Weight loss drug hype grows

elcome to our first issue of 2025! Generally, my focus in the New Year is around lifestyle and behaviour change, given that this tends to be the time of year when levels of motivation are at their highest. This year, however, I noticed a bit of a lull in bookings to see me. Don't get me wrong, there was still plenty to do, but I did have a few available slots, which is unusual. According to the reception staff, quite a few people asked to postpone their bloods to lessen the impact of their Christmas indulgences!

It's not unusual for people to put on a bit of weight at this time of year and to be looking for ways of losing the excess weight, but an increasing number of people are now turning to injectable incretin-based therapies. Many of the people I see with diabetes are now asking to be prescribed GLP-1 receptor agonist therapy but may not fit the current criteria recommended by NICE. It's a tricky situation when, as a clinician, you can foresee the benefits but would struggle to justify a decision to bypass other first-, second- and even third-line agents in favour of a GLP-1 or GIP/GLP-1 RA, particularly in those with an HbA₁ at or below target.

These days, I only see people with diabetes at the practice, but colleagues are also increasingly being asked to prescribe these agents for weight loss, and notifications of their initiation by private providers is now a regular occurrence. I've been quite surprised by the number of people willing to pay £180–£200 per month for these drugs privately.

The hype around these so-called "skinny jabs" does not appear to be abating in the media (particularly social media), despite there also being a few cautionary tales among the success stories. We know better than most that these agents offer significant benefits when used as indicated in appropriate individuals, but they are not a magic wand! I am tiring of the targeted advertisements for weight loss injections and even "GLP-1 patches" (there's no GLP-1 mimetic in them, by the way!) bombarding my social media. However, last week I did happen upon a really interesting and well-written comment piece in – of all places – the March issue of *Men's Health* magazine.

The article, titled The new world of weight loss, posed the question, "Are we truly on the brink of a cure for obesity? Or could neglecting the root causes risk worsening the very problems we seek to solve?" (Godwin, 2025). Drawing on reputable sources, including Danial Drucker, the Canadian endocrinologist who laid the groundwork for this therapy with the discovery of the role of glucagon-like peptides in the early 1980s, it is a balanced article that acknowledges the significant benefits of these drugs for type 2 diabetes and obesity, and potentially many other conditions in the future. The ease with which people acquire these prescription-only medications is, however, a concern, given that they are not without the potential to harm.

The other important point raised in the article is that, as availability of these agents increases over time and reduced cost makes them more widely accessible, this could divert attention away from preventing obesity in the future. Policy makers may be less determined to pursue prevention strategies, such as banning the advertisement of junk foods and adding health warnings to harmful foods.

These agents don't prevent obesity from developing in the first place and, like most drugs, they only work while you are taking them. The SURMOUNT-4 trial investigated the effect of continuing versus stopping tirzepatide treatment on the maintenance of weight loss (Aronne et al, 2024). Following an initial, open-label treatment period of 36 weeks, participants with obesity or overweight, but not diabetes, were randomised to continue with either tirzepatide or placebo



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In this issue

Diabetes Distilled: Reframing the definition and diagnosis of clinical obesity

Consensus report advises definitions of clinical and pre-clinical obesity, according to the presence of obesity-related conditions and dysfunction.

Diabetes & Primary Care **27**: 25–8

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Prescribing pearls: A guide to ACE inhibitors

Understanding ACE inhibitors: The essential information in one place. *Diabetes & Primary Care* **27**: 11–4

Click here to access

Prescribing pearls: A guide to angiotensin receptor blockers (ARBs)

Understanding ARBs: The essential information in one place. *Diabetes & Primary Care* **27**: 15–8 <u>Click here to access</u> for a further year. Having experienced a mean weight reduction of 20.9% in the lead-in period, those who switched to placebo experienced a 14% weight regain, whereas those continuing tirzepatide experienced an additional 5.5% weight reduction.

The other important point that really needs to be emphasised is that these therapies should be just one part of a holistic treatment plan, in which the medication is combined with lifestyle changes, a healthy, balanced diet and physical activity. Lasting changes are only likely to be possible if the medication is used in this way. If not, I believe the hype and the hope will be short-lived.

