2011: An eventful year for diabetes

Pam Brown, Colin Kenny

As we near the end of what has been a particularly eventful year in the diabetes world, it is a good time to look back at events that made the headlines and identify the changes most likely to impact on primary care teams as we move into 2012. This article summarises the changes to QOF, the use of HbA_{1c} for diagnosis of diabetes, new NICE guidance, diagnosis of diabetes in children, cancer and diabetes and new rules for drivers with diabetes.

Article points

1. We have pulled together all the impactful events in diabetes over the past year into this article, to provide an easy-access guide to the year that was 2011.
2. The World Health Organization published guidance on the use of HbA_{1c} for the diagnosis of diabetes early on in the year, and recently an expert group published similar guidelines for the UK.
3. Concern was expressed at the beginning of the year regarding the recognition of diabetes in children and the need for prompt admission. A number of NICE guidelines and new rules for drivers with diabetes were published.
4. There are many developments on the horizon and we look forward to bringing you the latest practical information in *Diabetes & Primary Care* throughout 2012.

Key words

- Cancer
- HbA_{1c}
- Hypoglycaemia
- NICE
- QOF

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Looking back at 2011, a number of events stand out as having a major impact on primary diabetes care. The World Health Organization (WHO, 2011) published guidance on the use of HbA_{1c} for the diagnosis of diabetes early on in the 2011, and recently an expert group published similar guidelines for the UK (see page 333). Hypoglycaemia became higher profile and the lowest QOF indicator returned to 7.5% (58 mmol/mol), among other changes to indicators. Concern was expressed at the beginning of 2011 regarding the recognition of diabetes in children and the need for prompt admission. In addition, a number of NICE guidelines and new rules for drivers with diabetes were published.

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Hypoglycaemia becomes higher profile

The availability of oral antidiabetes drugs that are associated with a low risk of hypoglycaemia, together with the amended DVLA driving regulations (Drivers Medical Group, 2011), have placed an increased responsibility on healthcare professionals to counsel people with diabetes fully about hypoglycaemia risks when initiating or reviewing sulphonylurea treatment. The reports of higher mortality rates in those with a history of previous severe hypoglycaemic events in the intensively treated arm of the ACCORD (Action to Control Cardiovascular Risk in Diabetes; ACCORD Study Group et al, 2011) study were widely publicised and raised awareness of the risks of hypoglycaemia, particularly in those with long-standing type 2 diabetes and cardiovascular disease. Teams can no longer argue that hypoglycaemia is an inevitable, or indeed acceptable, consequence of achieving good diabetes control.

QOF lowest HbA_{1c} threshold raised to 7.5% (58 mmol/mol)

Although we already aim to agree individualised HbA_{1c} targets with our patients, articles such as Currie et al (2010), demonstrating higher mortality rates in those with type 2 diabetes at both low and high HbA_{1c} values, have prompted many clinicians to opt for unnecessarily conservative targets. In Currie et al's cohort study, the nadir of the J-shaped mortality curve at an HbA_{1c} level of around 7.5% (58 mmol/mol), and slightly higher for insulin-treated groups, has been widely portrayed as suggesting that target levels below 7.5% (58 mmol/mol) are unsafe. However, evidence from the UKPDS (UK Prospective Diabetes Study; UKPDS Group et al, 1998) and its long-term follow-up study (Holman et al, 2008) make it clear that there is a "legacy effect" of cardiovascular benefit from tight, and early glycaemic control, aiming to

Page points

1. In 2011/12 the three main changes to QOF indicators were the controversial raising of the lowest HbA_{1c} threshold, a requirement to carry out risk assessment of diabetic feet, and tightening of the blood pressure thresholds.
2. Process indicators such as DM5 (percentage of people with diabetes who have a record of HbA_{1c} in the previous 15 months), DM11 (blood pressure) and DM16 (total cholesterol) were retired, but surprisingly the total cholesterol indicator for those with diabetes remained at 5 mmol/L rather than the lower levels many of us aspire to.
3. A statement has been published on behalf of an expert group, recommending an HbA_{1c} level of 48 mmol/mol (6.5%) as the cut point for diagnosing diabetes in the UK. A value of <48 mmol/mol (<6.5%) does not exclude diabetes diagnosed using glucose tests.

