GLP-1 receptor agonists associated with increased new chronic cough?

GLP-1 receptor agonist use, compared with other second-line drugs for type 2 diabetes, is associated with a 12% increased risk of new chronic cough within 5 years of initiation, according to this large retrospective cohort study of those initiated between 2005 and 2025, published in *JAMA Otolaryngology–Head & Neck Surgery*. After removing those with a history of gastro-oesophageal reflux (GORD) from analysis, the association strengthened to a 29% increased risk, possibly due to loss of protective effects of acid-suppressive drugs. An increased risk of GORD associated with GLP-1 RA use was confirmed, and other possible mechanisms for the cough, including laryngopharyngeal reflux and vagus nerve activation causing neurogenic cough, are discussed. The authors highlight that acid-suppressant drugs may not effectively manage the chronic cough. Alongside considering the findings from this study, primary care teams need to ensure they continue to follow NICE guidance on urgent investigation of people with chronic cough.

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Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used in people with type 2 diabetes for both glucose lowering and cardiovascular and renal protection, and are prescribed in higher doses for weight loss both on the NHS and privately. They are known to be associated with slowing of gastric emptying, gastro-oesophageal reflux disease (GORD) and stimulation of the vagus nerve. These mechanisms of action could increase the risk of chronic cough but this has not been investigated previously.

Chronic cough is defined as cough lasting 8 weeks or more. It is very common, with a global prevalence of 9.6%, and can have many causes, including infection, post-nasal drip, GORD, asthma and laryngopharyngeal reflux (silent or pharyngeal reflux). Around 75% of people with GORD have no gastrointestinal symptoms and, as a result, do not receive treatment, but may present with other symptoms such as chronic cough. Proton pump inhibitors are often ineffective for treating such cough.

The present study

In this large, retrospective cohort study of people with type 2 diabetes from the TriNet X research network in the US, Gallagher and colleagues compared the development of chronic cough within 5 years in 427,555 people initiated on GLP-1 RAs from 2005 to 2025 versus 1,614,495 people who initiated any other second-line glucose-lowering drugs (including sulfonylureas, SGLT2 inhibitors and DPP-4 inhibitors). Subgroups without a history of GORD were also identified, allowing increased clarity on the role of GORD in the association between GLP-1 RAs and chronic cough.

Results

After propensity score matching, those using GLP-1 RAs had a 12% higher probability of developing new chronic cough within 5 years of initiation than those using other second-line glucose-lowering agents. The study also confirms the known association between GLP-1 RAs and GORD (Khan et al, 2025). Adjusted hazard ratios between GLP-1 RAs and other second-line agents (collectively or separately) are shown in *Table 1*.

When people with a history of GORD were excluded, the association between GLP-1 RAs versus other second-line drugs and increased risk of new chronic cough was even stronger (adjusted

Citation: Brown P (2025) Diabetes Distilled: GLP-1 receptor agonists associated with increased new chronic cough? *Diabetes & Primary Care* **27**: [Early view publication]

Table 1. Adjusted hazard ratios for development of new chronic cough within 5 years of second-line glucose-lowering drug initiation.

Comparison	Adjusted hazard ratio (95% confidence interval)
GLP-1 RA vs any other second-line therapy	1.12 (1.08–1.16)
GLP-1 RA vs DPP-4 inhibitor	1.18 (1.11–1.26)
GLP-1 RA vs sulfonylurea	1.32 (1.24–1.40)
GLP-1 RA vs SGLT2 inhibitor	1.03 (0.98–1.09) – not significant

hazard ratio 1.29). The authors postulate that people with GORD are likely to have treatment with acid-lowering agents and that these may have some beneficial effects before chronic cough occurs.

Discussion

Possible mechanisms behind the association shown here include the gastroparesis effect of GLP-1 RAs increasing laryngopharyngeal reflux (sometimes described as silent or airway reflux), rather than conventional acid reflux; activation of the vagus nerve causing cough reflex activation and neurogenic cough; or dry mouth and dry larynx leading to cough. As a result, proton pump inhibitors may not effectively treat the cough.

Advice is available for management of laryngopharyngeal reflux (Krause et al, 2022), and if neurogenic chronic cough seems likely, referral for neuromodulators (opioids with or without cough suppressants), voice therapy, superior laryngeal nerve block or laryngeal botox can be considered (Wamkpah et al, 2022). In some cases, if cough is troublesome and refractory to all treatment options, a trial of stopping the GLP-1 RA may be the only option.

The authors highlight potential limitations of their study, including lack of data on medication adherence, dosage and drug use, GORD misclassification, and difficulties which may arise with coding in relation to variations in cough and reflux symptoms over time. They call for prospective studies with data on reasons for GLP-1 RA use, and use of patient-reported outcome measures to better understand the benefits of GLP-1 RAs versus the impact of chronic cough if it occurs.

Implications for practice

Iatrogenic cough is said to occur in at least 10% of people using an ACE inhibitor, although in clinical practice, anecdotally, it feels as if it is more common. This is the first study to suggest that GLP-1 RA use is associated with a small but significant 12% increased risk of developing chronic cough compared to treatment with other second-line agents for type 2 diabetes. Although the absolute increased risk remains small, when we consider the number of people being prescribed GLP-1 RAs for type 2 diabetes, and also the increasing numbers privately funding GLP-1 RAs for weight management, we may find that investigation and management of associated chronic cough could potentially translate into a significant workload. Many of these people may also be on an ACE inhibitor, further confusing management.

It will be important, as with people who present with chronic cough while prescribed an ACE inhibitor, that we do not attribute the cough to the GLP-1 RA without first considering the need for investigation to rule out other underlying lung conditions when appropriate, particularly in people with a smoking history. It is useful to review the NICE (2025) guidance on recognition and referral of lung and pleural cancers for guidance on who needs an urgent (within 2 weeks) chest x-ray.

As with any drugs that we prescribe, it is important that we stay abreast of newly recognised potential adverse events which may occur with the drugs we use for diabetes and obesity. With a portfolio of drugs that is likely to expand rapidly over the next few years, the Primary Care Diabetes & Obesity Society and its publications, including *Diabetes & Primary Care* and *Diabetes Distilled*, will help keep us all up to date.

Practice points

1. Be aware of the potential association between GLP-1 receptor agonists and new-onset chronic cough.
2. Referral for neuromodulators (opioids with or without cough suppressants), voice therapy, superior laryngeal nerve block or laryngeal botox can be considered if proton pump inhibitors are ineffective.
3. Be careful not to attribute the cough to the GLP-1 RA without first considering the need for investigation to rule out other urgent underlying lung conditions when appropriate, particularly in people with a smoking history.

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Glucagon-like peptide-1 receptor agonists and chronic cough

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