Type 2 diabesity

A staging strategy for individualised, holistic care

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In this opinion piece, the importance of individualised, holistic care for people with diabetes is discussed and a strategic framework that stages patients along the insulin resistance continuum to ensure stage-specific care proposed.

The pandemics of obesity and type 2 diabetes[1] can evoke pessimism among those caring for people with diabetes. First, they portend a cardiovascular disease (CVD) burden beyond our health means and, second, the drivers of the pandemics seem inexorable. Despite this gloom, recent US data indicate there is a significant decline in the incidence of diabetes complications, including a reduction in the myocardial infarction (MI) rate by 68%.[2] However, this promising trend may be generating a new challenge: increasing numbers of ageing survivors of diabetes. These people, often taking multiple, expensive medications, are at risk of iatrogenic harm if their doctor's once appropriate zeal for glycaemic control is not reigned in at the right time. Indeed, if the focus of care is too glucocentric, there can be missed opportunities for preventive general medicine in the diabetes clinic.

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Key points

- **Individualisation of care for people with diabetes is the gold standard to ensure treatment goals are appropriately set.**
- **Lapses in individualisation are manifest in lack of intensity of treatment early in the diabetes disease process and overly intensive glucose lowering strategies in the elderly.**
- **A strategic framework for staging a patient along the insulin resistance continuum may trigger stage-specific prevention strategies, more holistic prioritisation of care, and alertness to prevent iatrogenic morbidity.**
- **Each year, recalibration of goals and care can be triggered by reassigning the patient to one of the 'career' stages in the insulin resistance continuum; stage-specific medical therapeutic targets can then be reset.**

Commentary from the Editor-in-Chief

Although a 'one size fits all' approach to care can aid outcomes in many people with type 2 diabetes, it is much less desirable than more individualised diabetes care. Optimal approaches to individualising care in diabetes are, however, often imperfect as the diabetes care evidence base is lacking, including when applied to the real world. Given current applied knowledge, there are some common sense examples where personalised care in prediabetes and diabetes across the lifespan, especially related to comorbidities, is desirable. This opinion piece article describes targeted practical strategies with clinical examples where individualising care would be expected to aid patient outcomes.

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At the level of the individual patient, diabetes provides protean, rewarding prevention opportunities for the holistically minded clinician. These include diagnosing, managing and preventing diseases such as depression, sleep apnoea, silent CVD, sexual dysfunction and cancer that would otherwise be missed if only addressing glycaemia. An individualised approach is particularly important among the increasing number of older Australians with diabetes. Overall there was a 12% prevalence of diabetes in the Australian Diabetes, Obesity and Lifestyle study (AusDiab) cohort after 12 years' follow up,[3] and a 23% prevalence in people over the age of 75 years, according to Australian Institute of Health and Welfare data.[4]

Just as management of infectious diseases, such as tuberculosis and HIV infection, have involved pharmacotherapy as well as societal change, the diabesity pandemic should inspire in the clinic strategies to change how societies live. Specifically, we need motivational strategies to target overconsumption of high-energy foods and our technologically engineered lack of activity.

Individualisation of care: how it can become suboptimal

Individualisation of care for people with diabetes is the gold standard to ensure treatment goals are appropriately set,[5] and the latest joint Royal Australian College of General Practitioner (RACGP)/Diabetes Australia guidelines on the management of type 2 diabetes provide an excellent resource for such a patient-centric, holistic approach to 'individualisation'.[6] However, in busy practices the pressures of caring for patients with multiple morbidities can lead to understandable lapses in the quality of individualisation of care. These are manifest in lack of intensity of treatment early in the diabetes disease process and overly intensive glucose lowering strategies in the elderly. At the very least, a lack of a structured strategy for care can lead to missed opportunities to address important comorbidities that have an impact on quality of life and mortality. At worst, it can lead to

Table. A staging strategy for individualisation of care in patients with insulin resistance and type 2 diabetes

