

Appendix G:

35 Primary Research Questions and Related Research Questions

Research Questions, Related Questions, and Design Considerations:

This appendix outlines the primary research questions as well as related research questions and design considerations that were discussed at the November 2025 workshop and iteratively reviewed and revised. This list of research questions, related research questions, and design considerations is not all-inclusive; rather, it is a consolidation of examples that were developed during the year-long workshop. Additional factors to consider for the pediatric population specifically, when applicable, include the following domains.

Additional Factors for Consideration:

- **Individual pediatric patient and developmental factors** – Characteristics intrinsic to children or adolescents (e.g., age, developmental stage, pubertal status, genetics, disability status, and special health care needs) that influence treatment appropriateness and risk-benefit considerations.
- **Disease severity, functional status, and clinical risk factors** – Indicators of obesity severity and associated medical or psychiatric burden (e.g., quality of life, body mass index [BMI] class, comorbidities, genetics, family history, laboratory values, nutritional biomarkers, imaging, metabolic markers such as blood pressure, and other screening results such as mental health and eating disorders) that inform clinical urgency, therapeutic need, and treatment intensity.
- **Treatment history and therapeutic context** – Factors related to prior and concurrent interventions (e.g., response to lifestyle treatment, role of Health Behavior and Lifestyle Treatment (HBLT), sequencing of therapies, and timing within the treatment course) that shape escalation or modification decisions (this includes previous or current obesity medication use, combination obesity medication (OM) use, surgery, or other treatments that influence decision making).
- **Medication-specific safety, feasibility, and longitudinal management** – Drug-level considerations (e.g., contraindications, route of administration, anticipated adverse effects, drug-drug interactions, and adherence feasibility) that influence whether and how a pharmacologic agent can be safely initiated. Longitudinal management includes considerations for initiation, escalation/de-escalation, maintenance strategies, relapse prevention, transitions between treatments, and long-term follow-up.

- **HBLT-specific components, delivery, and feasibility** – The “what, how much, how, where, when, and by whom” of HBLT delivery for youth on obesity medications, including feasibility and access factors.
- **Psychological, family, and social factors** – Psychological, relational, and social factors (e.g., mental health status, family readiness, parental treatment for obesity, weight stigma and bias, cultural context, health literacy, and treatment preferences) that affect engagement, adherence, and shared decision-making. This also includes functional status (e.g., mobility, activities of daily living) health-related quality of life (HRQoL), and symptom burden (fatigue, pain, etc.).
- **Health system and care delivery factors** – Ethical, regulatory, structural, and practice-level considerations that may affect access to and delivery of treatment. For example, these may include care setting, including telemedicine; provider type and availability for treatment initiation and management, such as obesity specialty care or primary care; multidisciplinary capacity; insurance coverage and affordability; care coordination models; and structural drivers of health, such as access to healthy food and other resources that may influence a patient’s ability to initiate, receive, and continue treatment.

Question No.	Primary Research Question	Related Research Question
1	When should obesity medications (OMs) be initiated in youth?	• What clinical, developmental, and contextual factors should guide decisions about when to initiate OMs in children and adolescents? • What roles should different clinical settings (e.g., primary care vs. specialty care) play in initiating OMs, and how should pharmacotherapy be sequenced or paired with behavioral or lifestyle interventions? • What evidence-informed methods are needed to refine clinical practice guidelines and improve the precision, consistency, and equity of decisions regarding initiation, delay, or avoidance of OMs in youth? • What indicators—such as BMI classification, metabolic markers, functional status, or psychosocial factors—help determine when OM treatment may not be appropriate for youth? • How can genetic testing or other biological markers improve the precision of determining the optimal timing for initiating OMs in youth? • In earlier phases of elevated BMI, such as in youth with overweight and comorbidities or in youth with short-term or rapid-onset obesity, what is the relationship between earlier initiation of OM treatment and BMI trajectories, comorbidities, and long-term health outcomes?

