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Cost-utility models of continuous glucose monitoring in individuals with type 1 diabetes: a systematic review on methodology and quality

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de Jong LA[1], Li X[2], Emamipour S[3], van der Werf S[4], Postma MJ[1,5], van Dijk PR[6], Feenstra TL[2,7]

1 Department of Health Sciences, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands; 2 Unit of PharmacoTherapy, -Epidemiology & -Economics, University of Groningen, Groningen Research Institute of Pharmacy (GRIP), Groningen, the Netherlands; 3 Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands; 4 Central Medical Library, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands; 5 Department of Economics, Econometrics and Finance, Faculty of Economics & Business, University of Groningen, Groningen, the Netherlands; 6 Department of Endocrinology. University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; 7 Center for Nutrition, Prevention and Health Services Research, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Introduction

- Continuous glucose monitoring (CGM) devices have improved the quality of glucose management, and potentially improve quality of life, decrease disease burden and diabetes related hospital admissions in individuals with diabetes type 1[1,2].
- Though it has been shown that the devices improve glucose control, the affordability of these devices remain a point of discussion[3,4].
- Different types of glucose monitoring devices can be combined with different types of insulin administration. All of these can be compared to traditional finger pricking for monitoring of blood glucose in combination with insulin pens or injections, or to each other.
- Previous reviews showed that cost-effectiveness ratios and health benefits vary widely.
- Therefore, the current review aims to critically appraise differences in methodology and quality of model- and empirical-data-based studies.

Objectives

- To systematically summarize published model-based and empirical-data-based cost-utility studies of CGM in individuals with type 1 diabetes, by type of device.
- To systematically assess their quality and validity.

Methods

PROTOCOL AND REGISTRATION

- A protocol was registered with PROSPERO (registration number: CRD42023391284)[5] and published[6]. The review was conducted and reported in accordance with this protocol, following the updated PRISMA 2020 statement: an updated guideline for reporting systematic reviews[6].

SEARCH STRATEGY

- Several electronic databases were searched: MEDLINE, Embase, Web of Science, Cochrane Library (for Cochrane Central Register of Controlled Trials (CENTRAL)), and Econlit. A grey literature search was conducted using Google Scholar and references of previous systematic literature reviews on this topic and the reference lists of identified papers were hand checked for additional articles.
- The search strategy was based on three concepts: 1) type 1 diabetes, 2) continuous glucose monitoring and 3) cost-utility. Per concept a search block was developed.
- The search was limited to articles published between 2000 and 2023, since the first CGM device was approved by the FDA in June 1999[8]. Further selection criteria are listed in Table 1.

Table 1. Summary of eligibility criteria

Eligibility criteria (PICOT)
Individuals diagnosed with T1D
Any CGM intervention. Studies on bi-hormonal closed loops (e.g., artificial pancreas) and do-it-yourself hybrid closed loop devices were excluded as these interventions are still in development.
Any comparator
Studies reporting health benefits in terms of QALYs gained
Model-based and empirical-data-based cost-utility studies
January 1, 2000 to January 19, 2023
English

CGM, continuous glucose monitoring; T1D, type 1 diabetes; QALYs, quality-adjusted life years.

STUDY SELECTION AND DATA EXTRACTION PROCEDURES

- After deduplication, titles and abstracts were screened using Rayyan. Two reviewers independently assessed all studies against the eligibility criteria, in case of disagreement they met and discussed until consensus. Next, the same two reviewers did independent full text screening.
- Data extraction was then performed in excel, using a prespecified data extraction format with several tabs. Studies were distributed over 4 authors performing data extraction, such that each study was seen by two reviewers. Any disagreement between the two reviewers was resolved through discussion with a third independent reviewer.
- Data extraction concerned basic study information, model structure or type of empirical data study design employed, how effectiveness of CGM was modelled, input data used, handling of uncertainty, model validity and quality of study design. Additionally, incremental costs and QALYs and the ICER were collected, as well as COI statements and study funding. For quality of study design and model validity, the Philips et al. 2006 checklist[8] , the CHEC-extended checklist[9-10] and the AdViSHE[11] tool were applied.

DATA SYNTHESIS

- Results of data extraction were qualitatively synthesized, with a focus on methods and models applied.
- Extra attention was paid to CGM effectiveness modeling, intervention costing, sources for utilities and whether disutility values for hypoglycaemia or fear of hypoglycaemia were included.