Stage	Evidence base for stage	Significance	Suggested actions
1. Prediabetes	DPP, STOP-NIDDM	• Possibly equivalent CVD risk as diabetes • Significant preventive opportunities	• Medical lifestyle prescription • Metformin in some patients (not PBS subsidised)
2. Early career type 2 diabetes	UKPDS[9]	• Potential legacy effect of early tight BGL control in preventing later CVD outcomes	• Aggressive treatment of glycaemia and other CVD risk factors
3. Post-event type 2 diabetes	ACCORD[7]	• Potential danger of tight BGL control • Opportunity to prevent comorbidities	• Actively avoid hypoglycaemia • Consider setting higher HbA_{1c} targets depending on patient risk, e.g. <8% • Manage comorbidities
4. Senior 'celebratory' type 2 diabetes	ETDS[10]	• Risk of iatrogenic harm from chronic or acute hypoglycaemia • Overly intense regimens and testing	• *Primum non nocere* • Focus on improving quality of life and reducing frequency of capillary blood glucose testing

Abbreviations: ACCORD = Action to Control Cardiovascular Risk in Diabetes; BGL = blood glucose level; CVD = cardiovascular disease; DPP = Diabetes Prevention Program; ETDS = Edinburgh Type 2 Diabetes Study; STOP-NIDDM = Study to Prevent Non-Insulin Dependent Diabetes Mellitus; UKPDS = UK Prospective Diabetes Study.

potential harm from adverse effects of the diabetes treatments. Some of the reasons for suboptimal individualisation of care are described below.

Heterogeneity in the importance of glycaemic control along the diabetes continuum

Control of the symptoms of hyperglycaemia and prevention of microvascular complications are well-established benefits of treatment with antidiabetic medications. As mentioned previously, recent US data indicate success in slowing the rates of diabetes complications, including MI, stroke, amputation and end-stage renal disease.[2] Much of this reduction in morbidity, however, may be due to reduction in global CVD risk, by control of lipids and hypertension rather than lowering of the serum glucose concentration. Several large studies have also cast considerable doubt as to whether tight glycaemic control *per se* in patients with type 2 diabetes actually prevents premature CVD deaths.[7,8] Furthermore, the well-reported Action to Control Cardiovascular Risk in Diabetes (ACCORD) study signal of increased cardiac mortality from tight glycaemic control has changed the views of many of treatment targets in high-risk individuals.[7]

Confusion and complexity in pharmaceutical choice

As people with diabetes live longer and increasing numbers of newer agents are developed to lower blood glucose levels, clinicians face prescribing complexity created by several factors.

- **Avoidance of potential conflicts can create confusion.** The enormous shareholder investment in drug development understandably needs to be recouped by the marketing efforts of pharmaceutical companies. In the face of such marketing, doctors' attempts to avoid perceptions of conflicts of interest are ethically desirable and understandable but can, ironically, contribute to confusion in care plans. For example, the authors of treatment algorithms, trying to avoid declaring a preference for a particular compound or class of products, may cite them alphabetically or historically by development. GPs seeking guidance on treatment steps might interpret these drugs' position in the algorithm as an endorsement of their suitability for that particular step.
- **Data not reflecting real world settings.** Pharmaceuticals are often marketed on their ability to lower HbA_{1c}, despite limited data for lowering the incidence of the main cause of death in people with diabetes: CVD events. Practitioners may be influenced by the marketed 'benefits' while being less aware of diminishing returns and increasing harm in lowering blood glucose levels as patients age. Furthermore, treatment algorithms and guidelines are often developed from evidence derived from single-disease studies in research clinics. Hence, using these data to choose drugs might be less appropriate for patients with comorbidities in real world settings.
- **Disease-stage bias affecting prescribing choices.** A disease-stage bias can also influence prescribing choices. For example, although pharmaceutical marketing might exhort early adoption of newer drugs, GPs may look to hospital specialists for leadership and endorsement before introducing them. If specialist clinics tend to see patients referred only at later stages of this progressive disease, hospital specialists or their trainees may not themselves have much opportunity to use the newer agents and therefore may appear to preferentially use insulin therapy. This apparent preference might then influence the choice of referring GPs in escalation of treatment for their next such patient.

Attitudes and behaviours of healthcare professionals in diabetes care

No matter how well intentioned, all healthcare professionals involved in caring for people with diabetes are prone to human frailties exposed by large patient loads and complexity.