Question No.	Primary Research Question	Related Research Question
2	Which health factors, genotypes, and phenotypes inform obesity medication (OM) selection, dosing, treatment schedule, titration, and monitoring in youth?	• Which factors help determine the most appropriate OM choice and dosing strategy for youth? • How do different classes of OMs vary in safety, and effects on outcomes such as weight change, metabolic markers, and muscle mass or function? • How can genetic testing or other biological markers improve the precision of determining the optimal timing of OM use in youth across the treatment course (e.g., initiation, titration, adjustment, or discontinuation)? • To what extent could personalized dosing approaches, including the use of lower doses, minimize adverse effects in youth? • How should the magnitude of weight reduction be considered in relation to non-weight/weight independent outcomes when making dosing, titration, and timing decisions for OMs in youth? • How can the potency of different OMs be aligned with the severity of obesity and the presence of specific comorbidities to ensure youth receive the most appropriate treatment? • How should OM doses and lifestyle support be adjusted as BMI, clinical status, or comorbid conditions change over time? • In earlier phases of elevated BMI, such as in youth with overweight and comorbidities or in youth with short-term or rapid-onset obesity, how do health factors, genotypes, and phenotypes inform OM selection and management strategies, and how are these decisions associated with long-term weight and health outcomes? • What frequency and components of clinical monitoring, such as laboratory testing, physical examination, and assessment of treatment response, are needed to guide titration, continuation, or discontinuation of OMs in youth? • Which clinical monitoring elements, such as laboratory testing and physical examination, provide the information needed to guide these decisions? • What clinical red flags should prompt closer monitoring or adjustment of OM dosing in youth?
3	In younger children, what is the relationship between earlier initiation of obesity medication (OM) treatment and BMI trajectories, comorbidities, and health outcomes?	• What medical, developmental, or psychological risks and benefits are associated with initiating OMs earlier in childhood? • What dosing strategies are most appropriate for early initiation of OMs, and how should dose selection account for developmental stage (e.g., psychological, physical, organ development, pharmacokinetic), treatment goals, and safety considerations? • What long-term treatment, monitoring, maintenance, or follow-up is needed when OMs are initiated at an early age, and how does age and length of exposure influence outcomes over time? • To what extent can genetic testing or other biological markers inform expected treatment response or optimal timing of initiation, in young children on OM?

Question No.	Primary Research Question	Related Research Question
4	What is the relationship (e.g., correlation, causation, mechanism) between obesity medication (OM) treatment and 1) cardiometabolic outcomes and 2) comorbidities in youth?	- Comorbidities of interest may include, but are not limited to, hypertension, metabolic dysfunction–associated steatotic liver disease (MASLD), polyendocrine metabolic ovarian syndrome (PMOS), asthma, type 2 diabetes, obstructive sleep apnea, and orthopedic conditions. - What is the minimal clinically important BMI change that is associated with comorbidity change in youth treated with OM? - To what extent is the resolution of specific comorbidities in youth attributable to the direct pharmacological effects of OM versus effects mediated by total body weight reduction? - Which clinical, demographic, and physiological factors influence the likelihood of comorbidity resolution versus non-resolution in pediatric populations receiving obesity medicine treatment? - How do cardiometabolic outcomes associated with OM compare to those achieved through lifestyle-based interventions or metabolic bariatric surgery in youth? - What frequency and types of monitoring (e.g., laboratory measures, vital signs, anthropometrics, body composition, imaging, physical exam) are needed to assess treatment response and safety in youth on OMs? - What differences in cardiometabolic adaptation (e.g., energy expenditure, hunger/fullness hormones, metabolic substrate utilization) are observed across OM treatment phases (early, active weight loss, maintenance), and how do these differences relate to comorbidity outcomes independent of weight change? - To what extent do pre existing comorbidities (e.g., obstructive sleep apnea, type 2 diabetes) moderate the relationship between OM treatment and cardiometabolic and comorbidity outcomes in youth?
5	How does treatment response vary (effects and side effects) among youth on obesity medications (OM), what accounts for this, and how can it be modified?	- What distinct trajectories of treatment response (e.g., weight outcomes, weight-independent outcomes, and side-effect patterns) emerge among youth on OMs, and what factors contribute to these variations? - What is the relationship between biological, behavioral (e.g., eating behaviors), developmental and environmental characteristics, dosing/titration strategies, and 1) BMI response trajectories (e.g., early response, plateau, diminishing response, non-response) and 2) heterogeneity of non-weight outcomes among youth using OMs? - How do different treatment response patterns vary among youth, such as early response, plateau, or weight regain, inform clinical decisions to maintain, adjust, switch, or combine OMs? - How does variation in youth treatment response patterns and the tolerability/safety profile (benefit-risk balance) shape clinical decision-making, medication continuation or modification, and real-world treatment trajectories? - What is the relationship between patterns of side effects, treatment tolerability, and patterns of side effects and 1) real-world barriers to optimal use of OMs and 2) differences in treatment response trajectories (e.g., early response, plateau, non-response, or regain) among youth?

