What are we actually optimising for?

The headlines from the American Diabetes Association's 86th Scientific Sessions in New Orleans this June were about molecules and tech, as they usually are. A triple agonist with phase 3 data behind it, an agent you can dose once a month, continuous glucose monitoring making its case in people with type 2 diabetes not on insulin – by any measure, it was a strong year for the pipeline, as our conference report attests.

A quieter conversation has started this year though, one centred on several key questions. What kind of change have we produced with our interventions? What did it cost the person to get there? And was this the change that mattered to them in the first place? The topics in this issue of the journal, as varied as they look, mostly circle back to these themes.

It is worth being honest about the backdrop we are reading all of this against. The 10-Year Health Plan for the NHS has put neighbourhood health, prevention and the shift from hospital to community care at the centre of the agenda (Department of Health and Social Care, 2025), and at the same time the system is under real financial strain. This combination forces the question of value to the surface. When resource is tight, what we choose to measure, fund and define as a "good" outcome stops being an academic matter; it quietly decides who gets help and who does not.

Quality of weight loss, not just quantity

The awkward fact is that a fair slice of any weight loss comes from lean tissue, and with the newer, more potent agents for weight management, that slice can be larger. After a meal, the largest single site of insulin-stimulated glucose storage is the skeletal muscle (roughly 70–80% of a glucose load is taken up by muscle), and much of that is stored as glycogen rather than burned immediately (DeFronzo and Tripathy, 2009). Muscle holds the bulk of the body's glycogen by mass: around 400 g versus around 100 g in the liver (Jensen et al, 2011). In addition to this, muscle keeps up the resting energy expenditure, so losing it eats into the metabolic gains we were after and makes weight regain easier down the line.

Two potential answers to this conundrum can be proposed. One is pharmacological, using the likes of GLP-1 receptor agonists in combination with muscle-sparing agents, built to push the composition of weight loss towards fat. The early results were striking – pairing a GLP-1 RA with a muscle-sparing agent can direct the overwhelming majority of weight lost towards fat, and protect a meaningful share of muscle compared with the GLP-1 RA used on its own (Heymsfield et al, 2026; Pratley et al, 2026). It is a useful reminder that "how much?" and "what kind?" are two different questions.

The other answer is less cutting-edge and centres on many of the key messages we have been discussing with our populations for years: increase protein intake and do resistance training. Nicole Green discusses this in our At a glance factsheet. Tailored approaches are important though, and at the moment commissioning is not agile and the metrics we use to define "good" may be quietly letting down the person living with obesity.

Weight cycling: An assumption worth re-examining

This brings me to a connected question. Is weight cycling harmful? New review evidence has shed doubt on this (Magkos and Stefan, 2026; reviewed in *Diabetes Distilled*), and we may, as clinicians, need to become more sceptical around the idea that losing and regaining weight repeatedly is metabolically worse than keeping the weight on. A lot of what looked like harm may have its explanation in natural ageing processes, concurrent illness and the underlying predisposition to weight cycling in the first place.

There is a huge amount of stigma associated with weight cycling, and in extreme cases it has been a justification for not treating at all: the "you'll only put the weight back on" argument. We should be clearer about the goals and set longer timelines for review. Weight loss is not a

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short-term goal; it is a lifetime trajectory with natural fluctuations, and it should be linked to reductions in meaningful risk for the person and improvements in quality of life, not to a number on a scale.

This question has become far less theoretical now that we are prescribing weight-loss medicines at scale, because stopping an incretin therapy produces a textbook cycle of its own. Discontinuation is closer to the norm than the exception – around half of people stop within 12 months, and this figure is higher still in older people with diabetes. A systematic review published in the *BMJ* this January (and reviewed in our previous issue) found weight returning at roughly half a kilogram per month after stopping a weight-loss medication, putting people back towards their starting weight within around two years, and doing so faster than after a behavioural programme alone (West et al, 2026). Uncomfortably for us as clinicians, it is not only the weight that returns; blood pressure, glycaemia and lipids drift back towards baseline levels too.

None of this is an argument against treating. It is an argument for treating properly (Sun, 2026) – for commissioning the maintenance care and the wraparound support rather than the weight loss alone, which is exactly what NICE (2025) had in mind when recommending at least a year of post-treatment support.

The same question, beyond obesity

Our difficulty in defining meaningful care for populations goes well beyond obesity, and the article on competing risks of death versus renal replacement therapy in chronic kidney disease is the bluntest illustration of this. For a lot of people, the honest endpoint is not whether they reach dialysis but whether they live long enough to need it. Aiming at the wrong endpoint helps nobody. The multiple long-term conditions review asks the same question about the whole person, where tidying up each disease on its own can leave the individual worse off in the round.