Results

SEARCH RESULTS AND STUDY OVERVIEW

- In total 34 eligible studies were identified. Figure 1 represents the study selection process.
- The studies originated from 14 countries and had many different comparisons. (Figure 2) The most common comparison (15 out of 34) considered was real-time CGM (rt-CGM) plus sensor-augmented pump (SAP) to self-monitoring of blood glucose (SMBG) combined with either continuous subcutaneous insulin infusion (CSII), multiple daily injections (MDI) of insulin, or a combination of both (Figure 2).

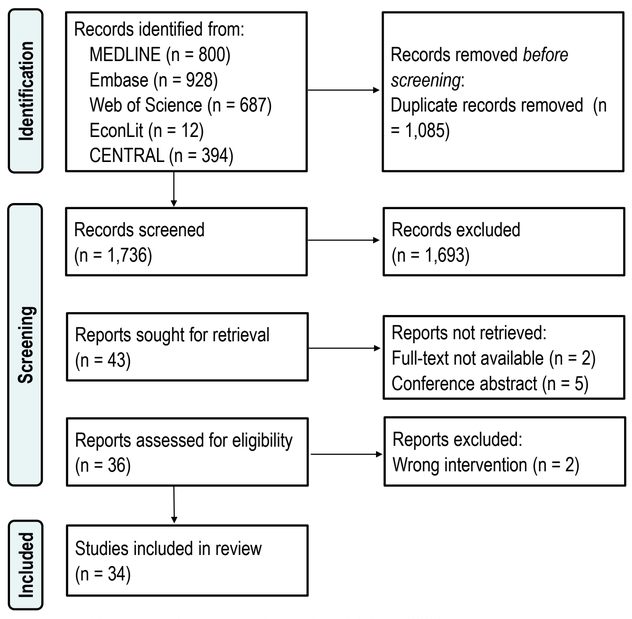

Figure 1. Study selection presented in the PRISMA 2020 flow diagram.

Results

- Most studies were model-based, we only found two trial-based (one of them also included a model-based analysis) and one observational data-based study. The majority of model-based studies (75%, 24 out of 32) used the CORE diabetes model. The remaining 8 studies used the Sheffield model (1), or a newly developed one (7), often building from previous studies' models.
- All three empirical-data based CUAs used a within study time horizon of up to 12 months and concluded that CGM is cost-effective. All except two model-based CUAs used a lifetime horizon. Only four model-based studies (which were all four publicly sponsored) concluded CGM to be not cost-effective. In total 25 studies were sponsored by the device producer, which all concluded the CGM devices to be cost-effective or cost-saving.

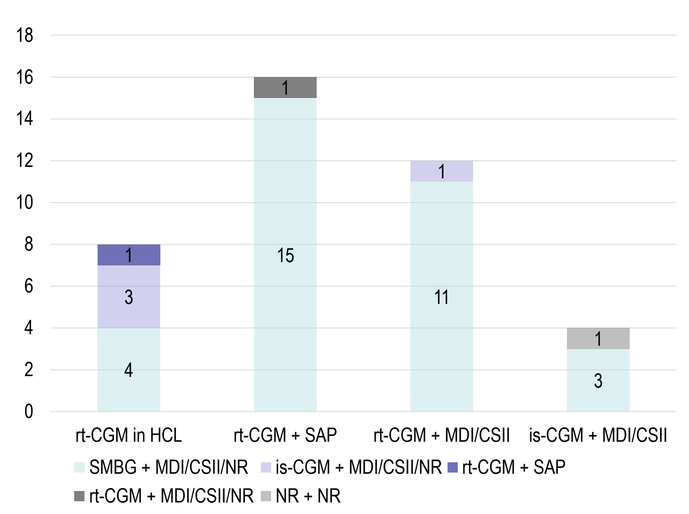

Figure 2. Overview of the comparisons included in the studies. Some studies included multiple comparisons. *CSII, continuous subcutaneous insulin infusion; HCL, hybrid closed loop, is-CGM, intermittently-scanned continuous glucose monitoring; MDI, multiple daily injections; NR, not reported; rt-CGM, real-time continuous glucose monitoring; SAP, sensor-augmented pump*

