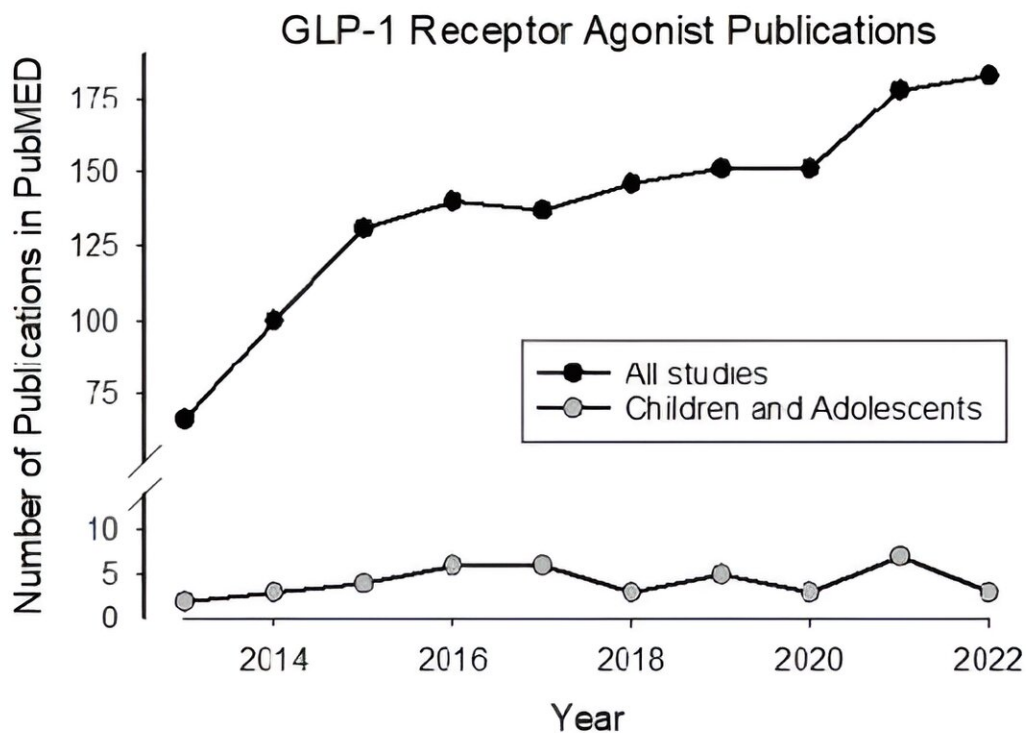


Researchers issue a warning that GLP-1RAs may be dangerous for children

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Dearth of research on GLP-1 RAs in children and adolescents. The use of these medications in the pediatric age range is likely to be long term. Little is known about the long term and lifespan effects of these drugs during critical periods of growth and development. Credit: University of California, Irvine

A team of clinicians, exercise scientists, pharmaceutical scholars,

ethicists, and behavioral experts at the University of California, Irvine, outlined their concerns that the use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) to treat childhood obesity and type 2 diabetes may have unintended and adverse consequences for children's health.

The commentary, "Unintended Consequences of Glucagon-like Peptide-1 Receptor Agonists Medication in Children and Adolescents—A Call to Action," was published as a Perspective in the *Journal of Clinical and Translational Science*. The article was led by Dan M. Cooper, MD, Distinguished Professor in the Department of Pediatrics, UCI School of Medicine.

In the perspective, the team noted that the GLP-1RA class of medications is transforming the care of obesity and type 2 diabetes in adults and noted recent studies indicating similar powerful effects in children and adolescents. Given the intractable pediatric obesity epidemic and associated rise in type 2 diabetes in youth, made worse by the COVID-19 pandemic related shutdowns and disruptions in opportunities for exercise and play in youth, this new class of medications will certainly benefit children with morbid obesity and type 2 diabetes. Ironically, it is the unprecedented success of these medications that has the team worried. The team believes that their overuse and abuse among youth is inevitable.

"Our major concern is the unbalance and inappropriate reductions in calorie or [energy intake](#) associated with these [weight loss drugs](#)," said Cooper, associate director of the UCI Institute for Clinical and Translational Science and interim director of the UCI Institute for Precision Health. "Unlike in adults, children and adolescents need energy and sufficient calories not only for physical activity, but for growth and development."