Question No.	Primary Research Question	Related Research Question
6	Among youth with medical complexity, which factors guide obesity medication (OM) treatment? Examples of medical complexity: • Neurodevelopmental conditions (e.g., autism spectrum disorder, ADHD, intellectual disability) • Genetic syndromes associated with hyperphagia or obesity (e.g., Prader-Willi syndrome, Bardet-Biedl syndrome) • Endocrine or hypothalamic disorders (e.g., panhypopituitarism, hypothalamic obesity after central nervous system tumors) • Serious mental illness (e.g., major depressive disorder, bipolar disorder) • Treatment-related factors (iatrogenic) (e.g., chronic steroid use, atypical antipsychotics, chemotherapy, cranial irradiation) • Cancer and cancer-treatment sequelae (e.g., craniopharyngioma, pituitary injury)	In youth with medical complexity: • What specific factors determine the timing for OM initiation and the selection of pharmacotherapy? • How do drug-drug interactions and concurrent treatment burdens guide the selection and safety monitoring of OM in youth? • Do altered developmental status and needs necessitate deviations from standard OM algorithms (e.g., titration, dosing, care delivery models)?

Question No.	Primary Research Question	Related Research Question
7	Which factors guide when and how obesity medication (OM) therapy is tapered or discontinued, and what supports are needed?	• What adverse effects/red flags (e.g., eating behaviors, rate of BMI reduction, new complicating diagnosis) serve as indicators to initiate the tapering or discontinuation of OM in youth? • What obesity-related factors (e.g., BMI and comorbidity response) serve as indicators to initiate the tapering or discontinuation of OM in youth? • Do age and pubertal status influence decisions about when and how OM therapy should be tapered or discontinued in youth? • What are the most effective and safe pharmacological protocols for tapering or adapting OM dosages in youth? • Which maintenance or supportive strategies, such as behavioral therapy, nutrition support, or HBLT components, are most effective in sustaining outcomes during OM tapering or discontinuation in youth?
8	What is the relationship between obesity medication (OM) discontinuation and clinical, psychological, and psychosocial functioning outcomes in youth?	• What medical or psychological risks are associated with weight regain or changes in health status following the discontinuation of OM in youth? • What is the relationship between the underlying reason for discontinuing OM (e.g., side effects, lack of response, access barriers, patient preference) and the outcomes observed after treatment discontinuation? • Is there a relationship between starting OM earlier in life and long-term weight and health outcomes following tapering or discontinuation?
9	What is the relationship between obesity medication (OM) treatment and body composition (e.g., fat mass, lean mass, bone mass) and physical function in youth?	• How does use of OM affect functional mobility, body composition, including fat mass, lean mass (skeletal muscle and organs), and bone health in children and adolescents? • How do specific components of body composition—such as fat mass (quality, magnitude, rate, regional distribution), lean mass (including skeletal muscle and organ tissue quality), and bone health (architecture, strength, linear growth)—change in youth undergoing OM treatment? • What are the impacts of OM on functional mobility and physical performance in youth, and how do these changes relate to shifts in body composition? • Which body composition changes (e.g., magnitude, regional distribution, quality of tissue) are most strongly associated with clinically meaningful outcomes in youth using OM? • What methods, measurement intervals, or clinical tools are most appropriate for tracking body composition and related functional outcomes over time in youth receiving OM?