achieve HbA_{1c} targets of 6.5–7% (48–53 mmol/mol) during the first 10 years after diagnosis. The benefits persist even when control later lapses. Therefore, it could be argued that the <7% (<53 mmol/mol) QOF indicator should have been retained for people with diabetes during the first 5–10 years after diagnosis to achieve cardiovascular benefits, with less tight control acceptable for the frail, elderly and those with established cardiovascular disease.

Changes to QOF indicators

Practices continued to achieve high scores in the diabetes domain of QOF. The data are summarised on page 336.

In 2011/12 the three main changes were the controversial raising of the lowest HbA_{1c} threshold, a requirement to carry out risk assessment of diabetic feet, and tightening of the blood pressure thresholds (British Medical Association and NHS Employers, 2011).

In DM26, the lowest HbA_{1c} threshold was raised again to ≤7.5% (≤58 mmol/mol) with 17 points on offer for achieving this in 50% of those aged ≥17 years with a diagnosis of diabetes. The other two thresholds and achievement indicators remain unchanged at 70% ≤8% (≤64 mmol/mol) and 90% ≤9% (≤75 mmol/mol). For the first time, all the HbA_{1c} indicators were listed in the new units (mmol/mol).

The second change was that DM29 now requires not just assessment of foot pulses and sensation, but also assessment of deformity and ulceration and classification of diabetic feet into low risk, increased risk, high risk or ulcerated, depending on the findings of clinical examination. Although initially challenging, many believe this has been useful in flagging up high-risk feet both to healthcare professionals and to people with diabetes.

The third change was the tighter blood pressure indicator in DM31, aiming for a blood pressure of ≤140/80 mmHg in 40–60% of those on the diabetes register, with a blood pressure of ≤150/90 with a 40–71% target.

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Use of HbA_{1c} for diagnosis

In January, the WHO published a document that stated: "HbA_{1c} can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values and there are no conditions present which preclude its accurate measurement" (WHO, 2011). It recommends using an HbA_{1c} level of ≥6.5% (≥48 mmol/mol) for diagnosing diabetes, but stresses that values of <6.5% (<48 mmol/mol) do not exclude diabetes that has been diagnosed by glucose tests.

A statement has been published in this issue of *Diabetes & Primary Care* (page 333) from Gary John (Clinical Biochemist, Norfolk), Rowan Hillson (National Clinical Director for Diabetes) and George Alberti (Chair, Diabetes UK) on behalf of an expert group, recommending an HbA_{1c} level of 48 mmol/mol (6.5%) as the cut point for diagnosing diabetes in the UK. A value of <48 mmol/mol (<6.5%) does not exclude diabetes diagnosed using glucose tests.

Since HbA_{1c} reflects blood glucose levels over the preceding 8–12 weeks, many feel more comfortable using this when diagnosing diabetes rather than fasting glucose or levels from an oral glucose tolerance test, which reflects levels on a single day only. It is important to check that there are no conditions present that may interfere with accurate use of HbA_{1c} as outlined in the appendix to the WHO guidance.

When choosing to use HbA_{1c} for diagnosis of diabetes or pre-diabetes, it is important to realise that this test will identify a slightly different group to those that would be diagnosed by a fasting glucose level or an oral glucose tolerance test (OGTT). If the person is asymptomatic, two abnormal tests are still needed – either two of the same test, or two

Page points

1. It is estimated that one in three children newly diagnosed with diabetes will have been seen by a healthcare professional with symptoms suggestive of diabetes in the weeks prior to diagnosis, which suggests that GPs and nurses may be missing opportunities to diagnose type 1 diabetes at an earlier stage and avoid diabetic ketoacidosis.
2. In March, NICE published 13 quality standards for the management of diabetes in adults.
3. In March, the Royal College of General Practitioners launched a report along with NHS Diabetes, which aimed to improve the diagnosis, classification and coding of diabetes.

separate diagnostic parameters, for example OGTT and HbA_{1c}.

