Should recent papers change our practice?

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I hope you have all been able to make time for a holiday this summer or at least to spend time relaxing, and are reading this edition of the Journal with your batteries recharged, ready to get the most from the enthusiasm and inspiration provided by our contributors as they tackle areas of real importance to our day-to-day practice.

Colin Kenny helps us decide when to stop aspirin in those without previous cardiovascular events, Mike Kirby steers us through the dyslipidaemia CPD module and Neil Munro provides a guided tour of the microbiome and its implications for diabetes. We hope you will choose to undertake Sam Seidu's latest audit looking at estimated glomerular filtration rate and incretin therapies, learn more about the law of consent in the second of Chris Cox's legal updates, and join Lesley Mills and Christopher Garrett as they explore our role in helping to prevent diabetic ketoacidosis. Finally, I suspect the Government's plans for the sugar tax have been somewhat overshadowed by recent political upheaval, but we will share your views from our survey on whether you believe such a tax will achieve its goals. NICE stresses the importance of individualising the care we provide and papers published over the last few months help inform our recommendations on diet, glucose-lowering drugs and blood pressure (BP).

Individualising diet advice

Understanding the nuances of different diets and individual nutrients is challenging, and, therefore, specialist dietetic input, not just at diagnosis but throughout the early years of diabetes, can help people make informed, beneficial choices about what they eat. However, this is not always available, so the only dietary advice many people receive comes from practice teams, the patient's friends and family and the media. The recent publication from the National Obesity Forum (National Obesity Forum and Public Health Collaboration, 2016) has been criticised for providing confusing messages, which have been widely publicised by the press. It is perhaps timely, therefore, that we review the dietary advice that we deliver and ensure our teams provide clear, consistent messages.

Food can be thought of as the only medication impacting lipids, glycaemia, BP and weight that everyone adheres to, taking large and small doses of suitable or unsuitable "drug" each day. Within minutes of each meal, snack or drink, nutrients are interacting with our microbiome and genome, switching pathways and enzymes off and on, and influencing our metabolism.

Although we would all agree that most people with type 2 diabetes would benefit from eating fewer calories and more "real" food, it can be difficult in short consultations to provide individualised advice which is specific enough to be useful, yet concise enough to be deliverable. The American Diabetes Association (ADA) recommends a Mediterranean-style diet rich in monounsaturated fats (MUFA), fatty fish, nuts and seeds, with carbohydrates focused on whole grains, fruit and vegetables that are high in fibre and with a low glycaemic load. This eating style has been demonstrated to reduce type 2 diabetes development, assist weight loss and glycaemic control (Esposito et al, 2015) and be beneficial compared to low-fat diets in primary and secondary prevention of cardiovascular disease (CVD). It is easy to prescribe the Mediterranean diet using the Patient leaflet (http://patient.info/health/mediterranean-diet) and online resources such as those at NHS Choices Living Well. However, it remains unclear which components of this diet actually deliver the benefit.

Two recently published studies further explore the effects of increased MUFA and polyunsaturated fats (PUFA) in those with diabetes. A meta-analysis (Imamura et al, 2016) including 102 randomised controlled feeding trials, reviewed effects of macronutrient intake on HbA_{1c}, insulin sensitivity, insulin levels and insulin secretion in 4222 adults. The studies within this meta-analysis explored the impact of swapping a proportion of

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dietary carbohydrate or saturated fat for other macronutrients, while maintaining calorie intake. Swapping 5% of carbohydrate or saturated fat (SFA) for increased MUFA or PUFA reduced HbA_{1c} and insulin resistance. However, only replacing with PUFA was linked to lower fasting glucose and improved insulin secretion. Previous studies have confirmed that both MUFA and PUFA have beneficial effects on lipid profiles, but cardiovascular benefits were only shown for some types of PUFA. These differences on glucose and insulin secretion may help to explain this.

A smaller systematic review and meta-analysis of randomised controlled trials (RCTs) comparing high-MUFA to high-carbohydrate diets demonstrated reduction in fasting glucose, triglycerides, body weight and systolic BP and increases in HDL-cholesterol with high-MUFA diets (Qian et al, 2016). Comparing high-MUFA to high-PUFA diets demonstrated a significant reduction in fasting glucose with MUFA.

Foods contain a mix of fats, making it difficult to translate such research into practice, but the evidence continues to support recommending Mediterranean-style eating, with increased intake of olive oil, nuts, fish and vegetables high in unsaturated fats and reduced intake of saturated animal fats or refined grains, starches and sugars. This broadly aligns with NICE's recommendations.