Question No.	Primary Research Question	Related Research Question
10	What is the relationship between nutrition and physical activity interventions and body composition outcomes in youth using obesity medications (OM)?	- Which components of usual clinical practice, such as higher protein intake, resistance training, or routine micronutrient supplementation, most effectively support preservation of lean mass and overall body composition in youth on OM? - How does timing—such as initiating nutrition or resistance-training interventions during titration, active weight loss, or weight stabilization—affect body composition outcomes among youth on OM? - What guidance can be drawn from bariatric surgery or other rapid-weight-loss interventions to inform nutrition and physical activity recommendations for youth treated with OM, and where do OM-specific patterns differ?
11	What is the relationship between obesity medication (OM) associated body composition changes and clinical outcomes?	Are there developmental periods during which youth are more vulnerable to changes in muscle mass, bone health, or other structural adaptations during OM treatment?
12	What criteria (e.g., comorbidities, risk factors) can guide the selection of combination obesity medication (OM) for youth with obesity?	- How do different combinations of OM influence clinical effectiveness and safety? - Are there youth-specific factors (e.g., phenotype, genotype, behavioral traits, comorbidity profiles) that help determine when combination therapy should be selected over monotherapy? - Are there sequencing strategies, such as adding, replacing, or tapering medications, that improve outcomes for youth?
13	What clinical, developmental, psychological, psychosocial, and surgical or other factors should guide when, how, and for whom obesity medications (OM) are used in combination with metabolic or bariatric surgery in youth?	- What are the clinical indications for the postoperative use of OM in youth (e.g., thresholds for suboptimal BMI reduction, early plateau or increasing BMI, persistent or incident comorbidities, ongoing hyperphagia or loss of control eating)? - Are there youth-specific factors (e.g., genetics, developmental stage, metabolic profile, behavioral/eating patterns) that inform whether OM should be initiated pre- or postoperatively to optimize outcomes? - Should OM selection, timing, route, or dosing be adapted when used as adjunct therapy in the preoperative or postoperative period for youth? - What safety considerations or monitoring needs arise when OM are used in combination with the physiological changes that occur after bariatric surgery (e.g., pharmacokinetics, over-suppression of appetite)?

Question No.	Primary Research Question	Related Research Question
14	What safety monitoring is needed for youth on obesity medications (OM)?	• What surveillance protocols are needed to routinely monitor safety, treatment response, and emerging concerns in youth receiving OMs? • How should adverse events be identified, tracked, and managed to ensure timely and appropriate clinical responses during OM treatment? • What clinical indicators or early warning signs should prompt additional monitoring, dose adjustment, or modification of OM treatment in youth? • How should medical teams assess and manage the effects of concurrent medications on the safety, tolerability, and effectiveness of OM treatment in youth?
15	What is the relationship between obesity medication (OM) use and 1) psychosocial functioning; and 2) psychological comorbidities in youth throughout treatment?	• How do youth describe changes in identity, motivation, self-confidence, or sense of agency as they progress through OM treatment phases? • How do emotional responses to rapid or substantial body changes shape youths' coping strategies, psychological adjustment, and overall treatment experience with OMs? • What is the effect of OM treatment on standardized measures of daily functioning, school engagement, and peer interactions in youth? • How do social dynamics, such as peer feedback, stigma reduction or emergence, and family reactions, affect psychosocial outcomes for youth receiving OMs? • To what extent does OM use relate to the clinical severity of pre-existing psychological comorbidities (e.g., major depressive disorder, generalized anxiety disorder, ADHD) in youth across different treatment phases? • What is the relationship between the physiological mechanisms of OMs (e.g., appetite suppression) and the incidence, resolution, or clinical masking of eating disorder psychopathology (e.g., binge eating disorder, extreme cognitive restraint) during active treatment? • Does the emergence of new-onset psychological symptoms, such as suicidal ideation or acute anxiety, correlate with specific OM classes or specific phases of treatment (e.g., rapid titration) in youth without a prior psychiatric history? • How do baseline psychological comorbidities and baseline psychosocial distress levels predict a youth's adherence to OM dosing protocols and their overall retention across longitudinal treatment phases?

