolescents diagnosed with anxiety growing by 29 percent and those diagnosed with depression growing by 27 percent[4] between 2016 and 2020. Moreover, the burden of mental health disorders is not equitably distributed. Children and adolescents of color; from low-income households; who identify as lesbian, gay, bisexual, transgender, queer or questioning, intersex, or asexual (LGBTQIA+); who have disabilities; or who have a combination of these factors[5-7] face a disproportionately higher burden of these disorders.[8] Ultimately, the growing prevalence and burden of mental health disorders among children and adolescents underscore the need for improved prevention and early detection.

The Bright Futures Periodicity Schedule and the U.S. Preventive Services Task Force (USPSTF) recommend screening and counseling for mental health disorders including substance use disorders among children and adolescents. Early identification and management through screening may minimize the severity and progression of illness, increase access to care,[9] and ultimately lessen the weight on an already stressed healthcare system and population. Likewise, counseling of children and adolescents suffering from a particular mental health disorder (e.g., depression) can serve as a preventive measure for a second condition (e.g., substance use disorder). However, implementation of such recommended preventive interventions appears to be limited, impeding early identification and treatment of mental health disorders and referral to appropriate services.[10, 11]

Understanding which implementation strategies or "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program"[12] are effective may help to improve the implementation of recommended clinical interventions to prevent mental health disorders more broadly. However, understanding which implementation strategies align with a setting's implementation goals is challenging. Implementation strategies should be tailored to a local context, but the appropriate selection of strategies is not always easily determined given the range of possible strategies and the settings in which they have been tested. For example, implementing screenings in school-based mental health systems looks different than implementing them in traditional primary care settings.[13] Thus, there is a need to understand the effectiveness of implementation strategies as they relate to different contexts.

Purpose of the Review

This systematic review will identify implementation strategies that are effective for achieving recommended preventive interventions for mental health disorders, including substance use disorders, in the United States.

II. The Key Questions

This review includes one Key Question (KQ):

- What is the impact of strategies to implement recommended screening and counseling interventions to prevent mental health disorders (including substance use disorders) in primary care settings for children and adolescents?
    a. Do the characteristics of the population, settings, care delivery, or implementation strategy lead to varying impacts in different population subgroups?
    b. Can implementation strategies improve equity in the delivery of recommended interventions to prevent mental health disorders for populations at risk for disparities (e.g., those of minority race, ethnicity, gender identity, and sexual orientation, and those with physical disabilities and low socioeconomic status)?

For the above KQ, the following PICOTS inclusion criteria apply (detailed PICOTS are listed in Table 1):

- **Population(s)**
    - Individuals 18 years of age or younger receiving primary healthcare services (studies with a mix of patients both younger than and older than 18 years of age will be included as long as at least 80 percent of the population is younger than 21 years of age)

- **Interventions**
    - Strategies to implement interventions (drawn from the Expert Recommendations for Implementing Change [ERIC][14] and the Effective Practice and Organisation of Care [EPOC] Taxonomy[15, 16]) that are recommended in the Bright Futures Periodicity Schedule and by the USPSTF (see Table 1) to prevent mental health disorders (including interventions with insufficient evidence)
    - Potential effect modifiers—population, setting, care delivery, and strategy characteristics

- **Comparators**
    - Other implementation strategy
    - No implementation strategy

- **Outcomes**
    - Implementation, service, patient, and adverse outcomes[17]

- **Timing**
  - Studies published in 2010 or later with any length of followup

- **Setting**
  - Primary care settings in the United States that traditionally deliver preventive interventions (including pre-visit, in waiting rooms, and during the encounter with clinician)