BASELINE CHARACTERISTICS AND TREATMENT EFFECT

- Populations varied from adult people with T1D in general to persons at increased risk of hypoglycaemia, or with uncontrolled HbA1c. Three studies included children and/or adolescents. As a result, baseline characteristics varied widely as well.
- Studies often used the same sources for the CGM effect on HbA1c and hypoglycaemic events. Frequently used sources were a meta-analysis by Pickup et al.[12] (7 out of 34), and RCTs by Ly et al[13] (7 out of 34), DIAMOND[14] (6 out of 34), and FUTURE[15] (4 out of 34). The remaining 10 studies used a variety of different RCTs.
- Many studies (20 out of 34) also included an effect on fear of hypoglycaemia in terms of QALYs, which was based on a reduction in Hypoglycaemic Fear Survey score sourced from either the DIAMOND[14] or INTERPRET trial[16].

INTERVENTIONS AND COSTING

- The intervention and comparator were rarely defined in the objectives or methods and had to be deducted from the clinical data or cost tables, reflecting lack of transparency.
- Intervention costs were also intransparent. Some studies only reported a lump sum cost, without specifying how these were estimated and what cost elements were included or not. (Figure 3)

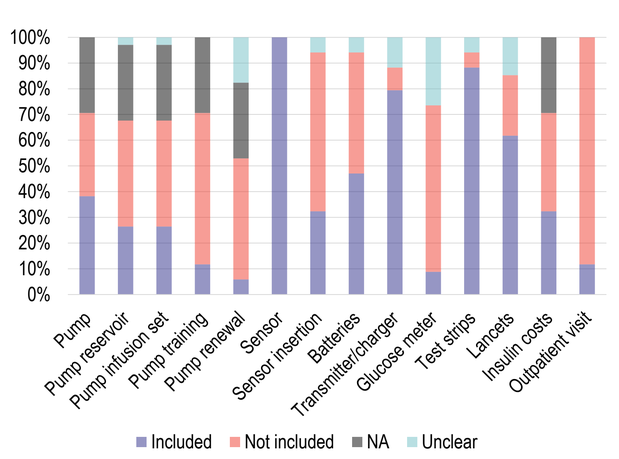

Figure 3. Proportion of studies that included CGM and insulin related cost items.

QUALITY AND VALIDATION

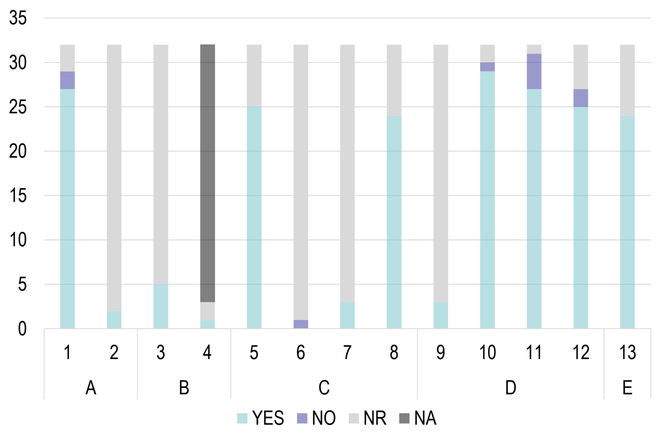

Figure 4. Model validation: total score per item of the AdViSHE checklist. *NA, not applicable; NR, not reported.*

- The studies that applied the CORE Diabetes model almost all referred to the original studies reporting on the structure of the model and its validation. Hence, they scored similar regarding model validity and model quality.
- Other studies varied in the amount of model validation efforts that were reported and in the details regarding model choices and uncertainty analyses provided.
- Model validity was in general well reported, but not for input data validity and code verification (Figure 4).
- It was hard to score the Philips consistently among the 4 co-authors involved.
- Model quality was moderate on average (56%) and varied per item in the Philips checklist (0%—100%) or paper (38%—85%).

Conclusions

- **A major concern of current cost-utility analyses is the lack of transparency on duration of treatment effects, indicating a need for long-term data to justify assumptions of a lifelong effect size.**
- **Another concern is the limited testing of structural uncertainty, while most analyses were based on the same model, which implies results should be interpreted with care.**
- **Studies perform well on basics of uncertainty analysis and model validation, but reporting can be improved.**

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Correspondence email: l.a.de.jong@rug.nl

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