Question No.	Primary Research Question	Related Research Question
16	What is the relationship between obesity medications (OM) and disordered and dysregulated eating-related behaviors in youth?	• To what extent does OM use change pre-existing dysregulated eating patterns (e.g., loss of control eating, eating in the absence of hunger) in youth? • How frequently do new-onset disordered eating symptoms, specifically restrictive presentations consistent with atypical anorexia, emerge across the phases of OM treatment in youth? • What biological, psychological, or treatment-related factors predict the development, worsening, or improvement of dysregulated and disordered eating behaviors during OM therapy in pediatric populations? • How do youth and caregivers qualitatively describe changes in hunger cues, food noise, and the daily experience of dysregulated and disordered eating behaviors following the initiation of OM? • How do present or emerging disordered eating behaviors influence a youth's adherence, clinical engagement, and overall metabolic response to OM treatment? • What is the association between a history of preexisting eating disorders and outcomes of OM treatment in youth? • What clinical criteria and patient-level factors are identified as necessary by health care providers to guide decision-making regarding OM treatment for youth with preexisting eating disorders?
17	What is the relationship between obesity medication (OM) use and addictive or other risk-related behaviors in youth?	• How do markers of brain development and neurobehavioral regulation (e.g., reward and impulse systems) manifest in youth on OMs? • What specific changes emerge in the frequency or intensity of chemical substance use (e.g., vaping, alcohol) and behavioral risk-taking (e.g., sexual risk behaviors, behavioral cross-addictions) among youth receiving OMs? • What developmental, psychological, familial, and environmental factors moderate the relationship between OM use and a youth's vulnerability to, or protection from, addictive and risky behaviors? • How do established or newly emerging patterns of addictive and risk-related behaviors impact the safety, tolerability, and overall clinical effectiveness of OM treatment in pediatric populations? • How do youth qualitatively perceive changes in their own motivation, reward-seeking, and risk tolerance while on OMs, and how can these patient-reported insights inform targeted clinical monitoring strategies?

Question No.	Primary Research Question	Related Research Question
18	What psychological screening and monitoring approaches are needed for youth receiving obesity medication (OM) treatment?	• How can baseline psychological factors (e.g., depression, anxiety, suicidality, and trauma history) inform the frequency and intensity of psychological monitoring for youth receiving OM treatment? • What level of ongoing monitoring is needed for youth on OM, based on their baseline psychological risk factors? • What targeted monitoring approaches, utilizing validated tools (e.g., Eating Disorder Examination Questionnaire (EDE-Q), Children's Eating Attitudes Test (ChEAT)) and specific clinical red flags, are required to safely manage youth with active or historical eating disorder symptoms, and to proactively detect disordered eating during OM therapy? • What specific evidence-based screening protocols (e.g., Car, Relax, Alone, Forget, Friends/Family, Trouble (CRAFT) questionnaire) and assessment cadences are necessary for the longitudinal detection and monitoring of shifts in addictive, impulsive, or risk-related behaviors during pediatric OM treatment? • What standardized clinical escalation pathways and multidisciplinary follow-up protocols must be implemented immediately when psychological, behavioral, or safety-related red flags emerge during OM therapy? • What are the critical methodological gaps in currently available psychological screening tools when applied to pediatric OM populations, and what specific adaptations or novel instruments must be developed to ensure accurate risk detection?
19	Which psychological interventions are associated with improved outcomes for youth receiving obesity medication (OM) therapy?	• How do structured individual psychological approaches, such as cognitive-behavioral therapy (CBT), skills-based training, and resilience-building programs, improve emotional regulation and behavioral outcomes in youth receiving OM therapy? • Which specific family-based psychological interventions and caregiver support strategies are most effective at sustaining youth engagement, medication adherence, and treatment continuity across the different phases of pediatric OM therapy? • To what extent do group-based psychological interventions and peer-support models mitigate weight-related stigma and enhance psychosocial well-being for youth navigating the physical changes of OM therapy? • How should a youth's specific emotional needs, baseline coping styles, and clinical preferences guide the personalized selection and tailoring of psychological interventions to maximize OM treatment success?

