"Exploring the unknown: treatment uncertainties in type 1 diabetes"

Report from Workshop 4th June 2009

Participants:

Patricia Atkinson, **Katherine Cowan**, **Sally Crowe**, **Jude Rogers**, James Lind Alliance

Rachel Connor, Juvenile Diabetes Research Foundation

Dr Patricia Eagan, the Royal London Hospital

Mark Fenton, Database of Uncertainties about the Effects of Treatments (DUETs)

Dr Iain Frame, Diabetes UK

Dr Roger Gadsby, **Dr Beth Hall**, NHS Evidence - Diabetes

Jenny Hirst, Insulin Dependent Diabetes Trust

Dr Gillian Hood, NE London Diabetes Research Network

Dr James Howard, GP, Staploe Medical Centre

Gillian Stokes, PhD Student, University of London

Ron Marsh, person with diabetes

Ann Middleton, person with diabetes

Prof Sandy Oliver, University of London

Apologies:

Krystyna Reczko, person with diabetes

André Tomlin, Information Scientist, Managing Director, Minervation Ltd.

Janice Turner, Patient advocate

1. Context for workshop

There has been interest in using the James Lind Alliance (JLA) approach to explore uncertainties in diabetes for quite some time. The workshop was an opportunity to bring interested parties together for the first time, and explore treatment uncertainties in type 1 diabetes. It was also timely for the James Lind Alliance to gauge interest in taking the process further.

2. Welcome and Introductions

Sally Crowe welcomed everyone to the workshop. Following introductions it was clarified that some of the participants were observers collecting data, but all of those present had interests in type 1 diabetes, with a breadth and depth of experience to contribute to the workshop.

Participants talked about their expectations of the workshop in pairs and then shared these with the rest of the group:

- Roger Gadsby highlighted the 'drivers' for research being to publish papers relevant to the Research Assessment Exercises (RAE). These were not necessarily to do with research relevant to people with diabetes, but more to do with researchers' career progression.
- Rachel Connor wanted to add to her 'to do' list and hoped to get a sense of the research questions that were at the top of people's minds. She was sure that there are uncertainties in type 1 diabetes that need addressing. She also hoped for improved communication about research in type 1 diabetes, as type 2 diabetes has attracted more interest recently.
- Ann Middleton was encouraged because she thought that the workshop would enable people to talk about "real life" research in diabetes, such as issues in day to day management.
- Jenny Hirst and Gillian Stokes wanted more acknowledgement in the research community of living with type 1 diabetes, and more understanding of the reality of this in studies that are funded.
- Iain Frame felt that research priorities in management of type 1 diabetes could be handled better, and described a 're-orientation' of type 1 diabetes research
- Ron Marsh described how in preparing for the workshop he had listed his personal treatment uncertainties, and these have been incorporated into this workshop report.
- Gillian Stokes wanted to see more progress in research for children and young people.
- James Howard was concerned about what someone living with diabetes needs to know, to optimise their health and reduce complications.
- It wasn't clear at this stage of the day what would be achieved by the discussions so it was important to be clear about what had been said, by whom and any next steps agreed.

With this in mind it was agreed that the workshop report would be a comprehensive record of all the day's discussions.

3. Presentation – 'Tackling treatment uncertainties together - case studies from the James Lind Alliance', Sally Crowe:

Sally's presentation concentrated on the background and structure of the JLA. The JLA is unusual in that it aims to look at priorities from different perspectives, and by developing a shared research agenda, challenge the status quo in current research commissioning.

The process of gathering treatment uncertainties and then narrowing them down to just 10 was illustrated using previous pilot partnerships in asthma and urinary incontinence. What the JLA has learnt so far is that priority setting partnerships reach different priorities from those reached by clinicians, researchers or patients working independently of each other. The JLA can provide a transparent and inclusive way of developing research priorities, and UK funding organisations are interested in receiving these.

4. Small Group discussions

Discussion points were captured on flip charts, and then key points were shared with all the participants at the end of the small group discussions. Where potential treatment uncertainties were identified these are contained in the main body of the report. Other issues relating to clinical research in type 1 diabetes are in appropriately titled appendices at the end of the report. Texts in italics are quotes taken from Ron Marsh's personal report on the treatment uncertainties that matter to him.

4.1 (Group 1) was facilitated by Gillian Stokes, and participants talked about **forms of insulin** and **insulin delivery mechanisms**.

