Clinical and cost-effectiveness of continuous subcutaneous infusion for diabetes: updating review

A response from:

[redacted]

AHP Research

and

[redacted]

AHP Research

Enquiries:

AHP Research Ltd
Brunel Science Park
Kingston Lane
Uxbridge
UB8 3PQ

T: [redacted]
E: [redacted]
W: www.ahpresearch.com

Introduction

In general, we consider the document to be sufficiently detailed and an adequate update on the previous NICE guidance. Reading the document from a health psychology perspective, there is little detail on the assessment of patient-reported outcomes, despite acknowledgement of the importance of the patients' perspective following previous guidance. Where research has been conducted, this has not been critiqued with consideration of the validity of the questionnaire measures used. The data presented in the document are overly simplistic and consider the authors' claims of quality of life and treatment satisfaction at face value. Particular issues are considered below and specific recommendations are highlighted in italic text. Our points are organised under the following headings, relating to important methodological issues when evaluating the benefits of CSII therapy from the patients' perspective:

1. The patients' perspective
2. Defining quality of life
3. Measurement of QoL/HRQL
   - 3a. Validity of measures
   - 3b. Domains of importance when evaluating QoL
   - 3c. Conceptual model
   - 3d. Proxy reporting of QoL/HRQL
4. Comparability of studies
5. Research needs
6. Miscellaneous issues
7. Specific corrections recommended
8. Conclusions

1. The patients' perspective

1.1 The patients' perspective can be measured systematically using patient-reported outcomes (PROs) measures. PROs are defined by the Food and Drug Administration (FDA; 2006) as "any report coming directly from patients about a health condition and its treatment" (lines 1079-1080) i.e. without interpretation by physicians or others. Subjective self-report measures place the patient at the centre of the assessment process providing unique and valuable insights, complementing clinicians' evaluation of symptoms.

1.2 Outcomes that can be provided only by the patient include symptom severity and bothersomeness, perceptions of daily functioning and well-being, impressions of the impact of treatment on daily life, satisfaction with treatment, health status and QoL.

1.3 *We would like to see a recommendation for further assessment of PROs, particularly given that the benefits of evaluation from the patients' perspective have recently been acknowledged by European and American drug regulatory agencies, which now call for the inclusion of PRO assessment in clinical trials of pharmacological therapies (EMEA, 2005; FDA, 2006).*

2. Defining quality of life

2.1 There is conceptual confusion in the document between various PROs, with some referred to as QoL, which might more accurately be referred to as health-related QoL

(HRQL), psychological well-being or health status/functioning. For example, on page 14 the authors discuss the benefits of CSII to include five separate factors, differentiating between "quality of life, including a reduction in the chronic fear of severe hypoglycaemia" and "more flexibility of lifestyle – no need to eat at fixed intervals, more freedom of lifestyle, easier to participate in social and physical activity". QoL is about the goodness of life in general and although there are no universally accepted specific definitions of QoL and many conceptual inconsistencies in the literature, there is general consensus that QoL is multidimensional, subjective and dynamic. The first benefit mentioned above refers to a "reduction in the chronic fear of severe hypoglycaemia". While such a fear will, of course, have an impact on many aspects of life that are important for QoL the fear itself is an aspect of psychological well-being (that can be measured alongside other aspects such as anxiety, distress, stress, depression, positive well-being). Thus, it would be better to label the first benefit mentioned here as "greater psychological well-being, including a reduction in the chronic fear of severe hypoglycaemia" and re-label the second as "improved quality of life, including elimination of the need to eat at fixed intervals, greater flexibility and freedom of lifestyle, and ability to participate with ease in social and physical activity"

2.2 The FDA provides useful guidance on the difference between QoL and HRQL. QoL can be defined as:

> "A general concept that implies an evaluation of the impact of all aspects of life on general well-being. Because this term implies the evaluation of non health-related aspects of life, it is too broad to be considered appropriate for a medical product claim" (lines 1082-1084)

HRQL is defined as:

