Smart Insulin Pens are Associated with Improved Clinical Outcomes at Lower Cost Versus Standard-of-Care Treatment of Type 1 Diabetes in Sweden: A Cost-Effectiveness Analysis

Johan Jendle (ID) · Åsa Ericsson · Jens Gundgaard · Jonas Bech Møller ·
William J. Valentine · Barnaby Hunt

ABSTRACT

Introduction: Real-world evidence has demonstrated improved glycemic control and insulin management following introduction of smart insulin pens in a Swedish type 1 diabetes (T1D) population. To understand the implications for healthcare costs and expected health outcomes, this analysis evaluated the long-term cost-effectiveness of introducing smart insulin pens to standard-of-care T1D treatment (standard care) from a Swedish societal perspective.

Methods: Clinical outcomes and healthcare costs (in 2018 Swedish krona, SEK) were projected over patients' lifetimes using the IQVIA CORE Diabetes Model to estimate cost-effectiveness. Clinical data and baseline characteristics for the simulated cohort were informed by population data and a prospective, noninterventional study of a smart insulin pen in a Swedish T1D population. This analysis captured direct and indirect costs, mortality, and the impact of diabetes-related complications on quality of life.

Results: Over patients' lifetimes, smart insulin pen use was associated with per-patient improvements in mean discounted life expectancy (+ 0.90 years) and quality-adjusted life expectancy (+ 1.15 quality-adjusted life-years), in addition to mean cost savings (direct, SEK 124,270; indirect, SEK 373,725), versus standard care. A lower frequency and delayed onset of complications drove projected improvements in quality-adjusted life expectancy and lower costs with smart insulin pens versus standard care. Overall, smart insulin pens were a dominant treatment option relative to standard care across all base-case and sensitivity analyses.

Conclusions: Use of smart insulin pens was projected to improve clinical outcomes at lower costs relative to standard care in a Swedish T1D population and represents a good use of healthcare resources in Sweden.

J. Jendle (✉)
Institute of Medical Sciences, Örebro University, Örebro, Sweden
e-mail: johan.jendle@oru.se

Å. Ericsson
Novo Nordisk Scandinavia AB, Malmö, Sweden

J. Gundgaard · J. B. Møller
Novo Nordisk A/S, Søborg, Denmark

W. J. Valentine · B. Hunt
Ossian Health Economics and Communications, Basel, Switzerland

Key Summary Points

Why carry out this study?

Digital health solutions are becoming increasingly established for chronic disease management, particularly in the treatment of diabetes; however, there is a need for evidence to support healthcare payers in making value-based decisions on the new digital technologies

Smart insulin pens record the timing and dose of insulin injections, while their data can be integrated with continuous glucose monitoring to improve diabetes self-management and address an unmet need for patients to become more actively engaged with their diabetes care

The aim of the present modeling analysis—which was informed by clinical data from a Swedish prospective, noninterventional study—was to evaluate the long-term cost-effectiveness of introducing smart insulin pens to standard-of-care treatment for type 1 diabetes (standard care) from a Swedish societal perspective

What was learned from the study?

Projections showed that smart insulin pens were associated with lower healthcare costs and improved health outcomes (i.e., a dominant treatment option) versus standard care in the base-case analysis and across all of the sensitivity analyses conducted

Our findings suggest that smart insulin pens are likely to be a good use of healthcare resources in Sweden in this patient population with type 1 diabetes, and they add to a growing body of evidence that digital technologies can add value to the treatment of chronic diseases

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13296119.

INTRODUCTION

Diabetes, including type 1 diabetes (T1D), is associated with the development of microvascular and macrovascular complications [1, 2], which have significant negative effects on quality of life [3, 4], and morbidity and mortality [5], with substantial costs to healthcare systems across patients' lifetimes [6]. The incidence of T1D is increasing worldwide [2]; new cases of T1D in Europe are rising at a rate of 3.4% annually, with projections showing that, if the current trend continues, incidence will double in the next 20 years [7]. In Sweden, the incidence of pediatric-onset T1D has doubled in the last 40 years to 43.9 per 100,000—the second highest incidence rate in the world [2, 8].

The development and implementation of new digital solutions are key to supporting the management of chronic diseases [9]. They offer potential innovative solutions to reduce the burden of chronic disease on patients and healthcare providers, address the lack of data to inform therapeutic decision-making, improve clinical outcomes, and reduce healthcare needs [10]. However, the cost of these digital solutions can be a barrier to their implementation [11], and healthcare payers need evidence to make value-based decisions on digital tools. Economic analyses are increasingly being used to support healthcare decision-making [12]. One such method is cost-effectiveness analysis, which provides evidence on health gains and resource implications of a certain intervention by comparing the costs of interventions with expected outcomes (most commonly measured in quality-adjusted life-years, QALYs) [13].