Forms of Insulin

- What are the best forms of insulin for treating type 1 diabetes?
- What evidence is there that the various forms of insulin available are the best forms?
- What are the long-term complication rates associated with the various forms of insulin?
- How is it possible to identify which type of insulin to prescribe?
- Why has the variety of insulins available been reduced so dramatically in recent years (was 85 now 12)?
- How much would patient choice improve the progression of type 1 diabetes?
- Have there been any studies of hypoglycaemic events?
- Are there any studies into the benefits/harm of running higher glycaemic control to reduce events?
- Are the levels of hypoglycaemia acceptable - given that they are a side effect induced by the treatment of type 1 diabetes with insulin and not diabetes itself?

Delivery Mechanisms

Pumps

- Insulin pumps - who most needs one? (Is their wide use preventing those most in need of getting one?)
- Who are the best patients to have pumps? (They require motivation/understanding from patients, to get the best benefit from the pump)
- Is it worth waiting for closed loop system?
- Does the method of insulin delivery (injection vs. pump) have any impact on rates of complications?

Injections

- How many times can you inject with a syringe?
- What are the best injection sites?
- Should injections sites be varied?
- What lengths of needles are available?
- How can people identify which is the correct needle length for them?

Pens

- How can pens be improved to display unambiguously that insulin has been delivered?
- What delivery mechanisms are available? (transdermal, oral, new technologies)
- What are the benefits of slow release mechanisms?

4.2 (Group 2) facilitated by Jude Rogers, this group talked about **delivery mechanisms** and **blood glucose testing**

Delivery Mechanisms

- What research can we do around pump therapy vs. multiple injection therapy?

Pen Delivery

- Do the majority of Type 1 and Type 2s use pens?
- What is the accuracy of pens when delivering small doses?
- Is the choice of pen and appropriateness for individuals important – if so why?
- What are the benefits of disposable pens vs. non disposable?
- How do we ensure that people who have had type 1 diabetes for a long time are aware of new delivery systems, and offered the choice of using them?
- Much research is pharmaceutical company sponsored. Does this introduce a bias?

Pumps

- What is the value and cost effectiveness of pumps vs. multiple daily injections?
- What are the benefits of the closed loop system (the pump 'talking to' a blood glucose monitor)?
- What is the interaction of delivery system with lifestyle issues e.g. carbohydrate intake, exercise etc?

Blood glucose monitoring

- There is a need for accurate, continuous, non-invasive monitoring – how can we achieve this?
- Trials are needed that address the difference between technical control in the laboratory and real life experience of blood glucose strips.
- What is the optimal level of blood glucose monitoring for the individual?
- How effective is using 72 hour blood glucose monitoring and educating individuals in the management of type 1 diabetes?
- Can telemedicine be used to raise the use of blood glucose monitoring in adolescent and young people, in particular?
- Does continuous glucose monitoring yield better self-management?

4.3 (Group 3) facilitated by Sally Crowe talked about **forms of Insulin** and **psycho-social care/treatment**

Forms of insulin

- Insulin response is always particular to the person with diabetes, especially how long the insulin effect lasts. Whereas in prescribing terms is it the deal that the Trust has done with a supplier that will determine the treatment choices?
- Insulins are marketed as new and interesting – but what the actual benefits to patients?
- Does toleration of adverse effects drive decision making in choice of insulin type, rather than a pro-active choice?
- How much are treatment decisions based on real and significant doubts of the patient, and/or having what everyone else has/convenience and/or the quality of working relationships between patient/clinician.
- What outcomes of insulin are of interest in research – what are they measuring and why?
- Synthetic insulin, should we tailor insulin to match pancreatic secretion?

Psychosocial care/treatment

- These interventions have a low profile and small capacity/resource – why?
- Do psychosocial treatments focus on risk of harm in children too much?
- Do children receive more psychosocial treatments than adult populations and if so why?
- What is the evidence for psychosocial treatments that enhance decision making/planning for good care in type 1 diabetes?
- Is “poor” management a trigger for exploration in psychosocial care?
- How do psychosocial interventions help people with type 1 diabetes cope with life events and challenges to the diabetes lifestyle? (For example meetings/trips/events where children can interact with each other as well as more traditional 1:1 or group therapy)
- How do we support and help diabetic children who are being bullied?
- How do we counter the view that ‘children are considered a health and safety risk in educational settings’? Does this matter?
- How do we support adult diabetic populations with the short and long term side effects of diabetes such as kidney problems, neuropathy, pregnancy, erectile dysfunction, retinopathy and changes in sexuality?
- How do we get to the real story from people with type 1 diabetes presenting in clinic and when they are wanting to/needing to present as compliant?
    - Will HbAIC reflect this?
    - Change the treatment?
    - Explore the compliance?
    - Self management – self medicate?
- Dose Adjustment for Normal Eating (DAFNE) system – does it work? *Has there been significant penetration of training? Any analysis of results? Detailed group training may need more resource than available – are there other methods of achieving better self-managed blood glucose control?*
- Children’s choices v parent attitude - what helps clinicians strike the balance in good treatment and care?
- How do we identify parents’ needs?