> "A multidomain concept that represents the patient's overall perception of the impact of an illness and its treatment. A HRQL measure captures, at a minimum, physical, psychological (including emotional and cognitive), and social functioning. Claiming a statistical and meaningful improvement in HRQL implies: (1) that the instrument measures all HRQL domains that are important for interpreting change in how the study population feels or functions as a result of treatment; and (2) that improvement was demonstrated in all of the important domains. An HRQL instrument is a particular type of PRO instrument" (lines 1058-1065)

2.3 In brief, an individual's QoL is affected by many factors, such as living in a safe environment, having adequate housing and hygiene standards and financial or political freedom. Health is one of the factors that affect a person's QoL, and therefore, a perception of QoL in general is usually not considered an appropriate concept or outcome to be used in the evaluation of health interventions. HRQL is also a multi-dimensional construct, but a narrower concept of QoL. HRQL represents the impact of a condition and its treatment on various domains that are important for the patient's QoL, e.g. family life, working life, social life, finances. HRQL and "social" QoL are therefore not distinct, as suggested by the assessment group (page 41). Indeed, the arguments put forward on page 41 indicate confusion with regard to the content of various PRO measures (see Section 3a)[a].

2.4 Health status/functioning refers to the ability of a person to function (e.g. to walk up a flight of stairs) or the extent to which they experience bodily pain or can self-care.

[a] NB It would be helpful if the studies referred to on page 41 (and elsewhere in the summary) were referenced so that the reader can identify which measures have been used and make a judgement about the suitability of the selected measure and subsequent interpretations of findings.

2.5 *Barnard and colleagues stress the importance of clarity surrounding the term QoL (page 102). We would propose that the authors make clear in the document the distinction between QoL, HRQL and health status/functioning.*

3. Measurement of QoL/HRQL

3.1 When clear definitions have been lacking, researchers have used the term QoL, or HRQL, to refer to a range of psychological outcomes, including treatment satisfaction, psychological well-being or functional/health status. The reasons for this lack of specificity are two-fold:

(a) In the absence of a universally agreed definition of QoL, the measurement of all psychological outcomes has tended to be encompassed under this broad heading. While all of these outcomes may be important for QoL, they are not QoL per se.

(b) The term QoL (or HRQL) has become a buzzword in healthcare research. QoL is recognised as an important outcome in its own right and most major trials in recent years have needed to include some measure of QoL. In the absence of theoretically-driven measures of the impact of a condition on QoL, any measure of psychological outcome has been used (and frequently interpreted as QoL/HRQL).

3.2 As such, "QoL" has been measured and evaluated using a variety of instruments, both generic and diabetes-specific, employing varying methods including questionnaires, scales and interviews (page 95). Generic measures assess concepts that represent basic human values that are relevant to most people's functional status and well-being (i.e. not age-, disease-, or treatment-specific). They enable assessment and comparison across various conditions but are rarely sufficiently sensitive to the benefits of diabetes-specific interventions or treatments. Evaluation of such interventions generally requires diabetes-specific measures.

3.3 Measures mentioned in the report that have been used in clinical evaluation of "QoL" among CSII users have included the DQOL/DQOL-Y, EQ-5D, SF-36, SF-12, DQOLCTQ, DTSQ, SED, CHQ-CF87, WHO well-being questionnaire, and TAPQoL. Other questionnaires were used but no detail was available (eg Bruttomesso et al, 2006; page 95). The variety of measures used in such studies can be considered both an advantage (in terms of assessing various aspects of the patients' experience) and a disadvantage. Not only does use of various measures across studies limit comparability between studies but it potentially dilutes the reported benefits of CSII if limitations of certain measures are not considered and all measures are treated as equivalent.

3.4 Where the same scale has been used in numerous studies, results have been inconsistent. For example, the DQOL has been used seven times in studies of multiple daily injections (MDI) vs CSII reported in chapter 4 (page 118-119). Findings have shown significant improvements in DQOL scores on three occasions and non-significance on three occasions. One result is unreported.

3.5 The summary of findings on observational studies regarding QoL is mixed (as indicated in Barnard et al's review and on page 102 and also commented on in an editorial by Speight and Shaw, 2007), and does not support the statement "Gains in QoL…" (page 98).