Question No.	Primary Research Question	Related Research Question
20	What is the relationship between chronic stress and clinical, behavioral, and psychosocial outcomes in youth receiving obesity medication (OM) treatment?	• How do adverse childhood experiences (ACEs), historical trauma, and superimposed acute stressors modify the baseline metabolic and psychosocial trajectories of youth initiating OM treatment? • Which biologically plausible biomarkers (e.g., indicators of allostatic load or systemic inflammation) and clinical screening tools can most accurately identify youth on OM who are at heightened risk for stress-mediated adverse outcomes? • How do observed patterns of chronic stress, including links to sleep, circadian rhythms, and metabolic functioning, relate to clinical considerations regarding potential OM dose adjustments for youth? • How does chronic stress interact with the pharmacological mechanisms of OM to influence appetite regulation, override physiological satiety cues, and drive stress-induced eating behaviors in pediatric patients? • How do psychological responses to chronic stress, such as emotional reactivity, irritability, and maladaptive coping patterns, impact treatment adherence, engagement, and the overall clinical experience for youth receiving OM therapy?
21	What is the relationship between social connectedness (e.g., family cohesion, peer support, parent support, community engagement) and outcomes for youth receiving obesity medication (OM) treatment?	• What is the relationship between family-level factors (e.g., family cohesion, caregiver support) and clinical engagement, medication adherence, and the overall metabolic response in youth receiving OM? • In what ways do peer relationships, friend-based social support, and structured peer-mentorship programs shape a youth's motivation, psychological resilience, and long-term persistence during OM treatment? • How does active participation in health behavioral lifestyle treatment programs, community programs, and neighborhood or cultural support networks impact the clinical outcomes and treatment experiences of youth on OM? • To what extent does robust multi-level social connectedness (the combination of family, peer, and community support) buffer against weight-related stigma and predict long-term weight maintenance for youth undergoing OM therapy?
22	What is the relationship between obesity medication (OM) use and malnutrition, including macronutrient or micronutrient deficiencies, in youth?	• Which biological or physiological markers should be monitored to detect nutrient deficiencies in youth receiving OM, and how should these findings inform clinical care? • What testing frequency is appropriate for monitoring nutrient-related biomarkers during OM treatment? • To what extent do nutrient biomarker levels correspond with youth self-reported dietary intake while on OM? • Is there a relationship between OM use in youth and nutrient absorption?

Question No.	Primary Research Question	Related Research Question
23	What factors inform the risk assessment and identification of malnutrition in youth on obesity medications (OM)?	• How does the risk and presentation of malnutrition during OM treatment compare to what is known from other pediatric rapid weight change interventions such as very low-calorie diets, other medications, or bariatric surgery? • What safety concerns, adverse events, or clinical red flags may indicate emerging malnutrition among youth treated with OMs? • What physiological or behavioral factors contribute to the risk of malnutrition among youth undergoing intentional weight loss with OMs? • Does risk for malnutrition vary across development (e.g., age, pubertal status)? • How do pre existing or emerging eating disorder behaviors (e.g., restrictive intake, loss of hunger cues, food avoidance) influence the assessment of nutritional risk and early identification of malnutrition in youth on OMs?
24	For youth receiving obesity medication (OM) treatment, when, where, how, and what nutrition education should be delivered to optimize outcomes, including non-weight outcomes?	• Are there any indicators, such as declines in food noise, appetite suppression, gastrointestinal tolerance, or treatment milestones, that help determine the most effective point to introduce nutrition education? • Should nutrition education be tailored differently across treatment phases (preceding OM initiation, maintenance, and dose escalation)?
25	For youth receiving obesity medication (OM) treatment, when, where, how, and what physical activity counseling should be provided to optimize outcomes, including non-weight outcomes?	• Are there any indicators such as gastrointestinal tolerance or treatment milestones that help determine the most effective point to introduce physical activity interventions? • Should physical activity interventions be tailored differently across treatment phases (precede OM initiation, occur during dose escalation)?
26	What is the relationship between diet quality, eating patterns, and fluid intake and the side effects experienced by youth receiving obesity medication (OM) therapy?	• How can nutrition intake, eating patterns, and fluid consumption be reliably measured in youth receiving OM therapy? • Which micronutrient or macronutrient deficiencies—or other nutrition-related factors—elevate the risk of OM-associated side effects? • What insights from bariatric-surgery nutrition management (e.g., nutrient deficiencies, eating-pattern adjustments, hydration strategies) can inform optimal outcomes for youth using OMs? • Which aspects of diet quality, meal timing, and eating behaviors are associated with improved tolerance or reduced side effects during OM treatment?

