Comparing guidance for the management of type 2 diabetes: SIGN versus NICE

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This article compares new guidance for the management of diabetes from the Scottish Intercollegiate Guideline Network (2010) with the NICE (2009) clinical guideline for the management of type 2 diabetes. Both guidelines share the same approach to diabetes care but the algorithms for type 2 diabetes highlight subtle differences in the recommended management of blood glucose levels. This article explores the background to the development of the SIGN guidance and suggests possible reasons for the differences between the two algorithms.

Article points

1. This article explores the background to the development of the SIGN guidance and suggests possible reasons for the differences between the two algorithms.
2. Although the evidence base has been critically appraised by similar groups both in NICE and SIGN, the algorithms produced for glycaemic control in type 2 diabetes are slightly different.
3. While it is inevitable that the main thrust of guidance in the two documents concords, there are clear differences in detail, emphasis and some clinical issues.

Key words

- Algorithm
- Guideline
- NICE
- SIGN

The Scottish Intercollegiate Guidelines Network (SIGN) has just published its updated guideline on the management of diabetes (SIGN, 2010). As the primary care representative on the glycaemic control subcommittee, the author has been afforded an insider's view of the guideline development process from start to finish.

There has already been much expert comment on the NICE clinical guideline 87 (NICE, 2009) within the diabetes community and in many peer-reviewed journals, including this one. This article explores SIGN itself, its purpose, its provenance and where it sits within the vast organisation that delivers health care to Scotland and compares the new SIGN guideline with that of NICE (2009).

SIGN: The organisation

By the late 1980s there was growing recognition that there was substantial variation in clinical practice across a wide range of clinical domains. At the same time, the growing ability of the NHS to record clinical outcomes in detail revealed unacceptable performance linked to this variation. The simultaneous emergence of evidence-based medicine provided a platform for a national initiative to address these concerns. SIGN was born in 1993, and therefore predates both NICE and devolved health care by 6 years. Since the first clinical guideline was produced in 1995, 116 guidelines and review reports have been published, although some topics have been visited more than once.

In 2005, SIGN was subsumed into NHS Quality Improvement Scotland. This, a special Health Board, not only issues guidance but also provides support for implementation and improvement, and a resource for assessment, measurement and reporting.

SIGN and diabetes

Up until now SIGN has issued no guidance on glycaemic control in type 2 diabetes. SIGN 55, published in 2001, did address various aspects of diabetes care, including cardiovascular (CV) disease, nephropathy and lifestyle. The increasing prevalence of type 2 diabetes (on the back of ageing populations and an obesity pandemic),

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Page points

1. Although the evidence base has been critically appraised by similar groups both in NICE and SIGN, and the documents have been subject to a wide range of stakeholder input and vigorous peer review, the algorithms produced for glycaemic control in type 2 diabetes are not identical.
2. The most striking difference between the two algorithms lies in the level of detail. NICE has chosen to cover a lot of the scenarios that the prescriber is likely to encounter augmented by management instructions such as "monitor for deterioration", whereas the SIGN pathway adopts a broader brush approach to drug class choice.
3. Insulin in the SIGN algorithm is given the same treatment and prominence as dipeptidyl-peptidase-4 inhibitors, thiazolidinediones and glucagon-like peptide-1 receptor agonists as third-line options.

coupled with a diabetes research pipeline pumping out new drugs and new drug classes, made this omission glaringly obvious by 2008.

Furthermore, these epidemiological imperatives meant that new drugs were heading straight to primary care where the type 2 diabetes population had firmly ensconced itself. Primary care professionals were therefore denied the usual comfort zone of prescribing new treatments for individuals that secondary care colleagues had researched and were comfortable in recommending.

Algorithms and guidance: NICE versus SIGN

Although the evidence base has been critically appraised by similar groups both in NICE and SIGN, and the documents have been subject to a wide range of stakeholder input and vigorous peer review, the algorithms (*Figures 1 and 2*) produced for glycaemic control in type 2 diabetes are not identical. While there are no fundamental differences in approach, it is arguable that the same prescriber with the same individual could manage them somewhat differently according to which guideline they follow.

The treatment algorithms will be important informers of prescribing behaviour. Given that both NICE and SIGN clinical guidelines are over 100 pages, it is clear that these are useful tools either to use directly in the clinical setting or to inform the production of local guidelines (such as those produced by the Managed Clinical Networks in Scotland).