For people with diabetes, there are a growing number of digital technologies available that enable optimized monitoring of lifestyle and pharmaceutical interventions, and also capture

accurate data that can aid healthcare professionals in decision-making [14]. Smart insulin pens are one such digital tool, able to record the timing and dose of insulin delivered, and they can be combined with intermittently scanned or real-time continuous glucose monitoring (CGM) data, for example. From a patient perspective, smart insulin pens have the added benefit over standard insulin pens of capturing data on insulin delivery. When smart insulin pens were introduced to a cohort of people with T1D already using CGM in Sweden, they resulted in improved glycemic control (greater time in range, TIR), reduced time in hypoglycemia, and fewer missed bolus insulin doses [15, 16]. As a result of these factors, smart insulin pen use led to a significant increase in the amount of bolus insulin being administered each day, with no change to basal insulin dosing [15].

In combination, smart insulin pens and CGM may lead to improved diabetes self-management, and address an unmet need for patients to become more actively engaged with their diabetes care in this population of people with T1D [15]. However, it is important to understand the implications for healthcare costs and expected health outcomes based on improvements in glycemic control, but also increased bolus insulin doses. The cost-effectiveness of this digital tool should therefore be investigated and, as such, the aim of the present analysis, informed by Swedish real-world evidence, was to evaluate the long-term cost-effectiveness of introducing smart insulin pens to standard-of-care treatment of T1D (standard care) from a societal perspective in Sweden.

METHODS

Swedish Prospective, Noninterventional Study Design

The design and results of the Swedish noninterventional study have been published previously [15]. In brief, a one-arm, prospective, observational, proof-of-concept study evaluated the introduction of a near-field communication (NFC)-enabled smart insulin pen (NovoPen® 6; Novo Nordisk A/S, Bagsværd, Denmark) in 94 adults with T1D receiving basal–bolus insulin therapy and using CGM, from 12 diabetes clinics in Sweden [15]. Participants were included in the study at the discretion of their healthcare team and received a smart insulin pen for basal and/or bolus insulin injections. Downloadable long-term injection data were blinded to participants during the baseline period (baseline until visit 1), but CGM data could be viewed, and the dose of the last injection was displayed on the smart insulin pen [15]. At visit 1, the first set of injection data was downloaded at the participant's diabetes clinic, and subsequent follow-up visits were scheduled according to standard clinical practice. Smart insulin pen and CGM data were downloaded at each visit (CGM data were also uploaded between visits), and discussed and acted upon by the participant and healthcare team [15].

Glycemic summary measures and the number of missed bolus dose injections were compared between the blinded baseline period and the follow-up period [15]. The follow-up period was defined as any point after the fifth visit, to allow for adequate discussion of available smart insulin pen data with the healthcare team [15]. All 94 participants were included in the TIR analysis, while the 81 participants who were using the smart insulin pen for bolus insulin dosing were included in the bolus dose analyses and missed bolus dose analysis [15]. TIR was defined as the time spent with sensor glucose within the acceptable range (3.9–10.0 mmol/L [70–180 mg/dL]) [17]. Time spent in hypoglycemia (divided into level 1, 3.0 to < 3.9 mmol/L [54 to < 70 mg/dL]) and level 2, < 3.0 mmol/L [< 54 mg/dL]) [17], total daily insulin dose, mean glucose level, and the coefficient of variation were additional outcomes [15].

Cost-Effectiveness Model Overview

A cost-effectiveness analysis was performed by projecting costs (2018 Swedish krona, SEK) and clinical outcomes over patients' lifetimes following the introduction of a smart insulin pen in a Swedish T1D population. This approach

aims to capture the development of diabetes-related complications and their impact on projected costs, life expectancy, and quality of life, in alignment with guidelines on the assessment of the cost-effectiveness of diabetes interventions [18]. The analysis was performed using the IQVIA CORE Diabetes Model (IQVIA, Durham, NC), a validated computer-simulation model of diabetes [19]. The model projected the development of diabetes-related complications, mortality, hypoglycemia over a 60-year time horizon (i.e., patients' remaining lifetimes) based on risk factors such as glycated hemoglobin (HbA1c), blood pressure, lipids, and body mass index. First-order stochastic uncertainty was captured via a Monte Carlo approach. Modeled outcomes included direct medical costs, indirect costs, life expectancy, quality-adjusted life expectancy, and the cumulative incidence and time to onset of diabetes-related complications in each simulation arm. It was assumed that patients continued to receive their set intervention (smart insulin pen in addition to standard care versus standard care) for the duration of their lifetime. Future costs and clinical outcomes were discounted at a rate of 3% per annum, in alignment with guidelines for economic evaluations in Sweden [20]. This article does not contain any new studies with human participants or animals performed by any of the authors.