4.4 Other potential areas of uncertainty

- Is there any evidence that target culture is beneficial in treating type 1 diabetes?
- Should other medicines be introduced if people cannot regulate blood sugar?
- Is there any evidence that a more gradual approach to 'Borderline Glucose Intolerance' targets would be beneficial?
- How do we deal with concerns over the influence of an individual pharmaceutical company potentially reducing choices on offer?
- What is the role of pain (threshold) in relation to blood glucose testing, especially in children?
- What are the cultural issues at play in treating type 1 diabetes?
- What will be the potential benefits of Smart insulin?
- How early is early to give statins?
- Problem with balance between reduced complications resulting from reduced HbAIC (better control) and patient engagement; must not "throw the baby out with the bath water" and seem in control to satisfy patient quota issues. Whilst insulins are imperfect patient lifestyle changes are a vital component**.**
- What value is HbA1c as a 'surrogate marker'? Is it too simplistic? Do we need a range of markers? Use one or more of blood glucose, blood pressure, lipids, ketones, others? (*Glycated haemoglobin gives an indication of blood glucose over a period but is not a definitive measure of the harmful effects of diabetes. HbA1c has become the accepted indicator due to relative ease of use but is by no means the only or the most important.*
- Type 1/Type 2 classification – is this too simplistic? Unclear definitions which has implications for treatment options *(Classifications change over time. e.g. IDDM/NIDDM to T1/T2. Patients don't understand significance of differences due to oversimplification/poor explanation by clinicians. Primary need is to agree definitions, then promote differences and need for specific treatment needs to diabetes community. Lack of insulin production and insulin resistance are widely different conditions and each needs quite distinct treatment options.*

  What are the options for diabetic hand issues? *Personal experience shows that options for treatment of hand conditions (cheiroarthropathy, Reynaud's and Dupuytren's syndromes, etc) are few/ineffective. Lack of interest and poor understanding by clinicians? Side-effects of current interventions make them unattractive but the needs are great.*

4.5 Whole group discussion comments

- What about *discussing how easy/hard it will be to implement research priorities from DUETs and the JLA process?*
- *Commercial interests need to be addressed as part of the process – a lot of interest and lobbying of pharmaceutical companies that produce and market insulin, delivery mechanisms, and glucose te***s**ting equipment
- Issues that are specific to Type 1 diabetes have an impact on Type 2 diabetes population. How will this be dealt with in JLA process?
- Lack of recognition of differences in diabetes generally
- Need to learn much more about Type 1 diabetes
- Importance of treatments for preventing longer term complications such as cardiovascular disease – for example how early is early to give statins?
- Risks and treatments in pregnancy with type 1 diabetes?
- Approaching newly diagnosed patients – to ask certain questions re vaccinations at a time when they are grappling with their diagnosis

5. Presentation: 'Collecting and publishing treatment uncertainties; Database of Uncertainties about the Effects of Treatments (DUETs)', Mark Fenton

Mark's presentation focused on: the aims of DUETs; the definition of an uncertainty; how to harvest uncertainties; problems encountered when defining uncertainties and how to establish that an uncertainty really is an uncertainty. Currently there are 58 diabetes uncertainties in the database.

Discussion then took place around the possibilities of including all of the potential stakeholders in gathering uncertainties and ensuring that enough people are asked about their treatment uncertainties.

6. Presentation: 'What treatment uncertainties are the most important? A JLA perspective on priority setting', Sally Crowe.

The afternoon session focused on priority setting. Sally used previous examples to show the challenges of priority setting, and the resources needed to achieve it. As the JLA accrues more experience with Priority Setting Partnerships it can help with putting together surveys, and advise on using other methods of gathering data such as message boards and advice lines.

Following some questions about priority setting methods, the group reviewed the workshop. The main themes of this discussion are presented as concluding remarks below.

7. Concluding remarks

- Treatment uncertainties do exist for type 1 diabetes.
- It is important to collect and use uncertainties in treatments for type 1 diabetes, to inform the clinical research agenda.
- Patient/Carer/Clinicians' perspectives of treatment uncertainties in type 1 diabetes can be collected through the organisations represented at the meeting using some simple methods, but resources and capacity need to be considered (see post workshop action 1).
- Other organisations should be invited to participate in further discussions (see post workshop action 2).
- There is a need for organisations to align any work on treatment uncertainties in type 1 diabetes with its own objectives.
- Despite enthusiasm for the idea, meeting participants did not identify a clear "next step" in the way forward for co-ordination and collection of treatment uncertainties in type 1 diabetes. It may be that the best placed people to lead such work would be those who have multiple 'hats' in diabetes treatment and care and can span several organisations and networks. Some participants suggested the Diabetes Research Network, others thought that specialist organisations should lead the work.