Advice on GLP-1-based drugs and contraception

Still on the subject of the incretin-based therapies, I was alerted to this new guidance from the Faculty of Sexual & Reproductive Healthcare (FSRH, 2025). The FSRH is advising that individuals use contraception whilst using GLP-1 agonists, with additional advice for those using tirzepatide, which has a clinically significant effect on the bioavailability of oral contraceptives.

Owing to a lack of safety data in pregnancy, people should be advised to use contraceptives whilst on a GLP-1 RA, and to observe the recommended washout periods before planning pregnancy. Additionally, individuals using tirzepatide and oral contraception should switch to a non-oral contraceptive method, or add a barrier method of contraception, for 4 weeks after initiation and for 4 weeks after each dose increase. The statement, along with a resource for clinicians to share with patients, is available here.

Redefining obesity

According to a UK Government statistical commentary, 64.0% of adults in England were estimated to be overweight or living with obesity in 2022–2023, and 26.2% were estimated to be living with obesity (Office for Health Improvement and Disparities, 2024).

For decades, we have used BMI as the barometer for measuring whether a person is overweight or obese. Of course, we know BMI has limitations, particularly where there is central obesity, and many of us will also be checking waist:height ratios (with measurement of waist circumferences). Overweight and obesity are usually a feature of, and potentially the trigger for, type 2 diabetes. The debate as to whether obesity should be classified as a disease continues, but we do now have an evidence-based consensus on how to diagnose excess adiposity, pre-clinical obesity and obesity, which is comprehensively summarised in *Diabetes Distilled*. Regular screening for the development of type 2 diabetes as well as other obesity-related conditions in those with pre-clinical and clinical obesity is recommended.

Obesity, diabetes and hypertension

Obesity, diabetes and hypertension are closely linked and share both risk factors and complications. Alongside diabetes medications and statins, antihypertensive therapies are probably the drugs most frequently prescribed in a diabetes review. Several antihypertensive medications are often required to achieve and maintain blood pressure targets, but the starting point for those with diabetes is almost always an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB). Therefore, it made sense to progress our **Prescribing pearls** series with summaries for both of these drug classes. Like me, you probably favour one or two agents within each class and, on encountering a less familiar one, you turn to the Summary of Product Characteristics for a reminder of key information and doses. This can be quite a time-consuming exercise, so I hope these guides are useful.

Forgotten SGLT2 inhibitors?

Despite clear health benefits that extend beyond glucose lowering, including weight loss (albeit more modest), the SGLT2 inhibitors do not command the same public attention as the incretin-based therapies. We rarely get people asking for an SGLT2 inhibitor, at least in my experience.

Current NICE (2022) guidance recommends offering SGLT2 inhibitor therapy to people with established atherosclerotic cardiovascular disease (CVD) or heart failure, and considering it for those at high risk of CVD (defined as a 10-year cardiovascular risk score of >10%). These agents are also included in the KDIGO 2022 care strategy for people with diabetes to reduce the risk of kidney disease progression and CVD (KDIGO Diabetes Work Group, 2022), and are recommended by the UK Kidney Association for people with type 2 diabetes and chronic kidney disease if eGFR is 20–45 mL/min/1.73 m² (or >45 if uACR is ≥25 mg/mmol), and in people with type 2 diabetes and coronary heart disease or symptomatic heart failure (irrespective of ejection fraction) (Roddick et al, 2023).

Despite this, only a small proportion of those who are eligible actually receive them. Indeed, a NICE (2022) resource impact report for type 2 diabetes in adults (available at: <u>https://bit.ly/3QyvDQW</u>) suggests that approximately 1.7 million people with type 2 diabetes in England (approximately 50% of this population) are eligible for SGLT2 inhibitor treatment, yet longitudinal prescribing data indicates only around 27% of this population are receiving them. According to a paper published last year, potential barriers to SGLT2 inhibitor initiation include "guideline fatigue, confusion and misconceptions regarding safety risks" (Seidu et al, 2024).

