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Cost-effectiveness of continuous subcutaneous insulin infusion versus multiple daily injections of insulin in Type 1 diabetes: a systematic review

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Abstract

Aim Continuous subcutaneous insulin infusion (CSII) is increasingly used in clinical practice for the management of selected patients with Type 1 diabetes. Several cost-effectiveness studies comparing CSII vs. multiple insulin injections (MDI) have been reported. The aim was systematically to review these analyses and test the hypothesis that CSII is a cost-effective use of healthcare resources across settings.

Methods A literature review was performed using MEDLINE, Cochrane Library and other databases. No time limit or language restrictions were applied. After two rounds of screening, 11 cost-effectiveness analyses were included in the final review, of which nine used the CORE Diabetes Model. A narrative synthesis was conducted and mean cost effectiveness calculated.

Results CSII was considered cost-effective vs. MDI in Type 1 diabetes in all 11 studies in 8 countries, with a mean (95% CI) incremental cost effectiveness ratio of 30 862 (17 997–43 727), US$40 143 (23 409–56 876) per quality-adjusted life year (QALY) gained. CSII was associated with improved life expectancy and quality-adjusted life expectancy (0.4–1.1 QALYs in adults), driven by lower HbA_{1c} and lower frequency of hypoglycaemic events vs. MDI. CSII was associated with higher lifetime direct costs due to higher treatment costs but this was partially offset by cost-savings from reduced diabetes-related complications.

Conclusions Published cost-effectiveness analyses show that in Type 1 diabetes CSII is cost-effective vs. MDI across a number of settings for patients who have poor glycaemic control and/or problematic hypoglycaemia on MDI, with cost-effectiveness highly sensitive to the reduction in HbA_{1c} and hypoglycaemia frequency associated with CSII.

Introduction

Continuous subcutaneous insulin infusion (CSII, insulin pump therapy) was introduced initially as a research procedure in the 1970s, and shortly afterwards became established as a routine treatment for selected patients with Type 1 diabetes [1,2]. CSII is now used primarily in Type 1 diabetes, where it represents a clinically effective alternative to multiple daily injections of insulin (MDI) in people with diabetes who are unable to achieve adequate glycaemic control on MDI, as evidenced by an elevated HbA_{1c} level, or who experience frequent and problematic hypoglycaemic events [2,3]. In children with Type 1 diabetes, CSII is recommended also when MDI is considered impracticable [3], and the therapy has been shown to be safe, effective and well tolerated in even young children with Type 1 diabetes [4,5]. The evidence base for the routine use of CSII in Type 2 diabetes is less well established and usage varies considerably between countries [3,6,7]. CSII is not usually recommended or reimbursed for Type 2 diabetes in many countries [3] but in other settings it may be reimbursed for some patients with poorly controlled Type 2 diabetes [7].

The clinical effectiveness of CSII vs. MDI in adults and children with Type 1 diabetes has been the subject of review in several meta-analyses of randomized controlled trials (RCTs) and observational studies [8–13]. There is good evidence for a reduction in HbA_{1c} and in the frequency of severe hypoglycaemia with CSII, with greatest improvements in those patients with the worst glycaemic control and hypoglycaemia at baseline [11,13]. Total daily insulin dose is also reduced [8] and quality of life often improved [14] with CSII vs. MDI.

In addition to clinical efficacy and the impact on quality of life, a further major consideration for usage of a treatment by a healthcare system is value for money. Costs associated with CSII are higher than those with MDI due to the initial cost of the pump and other consumables, as well as initial training time [3]. The lifetime of the pump may vary from four

to eight years or more, resulting in costs for replacing the pump at regular intervals. These higher initial acquisition costs may be partially, or wholly, offset by lower long-term costs vs. MDI due to reduced insulin requirements and better clinical outcomes, including lower frequency of hypoglycaemia and the reduced risk of long-term complications that is expected because of improved glycaemic control [15].