3.6 The Summary of the last Assessment Report also noted that "most trials did not report quality of life" (see page 41) and so obtained much of its information about the patients' perspective from a patient group (INPUT). In terms of reliable evidence, this is inadequate and we recommend that the authors note that more studies are required that reliably and systematically evaluate CSII from the patients' perspective.

3a. Validity of measures

3a.1 The authors of the report consider claims of QoL at face value. However, many of the QoL measures used in studies to date are not suitable for these claims (Speight and Shaw, 2007).

3a.2 For example, the SF-36 (Ware & Sherbourne, 1992) measures health status using a set of generic items originally generated from various physical and role functioning, well-being and health perception measures. The developers (John Ware and Cathy Sherbourne) have never considered the SF-36 a measure of QoL, although it is widely misinterpreted as one. The eight dimensions represent the most frequently measured concepts in widely-used health surveys and those most affected by disease and treatment. Thus, the SF-36 includes many items (e.g. self-care and mobility) that may be highly relevant for some conditions (e.g. arthritis, multiple sclerosis) but are largely irrelevant to understanding the impact of diabetes and its treatment on QoL. Indeed, Hoogma and colleagues (2006) found no significant differences in physical health scores between those using CSII and MDI (see page 120). Furthermore, as it was not designed to measure QoL, the SF-36 excludes many more pertinent and potentially important issues, such as working life and social life, which are likely to be important for QoL and impaired by diabetes and its treatment. Finally, and perhaps most importantly, as it was not designed specifically for use in diabetes, the SF-36 also excludes issues that are of particular relevance and importance for people with diabetes, e.g. dietary freedom. It is, therefore, highly unlikely that the SF-36 would be sensitive to differences between treatment groups and differences, where observed, are likely to be an underestimate of the true differences in terms of QoL outcomes. However, due to the fact that it is a well-validated generic instrument, many HRQL studies in diabetes now include the SF-36 (or one of its derivatives, e.g. SF-12, SF-6D).

3a.3 Similarly, despite its intended purpose as a measure of health status, the EQ-5D has been misinterpreted as a measure of QoL in numerous conditions including diabetes (e.g. page 31). Use of the EQ-5D is similar to the SF-36 in that self-care items such as bathing and dressing oneself are largely irrelevant to understanding the impact of diabetes on QoL.

3a.4 Diabetes-specific measures of QoL are likely to be more sensitive to the benefits of CSII than generic instruments, though in the seven uses of the DQOL (Jacobson et al, 1994), half have shown no benefits (e.g. as described on page 118). Whilst this may well be due to small sample sizes (as pointed out by the authors), there may be other reasons for this lack of sensitivity. Although the aspects of life measured in the DQOL were informed by prior research and input from clinicians, there is no scope, within the measure, for an individual to indicate that a given aspect of life is not applicable to him or her. For example, items concerning the impact of diabetes on 'family life', 'sex life' and 'ability to drive a car or use machinery' may not be applicable to everyone. In a subsequent study, the developers of the DQOL acknowledged that some items would not be applicable to all respondents and "only included scale data for any subject if they completed 12 of the 15 satisfaction items, 16 of the 20 impact items, 2 of the 4 diabetes worry items, or 5 of the 7 social/vocational worry items" (Jacobson et al, 1994, p268). However, the authors did not provide any further justification for this seemingly arbitrary method of excluding data e.g. were data included only if particular items were complete or only if a particular number of items were complete? Many respondents' data were completely excluded from the analyses, rendering their remaining responses worthless. This method was recommended in subsequent scoring guidelines [Jacobson & The DCCT Research Group, 1994]. Where a respondent does complete an item, there is no scope to indicate the importance of the aspect of life for his/her quality of life. If applicable, items concerning the impact of diabetes on 'family life', 'sex life' and 'ability to drive a car or use a machine' may be more or less important to an individual than 'school or

household activities', 'missing work', or 'how often one has to tell others about one's diabetes'. Thus, the applicability of various aspects of life and their relative importance for the individual is not accounted for in the calculation of the DQOL Impact subscale, which treats all items as equally important to each other. In the DCCT [1993], the impact of diabetes on QoL might be expected to have been greater in the intensified treatment group but as this was not the case, the validity of the Impact subscale is brought into question. In general, the DQOL has been shown to be sensitive to the benefits of major interventions (e.g. pancreas only versus pancreas/kidney transplant (Nathan et al, 1991)) but not for less extreme interventions (e.g. CSII versus MDI (Tsui et al, 2001)).