HbA_{1c} use to diagnose "pre-diabetes" (replacing impaired fasting glucose and impaired glucose tolerance, since these cannot be differentiated using HbA_{1c}) is possible, but debate continues regarding the threshold to use. WHO recommends HbA_{1c} levels of 6–6.4% (42–46 mmol/mol) as diagnostic of pre-diabetes, while the American Diabetes Association (2011) recommends interventions to reduce risk of diabetes for those with an HbA_{1c} of 5.7–6.4% (39–46 mmol/mol), since these people are at greatly increased risk of developing diabetes. The Diabetes Prevention Programme (Knowler et al, 2002) demonstrated that interventions were effective in reducing progression to diabetes when delivered to a group with a mean HbA_{1c} level of 5.9% (41 mmol/mol).

Opportunities to diagnose type 1 diabetes in children

There was controversy in 2011 about the ability of healthcare professionals to diagnose type 1 diabetes. The peak age of diagnosis of type 1 diabetes is around 10–14 years. The onset may be rapid, taking family, carers and even healthcare professionals by surprise, and around 25% of children with type 1 diabetes will present with diabetic ketoacidois (DKA) (Sundaram et al, 2009). It is estimated that one in three newly diagnosed children will have been seen by a healthcare professional with symptoms suggestive of diabetes in the weeks prior to diagnosis, which suggests that GPs and nurses may be missing opportunities to diagnose type 1 diabetes at an earlier stage and avoid DKA (Sundaram et al, 2009). This is important as 80% of deaths in newly diagnosed people with type 1 diabetes under the age of 20 in the UK are related to DKA (Roche et al, 2005).

Healthcare professionals should think about type 1 diabetes when children present with thirst, polyuria, dry mouth, weight loss or headache. Confirmation with either a urine dip test or a random capillary glucose test using a calibrated glucometer should be done immediately and any level of glycosuria or a random capillary glucose level over 7.8 mmol/L would justify a same-day referral (NICE, 2004).

NICE quality standards in diabetes published

In March, NICE (2011a) published 13 quality standards for the management of diabetes in adults. NICE suggests that "an integrated approach to provision of services is fundamental to the delivery of high quality care to people with diabetes". The standards range across a wide spectrum of approaches to diabetes care as well as separate areas where control is important and should be optimised. The standards will also enable commissioners to be confident of the high quality and cost-effectiveness of services.

Coding and classification on GP registers

In March, the RCGP launched a report along with NHS Diabetes, which aimed to improve the diagnosis, classification and coding of diabetes (RCGP and NHS Diabetes, 2011).

The report identified that miscoding, misclassification and misdiagnosis are prevalent in primary care computer systems, with around 5% of people having one or more errors, with 2.2% being misdiagnosed, 2.1% being misclassified and 0.9% miscoded. As a result, an easy-to-use algorithm has been prepared to help with diagnosis and coding of people with diabetes. This also recognises an "uncertain" category.

Laboratories move to reporting HbA_{1c} in mmol/mol and not %

Although there would appear to be considerable regional and national differences on the uptake of this change in 2011, most laboratories have signalled their intention to move from dual reporting of HbA_{1c} levels from percentages to mmol/mol. Healthcare professionals are becoming accustomed to the new figures and levels and guiding patients accordingly.

Diabetes prevention

Diabetes prevention studies have demonstrated that intensive lifestyle programmes in those with impaired glucose regulation could reduce the risk of progression to diabetes by more than half and

were more effective than drug therapy (Knowler et al, 2002). Attempts are now underway to translate those research findings into practice.