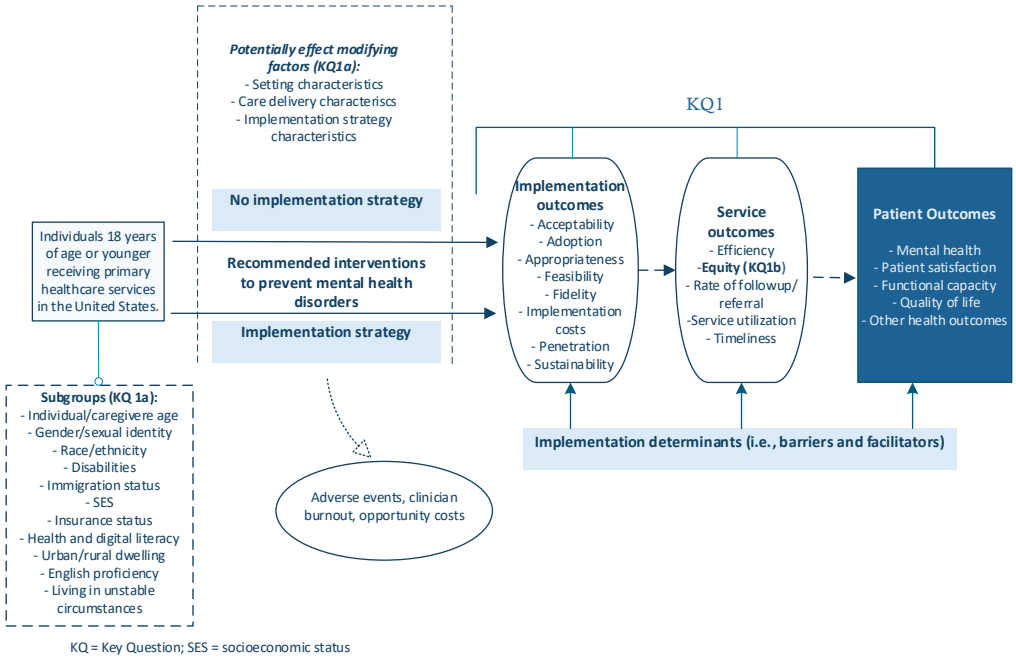
- **Study Designs**
  - Comparative studies that assess the impact of an implementation strategy compared with no strategy or another implementation strategy (randomized controlled trials [RCT], nonrandomized controlled studies, interrupted time series)

To assess the potential applicability of studies conducted outside the United States, we will identify any non-U.S. studies captured by our literature search that meet other inclusion criteria using a Contextual Question:

1. What strategies for implementing interventions to prevent mental health disorders (including substance use disorders) in primary care settings for children and adolescents were examined in seminal studies conducted outside the United States?
   a. What are the findings of these seminal studies?

III. Logic Model

Figure 1. Logic model



KQ = Key Question; SES = socioeconomic status

IV. Methods

For this review, we will follow the guidance in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[18] Our reporting will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline[19] and the extensions for reporting complex interventions[20] and equity. To determine study designs of nonrandomized studies, we will use criteria proposed by AHRQ for the classification of study designs.[21]

A. Criteria for Inclusion/Exclusion of Studies in the Review

The criteria for inclusion and exclusion of studies for the systematic review will be based on the KQ. These criteria are briefly described in the previous PICOTS section and are detailed in Table 1.

Table 1. PICOTS: Inclusion and exclusion criteria

PICOTS	Inclusion	Exclusion
Population at risk	Individuals 18 years of age or younger receiving primary healthcare services (studies with a mix of patients both younger than and older than 18 years of age will be included as long as at least 80% of the population is younger than 21 years of age)[a] Population subgroups: Child/patient or caregiver age, gender/sex identity, sexual orientation, race/ethnicity, physical or mental disability, socioeconomic status, insurance status/type (mental health coverage), families with low health or limited digital literacy, urban/rural dwelling with limited access to technology or the internet, those living in unstable circumstances, immigrants, refugees, and those with limited English proficiency	Individuals older than 18 years of age
Clinical interventions	Clinical interventions focused on individuals 18 years of age or younger or their caregivers to prevent mental health disorders in populations at risk recommended by • Bright Futures Periodicity Schedule – Maternal Depression Screening (for teenage mothers) – Behavioral/Social/Emotional Screening – Tobacco, Alcohol, or Drug Use Assessment – Depression and Suicide Risk Screening • USPSTF (including interventions with insufficient evidence) – Screening for Anxiety (B, I Grades) – Screening for Depression and Suicide Risk (B and I Grades) – Screening for Eating Disorders (adolescents only; I Grade) – Counseling regarding unhealthy Drug Use (adolescent only; B and I Grades) – Counseling regarding Illicit Drug Use (I Grade) – Counseling regarding Tobacco Use (B and I Grades) – Counseling regarding Unhealthy Alcohol Use (adolescents only; B and I Grades)	Clinical interventions • Interventions recommended in the Bright Futures Periodicity Schedule or by the USPSTF to prevent developmental disorders • Interventions to prevent mental health disorders not recommended in the Bright Futures Periodicity Schedule or by the USPSTF • Treatments of mental health disorders