3a.5 On page 95, the authors report on the use of the Insulin Pump Therapy Satisfaction Questionnaire (IPTSQ), designed specifically for a study of 22 parents and children. Whilst this may be a particularly relevant measure (given its encouraging name), the authors of the report do not comment on the measure's psychometric properties and consider the findings of the questionnaire at face value. It is not possible for this measure to have been fully validated with a sample of 22 and, thus, the findings of this study may be called into question, particularly if items have been summed to form scale scores.

3a.6 *We recommend that NICE evaluates the suitability of the instruments used to measure QoL (or other PROs) in trials of CSII and also to evaluate their psychometric properties (including reliability, validity and sensitivity). At a fundamental level, consideration of the instruments' content validity (i.e. the extent to which individual items and domains of the questionnaires actually measure outcomes of relevance and importance to the condition and its treatment) is key to appropriate measurement.*

3b. Domains of importance when evaluating QoL

3b.1 If QoL assessment is to be truly meaningful, it needs to take into account aspects of life that are important for an individual's QoL.

3b.2 It has been argued that QoL is a personal rating of how good or bad one's life is; a measure of the difference between an individual's hopes and/or expectations and the individual's present experience, concerned with the difference between perceived and attained goals. However, the problems with assessing QoL are not only conceptual, they are practical. As QoL is a highly subjective, multidimensional and dynamic construct, there is a case for adopting the principle that individuals should decide the extent to which their QoL is satisfactory based upon their own criteria for what constitutes good QoL for them personally. If this is accepted, then QoL needs to be defined as "what the patient says it is" rather than what the researcher decides to measure.

3b.3 The report refers to several measures of "QoL" that we argue here should not be interpreted as QoL (see section 3a). Furthermore, even where studies have included a measure of QoL/HRQL, they do not always use the same measures and thus, it is the domains of life assessed that need to be taken into account when considering the relevance or value of the evidence presented. In terms of assessing the impact of CSII on QoL, studies using the DQOL might be considered most relevant (though the DQOL also has severe limitations). Studies that have used the SF-36 or EQ5D are potentially irrelevant, particularly if the findings are negative because both measures of generic health status are likely to be insensitive to the benefits of CSII therapy. In Barnard et al's review, the study showing the largest effect (and coincidentally, also having the largest sample) used the DTSQ (Bradley, 1994) to measure the patients' satisfaction with treatment. Whilst treatment satisfaction is not equivalent to QoL per se, the benefits reported in that study are likely to have major advantages for QoL.

3c. Conceptual model

3c.1 Evaluation of the validity of QoL/HRQL assessment should be conducted through the development of a conceptual framework (showing how items are grouped according to subconcepts or domains). HRQL will be considered by the FDA/EMEA if demonstrated adequately through a good conceptual model and an appropriate instrument.

3c.2 The development of a conceptual framework involves three steps (FDA, 2006):

1. Identify concepts and domains that are important to patients.
2. Determine intended population and research application.
3. Hypothesize expected relationships among concepts.

3c.3 The development of a conceptual model allows for the evaluation of domains of life most important to individuals' QoL. The assessment group (page 41) noted that many of the gains in QoL were in "social" aspects of quality of life and correctly noted that these may not be picked up by existing utility (and QoL outcome) measures. The insulin pumps working group report (p 42-43) requested consideration of QoL issues, including the number of daily injections required to achieve optimal glycaemic control, frequent sick days, marked glycaemic swings or dawn phenomenon, impaired exercise capacity, and difficulties with shift work or travel across time zones. It is unclear why these domains of QoL were selected but none are covered by generic health status measures (e.g. SF-36 and EQ5D) and many are not covered by existing diabetes-specfic QoL measures.

