Analysis finds no increased risk of mental health issues among those using semaglutide for weight loss

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Taking the weight loss medication semaglutide did not increase the risk of depressive symptoms, suicidal thoughts, or suicidal behavior in

persons without known major mental health disorders, according to a new study led by researchers from the Perelman School of Medicine at the University of Pennsylvania published in *JAMA Internal Medicine*.

Both the Food and Drug Administration (FDA) and the European Medicines Agency are actively monitoring the psychiatric safety of semaglutide and similar medications after post-marketing surveillance reports of depression, suicidal thoughts (ideation), and suicidal behavior in patients taking the drugs for the management of type 2 diabetes or obesity.

Semaglutide has emerged as a significant advancement in the field of weight management. Initially developed as a treatment for type 2 diabetes, the drug gained widespread attention after clinical trials showed it reduced baseline body weight by approximately 10–15%. Weekly injectable medications like semaglutide have become a popular option for health care providers to prescribe for patients.

As many as 5 million Americans were prescribed semaglutide in 2023, with nearly four in ten taking it for weight management.

The new study, led by Thomas Wadden, Ph.D., a professor of Psychology in Psychiatry and the former director of Penn's Center for Weight and Eating Disorders, analyzed data from over 3,500 participants across four major clinical trials. Researchers examined data from the Semaglutide Treatment Effect in People with obesity (STEP) trials—STEP 1, 2, 3, and 5. These studies were crucial in gaining approval from the FDA to use semaglutide 2.4 mg for obesity.

"The STEP trials provide strong evidence that semaglutide 2.4 mg reduces body weight and improves numerous health complications associated with obesity. Our new analyses provide assurance that the medication, when taken by individuals who are free of significant mental

health concerns, does not increase the risk of depression, suicidal thoughts, or suicidal behavior," Wadden said.

He noted, however, that further study is needed of the psychiatric safety of semaglutide 2.4 mg when used by persons with current major depressive disorder, other serious mental illness (such as schizophrenia), or a history of suicide attempt. Individuals with such conditions were not included in the STEP trials.

The study examined changes in depressive symptoms using the Patient Health Questionnaire-9 (PHQ-9) and assessed suicidal ideation and behavior using the Columbia Suicide Severity Rating Scale.

Across the 68-week STEP 1–3 trials, semaglutide-treated participants, as compared to those who received placebo, did not show an increased risk of developing moderately severe symptoms of depression or of suicidal thoughts or behavior. Similar findings were observed in the 104-week STEP 5 study.

Examining all four STEP trials, researchers found that 1% or fewer of participants reported suicidal ideation or behavior during treatment, with no differences between semaglutide 2.4 mg and placebo.

Moreover, only 2.8% of the semaglutide-treated participants, versus 4.1% of those who received placebo, reported levels of depression at some point during treatment that required evaluation by a mental health professional. These rates are consistent with the risk of significant depression in the general population.

"It is certainly possible that individuals with overweight or obesity who take semaglutide may experience depressive symptoms or suicidal ideation or behavior, but the data suggest that persons not taking semaglutide—in the placebo group in this study—are equally likely to

experience these conditions," said Gregory Brown, Ph.D., a study co-author and Director of the Penn Center for the Prevention of Suicide at the Perelman School of Medicine.

Wadden and Brown noted that their study's findings for semaglutide are consistent with results of the FDA's most recent analysis of post-marketing surveillance data for this class of medications which did not find "evidence that use of these medicines causes suicidal thoughts or actions."

More information: *JAMA Internal Medicine* (2024). jamanetwork.com/journals/jama/ … ainternmed.2024.4346

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