Introduction

Although talk of patient-centred care is ubiquitous, one of the greatest challenges facing diabetes health care professionals is turning this rhetoric into a clinical reality and really engaging people with diabetes in shared decision making.

As medicine becomes more sophisticated with improved technological advances, there is a view that the doctor–patient relationship has become more constrained, more focused on measuring and recording biomedical outcomes (HbA1c, blood pressure, lipids, microvascular complications) at the expense of compassion, communication and the health outcomes that matter to patients. This is a particular concern for children and young people with type 1 diabetes, who are focused on the impact of diabetes and its treatment in their everyday lives and typically less motivated by the strict glycaemic control targets recommended by health professionals for improved long-term health outcomes. The National Paediatric Diabetes Audit highlights the urgent need to bridge this gap between our expectations of tight glycaemic control and the reality of actually achieving it, with only 15% of children and young people achieving an HbA1c below 7.5% (58mmol/mol). Similarly, only a minority of women with diabetes are adequately prepared for pregnancy, with fewer than 20% taking preconception folic acid supplementation and achieving a first trimester HbA1c level below 7.0% (53mmol/mol).1 Despite the well-recognised association between poor glycaemic control and increased risk of major congenital malformation (30% increased risk per 1% increase in HbA1c above 6.3% [45mmol/mol]), a majority of women are unable to achieve these targets.2

In real-life settings, health professionals may struggle to balance the requirement for improving glycaemic control with realism and appreciation of the patient’s sustained daily efforts.3 We may give conflicting information about the number and timing of blood glucose tests (before and after meals versus only before meals), inconsistent dietary advice (count only carbohydrates versus consider impact of glycaemic index and macronutrients on carbohydrate availability and absorption rate), and set unrealistic expectations about matching prandial insulin boluses to variable dietary intakes. We may also fail to acknowledge the limitations of treatment regimens and individual variability in carbohydrate metabolism and insulin pharmacokinetics.

Structured diabetes education

It is uncontroversial that intensive insulin therapy accompanied by intensive educational, dietary and psychological approaches to type 1 diabetes

Abstract

A gap exists between our expectations of tight blood glucose control for type 1 diabetes and the reality of safely achieving it, particularly during adolescence and pregnancy. Technological and pharmaceutical advances will not alone achieve near-normal blood glucose control and optimal health outcomes without recognising the social, cultural and behavioural context of those living with diabetes. Neither will educational programmes completely overcome the fundamentally disordered metabolic pathways and/or the additional physiological challenges of adolescence and pregnancy.

Improved integration of the technological, behavioural and educational aspects of care will pave the way for truly personalised, diabetes self-management and improved health outcomes for women and children with type 1 diabetes. Copyright © 2012 John Wiley & Sons.
psychological support improves glycaemic control and reduces the risk of microvascular complications; however, the means of routinely providing this support in real-life clinical settings are unclear.\textsuperscript{4} The UK DAFNE study demonstrated that, for adults with poor glycaemic control, a five-day programme teaching intensive insulin dose adjustment improved both quality of life and glycaemic control without worsening hypoglycaemia.\textsuperscript{5} However, the benefits on glycaemic control wane with time, with a mean fall in HbA1c reducing from 1% at six months to 0.5% at six months. Longer-term follow up in routine care suggests even more modest reductions of 0.3% at four to seven years’ follow up. The Irish DAFNE study, which focused on patient-centred goal setting in addition to intensive insulin dose adjustment, suggests that patients may judge reducing their risk of hypoglycaemia or improving their quality of life to be just as or even more important than lowering HbA1c. More detailed qualitative research is trying to unpick the longitudinal predictors of success of structured education, suggesting that in adults some key factors include embedded knowledge, continued responsive support, enduring motivation and being empowered.\textsuperscript{6}

