Patients With Type 2 Diabetes and Sleep Apnea Derive Greater Survival Benefit From GLP-1 Receptor Agonist Therapy: Analysis of 1.8 Million Records

Glenview, IL – A real-world study of nearly 1.8 million patients found that individuals with type 2 diabetes (T2DM) and obstructive sleep apnea (OSA) prescribed glucagon-like peptide-1 receptor agonists (GLP-1RAs) experienced greater survival benefits than those without OSA, suggesting that OSA status may enhance the mortality benefit of GLP-1RA therapy.

While GLP-1RAs such as tirzepatide, semaglutide, and dulaglutide are known to reduce cardiovascular and all-cause mortality in patients with T2DM, their effects in patients who also have OSA remain unclear. Building on the findings from the SURMOUNT-OSA1 trial, which demonstrated tirzepatide's efficacy in improving OSA in nondiabetic patients, this study investigated whether OSA modifies the mortality benefit associated with GLP-1RA use among individuals with T2DM in a large, real-world population.

The primary end point was all-cause mortality within one year of metformin ± GLP-1RA prescription. Propensity score matching (PSM) adjusted for demographics and comorbidities, and Cochran–Mantel–Haenszel testing assessed for effect modification by OSA status.

The study identified 1,799,261 patients with T2DM prescribed metformin, of which 1,083,492 (60.2%) had neither OSA diagnosis nor GLP-1RA prescription; 361,492 (20.1%) were prescribed GLP-1RA without OSA diagnosis; 207,947 (11.6%) were diagnosed with OSA without GLP-1RA prescription; and 146,330 (8.1%) were diagnosed with OSA and prescribed a GLP-1RA. The most prescribed GLP-1RA was semaglutide, followed by dulaglutide and tirzepatide. Following PSM (in which standardized mean differences were found to be <0.1, indicating successful matching), GLP-1RA-prescribed groups continued to show lower 1-year mortality, both without (acute respiratory distress (ARD) 0.9% vs 1.8%, respiratory rate (RR) 2.04, CI 1.95–2.13) and with OSA (ARD 1.0% vs 2.5%, RR 2.45, CI 2.29–2.61), all p < 0.001. The ratio of RRs for mortality between non-OSA and OSA cohorts was 1.2, indicating a 20% greater mortality benefit in the OSA population, and Cochran–Mantel–Haenszel statistic was significant (p < 0.001).

"We observed 1-year mortality in patients with type two diabetes who were prescribed GLP-1RAs to be substantially lower than patients not prescribed GLP1-RAs with a disproportionate benefit observed in those also diagnosed with OSA," said Cosmo Fowler, MD, lead researcher and CHEST 2025 presenter. "This large-scale analysis suggests that OSA status may act as an effect modifier in the association between GLP-1RA prescription and mortality."

The results of this study may lead to OSA diagnosis identifying T2DM patients more likely to derive mortality benefit from GLP-1RA therapy. The 20% greater relative mortality reduction in patients with OSA supports considering OSA status when making GLP-1RA prescribing decision. Future research should examine prospectively the relationship between OSA and T2DM diagnosis and long-term outcomes of GLP-1RA therapy.

Further results will be shared at the CHEST Annual Meeting 2025 as part of the *GLP-1* Agonists and Implications on OSA Comorbidities Rapid Fire original investigation presentations titled, Enhanced Survival Benefit for GLP-1 Receptor Agonist Prescription in Patients With Coexisting Type 2 Diabetes and Sleep Apnea: A Real-World Analysis of 1.8 Million Patients. The <u>study abstract</u> can be viewed on the CHEST® journal website.