Individualising glycaemic targets and drug therapy

When we are helping people individualise their glycaemic targets, the ADA/European Association for the Study of Diabetes (EASD) glycaemic goal-setting diagram (Inzucchi et al, 2015) provides a practical tool. Some clinicians prefer the "ABCD" *aide-mémoire* and an updated review of this now incorporates an additional "E" (Lyssenka et al, 2016). Similar to the ADA/EASD resource, this encourages us to consider **A**ge (as a risk factor and for life expectancy and mortality), **B**ody weight and fat distribution (as markers of insulin resistance), **C**omplications (in relation to suitability for drugs and doses, and in relation to complication prevention) and **D**uration of diabetes (short duration and tight control or long duration and less benefits). The authors added **E**tiology, reminding us of the variable contribution of the underlying "Ominous Octet" of defects in each individual. Targeting a variety of these defects by using drugs with different sites of action helps optimise therapy.

Many primary care teams find that helping people decide what to add to metformin is stressful and time-consuming due to the plethora of drugs and the freedom of choice afforded by the 2015 NICE guideline. The resulting "paralysis by analysis" increases the risk of clinical inertia and delayed intensification. A new meta-analysis of RCTs and network analyses comparing the clinical outcomes and adverse events associated with different glucose-lowering drugs (Palmer et al, 2016) reinforced metformin as first-line therapy and provided reassurance that all the other drugs had similar glucose-lowering effects when added to metformin, and none of the drug classes was associated with increased CVD or mortality. As expected, sulfonylureas (SUs) and basal insulin were associated with highest risk of hypoglycaemia (10% absolute risk difference compared with metformin), prompting the authors to remind us that we and our patients may prefer to avoid SUs and insulin to minimise hypoglycaemia.

The relationship between SU use, hypoglycaemia and CVD risk has been much debated in recent years. A meta-analysis (Rados et al, 2016) seeks to reassure us that SUs do not increase all-cause and CVD mortality, while a new review (Hanefeld et al, 2016) explores possible links between hypoglycaemia and CVD risk without being able to identify a definitive causal relationship. However, the authors of this latter paper, global experts on hypoglycaemia, conclude that severe hypoglycaemia appears to be able to trigger cardiovascular events in vulnerable patients and should therefore be "avoided at all costs in people with known cardiac disease".

A further analysis of the SAVOR-TIMI saxagliptin cardiovascular safety study demonstrated 16.6% of patients reported hypoglycaemia and nearly 2% suffered major hypoglycaemia, with SU or insulin use associated with increased risk of hypoglycaemia. This is a timely reminder that if we choose to continue SUs when intensifying oral therapy rather than switching to potentially safer drugs, we need to reduce the SU dose at least initially to avoid precipitating hypoglycaemia.

"This is a timely reminder that if we choose to continue sulfonylureas when intensifying oral therapy rather than switching to safer drugs, we need to reduce the dose at least initially to avoid precipitating hypoglycaemia."

So should these new papers change our prescribing? The evidence remains that SUs cause significant weight gain and hypoglycaemia. Other drugs provide similar glycaemic benefits, are weight neutral or facilitate weight loss, cause low hypoglycaemia risk and several have proven cardiovascular neutrality or benefit in high-risk groups. I will, therefore, continue to reserve SUs for rescue therapy in symptomatic individuals at diagnosis or if control is very poor, aiming to withdraw the gliclazide after a few months when control improves.

Individualising BP targets in older people

Following on from our hypertension CPD module in the last edition of the Journal (Gadsby, 2016), a supplement to the August edition of *Diabetes Care* summarised the 5th World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension 2015. A review (Solini and Grossman, 2016) of studies of older people with diabetes and hypertension recommended a target of <140–150/90 mmHg for otherwise healthy older people. This is similar to the 140–145/80–90 mmHg target recommended in older people in the hypertension CPD module (Gadsby, 2016). The same target was recommended, but avoiding aggressive BP lowering if co-existing coronary arterial disease, and also in isolated systolic hypertension (ISH) provided this can be achieved with a diastolic >60 mmHg. In those with ISH, if the diastolic is 60 mmHg or less, a systolic target of 160 mmHg may be adequate. Up to 30% of older people with hypertension suffer from orthostatic hypotension (>20 mmHg reduction in systolic or >10 mmHg in diastolic BP going from supine to standing position) and diabetic neuropathy may increase this. We should look for orthostatic hypotension, and review carefully the benefit–risk balance and consider relaxing targets if it occurs, especially in the frail elderly or those with cognitive decline. Discussion continues on optimal systolic targets in younger people with diabetes.

Referral for retinopathy screening

Finally, a reminder that NICE updated the type 1 diabetes (NICE, 2015a) and type 2 diabetes (NICE, 2015b) in adults guidelines to clarify that primary care teams should immediately refer all adults to the local eye-screening service at time of diabetes diagnosis, with a view to screening being performed as soon as possible and no later than 3 months from referral, with annual follow-up thereafter. This 3-month target may be challenging for services but hopefully can be used to influence increased funding. Two-yearly screening is recommended for low-risk people with type 2 diabetes in some areas; provided we are vigilant and request new appointments for non-attenders, the evidence supports this. Since retinal screening is no longer included in Quality and Outcome Framework targets, it is no longer included in the downloadable templates we use to prompt action in consultations and clinics. Spending 5 minutes this month amending our templates to add this and albumin:creatinine ratio screening back in could be time well spent. ■

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