We have covered SGLT2 inhibitor prescribing many times before in the journal, and our *Need to Know* on the licensed indications is one of our most frequently downloaded articles. To supplement this, in this issue we have now published a more detailed <u>SGLT2 inhibitor</u> *Prescribing pearl*. Please do share this with colleagues who may be less confident prescribing these agents.

Adding a mineralocorticoid receptor antagonist to the mix

Diabetes is a major risk factor for heart failure, and people living with both of these conditions often experience worse symptoms, are more likely to be admitted to hospital, and have a worse quality of life, a more rapid decline in kidney function and a shortened life expectancy.

We should be vigilant in identifying heart failure in diabetes reviews, but the

relationship between heart failure and diabetes is bi-directional, and people with heart failure are also at greater risk of developing diabetes. Any intervention with the potential to reduce this risk is most worthy of our attention. The FINEARTS-HF trial explored the use of finerenone in people with heart failure and mildly reduced or preserved ejection fraction, and demonstrated a 24% reduction in new incident diabetes in those treated with finerenone versus placebo.

Finerenone is a non-steroidal mineralocorticoid receptor antagonist (MRA) that inhibits receptormediated sodium reabsorption and decreases receptor overactivation, thereby reducing the inflammation and fibrosis that lead to kidney damage (BNF, 2025). The NICE (2023) Technology Appraisal for finerenone states that people with type 2 diabetes and chronic kidney disease can be prescribed finerenone in addition to an ACE inhibitor/ARB and an SGLT2 inhibitor (unless these are unsuitable), if eGFR is at least 25 mL/min/1.73 m².

Currently in the UK, finerenone is not licensed to treat heart failure, but studies like FINEARTS-HF will undoubtedly impact future practice, as extensions to the licence seem likely. As Pam Brown suggests in her *Diabetes Distilled*, having clear detail of the type of heart failure and ejection fraction is important to help identify those who may benefit from additional heart failure management interventions like this in the future.

Care of older people

Also in *Diabetes Distilled* this issue is a very useful new international consensus statement on the <u>management of diabetes in older people</u>. The recommendations and review, from the International Geriatric Diabetes Society, introduce us to the term "realignment", in preference to "deprescribing", as it is more holistic and encompasses aims such as reducing treatment burden, reducing hypoglycaemia risk and improving quality of life in addition to merely reducing or stopping medications.

This so-called 4S pathway can sit alongside other guidance and provides a comprehensive list of factors that, when spotted, should prompt us



Prescribing pearls: A guide to SGLT2 inhibitors

Understanding SGLT2 inhibitors: The essential information in one place.

Diabetes & Primary Care **27**: 7–10

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Diabetes Distilled: Finerenone reduces new diabetes and improves heart failure outcomes in the FINEARTS-HF trial

Some of the known excess risk of type 2 diabetes in people with heart failure attenuated, and outcomes improved.

Diabetes & Primary Care **27**: 21–3

Click here to access

Diabetes Distilled: The 4S Pathway – realigning management for older people with diabetes

Practical guidance from the International Geriatric Diabetes Society on the management of diabetes in older people.

Diabetes & Primary Care **27**: 29–31

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to re-evaluate our treatment targets and choices. Well worth a read!

An evolving PCDS

Finally, the publication of this editorial also coincides with the <u>news from Naresh Kanumilli</u> that the Primary Care Diabetes Society is evolving in response to the changing landscape of diabetes care and henceforth will be operating as the <u>Primary Care Diabetes & Obesity</u> (PCDO) Society.

As the official journal of the Society, *Diabetes* & *Primary Care* too will be adapting. Whereas previously we tended to cover obesity insofar as it was associated with type 2 diabetes, going ahead we will also be covering it as a condition in its own right, reflecting the growing number of guidelines and therapies available to treat it even in the absence of type 2 diabetes. We are currently in the process of expanding our Editorial Board to aid us in this, and we look forward to bringing practical information and advice on this fast-evolving topic.

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