Clinical Data

Model inputs for clinical outcomes were informed by the Swedish prospective, noninterventional study [15]. In the study, smart insulin pens were associated with an additional 1.89 h per day TIR compared with the baseline measurement (without a smart insulin pen; 9.19 h, over a median follow-up of 7 months), and daily bolus insulin dose increased from 25.1 units [U] to 32.1 U from baseline to visit 5 [15]. There are currently no published risk equations allowing TIR to be directly linked to incidence of diabetes-related complications and, therefore, a conversion from TIR to HbA1c was made, based on a previously identified linear relationship between the two parameters

[21]. A 10% change in TIR was considered equivalent to a change in HbA1c of 0.8% (9 mmol/mol) [21]. TIR as a percentage (baseline, 41.4%; end of trial, 49.9%; change in TIR, + 8.5%) was converted to HbA1c using the following regression equation (HbA1c = [TIR − 155.4]/− 12.762) [21]. This conversion allowed long-term outcomes to be modeled on the basis of published risk equations that use HbA1c as a risk factor for developing complications. These calculated HbA1c values at baseline (8.93%) and end of trial (8.27%) resulted in a HbA1c treatment effect of − 0.67% (− 7 mmol/mol), which was applied in the smart insulin pens arm, with no HbA1c treatment effect applied in the standard care arm. The HbA1c treatment effect was assumed to be constant in both arms of the analysis, with the difference maintained for the duration of the analysis. Hypoglycemic event rates were based on the study period of the Swedish prospective, noninterventional study for the smart insulin pens arm, and the baseline value for the standard care arm (3287.25 and 6574.50 events per 100 patient-years, respectively). For modeling purposes, hypoglycemia was defined as at least 15 min of below 54 mg/dL (< 3.0 mmol/L) in CGM data [22], and all hypoglycemic events were categorized as nonsevere. Mortality as a result of diabetes-related complications and background mortality based on Sweden-specific life tables [23] were applied.

Simulated Cohort

All baseline characteristics were taken from people with T1D enrolled in the Swedish National Diabetes Register [24], other than baseline HbA1c (calculated from baseline TIR from the Swedish prospective, noninterventional study) [15], number of cigarettes smoked per day, and mean weekly alcohol consumption (both assumed to be the same as the Swedish general population) [25, 26] (Table 1). The model simulated the lifetime progression of diabetes in a cohort of 1000 hypothetical patients and repeated the process 1000 times for each simulation arm. This simulation generated mean and standard deviation values of clinical effectiveness and costs.

Table 1 Simulated cohorts

Characteristic	Parameter	Unit	Source
Age	41.6	Years	SWE-NDR [24]
Duration of diabetes	26.1	Years	SWE-NDR [24]
Male	0.545	Proportion	SWE-NDR [24]
HbA1c[a]			
Smart pens arm	8.27/66.9	Percentage/mmol/mol	Adolfsson et al. 2020 [15]
Standard care arm	8.93/74.1	Percentage/mmol/mol	Adolfsson et al. 2020 [15]
NSHE			
Smart pens arm	3287.25	Events per 100 patient-years of observation	
Standard care arm	6574.50		
Blood pressure			
Systolic	128.7	mmHg	SWE-NDR [24]
Diastolic	73.6	mmHg	SWE-NDR [24]
Cholesterol			
Total	146.2	mg/dL	SWE-NDR [24]
HDL	62.6	mg/dL	SWE-NDR [24]
LDL	103.2	mg/dL	SWE-NDR [24]
Triglycerides	95.6	mg/dL	SWE-NDR [24]
BMI	25.3	kg/m^2	SWE-NDR [24]
Smokers	0.122	Proportion	SWE-NDR [24]
Cigarettes[b]	14	Number per day	Population data [25]
Alcohol consumption	5.98/177	Fluid ounces per week/mL per week	Population data [26]
Ethnicity			
White[c]	1.000	Proportion	Assumed

Data are mean, unless otherwise stated

BMI body mass index, *HbA1c* glycated hemoglobin, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *NSHE* nonsevere hypoglycemic events, *SWE-NDR* Swedish National Diabetes Register

[a] HbA1c data were derived from time in range and converted using a published regression equation [21]; the HbA1c value for the smart pens arm was calculated as 8.933–0.666 [derived treatment effect from the regression equation] = 8.267%, with all figures rounded to 2 decimal places

[b] Only applies to the smokers

[c] These data were not collected in the prospective, noninterventional Swedish study, so were assumed to be 100% white for simplicity in this analysis

Quality-of-Life Utilities

Quality-adjusted life expectancy was assessed using the CORE Default Method, which involves taking the lowest state utility associated with existing complications and adding event utilities for any events that occur in that year (Supplementary Table S1), to create annual utility scores for each simulated patient. Utilities associated with diabetes and disease-related complications were extracted from published sources (Supplementary Table S1).

Costs

Costs were estimated from a Swedish societal perspective to capture all direct medical costs (pharmacy costs, costs associated with diabetes-related complications, and concomitant patient management costs) and indirect costs as a result of lost productivity. Insulin doses applied in this model were based on the baseline values of patients enrolled in the Swedish prospective, noninterventional study for the standard care arm, and based on end-of-trial data for the smart insulin pens arm (daily bolus dose increased from 25.1 U at baseline to 32.1 U at visit 5) [15]. Resource use and costs relating to insulin delivery were based on prices in Sweden, and are shown in Supplementary Table S2. Smart insulin pens and conventional durable insulin pens (without smart technology) have the same cost in Sweden (SEK 536.05) [27]; these costs were excluded from the analysis for simplicity owing to the relatively low costs and the durability (up to 5 years) of the insulin pens (Supplementary Table S2). Resource use relating to patient management was assumed to be the same as the general population of people with T1D in Sweden and is detailed along with patient management costs in Supplementary Table S3.