Design and style

The SIGN schematic (*Figure 1*) has a relatively simple layout compared with the NICE algorithm. SIGN opted for highlighting a "usual care" or "alternative care (special considerations)" approach. It was felt advantageous pictorially that the new treatments should be embedded alongside the historical prescribing pattern of metformin, followed by a sulphonylurea and then on to insulin (which in large parts of Scotland, often meant hospital referral).

By contrast, NICE have produced a "pathway" of fairly detailed guidance linked by leading arrows. In addition, further advice is given in the form of ten footnotes on the NICE algorithm, which SIGN attempts to cover in the body of its algorithm, albeit in less detail. Metformin and sulphonylurea get their own "starting blocks" on opposite sides of the NICE flow chart, thus generating specific and detailed instructions for "step two."

Content and scope

The most striking difference between the two algorithms lies in the level of detail. NICE has chosen to cover a lot of the scenarios that the prescriber is likely to encounter, augmented by management instructions such as "monitor for deterioration", whereas the SIGN pathway adopts a broader approach to drug class choice. Interestingly, both bodies include different details of advice with respect to hypoglycaemia – SIGN mentioning driving and potential occupational hazards and NICE opting for "significant risk of hypoglycaemia or its consequences". This exemplifies the difficult problem of what to put in and what to leave out. Do healthcare professionals need to be reminded about occupational risk?

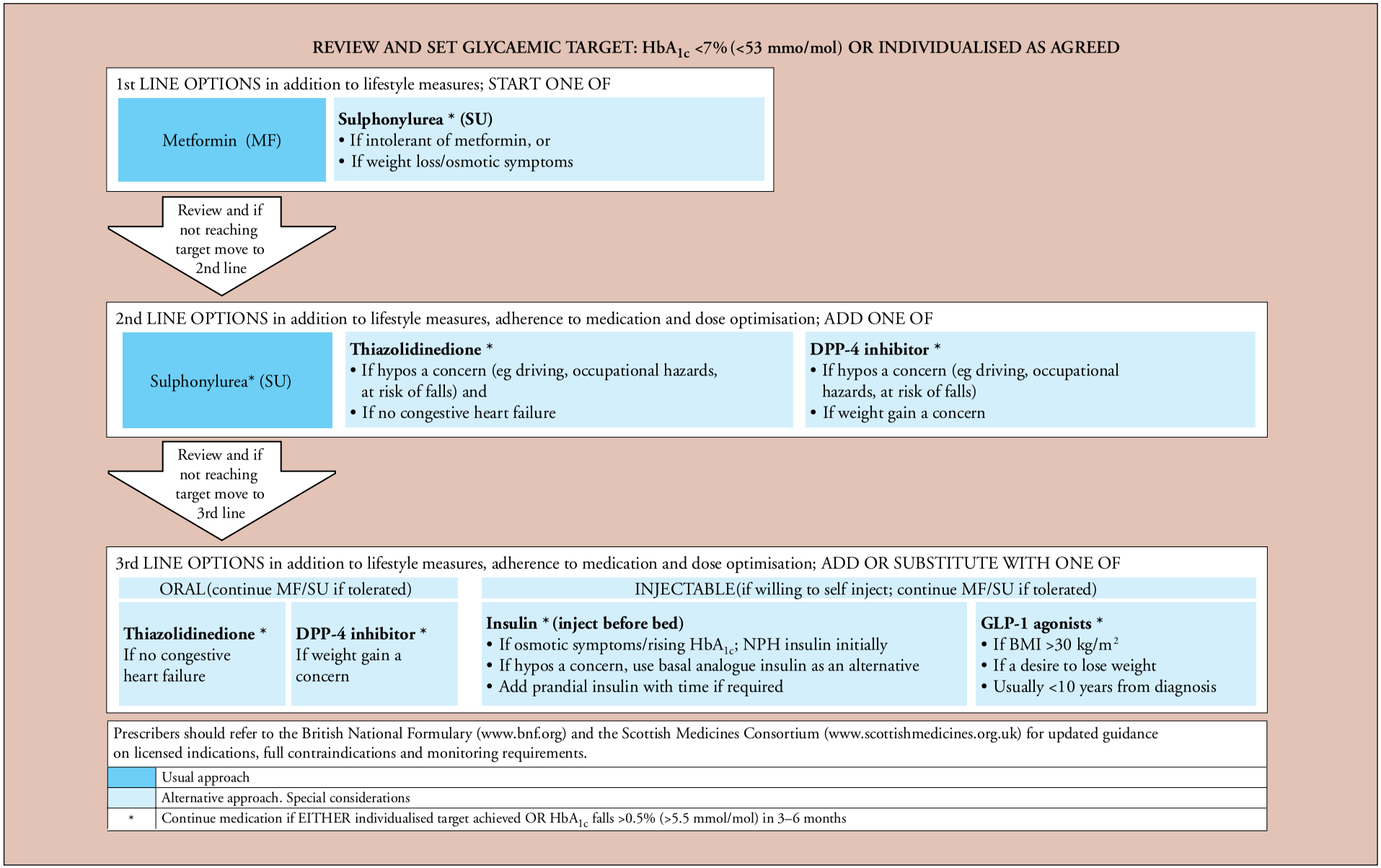
While both pathways work their way through traditional and newer agents, NICE gives insulin its own box and goes on further to discuss concomitant administration with pioglitazone (a licensed indication). Insulin in the SIGN algorithm is given the same treatment and prominence as dipeptidyl-peptidase-4 (DPP-4) inhibitors, thiazolidinediones (TZDs) and glucagon-like peptide-1 (GLP-1) receptor agonists as third-line options.