PICOTS	Inclusion	Exclusion
	Implementation interventions[b] drawn from the Expert Recommendations for Implementing Change (ERIC)[14] and the Effective Practice and Organisation of Care (EPOC) Taxonomy[15, 16]: • Evaluate and iterate implementation (e.g., conduct needs assessment, assess for readiness; develop implementation plan; develop quality monitoring systems; develop tools for quality monitoring, public reporting, audit, and feedback; conduct cyclical tests of change; obtain and use patient and family feedback; stage implementation scale-up) • Provide interactive assistance (e.g., provide local technical assistance, centralize technical assistance, provide facilitation, provide clinical supervision) • Adapt and tailor to context (e.g., use data experts, use data warehousing techniques, promote adaptability of the intervention, tailor implementation to address barriers and facilitators) • Develop relationships with internal and external partners (e.g., develop academic partnerships, conduct local consensus discussions to partner with community members, build a coalition, obtain formal commitments, use an implementation adviser, visit other sites, change organizational culture, involve executive boards, recruit and train leaders for implementation, use community advisory boards and workgroups, inform local opinion leaders, identify early adopters, identify and prepare champions, model and simulate change, promote network weaving, capture and share local knowledge, develop an implementation glossary) • Train and educate stakeholders (e.g., distribute educational materials, conduct educational meetings, conduct educational outreach visits, shadow other experts, create a learning collaborative, use a train-the-trainer model, conduct ongoing training, provide ongoing consultation) • Support clinicians (e.g., facilitate the relay of clinical data to providers, develop a resource sharing agreement, revise professional roles, create new clinical teams, provide clinicians with reminders) • Engage consumers (e.g., use mass media, increase demand, involve patients and families, intervene with patients and families to enhance intervention uptake and adherence, prepare patients and families to be active participants) • Utilize financial strategies (e.g., access new funding, alter incentive structures, place intervention on fee-for-service lists/formularies, make billing easier, use capitated payments, fund and contract for the intervention, develop disincentives for failure to implement interventions, alter patient fees) • Change infrastructure (e.g., change health system oversight, grow workforce, create or change credentialing or licensure standards, change accreditation or membership requirements, change liability laws, change intervention oversight, mandate change, change physical structure and equipment, change record systems, change service sites, modify workflow and processes, start a dissemination organization)	Implementation interventions • Screening, Brief Intervention, and Referral to Treatment

PICOTS	Inclusion	Exclusion
	Potential effect modifiers: • Setting characteristics: type of setting, type of practice/providers, structure, size, staffing, readiness for implementation, use of health information technology • Care delivery characteristics: accessibility, continuity, timeliness, equitability, cultural competence • Strategy characteristics: complexity, number of components, Intensity/frequency/duration, costs, etc.	
Comparators	• Other implementation strategy • No implementation strategy	No comparator
Outcomes	Implementation outcomes • Acceptability • Adoption • Appropriateness • Feasibility • Fidelity • Implementation costs • Penetration • Sustainability Service outcomes • Efficiency • Equity (KQ 1b) • Rate of followup/referral • Initiation of treatment • Service utilization • Timeliness • Professional satisfaction • Continuity of care Patient outcomes • Mental health • Progression to diagnosis • Patient satisfaction • Functional capacity • Quality of life Adverse outcomes • Adverse events • Clinician burnout • Opportunity cost of other services • Staff turnover • Unintended effects including stigma	Outcomes not listed
Timing	Studies published in 2010 or later with any length of followup	• Studies published before 2010
Setting(s)	Primary care settings in the United States that traditionally deliver preventive interventions (including pre-visit, in waiting rooms, and during the encounter with clinician) • Primary care practices (including FQHCs) • School-based clinics	• Settings outside of the United States • Urgent care, emergency departments, trauma centers, neonatal intensive care units • Schools (without school-based clinics) • Carceral system settings • Community-based settings

PICOTS	Inclusion	Exclusion
Study Design	Comparative studies that assess the impact of an implementation strategy compared with no strategy or another implementation strategy: • RCT • Nonrandomized controlled studies • Interrupted time series	• Systematic reviews, scoping reviews, and other types of evidence synthesis (will be used for searching reference lists) • Studies without a control group (except interrupted time series) • Pre/post studies • Narrative reviews, editorials, commentaries • Study protocols

[a] Includes clinical interventions focused on caregivers.

[b] May focus on caregivers and providers.

FQHC = Federally Qualified Health Center; KQ = Key Question; RCT = randomized controlled trial; USPSTF = U.S. Preventive Services Task Force.