- **Enthusiasm fatigue/nihilism.** After the 20th patient with diabetes that day or the 20th year of treating this disease, a certain jaded nihilism among healthcare professionals is understandable and perhaps inevitable: 'It's a progressive disease', 'They won't listen', 'What's the point?'
- **Professional silos.** Multidisciplinary team care is pivotal in managing diabetes, working best when the team members are motivating the patient to achieve patient-centric goals and re-emphasising each other's messages. However, with lack of time being the most commonly quoted reason, doctors will often 'outsource' to multidisciplinary team colleagues: dietary advice to the dietician, exercise prescription to the exercise physiologist, diabetes advice to the educator and even motivation to the psychologist. If multidisciplinary team follow up fails ('I've run out of visits on my enhanced primary care plan'), the dietary and exercise prescription may be overlooked by a medical practitioner with insufficient time or skills in 'prescribing' these crucial nonpharmaceutical interventions.
- **Professional chauvinism and drug bias.** It is no surprise that at medical conferences many well attended (and catered) symposia are those announcing results of the drug intervention trials, rather than those reporting allied health interventions. Hence a drug bias is natural among doctors over lifestyle change strategies. The outsourcing model above misses the crucial opportunity to improve compliance by having the nutrition, motivation and exercise 'prescriptions' written or at least re-emphasised by an influential member of the multidisciplinary team: the doctor.

A staging strategy to trigger individualisation of care

A strategic framework that consciously stages a patient along the insulin resistance continuum (analogous to oncological stage-specific treatment) is proposed below and summarised in the Table.[7,9,10] Its aims are to help trigger stage-specific prevention strategies, more holistic prioritisation of care, and more alert prevention of iatrogenic morbidity. The four case examples discussed in Box 1 illustrate how such a staging strategy could have helped improve patient care.

Individualisation of diabetes treatment goals should begin with the most powerful tool in medicine: a detailed clinical history of the person's life context, comorbidities and goals. The spouse/support person might be encouraged to attend the goal-setting consultation as a collaborator in maintaining motivation and accountability. Over the years, recalibration of goals and care might be simply triggered by the reviewing doctor mentally assigning the patient to one of four 'career' stages in the insulin resistance/type 2 diabetes continuum.

1. Case examples of how a diabetes staging strategy could improve patient care

Case 1. Preventive opportunity missed in the patient with prediabetes and the metabolic syndrome

A 38-year-old woman with a history of polycystic ovary syndrome, central adiposity and gestational diabetes was duly recalled for her postpartum oral glucose tolerance test (OGTT). Discussing the results, her doctor reassured her that instead of diabetes she had 'only impaired glucose tolerance (IGT)'. She received general advice to lose weight and re-attend for a check up and measurement of her fasting blood glucose level (BGL) in 12 months, but without a formal diagnosis of diabetes as a trigger, an aggressive lifestyle intervention was not implemented.

Six years later, after treatment for breast cancer, she had still not developed diabetes but was referred for lifestyle intervention for weight loss by her oncologist.

Comment

This patient might have been 'assigned' as stage 1 and thus counselled about her risk for various diseases that can cluster around insulin resistance and the metabolic syndrome and how this risk could be mitigated by addressing her central adiposity. Waist reduction goals and dietary and exercise prescriptions should have been made at the time of her postpartum OGTT result.

Case 2. Failure of timely escalation of treatment in an early 'career' person with diabetes

A 53-year-old sedentary professional woman who had had type 2 diabetes for six years was referred for specialist care and newly found to have background retinopathy and microalbuminuria. Her HbA_{1c} had fluctuated between 7.9% and 9.1% over the past three years while she had been taking what her doctor perceived to be 'maximal' doses of oral therapy (metformin and a sulfonylurea). Potential explanations for the three-year delay in escalation in her therapy include:

- *the patient's regularly stated reluctance to start insulin*
- *her doctor's perception that insulin was the only other effective option.*

Comment

History taking revealed this motivated woman of Indian origin to be at stage 2. She was not fearful of insulin but wanted to exhaust various lifestyle and oral agent options first. A motivational, culturally appropriate lifestyle strategy was designed around her family/life goals. Discussion of the mechanism of action of all the available oral agents was had, including side effects and PBS restrictions. The informed patient and physician jointly elected that she try a combination of a dipeptidyl peptidase-4 (DPP4) inhibitor with metformin while continuing taking the sulfonylurea temporarily on a clearly annotated 'non-PBS' prescription. In combination with her diet and exercise strategy, she lost several centimeters off her waist and was subsequently able to cease the sulfonylurea and achieve an HbA_{1c} closer to 7% while taking oral medications alone. She was fully aware that she might need insulin in the future regardless of her lifestyle measures.