The cost of diabetes-related complications in the year of the event and for annual follow-ups (applied in each year of the simulation subsequent to the event) were identified through a literature review, and costs were inflated to 2018 values (Supplementary Table S4). Indirect costs of diabetes-related complications were considered in both arms of the analysis. Working age was considered to be from 20 to 65 years of age, with an average annual salary of SEK 438,000 for men and SEK 391,200 for women [28], and the working year considered to be 250 days. Days off work estimates were taken from an analysis of Danish registry data [29] or a study on the annual cost of hypoglycemia in Sweden [30], or a conservative assumption was used when no estimates could be identified (Supplementary Table S5). Cost results are presented in SEK, with a conversion to euros (EUR) in the Supplementary Appendix using a SEK 0.091 exchange rate, correct as of 27 March 2020.

Sensitivity Analyses

As the extrapolation of clinical results by modeling long-term outcomes is associated with a level of uncertainty, sensitivity analyses were performed to assess the robustness of the findings and identify key drivers of modeled outcomes. Sensitivity analyses were performed by varying model parameters. The influence of time horizon on the outcomes projected by the model was investigated by running analyses over 3, 5, and 10 years. The base-case analysis used the baseline HbA1c from the Swedish prospective, noninterventional study, and sensitivity analyses were performed with variation in this input parameter. The calculated change in HbA1c (with the smart insulin pen relative to standard care) was varied to investigate uncertainty around the impact of smart insulin pens on glycemic control and the relationship between TIR and HbA1c. Further sensitivity analyses were conducted removing treatment effects in terms of HbA1c and hypoglycemic event rates, and with treatment switching from standard care to the smart insulin pen.

RESULTS

Base-Case Analysis

Projections showed that smart insulin pens were associated with improvements in mean

discounted life expectancy of 0.90 years per patient and mean discounted quality-adjusted life expectancy of 1.15 QALYs per patient, compared with standard care (Table 2). Clinical benefits resulted from a reduced incidence of all diabetes-related complications, with a single

Table 2 Results of the base-case analysis

	Smart insulin pen	Standard care	Difference
Outcomes, mean (SD)			
Discounted direct costs (SEK)	635,599 (19,290)	759,869 (21,883)	− 124,270
Discounted combined costs (SEK)	1,541,648 (55,546)	2,039,643 (61,753)	− 497,995
Discounted life expectancy (years)	20.20 (0.19)	19.31 (0.20)	+ 0.90
Discounted quality-adjusted life expectancy (QALYs)	14.74 (0.14)	13.59 (0.14)	+ 1.15
Cumulative incidence of complications, %			
Cardiovascular disease			
Myocardial infarction	15.04	16.20	− 1.16
Angina	12.22	13.09	− 0.87
Stroke	3.22	3.41	− 0.19
Congestive heart failure	3.83	4.07	− 0.24
Peripheral vascular disease	16.45	16.79	− 0.34
Renal disease			
Microalbuminuria	41.91	58.50	− 16.59
Gross proteinuria	21.71	33.28	− 11.57
End-stage renal disease	8.30	12.74	− 4.44
Death following end-stage renal disease	6.12	9.67	− 3.55
Eye disease			
Background diabetic retinopathy	76.61	88.25	− 11.64
Proliferative diabetic retinopathy	22.26	38.95	− 16.69
Macular edema	42.79	58.87	− 16.08
Severe vision loss	32.27	42.80	− 10.53
Cataract	21.81	20.64	+ 1.17
Neuropathic complications			
Neuropathy	63.51	75.26	− 11.75
Diabetic foot complications			
Foot ulcer	47.23	57.48	− 10.25
Amputation	17.70	21.78	− 4.08

QALY quality-adjusted life-year, *SEK* 2018 Swedish krona

exception (cataract) in the smart insulin pens arm compared with standard care over the 60-year time horizon of the analysis (Table 2). Treatment with smart insulin pens was also associated with a delayed mean time to onset of any diabetes-related complication (+ 2.9 years) versus standard care (Fig. 1).