3c.4 The literature is an ideal place to begin identifying concepts and domains that are important to patients. For example, Sanfield et al (2002, see page 123) reported that patients rated eating, working, sleeping, bathing and sexual activity as the most important aspects of life and sections 5.2.3.11 and 5.2.3.12 summarise the perceived benefits and challenges of pump use in children (note: separate conceptual models are needed for separate populations e.g. child, adolescent and adult)

3c.5 In addition, no PRO conceptual model is complete without input from patients. Barnard & Skinner's (2006) qualitative telephone survey can be considered sufficient for the development of a phase I model.

3c.6 We would encourage NICE to develop a conceptual framework for QoL assessment of CSII treatment in diabetes and evaluate the suitability of current questionnaires based on this framework.

3d. Proxy reporting of QoL/HRQL

3d.1 In many conditions there is generally only a small correlation between patient-reported outcomes and clinician accounts of the patient's experience. Furthermore, QoL data generally show a moderate correlation (at best) with objective or biomedical outcomes. For example, in a qualitative study, fifteen adolescents with Type 1 diabetes were asked to rate their QoL. Their diabetes specialist nurse (DSN) (who had known most of these patients since diagnosis of their diabetes) was also asked to rate each of the adolescents' QoL (Walker & Bradley, 2002). The DSN's rating was more closely related to HbA_{1c} results than to the adolescents' own ratings (although neither was significant). Whilst the sample was small, this finding confirms that estimating a patient's QoL is not intuitive and that routine measurement of psychological outcomes is needed if the patient's perspective is to be truly considered in treatment decisions. In this example, the DSN was making the erroneous assumption that if blood glucose control is good, then QoL is good and when blood glucose control is sub-optimal, then QoL suffers. In reality, the reverse is much more likely to be the case. Clinicians' ratings of their patients' QoL are generally based

upon health-related outcomes i.e. the aspects of a patient's life with which the clinician is familiar and potentially able to influence. Improvement in QoL is, however, not an automatic result of improved clinical status. Patients see beyond health status, considering aspects of their life such as vitality, social functioning, emotional well-being, and sexual functioning as well as the demands and side-effects of any treatment. Thus, despite good biomedical outcomes (e.g. HbA_{1c}), the individual with diabetes may report his/her QoL to be impaired due to the limitations placed on personal and leisure activities by the demands of his/her treatment.

3d.2 Parent and clinician ratings were used in some studies, although the suitability of the instruments for proxy-reporting is unclear. Furthermore, even a parent will have a different perspective of his/her child's diabetes and CSII treatment from that of child him/herself, which may render the parent-report, at best, inadequate and, at worst, irrelevant and misleading. The subjectivity of PROs is clear and applications of PRO measures may be affected by a host of variables outside the knowledge and understanding of others. In the reported study by Mednick and colleagues (2004, page 95-96), discrepancies in parent and child ratings were observed but are not accounted for.

3d.3 *We recommend that NICE discourages the use of proxy-reported outcomes (i.e. involving clinician or parent interpretation) in the evaluation of QoL, HRQL and treatment satisfaction, except in circumstances where it is the only possible method of subjective data collection. However, in such circumstances, the limitations of such methods need to be clearly stated and considered.*

4. Comparability of studies

4.1 The last assessment report concluded that the main value of CSII is in "improving QoL by allowing greater flexibility of lifestyle" (see page 40). However, it did not propose an adequate methodology for evaluating QoL and as such there has been inconsistency in studies. Differing inclusion/exclusion criteria, sample populations, PRO assessment (see above) and methodologies limit the ability to pool and compare cross-study results. Furthermore, the Assessment Group noted differences in hypoglycaemia outcomes between trials and observational studies, concluding that this might be due to trials recruiting "unselected patients from clinics, whereas the observational studies included people having particular problems such as hypoglycaemic episodes" (see page 41).

4.2 On page 122, the authors suggest that "as with much of the patient preference and quality of life literature, these results are difficult to interpret as patient characteristics and the reasons for receiving CSII are not well documented." In addition, Rodrigues et al (2005, see page 124) noted significant differences in SF-36 scores based on contraindications; a potential bias not reported by all authors.