Case 3. Fruitless and potentially harmful escalation of therapy without addressing comorbidities

A 66-year-old male truck driver was referred with an HbA_{1c} of 8.5% despite regular uptitration of his premixed insulin. His semi-regular visits to a hospital diabetes clinic had resulted in gradual increases in his premixed insulin doses and weight gain, and failure to attend the clinic. He had given up checking his BGLs, but kept long-life juice handy in his truck for when he 'felt low'.

Comment

Detailed history taking revealed 'indigestion' pain on exertion on a background of coronary artery bypass grafting and lapsed cardiology follow up. He had lost any interest or motivation to check his BGLs and on enquiry had erectile dysfunction and excessive daytime sleepiness.

Assigning this man to stage 3, priority was placed on avoidance of hypoglycaemia and attention to more pressing concerns: urgent cardiac testing, a sleep study (which he agreed to only after reassurance that the result would not cause him to lose his licence) and measurement of androgen levels.

Cardiac testing revealed significant coronary reocclusion. Hypoglycaemia and HbA_{1c} both improved with revascularisation and a new dietary, exercise and motivational strategy coupled with adequate continuous positive airway pressure therapy. Correction of his androgen deficiency and sleeve gastrectomy were discussed at subsequent visits.

Case 4. Overzealous treatment of the frail elderly patient worsening cognitive decline and falls risk

An 83-year-old woman with diabetes living semi-independently in a hostel was admitted to hospital with a fractured neck of femur after a fall. Her family had noticed no obvious hypoglycaemic episodes but significant cognitive decline and unsteadiness. Her HbA_{1c} was 6.8%; she was taking metformin, pioglitazone and gliclazide. The latter had been added four years earlier to improve her glycaemic control when BGLs were occasionally found to be in the teens and HbA_{1c} was perceived to be 'above target' at 8.3%. She had been checking BGLs three times per day, regularly taking her medications from her Webster pack but had been 'off her food' of late.

Comment

This case exemplifies how staging might have prevented iatrogenic morbidity. Had this woman been restaged as being at stage 4, more reasonable holistic goals might have been negotiated, perhaps avoiding the addition of a sulfonylurea that may have accelerated her cognitive decline and falls risk. With known osteoporosis, the glitazone might have been ceased long before it may have contributed to bone loss and less stringent blood glucose testing might have been in order rather than attempts to lower her HbA_{1c}.

2. Individuals at high risk of type 2 diabetes[6]

The risk of type 2 diabetes is considered to be high in people:

- at any age who have impaired glucose test results or impaired fasting glucose
- who have history of a cardiovascular event (acute myocardial infarction, angina, peripheral vascular disease or stroke)
- aged 35 years and over originating from the Pacific Islands, Indian subcontinent or China
- aged 40 years and over with body mass index (BMI) ⩾30 kg/m^2 or hypertension
- who are female with a history of gestational diabetes mellitus
- who are female with polycystic ovary syndrome who are obese
- who are taking antipsychotic medication

Stage-specific medical therapeutic targets can then be negotiated with the patient and family. For each of these stages, clinical trial evidence validates clinically useful staging boundaries.

Stage 1. Prediabetic states

'Diabesity' might usefully be seen as a part of a continuum of insulin resistant states that include an overweight child with acanthosis, a teenager with polycystic ovary syndrome, then becoming a woman with gestational diabetes (Box 2).[6] Take the sedentary person with a waist circumference greater than 100 cm, dyslipidaemia, hypertension and an abnormal ECG with 'only impaired fasting glucose'. These conditions represent an enormous opportunity for behavioural and educational intervention. While the UK Prospective Diabetes Study (UKPDS) provides evidence of the progressive nature of diabetes and loss of beta-cell function well before diabetes is diagnosed,[9] there is evidence that behavioural interventions in individuals with prediabetes can succeed in preservation of beta-cell function and improving insulin sensitivity.[11-17]