B. Literature Search Strategies to Identify Relevant Studies to Answer the Key Questions

Publication Date Range: We will search for studies published from January 1, 2010, through October 2023.

Literature Databases: To identify articles relevant to each KQ, we will begin with a focused MEDLINE search by using a variety of terms, including medical subject headings (MeSH) and by limiting the search to English-language, adult (18 years of age or older), and human-only studies. We will also search PsycINFO, the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature, and Embase (for primary studies only) using analogous search terms. The PubMed search strategy will be peer reviewed by another Evidence-based Practice Center (EPC) librarian, and any changes suggested will be considered by the team. We will conduct quality checks to ensure that the known studies are identified by the search. If they are not, we will revise and rerun our searches.

We will search the gray literature for unpublished studies relevant to this review and will include studies that meet all the inclusion criteria and contain enough methodological information for assessment of internal validity/quality. Gray literature sources will include ClinicalTrials.gov and the literature collection on AHRQ's Academy for Integrating Behavioral Health and Primary Care website.

Electronic literature searches will be updated while the draft report is posted for public comment to capture any new publications. Literature identified during the updated search will be assessed by following the same process of review as all other studies considered for inclusion in the report. If any pertinent new literature is identified for inclusion in the report, it will be incorporated before the final submission of the report.

Supplemental Evidence and Data for Systematic Reviews (SEADS): A SEADs notice will be posted on the Effective Health Care Program website for 4 weeks to receive supplemental evidence and data from the public.

Supplementary Searching: To avoid retrieval bias, we will conduct supplementary searches in reference lists of landmark studies and relevant reviews, editorials, and commentaries on this topic to look for any relevant citations that might have been missed by electronic searches.

Contacting Authors: In the event that information regarding methods or results appears to be unclear from the published results of a study, or if we are aware of unpublished data, we will query the authors to obtain this information.

Process for Selecting Studies: We will use DistillerSR for literature screening, leveraging its artificial intelligence (AI) capabilities to continually prioritize abstracts with a high likelihood of meeting our inclusion criteria. Two investigators will independently screen the top 70 percent of these prioritized abstracts against predefined inclusion and exclusion criteria. For the remaining 30 percent of abstracts, one investigator will be substituted with DistillerSR's AI function that has been trained based on the investigator's selections of the dual-screening abstracts.

Any discrepancies between human investigators and DistillerSR will be resolved through review by an additional investigator. We will employ DistillerSR's AI function to check for screening errors to vet dual exclusions of abstracts. Studies marked for possible inclusion will undergo a full-text review. For studies without adequate information to determine whether inclusion or exclusion of an abstract is appropriate, we will retrieve the full text and then make the determination. All results will be tracked in DistillerSR.

Two trained team members will independently review each full-text article for inclusion or exclusion based on the eligibility criteria described above. If both reviewers agree that a study does not meet the eligibility criteria, the study will be excluded. If the reviewers disagree, conflicts will be resolved by discussion and consensus or by consulting a third member of the review team. All results will be tracked in DistillerSR. We will record the reason that each excluded full-text publication did not satisfy the eligibility criteria so that we can later compile a comprehensive list of such studies.

C. Data Abstraction and Data Management

For studies that meet our inclusion criteria, we will extract and organize important information into evidence tables. To ensure a systematic approach, we will design data extraction forms in DistillerSR to gather pertinent information from each article, including characteristics of study populations, settings, interventions, comparators, study designs, methods, and results. We may employ Claude 2 (Anthropics), an advanced large language model, to assist us in extracting descriptive data related to population and general study characteristics (e.g., first author, funder, mean age, proportion of females), which will not have an influence on evidence synthesis. A recent proof of concept study demonstrated high accuracy when using this model for data extraction.[22] To ensure the reliability and accuracy of the extracted data, our team members will carefully review and verify all data extracted by Claude 2.

For data that can impact results and conclusions, such as implementation strategy characteristics and outcome data, a trained human reviewer will extract

the relevant data from each included article into the evidence tables. A second member of the team will review all other data extractions for completeness and accuracy.

D. Assessment of Methodological Risk of Bias of Individual Studies

To assess the risk of bias in the included studies, we will use the Cochrane Risk of Bias 2 (RoB 2.0) tool for RCTs,[23] the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool[24] for nonrandomized controlled studies of interventions with concurrent controls, and the Effective Public Health Practice Project tool[25] for interrupted time series analysis. Two reviewers will independently assess the risk of bias at the study and outcomes level.