For direct medical costs, projections indicated that the mean cost per patient was SEK 124,270 (EUR 11,309) lower in the smart insulin pens arm compared with standard care, over a patient's lifetime (Fig. 2a; Supplementary Table S6). Higher treatment costs in the smart insulin pens arm (SEK 154,047 [EUR 14,018]) compared with the standard care arm (SEK 136,461 [EUR 12,418]) (Fig. 2a; Supplementary Table S7) were a result of a higher bolus

insulin dose and increased survival, which led to further treatment over the long term. However, this higher treatment cost in the smart insulin pens arm was offset by cost savings arising from the reduced incidence of diabetes-related complications (Fig. 2a). For indirect costs, a mean saving of SEK 373,725 (EUR 34,009) per patient was projected for the smart insulin pens arm versus the standard care arm (SEK 906,049 [EUR 82,450] versus SEK 1,279,774 [EUR 116,459]) (Fig. 2b; Supplementary Table S7). When direct and indirect costs were combined, cost savings of SEK 497,995 [EUR 45,318] per patient with smart insulin pens were projected versus standard care (smart insulin pens, SEK 1,541,648 [EUR 140,290]; standard care, SEK 2,039,643
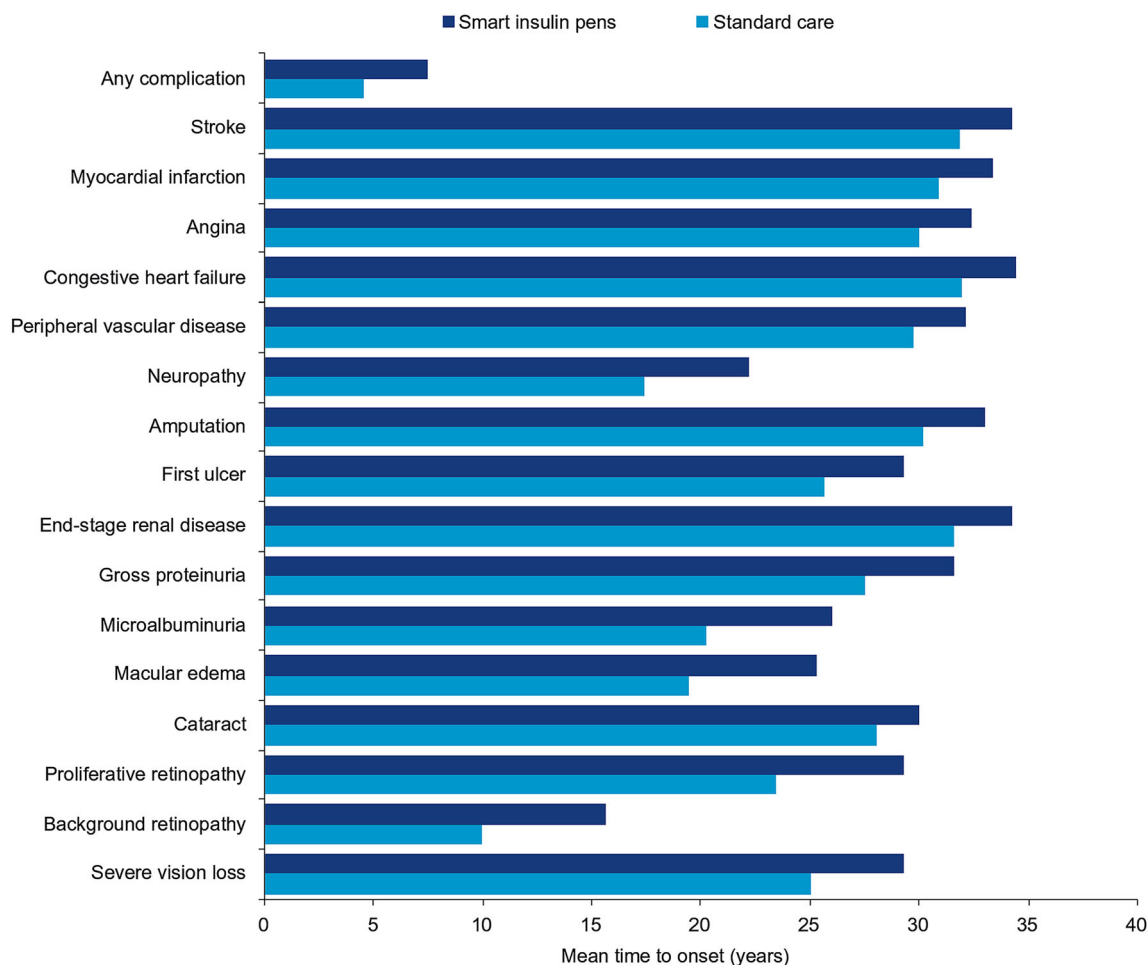