Question No.	Primary Research Question	Related Research Question
27	What is the relationship between obesity medication (OM) use and sleep outcomes (e.g., sleep duration, sleep quality, and sleep timing) in youth?	• How does OM use alter specific sleep-related behaviors in youth, specifically regarding the reduction of night eating, adherence to consistent sleep schedules, and the adoption of adaptive versus maladaptive sleep habits? • How do the effects of OMs on sleep outcomes vary across developmental stages, and what are the distinct comparative differences in sleep responses between early childhood, adolescence, and adulthood? • To what extent do specific pharmacological variables (e.g., medication type, dosing timing) and underlying clinical comorbidities influence the overall sleep outcomes and quality in youth receiving OMs? • How does baseline sleep quality influence the clinical efficacy of OMs, and conversely, how do the physiological changes driven by these medications subsequently alter sleep quality? • In pediatric patients with preexisting dysregulated sleep, does optimizing sleep health prior to initiating OMs yield superior clinical outcomes compared to initiating both interventions concurrently?
28	For youth on obesity medications (OM), which elements of health behavior and lifestyle treatment (HBLT) format and structure, including intensity, frequency, duration, timing, and provider type, are associated with improved outcomes, including non-weight outcomes?	• What specific dose of health behavior and lifestyle treatment—defined by total contact hours, session frequency, and duration—optimizes clinical and metabolic outcomes when paired with OM therapy in youth? • What modality of health behavior and lifestyle treatment—such as video, in-person, or other digital—optimizes outcomes and for whom, when paired with OM therapy in youth? • What unit of intervention of lifestyle support, including individual patient, caregiver/child, peer group, optimizes outcomes and for whom, when paired with OM therapy? • Do lifestyle supports mitigate risk for youth and improve non-BMI outcomes such as psychosocial function, eating disorder risk, and patient-centered outcomes among youth on OMs? What setting for lifestyle support—such as home, primary care, community, or specialty care—optimizes outcomes and for whom, when paired with OM therapy in youth? • What is the optimal timing for health behavior and lifestyle treatment initiation (e.g., before medication, concurrent, after) to maximize long-term outcomes of OM therapy in youth? • How do clinical, behavioral, and psychosocial outcomes differ for youth on OMs when adjunct health behavior and lifestyle treatment is delivered by clinically licensed providers (e.g., psychologists, registered dietitians) compared to non-clinical interventionists (e.g., health coaches, community health workers)?

Question No.	Primary Research Question	Related Research Question
29	For youth on obesity medications (OM), what health behavior and lifestyle treatment content and curricula are needed to support health, wellbeing, and improved outcomes and mitigate risk?	Within health behavior and lifestyle treatment: • How are success and outcomes described (e.g., non-weight-related outcomes, QOL, resilience) for youth on OMs? • What nutritional content is needed to address the nutritional needs, mitigate risk (e.g., associated side effects), and alter satiety for youth on OMs? • What physical activity content (e.g., resistance training and functional mobility) is needed to address the body composition changes and mitigate risk (e.g., lean mass and overall body composition changes) in youth on OMs? • What other behavioral routine content (e.g., sleep habits/hygiene, meal timing and screen time) is needed to support improved outcomes in youth on OMs? • What psychosocial skills and content (e.g., building resilience and managing weight-stigma and bias) are needed to support youth with rapid weight loss and the accompanying physical and emotional changes while on OMs? • What health literacy and self-management tools are needed to support youth and their families regarding OM mechanisms? • What curriculum topics are needed for specific clinical phenotype and developmental stage of youth on OMs? • What curriculum topics and skills are needed for the patient and/or caregiver while on OMs? • What curriculum topics and skills are needed to support the patient, caregiver, and family of youth on OMs who also have intellectual or developmental disabilities? • What curriculum topics and skills are needed to support the patient and/or caregiver during OM treatment? • What curriculum topics and skills are needed to prepare youth on OMs and their caregivers for the behavioral and metabolic shifts that occur across medication treatment phases (e.g., initiation, tapering, discontinuation)?
30	What models of co-management between health professional services (e.g., nutrition, behavioral health, physical activity) and the obesity medicine clinical prescribing practitioner lead to better outcomes for youth being treated with OMs?	• Do integrated care structures (e.g., co-location and communication pathways) relate to the effectiveness of co-management between health professional services and obesity medicine specialists for youth receiving OM treatment? • Which task-sharing approaches between health professionals and obesity medicine specialists best support coordinated care for youth receiving OMs? • How can multidisciplinary best practices for initiating and monitoring OMs be organized into clear and actionable clinical pathways for youth? • What training models and competency frameworks facilitate the delivery of integrated care by various health professionals for youth receiving OM treatment? • What reimbursement approaches and financial structures are associated with the sustainable delivery of integrated OM care across health professional services?