A number of cost-effectiveness studies of CSII vs. MDI have been published in recent years using a variety of methodologies and within the context of several settings (i.e. countries and healthcare systems), but there has been no systematic review of the results of these analyses. Indeed, multiple country-specific analyses are required due to differing cohort characteristics and the large differences in treatment and complication costs between settings. The aim of this study was, therefore, to systematically review all published cost-effectiveness analyses of CSII vs. MDI in patients with Type 1 diabetes and test the hypothesis that CSII provides a cost-effective treatment for Type 1 diabetes across different settings.

Methods

Identification and selection of studies

The protocol for the study is available from the corresponding author. Literature searches were performed using MEDLINE, the Cochrane Library, International Network for Healthcare Technology Assessment (INAHTA) and Google Scholar databases and the Agency for Healthcare Research and Quality website (http://www.ahrq.gov). We also searched conference proceedings from the European Association for the Study of Diabetes (EASD) and International Society for Pharmacoeconomics and Outcomes Research, as well as reviewing the cited literature in retrieved articles. Studies using CSII in combination with continuous glucose monitoring (sensor-augmented pump therapy) were excluded. For the

MEDLINE searches, the following search string was used, which combined Medical Subject Heading (MeSH) terms with free text terms: ((("insulin"[MeSH Terms] OR "insulin"[All Fields]) AND pump[All Fields] AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])) OR (continuous[Title] AND subcutaneous[Title] AND insulin[Title] AND infusion[Title] AND cost-effectiveness[Title])) OR (((continuous[All Fields] AND subcutaneous[All Fields] AND ("insulin"[MeSH Terms] OR "insulin"[All Fields]) AND infusion[All Fields]) OR CSII[All Fields] OR (CSII[All Fields] AND MDI[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR cost-utility[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])). Search terms were adapted as required for use in other databases. No limits in terms of timeframe (date of last searching December 2013), country or language were applied. Two groups of reviewers independently examined the retrieved articles: SR, JSP and WV had expertise in healthcare economics and JCP and KN expertise in clinical diabetes and CSII.

Outcomes measured

We extracted data from articles concerning total lifetime costs for MDI and CSII, quality-adjusted life years (QALYs) gained and cost-effectiveness as measured by the incremental cost-effectiveness ratio (ICER). To facilitate comparison, ICERs were reported as published, and also converted from the local currency and year (assumed to be the year preceding publication unless the cost year was otherwise stated) to 2013 Euro ( ) and US dollar ($) (using 2013 exchange rates sourced from www.OANDA.com/currency/converter/; inflation

rates were sourced from the International Monetary Fund World Economic Outlook Database).

Quality assessment

We rated reports for quality using an established checklist for economic evaluations in healthcare by Drummond and Jefferson [16]. The checklist incorporates a total of 35 items, with the maximum possible score for the evaluation being 35; however, not all items in the checklist are applicable to all economic evaluations. The results of the quality assessment are presented in the Supporting Information (Appendix S1).

Statistical analysis

Correlations were sought using Spearman's test. Summary results are presented as mean (SD) or mean [95% confidence interval (CI)], unless otherwise stated.

Results

Studies identified and quality assessment

A total of 106 reports were identified via databases sources and 17 via searches of relevant websites and reference sections of identified articles (Fig. 1). After removal of duplicates (n = 40), 83 unique reports remained. A further 57 hits were excluded during first-round screening of titles and abstracts because articles did not refer to cost/cost-effectiveness analysis of CSII vs. MDI, leaving 26 articles for full-text screening; these included 16 cost-effectiveness analyses (15 in patients with Type 1 diabetes and one in patients with Type 2 diabetes, which was excluded), five reviews containing cost/cost-effectiveness data or cost studies, one editorial, three letters to the editor commenting on cost-effectiveness analyses