**Paediatric diabetes education**

The UK paediatric diabetes education programmes have not yet identified how best to support adolescents to integrate the demands of intensive insulin dose adjustment into their daily routines. Parents recognise the negative impact of type 1 diabetes management on the ‘spontaneous nature of teenagers’, requiring them to accept ‘enormous responsibility at too young an age’.\textsuperscript{7} Family communication and sharing responsibility for daily self-management tasks to find a workable balance between delegating too much responsibility too soon or being too protective are crucial, across a variety of age ranges and cultures.\textsuperscript{8} Structured US programmes which support parents and young people to share diabetes responsibility are associated with improved biomedical outcomes, reduced family conflict and improved quality of life.\textsuperscript{9,10}

However, efforts to replicate these interventions in the UK have had only limited success, with two recent randomised studies (including ours) reporting a disappointing lack of efficacy on biomedical and/or psychosocial outcomes.\textsuperscript{12,13} This may also be related at least in part to a lack of embedded knowledge among patients, parents and health care professionals, and to the challenges of enhancing the communication skills required for continued parent and adolescent motivation and empowerment.

It remains unclear whether such programmes require specialist facilitators with health psychology/social scientist backgrounds or whether they can be delivered by existing multidisciplinary teams. It is also unclear whether delivering education to small groups of children and parents, which provide peer support for both parents and children, are sufficient to really embed the skills for intensive insulin therapy, to a range of children and adults of different socio-economic, demographic and educational backgrounds, and variable mathematical ability.

Our Families, Adolescents and Children Teamwork Study (FACTS) demonstrated that only between a third and a half of adolescents aged 11–16 years report frequently adjusting their pre-meal insulin doses.\textsuperscript{12} This may be due to a skills deficit, insufficient emphasis on parental input, and/or a lack of ongoing motivation and empowerment. Perhaps we need to start embedding the skills required for carbohydrate counting and insulin dose adjustment earlier, from immediately after diagnosis, with consistent structured and unstructured reinforcement thereafter. It is also clear that we need to understand better the barriers to blood glucose testing and sustained reflection among parents and young people, and develop new strategies for overcoming them before families enter the vicious circle of frustration and diabetes burn-out.

Decision aids including some of the paper, electronic and web-based apps for carbohydrate counting (www.carbsandcals.com) may help make consistent, reliable information more accessible. Blood glucose meters integrated with mobile phones may make blood glucose testing more socially acceptable to teenagers, and/or make recording blood glucose data less cumbersome. Reflecting on blood glucose data is recognised as key to optimal dose adjustment and it is unclear whether more sophisticated glucose meters facilitate or, with reduced need for paper-based diaries, may even hinder this task. Recent evidence suggests that poor mathematical skills are associated with poor glycaemic control in type 1 diabetes.\textsuperscript{14} Bolus calculator devices may help improve confidence with accuracy of insulin dose adjustment for those on pumps and multiple daily injections, with preliminary data suggesting they may allow people to dose adjust insulin with reduced fear of hypoglycaemia.\textsuperscript{15} However, there are no data to suggest that they are associated with additional biomedical benefit above and beyond structured carbohydrate counting and traditional insulin dose adjustment education, with most of the apparent improvements more directly related to the training provided rather than the bolus calculator device.\textsuperscript{16}

**Carbohydrate counting: challenges and constraints**

Highly motivated pregnant women, who participated in a 24-hour clinical research facility study, attributed their excellent overall glycaemic control (over 80% of time spent with plasma glucose levels within the recommended target range for pregnancy) to the ease with which they could accurately adjust insulin when provided with the precise carbohydrate content of supermarket bought ready-meals.\textsuperscript{17} It is also becoming increasingly clear that, while carbohydrate counting skills are key for optimal insulin dose adjustment, these skills are counterbalanced by new challenges and restraints. The increased challenges and demands of carbohydrate counting have recently been highlighted in qualitative studies, and can be summarised by the following comments from people with diabetes. ‘OK, constant monitoring, and watching, and counting has taken over. My life is not as free as it
used to be in so far as you took four injections a day, and you went about your business. But now every morsel of food over 10 grams of carbohydrate requires an injection. Another person describes altered eating behaviour following structured education, recognising that it may be easier to restrict carbohydrate intake and thereby limit the insulin dose and risk of postprandial hypoglycaemia: ‘I’m becoming a lot more conscious of my carb intake, and a lot of the time, like having a turkey breast or something; before I might have had rice with it, whereas now I’m thinking, I’ll just have salad. I’m realising that, because I’m not having rice, I don’t need my insulin, and then I won’t have a hypo.’