Lifestyle advice

The SIGN algorithm states that medication should be prescribed "in addition to lifestyle measures" compared with "after trial of lifestyle interventions" from the NICE algorithm. It may be a small difference as it reads, but the business of lifestyle advice in the management of type 2 diabetes is the subject of continual debate and widespread variation in practice – something that guidelines are meant to minimise.

Both NICE and SIGN are in a difficult position with lifestyle and glycaemic control advice. While the DESMOND (Diabetes Education and Self Management for Ongoing and Newly Diagnosed)

Figure 1. SIGN (2010) algorithm for blood glucose-lowering therapy in people with type 2 diabetes. Available from: http://beta.tiny.cc/8kaio. Reproduced with permission. This algorithm is not a substitute for the relevant section of the guideline. BMI = Body mass index; DPP-4 = Dipeptidyl peptidase-4; GLP-1 = Glucagon-like peptide-1; NPH = Neutral protamine Hagedorn.



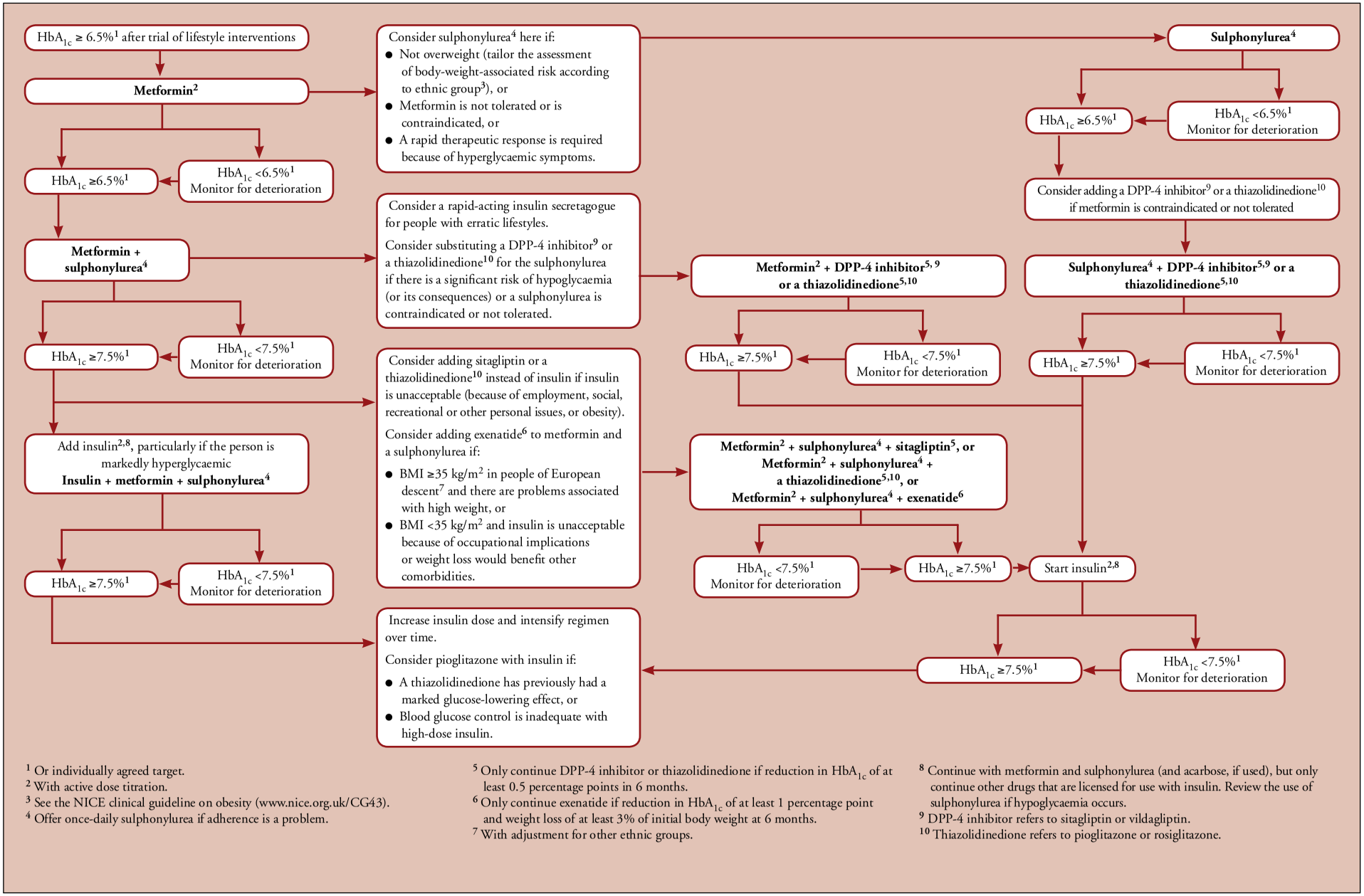


Figure 2. NICE (2009) algorithm for blood glucose-lowering therapy in people with type 2 diabetes. From NICE (2009). Adapted from: CG87 Type 2 Diabetes: The Management of Type 2 Diabetes. *NICE, London. Available from: www.nice.org.uk/CG87. Reproduced with permission. DPP-4 = Dipeptidyl peptidase-4.*

Page points

1. There are substantial differences in the algorithms in terms of glycaemic indicators and interventions.
2. Agreeing personalised targets with people with diabetes is considered important in both pathways, although in the author's opinion probably needs to be more prominent as it lies at the heart both of safe management and achievability.
3. The debate about how far to lower HbA_{1c} levels has subsequently been discussed in detail as new studies emerge, particularly one from Currie et al (2010), which proposes a "U-shaped" curve for HbA_{1c} and all-cause mortality, suggesting that there is more risk of harm with low and high HbA_{1c} levels.