included in the current review and one cost–benefit study from 1994, the full text of which was not available (Fig. 1). A further four cost-effectiveness analyses were excluded because two abstract/posters and one health technology assessment located via hand searches presented the same data as later full publications identified in the database searches and one publication compared sensor augmented pump therapy (rather than CSII) with MDI. Summary findings and review of the remaining 11 cost-effectiveness analyses in patients with Type 1 diabetes were performed by narrative synthesis and calculation of mean cost-effectiveness outcomes. (Tables 1 and 2) [17–27]. Of the included studies, nine were performed using the CORE (Center for Outcomes Research) Diabetes Model (CDM) [17,18,20–23,25–27] and two used Markov model analyses of CSII vs. MDI [19,24]. Cost-effectiveness analyses of CSII were performed in a number of different settings, including four from the UK [19,21,23,24], and one each from the USA [25], Canada [26], Australia [18], Spain [20], Denmark [22], Italy [27] and Poland [17]. Additionally, our search identified a cost-effectiveness analysis of CSII vs. MDI in Type 2 diabetes, and thus not included in the current review; this was conducted in a Chinese setting [28]. Of the 11 included manuscripts, 9 were industry sponsored by manufacturers of insulin pumps; the remaining 2 studies were commissioned on behalf of the National Institute for Health and Care Excellence (NICE) in the UK. Of the NICE-commissioned studies, only that by Cummins *et al*. [21] reported an ICER (51 614; $67 135 per QALY gained) [21]. In comparison ICERs reported from the industry-sponsored studies ranged from 3528; $4589 per QALY gained in Denmark [22] to 62 538; $81 343 per QALY gained for adults in Australia [18].

Results of the quality assessment showed that scores ranged from 10 to 24. However, the lowest scores were for abstracts/posters, where low scores were likely largely attributable to the limited amount of detail that could be included in abstracts/posters. Ambiguity around

methodology was another key factor for low scores in some studies. When limited to full text publications scores ranged from 17 to 24, with a total of seven analyses having a score of ≥ 20. Overall, seven studies scored ≥ 20 [18,20,22–26], with the remainder of studies scoring < 20 [17,19,21,27]. Results of the quality assessment should be interpreted with caution because not all checklist items are applicable to all studies. Detailed findings of the quality assessment are presented in the Supporting Information (Appendix S1).

Cost-effectiveness of CSII vs. MDI

The analyses reported higher lifetime costs for CSII vs. MDI [mean (SD) ratio CSII: MDI cost: 1.4 (0.4)], but also a higher life expectancy (in those analyses that investigated mortality) and higher quality-adjusted life expectancy associated with CSII. The mean (SD) gain in QALYs over a lifetime time horizon was 0.7 (0.3) (range 0.4–1.1) QALYs for adults. Cost-effectiveness, as measured by the ICER, ranged from 3528 ($4589) per QALY gained in the Danish setting [22] to 62 971 ($81 907) per QALY gained in the Australian setting [18] (Table 2). The mean (95% CI) ICER was 30 862 (17 997–43 727), $40 143 (23 409–56 876) per QALY gained.

The consensus among studies performed using the CDM (including analyses from the UK, USA, Canada, Denmark, Spain, Australia, Italy and Poland) was that CSII is cost-effective relative to MDI, with the ICER falling below generally accepted willingness-to-pay thresholds for cost-effectiveness (Table 2). Three studies performed using the CDM investigated the cost-effectiveness of CSII in both adult and adolescent populations [17,18,25]. Interestingly, in the Polish analysis by Clegg *et al*. [17], the ICER was lower in adolescents than in adults (18 670 vs. 25 917 per QALY gained; $24 285 vs. 33 711 per QALY gained). By contrast, in an analysis in a US setting by St Charles *et al*. [25], CSII was

more cost-effective in adults than in adolescent patients (23 464 vs. 14 661 per QALY gained; $30 520 vs. 19 069 per QALY gained). In the analysis by Cohen *et al*. [18] conducted in the Australian setting, the difference in cost-effectiveness between adults and adolescents was minimal.