Fig. 1 Projected mean time to onset of complications. Base-case analysis, treatment effects were maintained for patient lifetimes
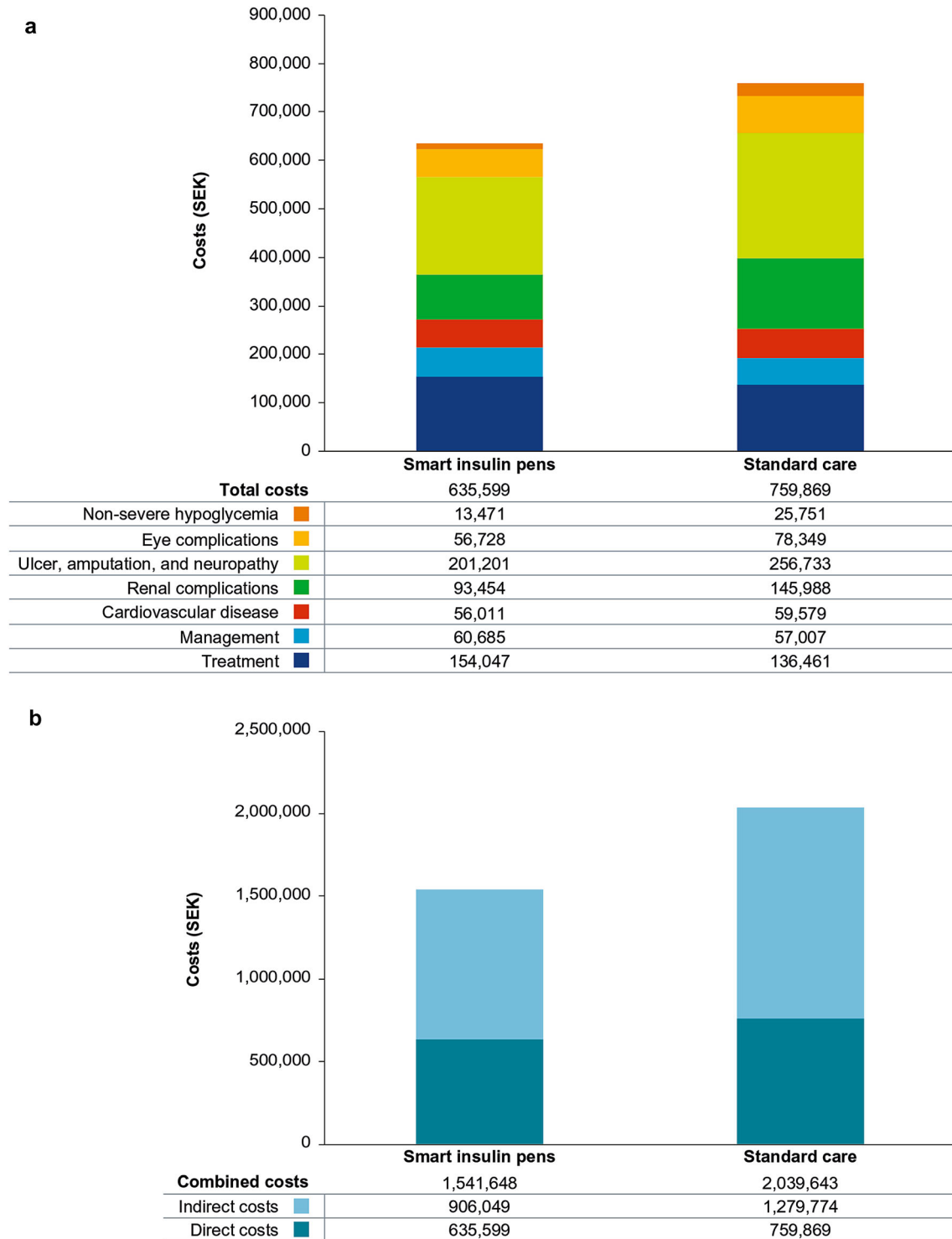
a

	Smart insulin pens	Standard care
Total costs	635,599	759,869
Non-severe hypoglycemia ■	13,471	25,751
Eye complications ■	56,728	78,349
Ulcer, amputation, and neuropathy ■	201,201	256,733
Renal complications ■	93,454	145,988
Cardiovascular disease ■	56,011	59,579
Management ■	60,685	57,007
Treatment ■	154,047	136,461

b

	Smart insulin pens	Standard care
Combined costs	1,541,648	2,039,643
Indirect costs ■	906,049	1,279,774
Direct costs ■	635,599	759,869

Fig. 2 Mean **a** direct costs and **b** combined (direct and indirect) costs over patients' lifetimes. Base-case analysis, treatment effects were maintained for patient lifetimes. SEK, 2018 Swedish krona

[EUR 185,607]) (Fig. 2b; Supplementary Table S7).

Estimation of long-term cost-effectiveness outcomes indicated that both life expectancy and quality-adjusted life expectancy were improved with smart insulin pens compared with standard care, at a decreased cost from a healthcare payer and a societal perspective. Therefore, treatment with smart insulin pens was considered dominant over standard care from both a healthcare payer and a societal perspective.

