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Optimizing clinical trials for pediatric obesity treatment

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About 1 in 5 children in the U.S. and more than 124 million children and adolescents worldwide are affected by obesity.[1] The complexity of both obesity risk and treatment is influenced by several key social determinants of health, as obesity disproportionately affects children and adolescents who have low socioeconomic status, live in under-resourced communities, have immigrated,[2] have experienced discrimination or had adverse childhood experiences.[3]

Obesity, now recognized as a chronic disease and defined in the pediatric population as having a BMI ≥ 95th percentile based on age and sex, has become one of the most common chronic pediatric diseases. Beyond the health implications in children and adolescents, obesity also has a high risk of persistence into adulthood with the development of comorbidities with high morbidity and mortality.

To help drug development sponsors address unmet medical needs for pediatric patients, this article provides an overview of the evolving treatment landscape, current challenges in pediatric obesity trials and considerations for optimizing clinical research.

Navigating an evolving treatment landscape

The scientific and medical understanding of obesity continues to evolve. Historically, treatments focused solely on lifestyle therapy through modification of diet and physical activity. However, lifestyle therapy alone was observed to often be insufficient for achieving clinically significant and specifically durable BMI reduction in children and adolescents.[4]

Over the last two decades, metabolic and bariatric surgery (MBS) has been recognized as a durable treatment for adolescents with severe obesity, but insufficient information from medical providers to adolescents and their families about this treatment, limited accessibility/affordability and perceived social stigma around MBS have created barriers to this treatment option.[5]

In 2023, the American Academy of Pediatrics (AAP) published its first edition of the *Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity*.[6] In this guideline, the AAP recommended that pediatric healthcare providers should offer anti-obesity medication (AOM) to adolescents ≥12 years of age with obesity as an adjunct to lifestyle therapy.

Several pediatric AOM clinical trials have examined pharmacological interventions for obesity and contributed to progress in the field. Glucagon-like peptide-1 (GLP-1) receptor agonists, such as exenatide, liraglutide, and semaglutide, affect appetite-control centers of the brain, increase insulin secretion and can increase satiety and regulate satiation.[7] Of note, semaglutide was observed to also improve cardiometabolic risk factors and quality of life.[8]

The next generation of pharmacotherapy continues to build on this progress by exploring various combinations of GLP-1, glucose-dependent insulinotropic polypeptide (GIP), amylin and glucagon.[1]

Current gaps in pediatric obesity research

While the pipeline of pediatric AOM is promising, clinical research still must address many questions and provide additional information about several factors, such as:

- **Treatment choice and timing**: There are different perceptions not only among pediatricians and healthcare providers but also among patients and families regarding the need for pharmacotherapy, as well as efforts to minimize the use of pharmacotherapy in pediatrics
- **Evaluating response**: Healthcare providers need guidance for meaningful predictors of response, as well as guidance for trying an alternate drug or add-on therapy after treatment discontinuation
- **Long-term data:** Many clinical trials are often around one year in duration and lack long-term safety and efficacy data. Additional research can shed light on the durability of treatment response and provide more insights into chronic disease management
- **Representative patient populations**: Future studies should examine a treatment's effect in a broader, more generalizable population and increase racial/ethnic diversity of the enrolled participants as obesity disproportionately affects youth of color[1]

Addressing major challenges for trials in pediatric patients with obesity

Running a randomized controlled trial of an AOM requires specific considerations to overcome inherent challenges. These include:

- **Selecting optimal sites**: Drug development sponsors must consider community sites versus an academic setting. Community health centers could provide access to more diverse patient populations, reduce the travel time required and may have existing community-clinic partnerships in place to tackle pediatric obesity education and interventions at a local level.[9] While an academic setting may have pharmaceutical-research experienced staff, have more experience delivering multidisciplinary weight loss treatments, and may address some of the primary care attitudes that anti-obesity medications should be managed by specialists.[10]
- **Defining the patient population**: Most trials so far excluded children and adolescents with mobility impairments, other chronic diseases, mental health issues or those using medications. Increasing the diversity of the patient population based on risk factors for obesity could enhance the generalizability of clinical trial results and support broader implementation of a treatment. Further, identification of known genetic variants through genetic screening (e.g., MC4R, LEPR mutations) could help to implement an obesity precision medicine approach with drugs in development.[11,12]
- **Incorporating patient-centric endpoints**: Sponsors should incorporate the voice of the patient to determine what matters to the patients and their families and what they consider clinically meaningful endpoints. Only a few studies included patients and families in the development of interventions, limiting the ability to ensure these are meeting the preferences and needs of the population highlighting the need for true patient engagement.
- **Supporting recruitment and retention**: Recruiting a pediatric patient with obesity involves recruiting an entire family; caregiver involvement is critical to support shared decision-making in treatment choices,[13] but also to support the patient to comply with lifestyle coaching or dietary commitments that may be combined with the AOM in a trial design. Healthcare professionals working with interventions in these families need to consider how to deal with family identity and dynamics within the family to secure support.

  Dropout rates greater than 25% have not been uncommon in previous studies; however, factors associated with it have not been systematically studied. It is important to note that even with increasing autonomy in adolescent patients, family support is still needed.[14] Previously, factors most closely related to better adherence were digital engagement strategies (e.g., text message reminders) as well as social and financial incentives. Elements of telehealth/mobile clinical services should be implemented to reduce barriers of patient and family participation.
- **Diversity in clinical trials:** Recruitment should also include under-resourced communities, as they experience higher levels of obesity. However, recruitment from these communities faces additional challenges such as lack of trust in healthcare providers, language barriers or different cultural values. A diversity and inclusion plan such as required by the FDA will help to address these recruitment challenges proactively.[15]
- **Recognizing cultural values**: Study materials should be tailored to specific cultures and written in an accessible format that is appropriate to the literacy level of a family when working with families that may have limited working proficiency in a secondary or tertiary language.[16] Any lifestyle and dietary coaching should be culturally relevant to the participant.

Looking ahead

Children and adolescents affected by obesity face many medical and social comorbidities and serious risk for adverse health outcomes that extend into adulthood, stressing the importance of advancing pediatric research and providing early intervention through effective, evidence-based obesity treatment. Clinical research in a pediatric population is challenging and should be thoughtfully designed to recognize potential barriers to participation, increase patient and caregiver engagement and address the needs of patients and their families.

How can we at Fortrea support your pediatric obesity program?

Fortrea has gained extensive experience in conducting pediatric trials over the past decades. A team of well-versed medical and operational SMEs, our Rare Diseases, Advanced Therapies and Pediatrics Team, as well as our regulatory experts are here to support the strategic planning and conduct of your pediatric development program and to optimize your trials for pediatric obesity treatment.

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