Input data used for cost-effectiveness studies

The most commonly used source for clinical input data for the change in HbA_{1c} associated with CSII in comparison with MDI was a 2003 meta-analysis of 52 studies by Weissberg-Benchell *et al*. [9], in which an HbA_{1c} reduction of 10–13 mmol/mol (0.95–1.2%) in favour of CSII was reported. Notably, this meta-analysis included data from both RCTs and observational studies. Nearly all of the analyses performed using the CDM utilized this meta-analysis as a source of clinical data. Other sources for expected change in glycaemic control with CSII that were utilized included a 2002 meta-analysis by Pickup *et al*. [8], a 2008 meta-analysis by Pickup and Sutton [11] and data from the Insulin Pump Clinical Database maintained at the University of Leeds (described as 'academic in confidence'). Interestingly, the 2003 UK-based analysis by Scuffham and Carr [24] assumed no HbA_{1c} benefit for CSII vs. MDI, basing their analysis exclusively on incidence of hypoglycaemic events and incidence of ketoacidosis, thereby representing a conservative approach. This study reported a gain in quality-adjusted life expectancy of 0.48 QALYs for CSII vs. MDI over a time horizon of 8 years, resulting in an ICER of £11 461 per QALY gained (2001 values).

Determinants of cost-effectiveness and sensitivity analyses

Within studies, the largest drivers of outcomes were change in HbA_{1c} and reduction in frequency of hypoglycaemic events associated with treatment by CSII vs. MDI. In most

analyses using the CDM, the HbA_{1c} benefit associated with CSII relative to MDI was taken to be 13 mmol/mol (1.2%) in the base-case, but in sensitivity analyses lower HbA_{1c} reductions were explored. In these scenarios, the ICER was typically increased relative to the base-case, e.g. from 39 157 ($50 932; 2013 values) per QALY gained for 13 mmol/mol (1.2%) HbA_{1c} change to 93 990 ($122 254) per QALY gained for a 6 mmol/mol (0.51%) HbA_{1c} change [23].

In CDM-based analyses, no benefit in terms of a reduction in the frequency of hypoglycaemic events was assumed in the base-case. Sensitivity analyses were performed in which CSII was associated with a reduction in the severe hypoglycaemic event rate of 50% and 75%. In these scenarios, the ICER was typically substantially reduced, e.g. from 39 157 ($50 932) per QALY gained in the base-case to 30 693 ($39 923) per QALY gained for a 50% hypoglycaemia reduction and 27 552 ($35 837; 2013 values) per QALY gained for a 75% hypoglycaemia reduction [23].

Discussion

This review of 11 cost-effectiveness studies across 8 settings showed that the mean (95% CI) for the ICER comparing CSII vs. MDI in Type 1 diabetes was 30 862 (17 997–43 727 per QALY gained) [$40 143 (23 409–56 876) per QALY gained] for the base-case, with a mean baseline HbA_{1c} of 72 mmol/mol (8.7%). For hypoglycaemia-prone people with Type 1 diabetes, where the mean frequency of severe hypoglycaemia is expected to be reduced by ~ 75% by switching to CSII [11], the base-case ICER would be expected to be reduced by ~ 30% [23], so that a mean ICER of 21 603 (12 598–30 609) per QALY gained, $28 099 (16 386–39 813) per QALY gained can be estimated. The willingness-to-pay threshold will, of course, vary between countries and healthcare systems; the UK National Institute for Health and Care Excellence (NICE), for example, has an informal threshold of £20 000–

30 000 (24 107–36 158), although this has not been adjusted for inflation since the inception of NICE [29]. It is evident, then, that for both of the two main clinical indications for CSII – elevated HbA_{1c} or frequent hypoglycaemia during MDI – insulin pump therapy may be considered a cost-effective treatment in Type 1 diabetes over most settings. In these patient groups, cost-effectiveness was driven by a lower incidence of long-term complications due to improved glycaemic control, leading in turn to improved quality-adjusted life expectancy and lower lifetime complication costs.