4.3 The generalisability and translation from clinical trial to clinical practice is also jeopardised by differing methodologies.

4.4 *We recommend that NICE needs to state explicitly that summaries are based on differing methodologies, influenced by different factors (e.g. selection criteria). As such, each study needs to be evaluated independently and some may carry more weight than others.*

5. Research Needs

5.1 In section 7.3, the authors make a suggestion that CSII should be compared to DAFNE. It is important that any comparison uses the same outcome measures. The primary psychological outcomes evaluated in the DAFNE trial (DAFNE Study Group,

2002) were the impact of diabetes on QoL (measured using the ADDQoL (Bradley et al, 1999; Bradley and Speight, 2002)) and treatment satisfaction (Bradley, 1994). Highly significant improvements were shown in the average weighted impact (AWI) of diabetes on QoL and also for 'present QoL', a single-item generic measure of QoL. In addition, highly significant improvements were show in satisfaction with treatment. Whilst the ADDQoL has never been used in a study of CSII therapy, it is likely (given the benefits demonstrated by the DAFNE programme) that similar improvements in QoL would be observed for CSII in comparison to MDI. Furthermore, it has been noted above (see section 3b) that the DTSQ has shown the largest patient-reported effect in any study of CSII conducted to date. Given that the DTSQ has shown benefits for both DAFNE and CSII (in separate studies), it would be useful to see a study in which the two treatment option were compared using the DTSQ and also the ADDQoL (given the already demonstrated benefits of DAFNE for QoL).

5.2 In their qualitative study (page 125), Barnard & Skinner suggest that some patients remain on CSII for only a short period of time. To maximise adherence/concordance and to evaluate long-term benefits of the therapy, a reliable and valid patient-based assessment of psychological suitability/preparedness is required. Such a measure would assess not only whether the patient was psychologically suited to such a form of treatment but also the extent to which they were prepared for the treatment (e.g. realistic expectations, readiness to embrace the demands as well as the benefits of the therapy). Previous NICE guidance indicates when a patient should be prescribed pump therapy, but does not assess the likelihood of the patient adhering to the treatment over time. A measure of psychological suitability is required.

6. Miscellaneous issues

6.1 On page 157, the report indicates "that the opinion of individual diabetologists and paediatricians had a major effect on provision, and that there are "anti-pump" professionals". In our recent study, we have identified that clinicians display various attitudes towards CSII therapy that may be a factor in local provision (though this was not established in our study) (Reaney et al, 2007; see Appendix A). Of particular note was the finding that clinicians had definitive attitudes regarding biomedical/clinical aspects of CSII but held less definitive views regarding the patients' experience, suggesting that further work is needed to enable clinicians to understand CSII from the patients' perspective.

7. Specific corrections recommended

7.1 Page 14: correction to the benefits of CSII listed (as indicated in Section 2.1 of this response).

7.2 Page 17: "The two studies that reported quality of life outcomes found no differences". Replace "quality of life outcomes" with "patient reported outcomes".

7.3 Page 37: the 4th bullet point needs to be corrected to read "and other aspects of health-related quality of life". It is important to note that just because a benefit is not demonstrated by the EQ-5D, it does not make is "non-health-related". The EQ-5D measures health status, not HRQL.

7.4 Page 41 (line 13): reword to read "…but were gains in social aspects of life, which might not be picked up by the usual utility measures".

7.5 Page 95: the first paragraph suggests that "nine studies evaluated aspects of quality of life associated with CSII use from the perspective of health care professionals, parents or children". However, only eight references are cited (reference 135 is cited twice) and ten studies are discussed (the eight cited plus references 147 and 166).

7.6 Page 153 (last bullet): reword to read “improved health-related quality of life arising from greater flexibility of lifestyle” (see point 3 in this section).