NICE (2011b) published public health guidance in May this year entitled *Preventing Type 2 Diabetes: Population and Community Level Interventions in High Risk Groups and the General Population*. It stressed that diabetes shares risk factors with other diseases, such as cardiovascular disease and some cancers, so interventions to reduce diabetes risk should also impact favourably on these other conditions. The guidance reiterated the importance of supporting behaviour change, achieving and maintaining a healthy body weight, making available effective weight loss programmes and increasing physical activity levels, and stressed that these must be delivered in culturally appropriate ways. Although much of the guidance was targeted at commissioners and public health teams, we in primary care are already helping to identify those who will benefit and signposting them to available resources in our communities.

The NICE public health draft guidance on *Preventing Type 2 Diabetes: Risk Identification and Interventions for Individuals at High Risk* is out for consultation until January 2012 (available at http://bit.ly/uPRuC4) and the completed guidance document is expected in summer 2012. This focuses on the use of risk assessment scores and blood testing to identify those at high risk of developing type 2 diabetes, and explores recommendations on how to provide information, advice and tailored support to help people make lifestyle changes that may help to reduce or delay their risk of developing diabetes. The first section of this document, which summarises the recommendations, is well worth reading and the programme development group would value input from the full range of stakeholders.

Cancer and diabetes – controversy continues

Meta-analyses have demonstrated higher rates of hepatic, pancreatic, colon, endometrial, bladder and breast cancer in people with diabetes (Vigneri et al, 2009).

Metformin

Metformin is widely accepted as a first-line agent in type 2 diabetes because of its efficacy and favourable cardiovascular outcomes (Holman et al, 2008). More recently it has been reported that metformin may also lower cancer risk in people with diabetes. Bowker et al (2006) demonstrated lower cancer mortality with metformin therapy when compared with sulphonylureas and insulin therapy in people with type 2 diabetes as well as better outcomes following chemotherapy for breast cancer in women with type 2 diabetes on metformin versus those not on metformin (Jiralerspong et al, 2009).

Postulated mechanisms include the effect of metformin on weight loss, which may play a small role since adiposity is linked to increased cancer risk. Metformin may also lower insulin resistance, which in turn lowers insulin levels. This could be important because hyperinsulinaemia may promote carcinogenesis (van der Burg et al, 1988). In addition, metformin appears to influence signalling molecules, such as tumour suppressors (Ben Sahra et al, 2008). This is all observational data but it is sufficiently intriguing to lead investigators to urgently consider randomised trials.

Insulin

The role of both human and analogue insulins in the development of cancer remains controversial. In 2009 the European Medicines Agency (EMA, 2009) reviewed the available data and concluded that there was no cause for concern and that changes to the prescribing advice were therefore not necessary. This year the US Food and Drug Administration (2011) suggested continuing treatment with insulin analogues to avert the long-term complications of diabetes until randomised, prospective studies are available to confirm a correlation with cancer and insulin.

Pioglitazone

Data emerged in 2011 that suggest a small increased risk of bladder cancer with pioglitazone-containing products, and the EMA

Page points

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3. Meta-analyses have demonstrated higher rates of hepatic, pancreatic, colon, endometrial, bladder and breast cancer in people with diabetes.
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Page points

1. The Primary Care Diabetes Society (2011) published guidance suggesting that use of pioglitazone is now contraindicated in people with current active bladder cancer, a history of bladder cancer and uninvestigated macroscopic haematuria.
2. Linagliptin is a dipeptidyl peptidase-4 inhibitor for the treatment of type 2 diabetes. Linagliptin (once-daily) was approved by the European Medicines Agency in September 2011.
3. A once-weekly version of the glucagon-like peptide-1 receptor agonist exenatide was also launched this year.
4. Changes to the DVLA guidance are already having an important impact on primary healthcare teams and will likely impact future prescribing costs.

has published new guidance on the drug (EMA, 2011). The EMA's Committee for Medicinal Products for Human Use (CHMP) reviewed all published and unpublished data and confirmed that medicines containing pioglitazone "remain a valid treatment option for certain patients with type 2 diabetes, but there is a small increased risk of bladder cancer in patients taking these medicines" (EMA, 2011).