The ICER estimates were highly sensitive to the HbA_{1c} benefit associated with CSII, as well as to the reduction in the incidence of hypoglycaemic events associated with CSII vs. MDI. In most of the analyses performed using the CDM and, in the majority of the commercially funded analyses, clinical input data for the base-case relating to expected HbA_{1c} change with CSII were derived from a 2003 meta-analysis by Weissberg-Benchell *et al.* [9] in which an HbA_{1c} treatment effect of 10–13 mmol/mol (−0.95 to −1.2%) was reported. The use of these data across several cost-effectiveness analyses in different settings and among similar patient populations is likely to contribute to the similar findings across settings. However, it has been argued [30–32] that the inclusion of non-randomized studies in this meta-analysis may have resulted in selection bias and an overestimate of the HbA_{1c} benefit of CSII compared with an earlier RCT-based meta-analysis by Pickup *et al.* [8], in which the mean HbA_{1c} difference between treatments was 6 mmol/mol (0.51%). Similarly, 2007 meta-analyses by Jeitler *et al.* [10] and Monami *et al.* [12] report treatment differences of just 3–4 mmol/mol (0.3–0.4%) in favour of CSII. Because sensitivity analyses showed that the treatment effect in terms of HbA_{1c} were a key drivers of outcomes, it is likely that the use of clinical input data from meta-analyses based only on RCTs would have led to substantially higher ICERs in many of the included analyses. Conversely, the inclusion of observational studies could provide a

more accurate representation of real life clinical practice compared with the stringently controlled clinical trial environment [13]. For example, adherence to therapy may be different in routine clinic patients with diabetes compared with trial volunteers and they may be more likely to present with the clinical problems of hypoglycaemia and elevated HbA_{1c} than volunteers [13]. In any case, RCTs and observational studies indicate that the greatest change in HbA_{1c} with CSII occurs in patients with the highest baseline HbA_{1c} [11,33,34]; a CSII-related HbA_{1c} change of 11–16 mmol/mol (1.0–1.5%) would be expected from a baseline HbA_{1c} of, say, 75 mmol/mol (9%) [11,33] and therefore justifies the HbA_{1c} 13 mmol/mol (1.2%) input used in many of the studies reviewed here.

Authors of CDM-based cost-effectiveness analyses also consistently performed sensitivity analyses around the HbA_{1c} treatment effect, using data on HbA_{1c} benefit from meta-analyses studies [8,11]. The study of Cummins *et al.* [21], which incorporated the findings of an earlier analysis performed for NICE [3] was based on a base-case HbA_{1c} treatment effect of 10 mmol/mol (0.9%) reduction vs. MDI, based on preliminary data from the Insulin Pump Clinical Database (as well as a 50% reduction in the rate of severe hypoglycaemic event rates), resulting in an ICER of £37 712 per QALY gained in the UK setting. This study also performed sensitivity analyses using HbA_{1c} reductions of 6 mmol/mol (0.6%), based on Pickup and Sutton [11], and 15 mmol/mol (1.4%) based on a study by Pickup *et al.* [35]. In the studies included in this review, a range of baseline HbA_{1c} values were used as input data, from 66 to 79 mmol/mol (8.2–9.4%) but, across studies, we did not find a significant correlation between the baseline HbA_{1c} and ICER, probably because of variations in cost-effectiveness modelling methods, MDI and CSII costs and handling of factors such as the predicted change in hypoglycaemia (see below).

Analyses performed using the CDM typically adopted a conservative approach, where (in most cases) no benefit in the frequency of hypoglycaemic event rate for CSII vs. MDI was

assumed in the base-case analysis. In comparison, the Scuffham and Carr analysis [24] was based exclusively on hypoglycaemic event rates (resulting in an ICER of £11 461 per QALY gained), which again represents a conservative scenario as no benefit in terms of HbA_{1c} was assumed. Palmer *et al.* [36] note that the failure of Scuffham and Carr to capture the HbA_{1c} improvement usually recorded with CSII, together with the relatively short time horizon used (8 years), represent major shortcomings in this analysis. This time horizon is insufficient to capture long-term benefits in life expectancy and quality-adjusted life expectancy associated with a reduced incidence of micro- and macrovascular complications due to improved glycaemic control. Published analyses generally also did not capture indirect costs associated with complications such as hypoglycaemia, which may further underestimate the benefit of CSII relative to MDI. Non-severe hypoglycaemic events, for example, lead to costs of $15–93 per month in lost productivity due to absenteeism [37].