Even carbohydrate counting in type 2 diabetes sits here. It is a genuinely powerful tool for the appropriate, engaged individual, but a waste of everyone's time – or worse – for those who are not suited to it. What is actually being tested in all of these is not whether you know the protocol; it is whether you know what you are treating, in whom and to what end.

Optimising for whom?

There is an equity dimension running underneath all of this that cannot be left unsaid. Obesity, diabetes and their complications fall hardest on our most deprived communities, and yet access to the newer therapies and technology, to structured education, and to the time and continuity that good metabolic care needs, too often runs the other way. If we design services around the people who find it easiest to engage, we will widen the very gap we are meant to be closing. NHS England's (2021) CORE20PLUS5 approach is not a box to tick at the end of a business case; it is a question to ask at the start – are we building this for the population with the most to gain, or for the population most like us? Optimising for the average can quietly mean optimising for the already advantaged.

The practical backdrop

This doesn't replace the everyday work, and this issue of the journal covers that as well. David Morris' latest interactive case study covers the NICE (2026) NG28 update, while Nicola Milne and Julie Lewis present abbreviated advice to deal with the discontinuation of Levemir (insulin detemir) – a reminder that the "right" choice is sometimes the one that supply leaves you with rather than the one the guideline would pick. There are also the new PCDO Society diagnosis modules for people still putting the foundations in. The work underpinned by these sorts of guidelines and resources is the bedrock of good, safe care and, as we develop Integrated Neighbourhood Team working, they will be our cornerstones.

Building Integrated Neighbourhood Teams is the part I keep coming back to. The promise of neighbourhood working is that we can finally organise around the person rather than the disease, but that promise only holds true if we measure the right things. If our dashboards still reward the amount of weight lost this quarter, prescriptions issued or single-condition targets hit, we will simply have rebuilt the old

incentives inside a new structure. The harder and more valuable task is to agree, locally and with our populations, what good outcomes over years actually look like – preserved function, meaningful risk reduction, fewer crises, a life that works – and then to commission and measure against that.

Simultaneously though, we recognise that the richer the toolkit gets, and the more impressive the molecules are, the more refined our skills need to become to avoid blindly following the guidance. We need to define our roles in having the judgement to use the guidance as a starting point, to spot when the numbers we are chasing might not be the ones that will change a person's life, and to have the nerve to go after the one that will. ■

DeFronzo RA, Tripathy D (2009) Skeletal muscle insulin resistance is the primary defect in type 2 diabetes. *Diabetes Care* **32**(Suppl 2): S157–63

Department of Health and Social Care (2025) *The 10 Year Health Plan for England: Fit for the future*. Available at: https://bit.ly/3QxZY5Z

Heymsfield SB, Aronne LJ, Montgomery P et al; BELIEVE trial investigators (2026) Bimagrumab plus semaglutide alone or in combination for the treatment of obesity: A randomized phase 2 trial. *Nat Med* **32**: 869–82

Jensen J, Rustad PI, Kolnes AJ, Lai YC (2011) The role of skeletal muscle glycogen breakdown for regulation of insulin sensitivity by exercise. *Front Physiol* **2**: 112

Magkos F, Stefan N (2026) Is weight cycling clinically harmful? *Lancet Diabetes Endocrinol* 14 May [Epub ahead of print]. https://doi.org/10.1016/S2213-8587(26)00037-9

NHS England (2021) *Core20PLUS5 (adults) – an approach to reducing healthcare inequalities*. Available at: https://bit.ly/4ffmxFR

NICE (2025) *Overweight and obesity management* [NG246]. Available at: https://www.nice.org.uk/guidance/ng246/

NICE (2026) *Type 2 diabetes in adults: management* [NG28]. Available at: https://www.nice.org.uk/guidance/ng28

Pratley RE, Denham DS, Trivedi R et al (2026) Apitegromab for lean mass preservation during tirzepatide-induced weight loss: A randomized, double-blind, placebo-controlled phase 2 trial. *Nat Med* 8 Jun [Epub ahead of print]. https://doi.org/10.1038/s41591-026-04440-4

Sun Q (2026) Weight regain after cessation of GLP-1 drugs. *BMJ* **392**: r2586

West S, Scragg J, Aveyard P et al (2026) Weight regain after cessation of medication for weight management: Systematic review and meta-analysis. *BMJ* **392**: e085304