Using new technologies to personalise diabetes education

While group education undoubtedly provides additional benefits of peer support, tailoring the insulin dose adjustment advice to each person’s individual dietary and lifestyle preferences can be challenging in a group setting. Continuous glucose monitoring (CGM) provides unprecedented insights into the inter- and intra-individual variability of glucose control.

Retrospective CGM whereby the patient provides detailed 24-hour glucose profiles and expertise regarding lifestyle can be used as an educational tool to support shared decision-making. The health professional brings understanding of carbohydrate metabolism, insulin kinetics and therapeutic options alongside the patient’s knowledge of their daily routines, to support collaborative problem solving in a very concrete fashion. It also allows for reflection on the changes made, providing precise feedback for patients and health professionals. For example, having viewed her seven-day CGM profile, a woman with very tight glycaemic control (booking HbA1c 6.3% [45mmol/mol]) and loss of hypoglycaemia awareness at eight weeks’ gestation was able to make the changes required (reduced insulin to carbohydrate ratio with lunch and decreased basal insulin rates during the afternoon) and to restore her hypoglycaemia warning symptoms. Her subsequent CGM profile provided visual confirmation that these changes had been successful, with HbA1c at 12 weeks’ gestation of 5.2% (33mmol/mol), alleviating her concerns about substantially compromising overall glycaemic control. The use of CGM supports shared decision making and can, for some individuals, be a powerful motivator for behavioural change.

In our randomised controlled trial of retrospective CGM during pregnancy, 71 women with type 1 (n=46) and type 2 diabetes (n=25) were allocated to routine capillary glucose monitoring (7–8 tests per day) either with or without supplementary CGM. The CGM was used 3–4 times during pregnancy at 4–6 weekly intervals and worn for 5–7 days to incorporate both weekdays and weekends. Women with access to supplementary CGM had significantly lower HbA1c levels at the end of the third trimester (32–36 weeks’ gestation): 5.8±0.6% (40±6mmol/mol) compared to women with only routine capillary glucose testing 6.4±0.7% (46±8mmol/mol). There were trends towards fewer emergency caesarean section deliveries and reduced infant birth weight in the CGM group (p=0.07 and 0.08 respectively), with significantly reduced birth weight standard deviation score, birth weight centile and risk of macrosomia (Figure 1).

Limitations of this study were the relatively small number of participants, the combination of women with type 1 and type 2 diabetes and the relatively late onset of CGM, which would ideally have been introduced before pregnancy to optimise glycaemic control during the periconception period. An international, multicentre, randomised controlled trial (Continuous glucose monitoring in women with type 1 diabetes during pregnancy trial – CONCEPTT) assessing the impact of real-time CGM pre- and post-conception will commence later this year.

Real-time CGM: benefits and limitations

Outside pregnancy, a meta-analysis of individual patient data (n=882), from six large randomised controlled trials, suggests that CGM is associated with a significant reduction in HbA1c, with greater benefits in those who use it daily and those with higher baseline HbA1c. Model estimates suggest a 0.9% (9mmol/mol) lowering for those with HbA1c of 10% (86mmol/mol) and 0.5% for those with baseline HbA1c of 7.0% (53mmol/mol). If these data are confirmed in women preparing for pregnancy, substantial reductions in the risk of major congenital malformation would be anticipated. While this meta-analysis did not demonstrate an independent
effect of age, the lack of benefit of CGM in children and young people is striking from the Juvenile Diabetes Research Foundation CGM data.21 The challenges of engaging adolescents in diabetes self-management are well recognised, but it is surprising that even those motivated to participate in an intensive study did not find CGM sufficiently useful to wear the device continuously and/or integrate the learning from CGM into their daily routines.