8. Post workshop actions

1. Organisations represented around the table agreed to think about and discuss with their respective organisations collecting uncertainties in type 1 diabetes, taking into consideration their resources and capacity. To assist with this the JLA would provide some indicative costs of the various stages of the process and share these with the group. Crucially this would include work on refining harvested uncertainties and entering them into DUETs. This would need the skills of a health information specialist.

2. Organisations that should be part of any further work on treatment uncertainties in type 1 diabetes.
    - Diabetes Specialist Nurses Networks
    - Input – 'Pump People'
    - Children with Diabetes
    - Diabetes UK
    - IDDT International
    - Diabetes Research and Wellness Foundation

- Diabetes Research Networks – 8 in England (training for patients July 09 do opportunities exist to access their ideas/thoughts?)
- Scottish Diabetes Research Network
- Diabetes Clinical Studies Advisory Group (Simon Heller chairs)
- Juvenile Diabetes Research Foundation
- Association of British Clinical Diabetologists
- Primary Care Diabetes Society
- Royal College of Physicians
- British Diabetes Association

3. The JLA will collate the discussion notes and send all participants a report of the workshop, by end of July 2009.

4. The four representatives who organised the day (from JLA, Diabetes Research Network, Juvenile Diabetes Research Foundation and the Independent Insulin Diabetes Trust) will reconvene in the autumn to consider the workshop report and other related progress.

9. Summary of workshop evaluations

Ten evaluation forms were completed. The feedback was broadly positive, and constructive.

Patient - many thanks for inviting me to the workshop yesterday. I was very pleased to have the opportunity to contribute to the discussion. I hope the process continues and that the Diabetes Research Network sign up to driving this particular topic - there are aspects of managing diabetes that are of much importance (and often frustration!) to those of us who live with it, day in and day out.

Charity leader - I would like to thank you for today's Workshop. I thought the day was excellent. As you know my feelings were that if we established that there are uncertainties in type 1 diabetes, it was a good step forward – so for me the day was a success. Discovering that there are uncertainties is difficult and uncomfortable for patients, and equally uncomfortable and difficult for charities.

Clinician – Interesting strategy for identifying priorities for research. Disappointing that no clear way for doing the work to implement the strategy was agreed.

Charity leader – I found the meeting an incredibly positive way to open up debate and begin to identify uncertainties. However, at the end of the meeting I felt under pressure to commit

financial resources to the project on the spot, which I simply could not do.

10. Appendices

General comments about type 1 diabetes research

- Why is there so little qualitative evidence available on type1 diabetes?
- Why is there so little investment in training of professionals with regard to pumps?
- There is an unmet need for a pain free, non-invasive, and convenient way of delivering insulin.
- Need some understanding of pump use in the UK vs. Europe
- Choice of insulin but individualised to clinician rather than to patient
- Different types of insulin are actually 'me too':
    - Animal (natural)
    - Human (synthetic)
    - Insulin analogues (synthetic)
- Clinicians working more in isolation, e.g. in community, probably rely more on marketing of insulin producers and staying in their own comfort zone. In a teaching hospital/centre there are more opportunities for dialogue with colleagues about relative benefits and drawbacks of different types.
- Insulin to be registered:
    - Equivalence to existing treatments
    - Safety
    - Lab measures + patient important outcomes
- Once we know what we ought to be doing, how do we best get it implemented across all Primary Care?

Comments about type 1 diabetes treatments

- No successful, continuing way of measuring blood glucose

Comments about outcomes measurement in type 1 diabetes clinical research

- Why are there no quality of life (QOL) studies?
- Why are QOL measures not built into clinical trials as a standard procedure?
- Are there specific QOL measures validated for type 1 diabetes?

- What should be the primary outcomes in studies looking at the effectiveness of psychosocial care?
- How do we measure wellbeing in type1diabetes?
- Is Body Mass Index the best way of measuring obesity in diabetics?

Comments about costs and resources in type 1 diabetes

- How can the cost of insulin to the NHS be reduced while increasing the benefit to people with diabetes?
- How much does the cost of insulin affect patient choice, in hospitals, GP practices, and clinics?
- Prescription revolves around cost
- Why do blood glucose strips go out of date so quickly? This represents wastage in the NHS