A number of CDM analyses performed sensitivity analyses around severe hypoglycaemic event rates, in which 50% and 75% reductions in frequency with CSII were modelled, which had the effect of decreasing the ICER. However, reported direct costs of severe hypoglycaemia varied substantially across settings, partly due to the different healthcare costs and to different definitions of severe hypoglycaemia across studies. For example, in the Canadian analysis by St Charles *et al.* [26], the cost of a severe hypoglycaemic event was estimated at CA$125. In comparison, in a US-based analysis by the same authors, the reported cost for a severe hypoglycaemic event was $1234 [25].

There were also large differences between settings in the costs of MDI and CSII therapy and the costs of diabetes-related complications. For example, in the Australian analysis by Cohen *et al.* [18] the cost of myocardial infarction was taken as AU$10 905 (2006 values), whereas the cost of the same event was taken as $38 783 in the US setting [25], and £4486 and

19 276 for UK and Spanish analyses, respectively [20,23]. The large variation between settings in both complication and therapy costs is therefore likely to have been a key driver in terms of the range of ICERs reported between settings.

This review was mainly designed to identify cost-effectiveness analyses of CSII in patients with Type 1 diabetes. However, one cost-effectiveness analysis of CSII vs. MDI in patients with Type 2 diabetes in the Chinese setting was also identified [28]. This reports that CSII was cost-effective vs. MDI for treating newly hospitalized patients with Type 2 diabetes in the Chinese setting over a short time horizon. However, this may reflect the cost-effectiveness of using CSII in Type 2 diabetes patients to temporarily restore normal glucose tolerance rather than as a long-term management practice. Corresponding analyses in Type 2 diabetes patients from North American and European settings are lacking.

Only three articles included here conducted analyses also in paediatric populations with Type 1 diabetes. Analysis from the Polish setting showed that CSII was more cost-effective in adolescents than adults [17], although in the US setting the reverse was true [25]. However, both analyses were performed using the CDM, which has not been validated for use in paediatric populations, which may contribute to the uncertainty around these findings.

A potential limitation of the current review was that several of the authors are also authors of some of the individual analyses included in the current review, which has the potential to introduce bias, particularly in terms of quality assessment. To reduce the potential for bias, the quality assessment of studies was performed by a researcher who was not an author of any of the cost-effectiveness analyses included in the present review. Additionally, the objective nature of the quality assessment instrument used (Drummond checklist) minimizes the potential for introducing bias.

Our review and the included studies are maybe limited because analyses did not take into account a possible deterioration in the effectiveness of CSII in a subset of subjects in the long term [38]. However, we recently found that 88% of patients receiving CSII maintained improved glycaemic control compared with MDI over at least 5 years [38]. Another possible limitation is that a proportion of patients who initiate CSII might eventually return to MDI. For example, UK guidelines [3] note that not all patients who switch from MDI to CSII will demonstrate improvements in HbA_{1c}, frequency of hypoglycaemia and quality of life, stating that in these instances 'continued use of an expensive therapy in the absence of demonstrable benefits would be an inappropriate use of resources.' [3]. Although the switching back of patients to MDI is likely to influence cost-effectiveness in the overall population, we have previously noted that the discontinuation rate is very small for CSII (<5%) [2] so this factor is likely to have minimal influence on cost-effectiveness calculations. For many settings, the availability of CSII is restricted principally to patients with poor glycaemic control and/or frequent or severe hypoglycaemic events. But from the foregoing considerations, the view that CSII is cost-effective is likely to be a robust conclusion for both short and long-term treatment for the patient population for which it is intended.

In summary, cost-effectiveness analyses identified in the current review show that for patients with Type 1 diabetes who have poor glycaemic control and/or frequent and/or problematic hypoglycaemia CSII is cost-effective in comparison with MDI across multiple settings; the reimbursement of CSII for Type 1 diabetes in many countries is therefore justified.