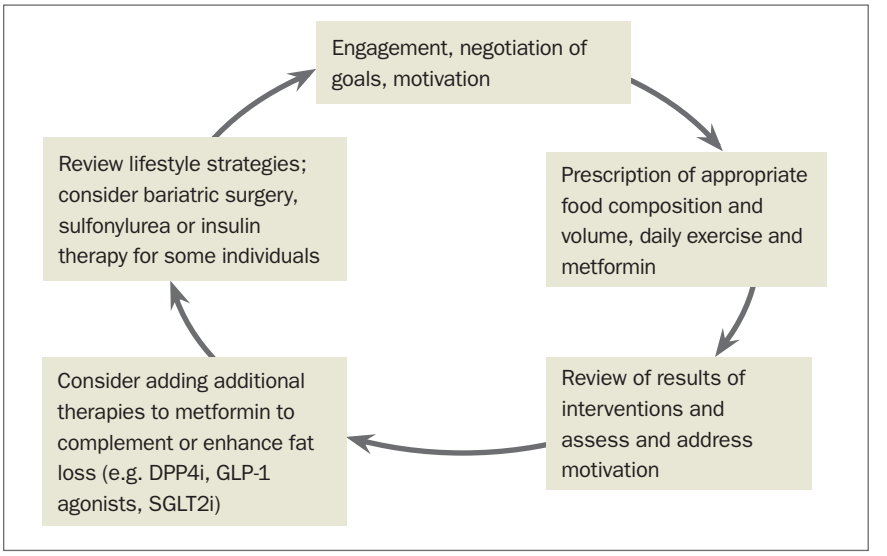

Figure. Treatment escalation algorithm for early career or stage 2 diabetes

Abbreviations: DPP4i = dipeptidyl peptidase-4 inhibitor; GLP-1 = glucagon-like peptide-1 receptor; SGLT2i = sodium glucose cotransporter 2 inhibitor.

Would we wait and only intervene if a patient is officially diagnosed as having diabetes with a fasting blood glucose level above 7 mmol/L? Or are we so focused on preventing or treating diabetes that we forget to manage the often present, very real total metabolic risk.

The person with mental illness and insulin resistance exacerbated by psychotropic drugs exemplifies someone who might benefit from an intervention triggered by staging when they present for routine follow up in the psychiatry clinic. Similarly, in the 60-year-old presenting for their osteoarthritic knee, examination and history might well reveal hypertension, central adiposity and fatigue presenting important opportunities to improve their quality of life as well as longevity. Simply completing the Australian type 2 diabetes risk assessment tool (AUSDRISK),[18] or empirically assigning an individual to stage 1 of the diabesity continuum, might lead us to more aggressively motivate our patients to achieve metabolic goals by dietary and exercise prescriptions.

This staging of an individual might also trigger enquiry for conditions that often cluster with metabolic syndrome, before any formal diagnosis of diabetes, such as sleep apnoea, depression,[19] ischaemic heart disease and cancer, all of which can be potentially worsened by weight gain associated with specific diabetes therapies.

Stage 2. Early 'career' type 2 diabetes

Shortly after a patient has been diagnosed with type 2 diabetes, emphasis on this early 'career' stage is justified by the strong trial evidence for prevention of microvascular complications by achieving tight glycaemic control. A further call to arms in this stage is the indication of a 'legacy' benefit of aggressive control early in the disease progress in terms of future CVD prevention.[9] At diagnosis, despite the risk of stigmatisation of having an incurable disease for life (when arguably diabetes is merely a risk factor for future vascular disease), there are undoubted opportunities for patients:

- a powerful motivational opportunity and enforced start time for major dietary and activity changes that will be beneficial for life
- a closer relationship with their GP through a formalised diabetes cycle of care that allows preventive checks for other insidious illness.

The management algorithm for aggressive achievement of tight control (Figure) should include a holistic approach to treatment escalation, not just a pharmaceutical strategy.