Sensitivity Analyses

Overall, results of the sensitivity analyses indicated that the result of the base-case analysis was robust to changes in the input parameters and assumptions used, with smart insulin pens found to be dominant relative to standard care in all sensitivity analyses (Table 3; in EUR in Supplementary Table S6). Shortening the time horizon led to smaller clinical benefits and cost savings with smart insulin pens compared with standard care; however, smart insulin pens remained dominant over standard care for even the shortest time horizon of 3 years (Table 3). The HbA1c improvement with smart insulin pens was a key driver of outcomes, as demonstrated through abolishing the treatment effect in HbA1c and hypoglycemic events in turn. When the HbA1c difference between arms was not applied, the clinical benefit fell from 1.15 QALYs (base-case analysis) to 0.24 QALYs, with smart insulin pens remaining dominant over standard care (Table 3). When hypoglycemic event rates were assumed equal in both arms, the clinical benefit fell from 1.15 QALYs (base-case analysis) to 0.90 QALYs (Table 3). Compared with the base-case analysis (treatments maintained for the full 60-year time horizon), switching patients in the standard care arm to smart insulin pens after 3–10 years of the simulation yielded smaller differences in costs and clinical benefits between the simulation arms, as the treatment effects in HbA1c, hypoglycemia, and treatment costs were abolished during the analysis, rather than being maintained for the entire time horizon as in the base case.

DISCUSSION

In this analysis, clinical outcomes and healthcare costs were modeled following the introduction of a smart insulin pen versus standard of care for adults in Sweden with T1D to determine cost-effectiveness. Direct cost savings with the smart insulin pen were projected to be SEK 124,270 (EUR 11,309) per patient and combined cost (direct and indirect costs) savings to be SEK 497,995 (EUR 45,318) per patient. Use of smart insulin pens was associated with increases in both mean discounted life expectancy of 0.90 years per patient and mean quality-adjusted life expectancy of 1.15 QALYs per patient, compared with standard care.

There is a growing market for digital health solutions in chronic disease management [9] and they are becoming increasingly established in the management of diabetes [14]. Smart insulin pens are one such innovation that have the ability to integrate refillable insulin cartridges, wireless communication, and insulin delivery tracking, and display information to the user [31]. Our analysis, modeled on the efficacy of a smart insulin pen in the Swedish prospective, noninterventional study [15], provides important information on long-term cost-effectiveness. Ultimately, it is the cost and payer coverage that will determine uptake of smart insulin pens, but this is likely to increase on the basis of demonstrable cost-effectiveness [31].

Improvements in life expectancy with a smart insulin pen occurred as a result of a reduced frequency and increased time to onset of almost all diabetes-related complications over the 60-year time horizon, owing to a reduction in HbA1c with smart insulin pens (converted from TIR). Cataract was the only diabetes-related complication that had a higher projected cumulative incidence rate in the smart insulin pens arm versus standard care, likely to be as a result of increased survival. As such, it is important to note that the cumulative incidence of all other diabetes-related

Table 3 Results of the sensitivity analyses

Analysis	Discounted direct costs (SEK)			Discounted combined costs (SEK)			Discounted quality-adjusted life expectancy (QALYs)			ICER (SEK per QALY)[a]
	Smart insulin pen	Standard care	Difference	Smart insulin pen	Standard care	Difference	Smart insulin pen	Standard care	Difference	
Base case	635,599	759,869	− 124,270	1,541,648	2,039,643	− 497,995	14.74	13.59	+ 1.15	Smart insulin pens dominant
3-year time horizon	39,204	42,490	− 3286	95,520	141,403	− 45,884	2.21	2.17	+ 0.04	Smart insulin pens dominant
5-year time horizon	68,034	76,006	− 7972	171,264	251,522	− 80,258	3.55	3.47	+ 0.08	Smart insulin pens dominant
10-year time horizon	147,293	172,482	− 25,190	403,989	579,865	− 175,876	6.45	6.26	+ 0.19	Smart insulin pens dominant
Baseline HbA1c of 7.96% (64 mmol/mol)	503,716	590,549	− 86,833	1,232,903	1,630,768	− 397,865	15.80	14.86	+ 0.94	Smart insulin pens dominant
Baseline HbA1c of 7.1% (54 mmol/mol)	425,384	483,414	− 58,030	1,046,641	1,383,286	− 336,645	16.52	15.74	+ 0.78	Smart insulin pens dominant
HbA1c reduction of 0.4% (4 mmol/mol)[b]	684,446	759,869	− 75,422	1,656,833	2,039,643	− 382,810	14.38	13.59	+ 0.80	Smart insulin pens dominant
HbA1c reduction of 0.8% (9 mmol/mol)[b]	615,900	759,869	− 143,969	1,489,429	2,039,643	− 550,214	14.91	13.59	+ 1.33	Smart insulin pens dominant
HbA1c treatment effect not applied	758,052	759,869	− 1817	1,840,469	2,039,643	− 199,173	13.83	13.59	+ 0.24	Smart insulin pens dominant
Hypoglycemia difference not applied	649,065	759,869	− 110,803	1,755,774	2,039,643	− 283,869	14.48	13.59	+ 0.90	Smart insulin pens dominant
Treatment switched after 3 years[c]	635,598	663,626	− 28,028	1,541,634	1,648,193	− 106,559	14.74	14.48	+ 0.25	Smart insulin pens dominant
Treatment switched after 5 years[c]	635,598	680,623	− 45,025	1,541,635	1,718,398	− 176,763	14.74	14.33	+ 0.40	Smart insulin pens dominant