E. Data Synthesis

We will summarize data narratively, structuring the synthesis of the evidence following the Cochrane EPOC[15] and the ERIC[14] frameworks. If we find three or more similar RCTs addressing an outcome of interest, we will consider meta-analysis of the data from those studies. For all meta-analyses, we will use random effects models to estimate pooled effects. To determine whether quantitative analyses are appropriate, we will assess the contextual, clinical, and methodological heterogeneity of the studies under consideration following established guidance.[26] If we conduct meta-analyses, we will assess statistical heterogeneity in effects between studies by calculating the chi-squared statistic and the I2 statistic (the proportion of variation in study estimates attributable to heterogeneity).

To leverage the expected heterogeneity, we will use the Qualitative Comparative Analysis (QCA) to identify potential relationships between implementation strategies and the desired outcomes. QCA can integrate qualitative (or categorical) and quantitative data to identify relationships between combinations of contexts, strategies, or other factors and the desired outcome (i.e., "recipes" for success). QCA can offer valuable insights, especially when the number of studies is limited and the outcomes of interest are context dependent.[27, 28]

F. Grading the Strength of Evidence for Major Comparisons and Outcomes

We will grade the strength of evidence based on the guidance established by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[29] We will ask the Technical Expert Panel (TEP) to rate the relative importance of outcomes using a modified Delphi approach. We will grade the seven outcomes, rated as most important for decision making. Two trained reviewers will assess each domain for each key outcome, and differences will be resolved by consensus. One of the two reviewers will always be a senior researcher with experience in grading the certainty of evidence.

G. Assessing Applicability

To provide users of our review with the necessary information to determine the applicability of findings, we will extract detailed data on contexts,[30] settings, interventions,[30] and implementation strategies. We will use Proctor et al.'s recommendations for specifying implementation strategies[12] to guide our data abstraction and reporting so that end users of the review are able to operationalize the strategies in practice and replicate their effectiveness.

H. Use of Artificial Intelligence and/or Machine Learning

During abstract screening, we will use DistillerSR's AI capabilities to continually prioritize abstracts with a high likelihood of meeting our inclusion criteria. For the bottom 30 percent of prioritized abstracts, one investigator will be substituted with DistillerSR's AI function for screening. Any discrepancies between human investigators and DistillerSR will be resolved through review by an additional investigator. We will also use DistillerSR's AI function to check for screening errors to reduce the risk of falsely excluded abstracts.

For data extraction, we will use Claude 2 (Anthropics), a large language model, to support us with extracting population and general study characteristics. A proof of concept study demonstrated high accuracy when using this model for data extraction.[22] A human investigator will double-check results of the automated data extraction.

V. References

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VI. Definition of Terms

None.

VII. Summary of Protocol Amendments

None.

VIII. Review of Key Questions

AHRQ posted the KQs on the AHRQ Effective Health Care Program website for public comment. The EPC refined and finalized them after reviewing the public

comments and seeking input from Key Informants and the TEP. This input is intended to ensure that the KQs are specific and relevant.

IX. Key Informants

Key Informants are the end users of research; they can include patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of healthcare, and others with experience in making healthcare decisions. Within the EPC program, the Key Informant role is to provide input into the decisional dilemmas and help keep the focus on KQs that will inform healthcare decisions. The EPC solicits input from Key Informants when developing questions for the systematic review or when identifying high-priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report. They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The AHRQ Task Order Officer (TOO) and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts constitute a multidisciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. The TEP is selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that fosters a thoughtful, relevant systematic review. Therefore, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and suggest approaches to specific issues as requested by the EPC. Technical Experts do not perform analysis of any kind; neither do they contribute to the writing of the report. They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

Members of the TEP must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The AHRQ TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparing the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers.

The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published 3 months after publication of the evidence report.

Potential peer reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited peer reviewers with any financial conflict of interest greater than $5,000 will be disqualified from peer review. Peer reviewers who disclose potential business or professional conflicts of interest can submit comments on draft reports through the public comment mechanism**.**

XII. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Direct financial conflicts of interest that cumulatively total more than $1,000 will usually disqualify an EPC core team investigator.

XIII. Role of the Funder

This project was funded under Contract No. 75Q80120D00007, Task Order No. 75Q80123F32007 from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The AHRQ Task Order Officer reviewed the EPC response to contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by either the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

XIV. Registration

This protocol will be registered in the international prospective register of systematic reviews (PROSPERO).