The balance of energy intake (diet) and energy expenditure (such as

physical play and exercise) influences a child's growth and health across their lifespan, and any change in the balance of these two factors can adversely impact health much later in life. For example, optimal levels of both diet and exercise increases bone mineralization during childhood, a critical period of growth and development, and this lessens their risk of osteoporosis and bone fractures later in life.

The team also pointed out the likelihood of abuse among patients with diagnosed eating disorders and children and adolescents involved in competitive sports like wrestling, [martial arts](#), gymnastics, and ballet.

"The benefit vs. cost (economic and quality of life) relationship of long-term use in youth needs to be carefully studied," said Jan D. Hirsch, one of the co-authors, dean of the School of Pharmacy and Pharmaceutical Sciences at UCI. "With the increase in social media, young people are already exposed to a diet culture and body images which may not be attainable and, ultimately, unhealthy. These drugs administered without proper supervision could cause a minefield of health and emotional problems for children as they age."

Cooper also noted that conditions like pediatric obesity have become epidemic in large measure because of environments without adequate venues for safe play and exercise for children and adolescents coupled with the availability of popular, inexpensive, high-calorie fast-foods. Not surprisingly, the epidemic of poor physical fitness and obesity has impacted underrepresented minorities disproportionately.

With the growing efficacy and popularity of these medications, drug manufacturers are quickly developing oral forms of the drugs, which researchers believe could limit oversight and cause cases of abuse. Anecdotal clinical experience suggests that there is already widespread knowledge in the pediatric population about the GLP-1RA effectiveness as satiety medications aiding weight loss, not helped by apparent

widespread use documented in the popular media.

"News about GLP-1RA agonists has infiltrated [social media](#) outlets, and is being spoken about by celebrities, fashion models and influencers. It's reasonable to assume that as access becomes easier, more children will engage in unsupervised use of GLP-1RA agonists in order to facilitate reaching societal beauty standards,": said Emma Cooper, MD, Department of Psychiatry & Human Behavior, UCI School of Medicine, "As the rate of mental health disorders, including eating disorders, continues to rise, health care providers should be screening for and intervening on inappropriate use of these medications."

Researchers believe appropriate pediatric health could also be threatened, not only by the rise of counterfeit drugs that have been well documented, but by illegitimate access through the internet.

As a result of their research and [clinical experience](#) with exercise, diet, and obesity prevention, the UCI team outlined a call-to-action. Targeting the National Institutes of Health network of academic centers, like UCI, that are recipients of Clinical and Translational Science Award (CTSA, led by the National Center for Advancing Translational Sciences) hubs across the nation, the call-to-action includes:

1. Build and support multidisciplinary teams of frontline clinicians, [community partners](#), physiologists, and behavioral and pharmaceutical scientists to address the knowledge gap in GLP-1RA effects in children and adolescents.
2. Address the translational bioethics research issues that will result from approval of pediatric formulations of the GLP-1RA medications in particular, and in general, that have evolved from the medicalization of health conditions like [pediatric obesity](#)
3. Engage and improve the quality and accessibility of relevant real-world data such as school based physical fitness testing (SB-

PFT), mandated in sixteen states covering ~ 60% of American school children.

4. Work with the FDA and other agencies to update guidelines for lifestyle interventions in pediatric clinical trials that incorporate state-of-the-art approaches to quantifying, monitoring, and evaluating [physical activity](#), adherence to diet, and accurate measurement of body composition beyond the current reliance on the [body mass index](#) (BMI), a suboptimal metric of overweight and obesity in adolescents.
5. Elevate and enhance training of the clinical trial workforce on state-of-the-art understanding of effective lifestyle interventions. Such training should also target primary care pediatricians whose exposure to exercise and nutritional science is currently quite limited
6. Develop, demonstrate, and disseminate learning modules for school personnel (teachers, coaches), parents, school-aged children, and primary care pediatricians and child mental health professionals about the GLP-1RA medications, their appropriate uses and possible abuse.

More information: Dan M. Cooper et al, Unintended Consequences of Glucagon-like Peptide-1 Receptor Agonists Medications in Children and Adolescents—A Call to Action, *Journal of Clinical and Translational Science* (2023). [DOI: 10.1017/cts.2023.612](https://doi.org/10.1017/cts.2023.612)

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