8. Conclusions

The report is highly detailed and provides a useful update on the evidence for and against use of CSII therapy in the UK. While it is encouraging that NICE is eager to understand the benefits/demands of CSII therapy from the patients’ perspective, further work is needed to encourage PRO evaluation but also to ensure that PRO assessment is critiqued adequately:

1) to avoid misinterpretation of data and misleading conclusions
2) to ensure that recommendations are put forward for the rigorous assessment of the impact of CSII on QoL.

We have identified several ways in which the report can be improved to ensure that the patients’ perspective is accounted for in a satisfactory manner:

8.1 The authors need to be clear in their use of terms such as QoL, HRQL, health status and, related to this, about which measures assess which outcomes, i.e. the SF-36/EQ-5D assess health status, not HRQL and misinterpretation of these measures has serious consequences for the recommendations made in the NICE report.

8.2 We would urge NICE to recommend that further research is conducted which rigorously considers the domains of life that are of importance to people with diabetes and how they are affected by treatments (i.e. show evidence of a conceptual model when selecting PRO measures) in order to identify and demonstrate ways in which QoL might be improved (or impaired) with CSII therapy.

8.3 We would discourage the use of proxy-reported measures of subjective outcomes such as QoL/HRQL and treatment satisfaction except in exceptional circumstances where the patient is unable to respond for him/herself. Studies have shown that children as young as eight years old can comment on how diabetes affects their QoL and that their perspective can differ substantially from that of their parent(s). Where proxy ratings are used, the limitations of such methodologies and the comparability with other studies should be clear.

8.4 We would encourage NICE to recommend that further research is conducted comparing CSII with the flexible intensive insulin therapy (FIIT, e.g. DAFNE, BERTIE), to demonstrate the demands and benefits of each form of treatment and to identify which patients might benefit from CSII over and above the benefits to be obtained from FIIT.

8.5 Finally, we would urge NICE to recommend that a tool be developed to help clinicians to make decisions about which patients would benefit from use of CSII therapy. Such a tool would include biomedical outcomes but, most importantly, assess patient’s understanding of both the benefits and demands of CSII therapy and their readiness to adopt such a treatment approach. However, in order to develop such a tool, a study is needed to determine who benefits most from CSII and why and this will require a significant investment of resources.

References

Barnard KD & Skinner C (2006). Qualitative study into quality of life benefits associated with insulin pump use. *Diabetes*, 55:A612.

Bradley C (1994). Diabetes Treatment Satisfaction Questionnaire (DTSQ), in C Bradley ed., *Handbook of Psychology and Diabetes: a guide to psychological measurement in diabetes research and practice.* Chur, Switzerland, Harwood Academic Publishers, p. 111-132.

Bradley C, Todd C, Gorton T, Symonds E, Martin A, Plowright R (1999). The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. *Quality of Life Research*, 8:79-91.

Bradley C & Speight J (2002). Patient perceptions of diabetes and diabetes therapy: assessing quality of life. *Diabetes Metabolism Research and Reviews*, 18(Suppl 3):S64-S69.

DAFNE Study Group (2002). Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. *British Medical Journal*, 325, 746-749.

The European Medicines Agency (EMEA) (2005). Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQL) measures in the evaluation of medicinal products. http://www.emea.europa.eu/pdfs/human/ewp/13939104en.pdf.

The Food and Drug Administration (FDA) (2006). Guidance for industry: patient-reported outcome measures: use in medical product development to support labelling claims: draft guidance. *Health and Quality of Life Outcomes*, 4:79.

Hoogma RP, Hoekstra JB, Michels BP, Levi M (2006). Comparison between multiple daily insulin injection therapy (MDI) and continuous subcutaneous insulin infusion therapy (CSII), results of the five nations study. *Diabetes Research & Clinical Practice*, 74 Suppl 2:S144-S147.

Jacobson AM, de Groot M, Samson JA (1994). The evaluation of two measures of quality of life in patients with type I and type II diabetes. *Diabetes Care*, 17(4):267-274.

Mednick L, Cogen FR, Streisand R (2004). Satisfaction and quality of life in children with type 1 diabetes and their parents following transition to insulin pump therapy. *Children's Health Care*, 33:169-83.