pilot hinted at the possibility of improved glycaemic control, the randomised controlled trial carried out subsequently showed no benefit for HbA_{1c} after 12 months, although benefits for health beliefs, weight loss and smoking were observed (Davies et al, 2008). The evidence for dietary interventions impacting on hard clinical endpoints in people with type 2 diabetes is similarly lacking (Nield et al, 2007). Exercise fares a little better, with some evidence for improved glycaemic control on a systematic review. The studies were, however, of short duration for the most part and may have limited applicability in the chronic disease setting in primary care (Thomas et al, 2006).

Glycaemic indicators and intervention

There are substantial differences in the algorithms in terms of glycaemic indicators and interventions. NICE recommends an HbA_{1c} indicator of <6.5% (<48 mmol/mol) at the stages of mono or dual therapy, increasing to <7.5% (<58 mmol/mol) when considering a third agent. The SIGN algorithm recommends <7.0% (<53 mmol/mol) throughout. In 2009, QOF introduced a three-tier payment with a new emphasis on a threshold of ≤7.0% (≤53 mmol/mol) for HbA_{1c} (previously 7.5% [58 mmol/mol]) (NHS Employers and the General Practitioners Committee, 2008).

The reason for the different glycaemic indicators lie in the somewhat confusing messages emerging from recent research. Since the UKPDS began reporting in 1998, a trend towards reduced CV risk by lowering HbA_{1c} began to emerge, and became significant in 2008: (Holman et al, 2008). However, data emerged from three other large studies in 2008 (ACCORD [Action to Control Cardiovascular Risk in Diabetes] Study Group, 2008; ADVANCE [Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation] Collaborative Group, 2007; and VADT [Veterans Affairs Diabetes Trial]; Duckworth et al, 2009). All three studies also showed a trend towards CV risk reduction with improved glycaemic control, but none achieved statistical significance. In addition, the ACCORD study increased-all cause mortality risk in the intensively treated group. This was entirely unexpected and that arm of the trial was stopped and the participants withdrawn.