The Primary Care Diabetes Society (2011) published guidance suggesting that use of pioglitazone is now contraindicated in people with current active bladder cancer, a history of bladder cancer and uninvestigated macroscopic haematuria. Current users of the drug, who are well controlled, should be guided by their healthcare professional to make an informed decision about the drug.

New diabetes pharmaceutical products launched

Linagliptin

Linagliptin is a dipeptidyl-peptidase-4 (DPP-4) inhibitor for the treatment of type 2 diabetes. Linagliptin (once-daily) was approved by the EMA in September 2011.

Linagliptin stimulates the release of insulin in a glucose-dependent manner and decreases the levels of glucagon in circulation. It is marketed as being particularly suitable for patients at all levels of renal impairment (Electronic Medicines Compendium, 2011).

Exenatide once-weekly

A once-weekly version of the glucagon-like peptide-1 receptor agonist exenatide was also launched in 2011. It is an extended-release medication for type 2 diabetes designed to deliver continuous therapeutic levels of exenatide in a single weekly dose.

New NICE hypertension guidance

In August, NICE (2011c) published clinical guidance for hypertension. It offers evidence-based advice on the care and treatment of adults with primary hypertension. The active treatment of hypertension in people with diabetes remains one of the most important evidence-based interventions.

The new guidance suggests that ambulatory blood pressure monitoring should be offered more widely by practices. The guidance recommends treating hypertension at the level of 140/90 mmHg in clinic blood pressure readings and suggests that angiotensin-converting enzyme inhibitors should be first-line followed by calcium channel blockers (CCBs) and non-thiazide diuretics if CCBs are not suitable.

Updated DVLA guidance should be flagged to all people with diabetes

Changes to the DVLA guidance are already having an important impact on primary healthcare teams and will likely impact future prescribing costs (Drivers Medical Group, 2011). From November 2011, any driver on insulin or a sulphonylurea who has more than one severe episode of hypoglycaemia requiring third party assistance in the previous 12 months must inform the DVLA and is at risk of losing their licence. Likewise, any driver with loss of hypoglycaemia awareness must inform the DVLA and they too may lose their licence.

Diabetes UK are widely publicising the changes, but the onus is also on all healthcare professionals prescribing these drugs to ensure that people with diabetes understand the guidance and report these adverse events. Most practices will choose to provide the Diabetes UK (2011) leaflet and to document this in the electronic record when seeing patients for review.

All drivers being treated with sulphonylureas will need to be educated about their risk of hypoglycaemia and the importance of testing blood glucose before driving. The hypoglycaemia risk is likely to foster reluctance to accept initiation of a sulphonylurea in future, when drugs such as the DPP-4 inhibitors that do not carry this risk are available.

Many more individuals will need and want to undertake self-monitoring, with the attendant costs, and it is hard to argue for restricting this. There are also implications for ambulance services, who are regularly called to assist those suffering severe hypoglycaemia, but who currently allow people with diabetes to decide

whether to inform their GP if they are not admitted. This will almost certainly change.

Specialists will make decisions on which people on insulin will be permitted to hold Group 2 (larger goods vehicle and passenger carrying vehicle) licences, but these people are likely to seek initial advice (and copious supplies of glucose-monitoring strips) from their primary care providers.

Conclusion

This article has summarised the main events in diabetes this year and their relevance for healthcare professionals in primary diabetes care. There are many developments on the horizon and we look forward to bringing you the latest practical information in *Diabetes & Primary Care* throughout 2012. ■

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