A more recent study of real-time CGM in younger school-aged children (n=146 aged 4–9 years old), in whom the parents would be highly engaged, motivated and involved in diabetes management, also failed to demonstrate a beneficial effect on HbA1c.22 This is all the more surprising considering their baseline HbA1c of 7.9±0.8% (63±29nmol/mol) and the fact that 64% were using insulin pump therapy. Indeed, these children spent almost 5 hours per day with glucose levels above 13.9nmol/L, with the authors suggesting that parents were unable to optimise prandial dose adjustment, due to their unremitting fear of hypoglycaemia. No data regarding dietary intake are available but it seems that, even among this highly motivated cohort with access both to CGM and insulin pump therapy, current insulin analogues could not limit exposure to postprandial hyperglycaemia.

**Postprandial hyperglycaemia**

The substantial contribution of postprandial glucose excursions to overall glycaemic control are best defined in patients with type 2 diabetes, with studies suggesting that in non-insulin treated patients with an HbA1c <7.5% (56nmol/mol) postprandial glucose levels make about a 70% contribution to overall glucose control, equating to about 1% HbA1c.23

Outside pregnancy, any reduction of 1% in HbA1c normally results in a substantial reduction in microvascular complications. During the first trimester, a 1% reduction in HbA1c would be associated with a 30% reduction in risk of major congenital malformation.2 A 1% reduction in HbA1c during the second and third trimester would be associated with a 50% reduction in pre-eclampsia the major cause of preterm delivery.24

Reductions in these complications alone would be associated with substantial improvements in maternal and neonatal morbidity (fewer neonatal care admissions etc.). However, improving postprandial glucose control during the second and third trimesters is necessary to reduce the risk of fetal growth acceleration and large-for-gestational age infants.25 Thus, better understanding of the pathophysiology of postprandial hyperglycaemia in pregnancy may help inform therapeutic options.

The postprandial glucose excursion is defined by interactions between total postprandial glucose appearance (Ra), endogenous glucose production (EGP) and glucose utilisation/disposal (Rd). Figure 2.)

![Figure 2. Postprandial glucose excursion](image)

The post-prandial rate of glucose absorption (Ra meal) is dependent on the rate at which glucose is emptied from the stomach and absorbed across the intestinal membrane and on the extent of extraction during the first pass of the liver and splanchnic tissues. Unlike endogenous glucose production and the rate of glucose utilisation, the gut absorption of glucose is not dependent on plasma insulin concentration by the quality and quantity of carbohydrate, protein and fat ingested; it is further influenced by the rate at which glucose is emptied from the stomach and absorbed across the intestinal membrane and by the extent of extraction during the first pass of the liver and other splanchnic tissues, before reaching the systemic circulation.

We have recently described the inter-individual variability in carbohydrate metabolism and insulin pharmacokinetics in pregnant women with type 1 diabetes using stable label isotope tracers and computational modelling techniques.27 The rate and timing of postprandial glucose appearance were largely determined by the type of carbohydrate ingested with a significantly more rapid appearance of glucose after a 60g carbohydrate breakfast of orange juice and two slices of toast with jam, compared to an 80g carbohydrate evening meal. Half of the glucose from breakfast appeared in the systemic circulation after 1 hour (60±20 minutes). For the evening meal, it took almost 2 hours, again with substantial individual variability (110±25 minutes). Despite the very different rates of postprandial glucose appearance between the evening and breakfast meals, the glucose disposal rates were quite comparable (both approximately 100±20 minutes).
The postprandial hyperglycaemic spike is a consequence of the mismatch between glucose appearance and glucose disposal, which was most apparent after the rapidly absorbed breakfast meal (glucose appearance vs glucose disposal 60±20 vs 100±20 minutes) and less challenging after the slowly absorbed evening meal (110±25 vs 100±20 minutes).

Contrary to our expectations of delayed gastric emptying there was no difference in the glucose appearance rates between early and late gestation. However, as pregnancy advances, there are further physiological changes with significantly increased insulin resistance (both hepatic and peripheral), significantly more delayed glucose disposal (now approximately 130±30 minutes after dinner and breakfast) and slower absorption of insulin from the subcutaneous site (taking 80±30 minutes compared to 50±10 minutes in early pregnancy).