3. A diabetes staging strategy for individualising care

- At least subconsciously stage the patient along the diabesity continuum and reconsider their stage and goals yearly.
- Engage the patient and, if appropriate, their family in setting outcome goals at each stage.
- To maximise motivation, ensure outcomes goals are personally compelling to the individual (i.e. not just pertaining to the HbA_{1c}) and duly note achievements such as reduction/cessation of antidiabetic therapies with reduction in waist circumference.
- Determine the degree of glucose testing appropriate for that stage and its treatment.
- Place all therapeutic (dietary, exercise, medical, surgical) options on the table for each stage.
- Review the safety of therapy at each restaging and discuss its risk–benefit status. Be alert for iatrogenic morbidity related to treatment – e.g. osteoporosis and hypoglycaemia-related cognitive impairment and falls.
- Holistically and systematically review a checklist of potential comorbidities at each stage.
- 'Celebrate' achievement of prevention goals in patients at stage 4 with aggressive focus on quality of life rather than glycaemic goals and consider pruning the medications list and blood testing frequency and easing dietary restrictions.

Crucially, the motivation, fat loss and muscle gain strategies should be measured at each clinic visit. At the least, this approach should mitigate the vicious cycle of weight gain that can be seen when, for example, a patient's premixed insulin dose is increased every three months when the HbA_{1c} level does not fall without adjusting the exercise or energy input dose.

Stage 3. Diabetes care after the first ischaemic event or revascularisation

The cause of the increased mortality in the aggressive treatment arm of the ACCORD study in patients with diabetes post-acute MI is still the subject of speculation. However, whether from increased hypoglycaemic events or the medications used themselves, the ACCORD study evidence provides a rationale for restaging a patient after a significant CVD event.[7] At this stage, although global preventive measures such as statins and blood pressure control might remain aggressive, the balance of evidence ought to lead us to be less aggressive with our glycaemic targets in these patients, if they cannot be met easily, with a rationalisation of antidiabetic treatments to avoid harm. The holistic approach to diabetes care, including ongoing screening for comorbidities, should remain a priority in this stage.

Stage 4. Senior ('celebratory phase') type 2 diabetes care

Patients at risk of iatrogenic morbidity due to biological frailty, such as hypoglycaemia, which can contribute to cognitive decline, falls and fractures,[10] might be categorised as being at stage 4. These patients may have altered pharmacokinetics for medications, polypharmacy and reduced hypoglycaemic awareness. Furthermore, they may have variable oral intake and less control of their dosing if using aids such as Webster packs. Intense therapeutic regimens that carry a hypoglycaemia risk, including those with insulins and sulfonylureas, should be rationalised with a priority placed on the *primum non nocere* principle. Similarly, intensive glucose monitoring regimens might be scaled back, with a focus on avoiding hypoglycaemia.

Recognition of several years' struggle with multiple comorbidities and an ever-growing medications list, should prompt a celebration of a patient's success in avoiding premature vascular death from years of diabetes self-management. This stage presents opportunities for review of medications and possible pruning of drugs (e.g. statins and antihypertensives in some cases) for a senior person whose benefit–risk ratio has waned. To avoid the misperception by family members that medical support is being withdrawn, sensitive communication is needed to engage them in negotiation of patient-centric goals for their older relative. Practically, this may take the form of emphasising that henceforth an aggressive approach ought to be taken to maximise their loved one's quality of life rather than their blood test results.

Summary

Although individualisation of care for people with diabetes is well known to be the gold standard, this can be challenging in busy practices. Even in a dedicated long enhanced primary care consultation, the engagement of the patient or the skills set of the practitioner may not engender an adequate understanding of the patient's personal life context and goals. Implementation of a simple staging strategy would make it more likely that every member of the healthcare team would consciously stage the patient along the insulin resistance continuum at clinic visits. This staging might then trigger stage-specific prevention strategies early in the continuum, provide more holistic prioritisation of care and search for comorbidities later in the diabesity 'career', and prevent iatrogenic morbidity from hypoglycaemia and weight gain. The steps involved in implementing such a strategy are summarised in Box 3. **ET**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: Dr Swaraj has accepted honoraria for lectures and travel grants from several pharmaceutical companies that manufacture medicines used in the treatment of diabetes, including Novo Nordisk, Novartis, Merck Sharp & Dohme, AstraZeneca, and Eli Lily. These and visits from company representatives presenting their trial data may well influence his choice of drugs for any individual patient. To mitigate this potential for bias, the sponsorships are declared to patients and all the drug and nondrug options are discussed with each patient, along with an emphatic bias for drugs that are nonadipogenic and less likely to cause hypoglycaemia.

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