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FIGURE 1 Summary diagram of literature review process.

Supporting information

The following supporting information is avalable online:

Appendix S1. Quality assessment checklist.

Table 1 Summary of total lifetime costs and quality-adjusted life expectancy in cost-effectiveness analyses of CSII vs. MDI

Study (setting)	Currency	Time horizon	Total cost MDI	Total cost CSII	Δ Cost	QALYs MDI	QALYs CSII	Δ QALYs
Clegg *et al.* 2008 (Poland) [17]	EUR	Not stated	—	—	9 309 (adults), 19 294 (adolescents)	—	—	0.35 (adults) 0.46 (adolescents)
Cohen *et al.* 2007 (Australia) [18]	AUD	Lifetime	88 760 (adult), 107 139 (adolescents)	123 402 (adult) 148 918 (adolescents)	34 642 (adults), 41 779 (adolescents)	7.48 (adult), 9.08 (adolescents)	7.95 (adult), 9.64 (adolescents)	0.47 (adults), 0.56 (adolescents)
Colquitt *et al.* 2004 (UK)	GBP	10 years	—	—	—	—	—	—

Study (setting)	Currency	Time horizon	Total cost MDI	Total cost CSII	Δ Cost	QALYs MDI	QALYs CSII	Δ QALYs
[19]								
Conget Donlo *et al.* 2006 (Spain) [20]	EUR	Lifetime	79 916	105 439	25 523	10.28	11.14	0.85
Cummins *et al.* 2010 (UK) [21]	GBP	50 years	36 915	59 592	22 677	8.97	9.57	0.60
Nørgaard *et al.* 2010 (Denmark) [22]	DKK	60 years	2 344 398	2 365 768	21 370	11.56	12.52	0.96
Roze *et al.* 2005 (UK) [23]	GBP	60 years	61 104	80 511	19 407	11.27	12.03	0.76
Scuffham and Carr 2003 (UK) [24]*	GBP	8 years	4 052	9 514	5 462	6.85	7.32	0.47
St Charles *et al.* 2009 (USA) [25]	USD	60 years	186 170 (adults), 190 862 (adolescents)	204 192 (adults), 212 597 (adolescents)	18 022 (adults), 21 735 (adolescents)	11.79 (adults), 13.62 (adolescents)	12.85 (adults), 14.42 (adolescents)	1.06 (adults), 0.80 (adolescents)
St Charles *et al.* 2009 [26] (Canada)	CAD	60 years	147 216	162 807	15 591	9.37	10.03	0.66
Lynch *et al.* 2008 (Italy) [27]	EUR	60 years	220 997	254 871	33 874	—	—	1.06

*Cost over 8 year period.

Table 2 Summary of published cost-effectiveness analyses

Study (setting)	Analysis	Cohort characteristics	Study sponsor/source of funding	Discount rate and time horizon	Currency (year)	ICER (per QALY gained, local currency)	ICER (per QALY gained 2013 EUR)*	ICER (per QALY gained 2013 USD)*
Clegg *et al.* 2008 (Poland) [17]	CORE model analysis of CSII versus MDI in adults and adolescents	Adults, mean age 37.8 years, duration of diabetes 10.4 years, HbA_{1c} 9.40% Adolescents, mean age 14.0 years, duration of diabetes 1.0 year, HbA_{1c} 9.40%	Commercial funding (Medtronic)	5% Not stated	EUR (2006)	20 778 (adults) and 14 968 (adolescents)	25 917 (adults) and 18 670 (adolescents)	$33,711 (adults) and $24,285 (adolescents)
Cohen *et al.* 2007 (Australia) [18]	CORE model analysis in adult and adolescent patients	Adults, mean age 43.3 years, duration of diabetes 17.2 years, HbA_{1c} 8.2% Adolescents, mean age 17.1 years, duration of diabetes 6.3 years, HbA_{1c} 8.9%	Commercial funding (Medtronic)	5% Lifetime	AUD (2006)	AU$74 147 (adults) and AU$74 661 (adolescents)	62 538 (adults) and 62 971 (adolescents)	$81 343 (adults) and $81 907 (adolescent)
Colquitt *et al.* 2004 (UK) [19]	Markov model analysis of CSII versus MDI	Not presented	Commissioned by UK NHS on behalf of NICE	1.5% for clinical outcomes and 6% for costs 10 years	GBP (year not stated)	Not presented	—	—
Conget Donlo *et al.* 2006 (Spain) [20]	CORE model analysis of insulin pumps versus MDI	Mean age 35.9 years, duration of diabetes 15.2 years, HbA_{1c} 8.30%	Commercial funding (Medtronic)	3% Lifetime	EUR (2005)	29 947	36 323	$47 245