Thus, for the same breakfast and evening meals the slower insulin absorption and delayed glucose disposal during the third trimester resulted in an even greater postprandial mismatch between glucose appearance and disposal. During the third trimester this was even more apparent after the rapidly absorbed breakfast (60±20 vs 130±30 minutes) compared to the more slowly absorbed evening meal (110±25 vs 130±30 minutes).

The therapeutic implications of this are that earlier prandial insulin administration and/or more slowly absorbed carbohydrates, particularly at breakfast, may help to reduce postprandial hyperglycaemia. This can be achieved in practical terms by giving an earlier pre-meal bolus (up to 30–40 minutes before meals) and adding protein and fat to slow down the absorption of breakfast carbohydrates (e.g. replacing ready-made breakfast cereals with granary or oat bread toast accompanied by egg, cheese or ham).

Closed-loop insulin delivery
Clearly, it is a complicated task in real life to compute the optimal timing and dose for the pre-meal insulin bolus and adjust this according to the nutritional content of the meal, current glucose level and prevailing insulin sensitivity. Closed-loop technologies use a control algorithm (set of mathematical instructions) to integrate insulin pump delivery with real-time CGM glucose levels. This means that insulin delivery is more responsive both to current and predicted changes in glucose and insulin concentrations. The model predictive controller used in Cambridge re-calculates the insulin dose every 15 minutes, attempting to minimize the distance between the forecasted glucose and target glucose concentration. It is proactive in that, with user input regarding the meal carbohydrate quantity and prandial insulin dose, it can anticipate changes in postprandial glucose appearance and insulin action over a 1.5–3 hour window. This is important given the slow absorption and delayed action of even the most rapid acting insulin analogues. The closed-loop system can operate in a fully automated fashion (without user input) between meals and overnight, but user input is required for optimal postprandial glucose control.

Preliminary studies in laboratory settings have focused on overnight closed-loop, demonstrating 20–30% increased time in target and reduced nocturnal hypoglycaemia, compared to conventional pump therapy, in children and in adults.28,29 Overnight studies in pregnancy also demonstrate the safe achievement of near-normoglycaemia in the clinical research facility, during early, mid and late gestation.30 It is worth noting that, during our 24-hour randomised crossover trial, the study participants (highly motivated pregnant women in specialist pump centres) achieved exceptionally good glycaemic control (80% time in target) both with conventional pump therapy and with closed-loop, perhaps suggesting that the strict glycaemic control targets recommended during pregnancy can be achieved by selected women, in selected centres.

The attraction of closed-loop is that it may make tight glucose control more safely achievable over a longer time frame and to a wider range of individuals. However, the demands of engaging those who might most benefit from these technological advances should not be underestimated.

Patients will need to wear an insulin pump and CGM sensor with all the necessary set changes, calibration tests etc and to carry the algorithm device (currently a tablet PC but with smaller devices such as smart phones anticipated in the future). However, the greater challenge will be how users interact with the technology, particularly around meals and exercise.

User education, in particular carbohydrate counting skills will remain key with communication between the user and the device absolutely essential for safe effective closed-loop control. Improved integration of the technological, behavioural and educational aspects of care will pave the way for truly personalised diabetes self-management and improved health outcomes for women and children with type 1 diabetes.

Acknowledgements
I would like to thank all the young people, pregnant women and their families who have graciously contributed to our research.

I am grateful also for the extensive input, expertise and experience provided by all the diabetes nurse specialists, dietitians, health psychologists and clinicians, in particular the Families, Adolescents and Children Teamwork Study (FACTS) group, the East Anglia Study group for Improving Pregnancy Outcomes in women with Diabetes (EASIPOD), and the Cambridge Artificial Pancreas team.

The FACTS project was funded by Diabetes UK Project Grant: 06/0003354.

The Closed-Loop In Pregnancy (CLIP) project is funded by Diabetes UK Project Grant BDA 07/005551.

HR Murphy is funded by a National Institute for Health Research (NIHR) research fellowship (PDF/08/01/036).

Declaration of interests
There are no conflicts of interest declared.

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State of the art lecture

The 2012 Janet Kinson lecture

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