The debate about how far to lower HbA_{1c} levels has subsequently been discussed in detail as new studies emerge, particularly one from Currie et al (2010), which proposes a "U-shaped" curve for HbA_{1c} and all-cause mortality, suggesting that there is more risk of harm with low and high HbA_{1c} levels. This has been discussed in detail in this journal (Hadley-Brown, 2009; Frier, 2010). It is no surprise, then that with such a confusing dataset there are differences in HbA_{1c} indicators between NICE and SIGN, evidenced by their algorithms. NICE follows the data reasonably closely by encouraging early, tight glycaemic control with more relaxed indicators for those individuals with more mature disease. SIGN, however, stays with a single indicator for all individuals.

Agreeing personalised targets with people with diabetes is considered important in both pathways, although in the author's opinion probably needs to be more prominent as it lies at the heart of both safe management and achievability.

Named agents

The issue of whether or not to name specific agents in the algorithm highlights the problem of timing guideline publications. The guidance for DPP-4 inhibitors in the NICE algorithm is limited to sitagliptin, which was the only licensed agent in its class at the time of publication. SIGN has opted for naming the class only, there are pros and cons with either approach. The NICE guideline does not intended to deny the prescriber a choice of agents within a class, but it could be interpreted as such. The same argument applies to exenatide or GLP-1 receptor agonists, although NICE is due to publish a technology appraisal for liraglutide later this year. Conversely, the SIGN algorithm potentially allows for all DPP-4 inhibitors (some without a triple therapy licence) to be used in this way.

What the guidance is saying here, is that some additional knowledge and judgement is required. One danger is that algorithms may be seen as "prescribing aids" that may be used widely and perhaps adhered to more rigorously by healthcare professionals in primary care without a special interest in diabetes.

In the past 2–3 years the safety of thiazolidinediones – rosiglitazone in particular – has been questioned (Nissen and Wolski, 2007). Both algorithms make no distinction between the two licensed agents (save for pioglitazone and insulin) and confirm, by their inclusion, the positive risk–benefit balance expressed by the European Medicines Agency (2007). The thiazolidinedione safety issue does merit a key question in the text of NICE (2009) CG87 and a good practice recommendation from SIGN that rosiglitazone should not be prescribed for people with acute coronary syndrome or with a history of myocardial infarction.

Futhermore, insulin analogues do make it into the SIGN algorithm after neutral protamine Hagedorn (NPH) insulin and where special concerns around hypoglycaemia arise. NICE restricts itself to intensifying insulin regimens.

Miscellaneous differences

Considerations for ethnicity merit considerable space in the NICE algorithm with further reference to obesity guidance (NICE, 2006). Ethnicity is further alluded to when considering exenatide therapy. This information, however, is in the remit of SIGN obesity guidelines and only receives brief consideration in this setting.

Regarding GLP-1 receptor agonists, the SIGN guideline restricts their use to obese people with a BMI over 30 kg/m^2, whereas NICE uses the higher cut-off point of 35 kg/m^2, albeit with the statement that people with a lower BMI but with significant obesity-related comorbidities may receive this treatment.

It is noteworthy that both sets of guidance advise withdrawal of therapy if there has been no improvement in glycaemic control. This may well prove important where drugs lack long-term safety data. Finally, rapid-acting insulin secretagogues and acarbose were not mentioned in SIGN, but are mentioned in the NICE pathway.

Conclusion

While it is inevitable that the main thrust of guidance in the two documents concords, there are clear differences in detail, emphasis and some clinical issues.

From a Scottish perspective, it is relevant to note that guidance on newly licensed medications (and in particular pharmaco-economic and budget impact assessments) are considered by the Scottish Medicines Consortium (SMC), a separate organization. This has stated a completion target of 12 weeks for submissions and informs all stakeholders in Scotland regarding the treatment of people with diabetes. SMC approval, therefore, carries great importance both for the pharmaceutical industry and prescriber. The use of class names throughout the SIGN algorithm should facilitate the use of new agents in glycaemic control as they emerge through this process. ■

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