Study (setting)	Analysis	Cohort characteristics	Study sponsor/source of funding	Discount rate and time horizon	Currency (year)	ICER (per QALY gained, local currency)	ICER (per QALY gained 2013 EUR)*	ICER (per QALY gained 2013 USD)*
Cummins *et al.* 2010 (UK) [21]	CORE model analysis of CSII versus MDI in adults	Age 20–39 years, HbA_{1c} 8.8%	Commissioned on behalf of NICE	Not stated 50 years	GBP (2006)	£37 712	51 614	$67 135
Nørgaard *et al.* 2010 (Denmark) [22]	CORE model analysis of CSII versus MDI	Mean age 26 years, duration of diabetes 12 years, HbA_{1c} 8.68%	Commercial funding (Medtronic)	3% 60 years	DKK (2005)	kr 22 337	3 528	$4 589
Roze *et al.* 2005 (UK) [23]	CORE model analysis of CSII versus MDI in adults	Mean age 26 years, duration of diabetes 12 years, HbA_{1c} 8.68%	Commercial funding (Medtronic)	3% 60 years	GBP (2003)	£25 648	39 157	$50 932
Scuffham and Carr 2003 (UK) [24]	Markov model analysis of CSII versus MDI	Not presented	Commercial funding (Medtronic)	1.5% for clinical outcomes and 6% for costs 8 years	GBP (2001)	£11 461	17 962	$23 363
St Charles *et al.* 2009 (USA) [25]	CORE model analysis of CSII versus MDI in adults and children/young adults	Adults, mean age 27.0 years, duration of diabetes 9.0 years, HbA_{1c} 8.95% Adolescents, mean age 13.0 years, duration of diabetes 5.2 years, HbA_{1c} 8.2%	Commercial funding (Medtronic)	3% 60 years	USD (2007)	$16 992 (adults) and $27 195 (children/young adults)	14 661 (adults) and 23 464 (adolescents)	$19 069 (adults) and $30 520 (adolescents)
St Charles *et al.* 2009 (Canada) [26]	CORE model analysis of CSII versus MDI in adult patients	Mean age 27.0 years, mean duration of diabetes 9.0 years, HbA_{1c}	Commercial funding (Medtronic)	5% 60 years	CAD (2006)	CA$23 797	19 988	$25 998

Study (setting)	Analysis	Cohort characteristics	Study sponsor/source of funding	Discount rate and time horizon	Currency (year)	ICER (per QALY gained, local currency)	ICER (per QALY gained 2013 EUR)*	ICER (per QALY gained 2013 USD)*
	with Type 1 diabetes	8.95%						
Lynch *et al.* 2008 (Italy) [27]	CORE model analysis of CSII versus MDI in adult patients with Type 1 diabetes	Mean age 27.0 years, duration of diabetes 9.0 years, HbA_{1c} 8.95%	Commercial funding (Medtronic)	3% 60 years	EUR (2007)	31 879	36 502	$47 490

*Costs were inflated to 2013 values using average consumer price index sourced from International Monetary Fund World Economic Outlook Database, available at: http://www.imf.org/external/pubs/ft/weo/2013/02/weodata/index.aspx. Exchange rate conversions were performed using historical exchange rates for 01 July 2013, available at: www.OANDA.com/currency/converter/

Figure 1