Nathan DM, Fogel H, Norman D, Russell PS, Tolkoff-Rubin N, Delmonico FL, Auchinloss H, Camuso J, et al (1991). Long-term metabolic and quality of life results with pancreatic / renal transplantation in insulin-dependent diabetes mellitus. *Transplantation*, 52(1), 85-91.

Reaney M, Barnard C, Skinner TC, Speight J (2007). Pilot study of clinician attitudes to insulin pump therapy: International differences and the need for a greater understanding of the patient perspective. *Value in Health* (in press) – *Abstract presented in Appendix A.*

Rodrigues IA, Reid HA, Ismail K, Amiel SA (2005). Indications and efficacy of continuous subcutaneous insulin infusion (CSII) therapy in Type 1 diabetes mellitus: a clinical audit in a specialist service. *Diabetic Medicine*, 22:842-9.

Sanfield JA, Hegstad M, Hanna RS (2002). Protocol for outpatient screening and initiation of continuous subcutaneous insulin infusion therapy: impact on cost and quality. *Diabetes Educator*, 28:599-607.

Speight J & Shaw JAM (2007). Does one size really fit all? Only by considering individual preferences and priorities will the true impact of insulin pump therapy on quality of life be determined. *Diabetic Medicine*, 24(7): 693-695.

Tsui E, Parkes R, Barnie A, Zinman B, Ross S (2001). Intensive insulin therapy with insulin lispro: A randomised controlled trial of continuous subcutaneous insulin infusion versus multiple daily insulin injection. *Diabetes Care*, 24(10):1722-1727.

Walker J & Bradley C (2002). Assessing the quality of life of adolescents with diabetes: using the SEIQoL, DQOL, patient and diabetes specialist nurse ratings. *Practical Diabetes International*, 19(5), 141-144.

Ware JE & Sherbourne CS (1992). The MOS 36-Item Short-Form Health Survey (SF-36). *Medical Care,* 30(6), 473-481.

Appendix A

Pilot study of clinician attitudes to insulin pump therapy: International differences and the need for a greater understanding of the patient perspective

Reaney M[1], Barnard K[2], Skinner C[3], Speight J[1]

[1] AHP Research, Uxbridge, UK; [2] University of Southampton, UK; [3] University of Wollongong, Australia

OBJECTIVES: To identify and survey healthcare professionals (HCPs) attitudes to insulin pump therapy (CSII).

METHODS: Eight specialists were interviewed to explore their attitudes and beliefs about CSII. Responses were analysed thematically and used to inform the design of a new 22-item questionnaire: the Attitudes to Pump Therapy (APT) Survey. The APT was pilot-tested among 95 HCPs (54% male; 75.5% diabetologists/DSNs, 13.8% general practitioners) at the International Diabetes Federation (IDF) conference, 2006. Results were analysed using non-parametric statistics with bonferroni correction.

RESULTS: Analyses of interview data identified 9 themes: biomedical, perceived control of care/diabetes, technology, quality of life, financial resources, training, education & support, suitability, and evidence-base. Items were designed to reflect these themes with responses scored on a 5-point Likert scale (strongly agree – strongly disagree). No statistically significant differences were found by gender, HCP speciality, country (and continent) of origin or proportion of patients using CSII. Most notable differences were found in relation to gross domestic product (GDP) and the potential for pump therapy to achieve tight blood glucose control (lower GDP = more agreement: $p=0.001$), and result in diabetic ketoacidosis (DKA) (lower GDP = less agreement: $p<0.005$). Ranked mean scores showed a split between biomedical/clinical items (N=11) and items concerned with patient experience (N=11). Attitudes about biomedical/clinical issues were generally clear (i.e. for 7/11 items, the mean score was “agree”) but less decisive about patient experience (i.e. for 8/11 items, the mean score was “neither agree nor disagree”).

CONCLUSIONS: Few subgroup differences existed, but those that did may be explained by lack of access to treatment (directly corresponding to GDP). Clinicians’ were generally clear in their attitudes regarding biomedical aspects but less so regarding patient experience. Research focusing on patient-reported outcomes is likely to offer clinicians a greater understanding of the patients’ perspective of insulin pump therapy.