Question No.	Primary Research Question	Related Research Question
31	From the patient and family perspective, what factors influence their choice of HBLT, obesity medication (OM) treatment (including selection of a specific medication), or bariatric surgery for youth?	• How do youth and caregiver beliefs, values, prior treatment experiences, and expectations shape decisions to pursue OM instead of HBLT or bariatric surgery (or vice versa, i.e., pursue HBLT or bariatric surgery instead of OM)? • How do factors such as youth and caregiver beliefs, values, prior treatment experiences, and expectations inform treatment selection within a continuum of care that includes OM, HBLT, and bariatric surgery? • How do factors such as access to specialty care, insurance coverage, program availability, travel burden, and waiting periods inform treatment selection within a continuum of care that includes OM, HBLT, and bariatric surgery? • How do clinical factors such as comorbidities, severity of obesity, developmental stage, and anticipated long-term outcomes inform treatment selection for youth within a continuum of care that includes OM, HBLT, and bariatric surgery?
32	From the clinical perspective, which factors (e.g., medical, behavioral, and operational) enable best practices for shared decision-making in obesity medication (OM) treatment?	• How can expectations for different evidence-based obesity treatments, including OM, be clearly communicated to youth and their caregivers to support informed decision making? • Which communication strategies best support shared decision making about dose titration, anticipated side effects, and ongoing medication management in youth? • At what point in the clinical care process should health care providers begin discussions about OM as a treatment option for youth, and what factors should guide the timing of these conversations? • How do youth and caregivers access, interpret, and weigh information about OM, including information from online sources, social media, or peers, when making treatment decisions? • How do youth, caregivers, and clinicians define treatment success within a shared decision-making framework, and how do these definitions influence treatment choices? • What supports help families navigate access barriers, medication changes, and care transitions while participating in shared decision-making about OM therapy?
33	From the multidisciplinary team perspective, what factors (e.g., clinical, operational, and safety) could enable best practice for initiating and monitoring obesity medication (OM) treatment in youth?	• How are youth and their support systems currently integrated into safety monitoring protocols during OM treatment (e.g., side effect reporting, nutritional intake)? • What clinical and operational strategies support the development of a collaborative relationship between health care providers, youth, and their support systems throughout OM treatment? Providers and youth and their support systems?

Question No.	Primary Research Question	Related Research Question
34	Which factors (e.g., patient-directed, clinical, behavioral, operational, and safety) should define “success” for youth receiving obesity medication (OM) treatment?	• Which time periods, including short-term, intermediate, and long-term phases, are most relevant when evaluating success for youth receiving OMs? • How does the definition of success vary across developmental stages such as childhood, puberty, and late adolescence, and how does this differ from adult expectations of treatment success? • How do different stakeholders, including youth, caregivers, clinicians, and payers, define and prioritize treatment success in the context of OM use?
35	How do youth and their caregivers characterize their experiences of obesity medication (OM) treatment?	• How do youth and caregivers describe changes in physical, mental, and psychosocial well-being while using OMs? • How do youth and caregivers view their long-term treatment trajectory, including whether and when they anticipate continuing, tapering, or discontinuing OMs?