Table 3 continued

Analysis	Discounted direct costs (SEK)			Discounted combined costs (SEK)			Discounted quality-adjusted life expectancy (QALYs)			ICER (SEK per QALY)[a]
	Smart insulin pen	Standard care	Difference	Smart insulin pen	Standard care	Difference	Smart insulin pen	Standard care	Difference	
Treatment switched after 10 years[c]	635,598	707,083	− 71,485	1,541,635	1,848,503	− 306,868	14.74	14.04	+ 0.70	Smart insulin pens dominant

HbA1c glycated hemoglobin, *ICER* incremental cost-effectiveness ratio, *QALY* quality-adjusted life-year, *SEK* Swedish krona

[a] ICER is reported for both direct and combined costs and, in all sensitivity analysis simulations, the outcome of dominance was the same when either direct or combined costs were considered

[b] For the smart insulin pen relative to standard care

[c] In the standard care simulation arm to smart insulin pen use, performed by removing differences in HbA1c, hypoglycemic event rates, and treatment costs from the time of switch until the end of the time horizon

complications was lower than in the standard care arm despite the longer survival. Results of the sensitivity analyses confirmed that the reduction in HbA1c, as determined by TIR in the Swedish prospective, noninterventional study [15], associated with smart insulin pen use was a key driver of improved outcomes. However, even when the HbA1c treatment effect was abolished, smart insulin pens remained dominant versus standard care.

In the Swedish one-arm, prospective, observational, proof-of-concept study, the introduction of smart insulin pens was associated with significantly fewer missed bolus insulin doses than at baseline, most likely as a result of patients evaluating their past dosing data with their healthcare team, assisting with remembering to deliver mealtime insulin, improving insulin dose timing relative to meals, and adjusting insulin appropriately [15, 16]. This improved insulin management following the introduction of the smart insulin pen is likely to have contributed to the increased TIR, through more consistent and stable glucose levels [15, 16]. Following the publication of the Swedish prospective, noninterventional study findings, healthcare payers may have had financial concerns regarding overall cost-effectiveness, due to the higher bolus insulin use with smart insulin pens over standard care. Accordingly, in the present analysis, it was projected that smart insulin pens were associated with higher treatment costs than standard care (SEK 17,586 [EUR 1600] per patient), driven by higher bolus insulin use, as well as increased patient survival and, therefore, a longer duration of treatment over patients' lifetimes. However, the cost of optimized insulin management with the smart insulin pen was offset by savings from a reduced incidence of diabetes-related complications in comparison with standard care from a lifetime perspective. Furthermore, the durability of smart insulin pens, with a life-span of up to 5 years [32], should alleviate concerns from payers regarding their upfront cost. Over patients' lifetimes, projected cost savings to the Swedish public healthcare payer with smart insulin pens (versus standard care) might free up some of the limited healthcare budget allocated to T1D (refer to

simulated cost distribution in Fig. 2a), and this could be directed towards other aspects of the care and management of people with T1D, for instance diabetes education and the prevention of complications.

Combined (direct and indirect) cost savings of almost SEK 500,000 [EUR 45,500] per patient were projected over a lifetime time horizon, with greater workplace productivity in the smart insulin pens arm than in the standard care arm. Smart insulin pens are designed to improve insulin administration and record data to facilitate discussion and action by patients and healthcare professionals [31], but from a global perspective are not yet widely funded. Smart insulin pens were dominant from both a public healthcare payer perspective (direct costs only) and a societal perspective (combined costs), with increased life expectancy and cost savings compared with standard care. While the base-case analysis was performed over a 60-year time horizon, with a 3% annual discount rate applied to projected outcomes, additional sensitivity analyses confirmed cost-effectiveness over time horizons as short as 3 years. Therefore, the findings of the present analysis add to a growing body of evidence that digital technologies can add value to the treatment of chronic diseases. To the best of the authors' knowledge, this is the first economic evaluation of a smart insulin pen.

Limitations

Some limitations of this analysis should be acknowledged. Only TIR data were available from the Swedish prospective, noninterventional study [15] and, therefore, change in TIR was converted to change in HbA1c using a published regression equation [21], as there are no published risk equations allowing TIR to be directly linked to incidence of diabetes-related complications. While there is some uncertainty when making this conversion, sensitivity analyses were performed for various HbA1c levels to check the robustness of this conversion and the cost-effectiveness result, which all demonstrated that smart insulin pens were dominant versus standard care. Also noteworthy is that

TIR has been associated with the risk of microvascular complications, and is an acceptable outcome measure for clinical trials [33]. A limitation of the Swedish prospective, noninterventional study, and therefore of the present analysis it informed, is the small study population and single-arm design [15]. Accordingly, baseline data were extrapolated for a hypothetical cohort who continued their previous regimen without a smart insulin pen, to make the comparison with the smart insulin pen simulation arm. In common with other health-economic analyses of diabetes interventions, the projections reported herein were reliant on relatively short-term clinical data. However, in the absence of long-term clinical data, modeled projections represent the best available alternative, while a long-term perspective is recommended by guidelines for cost-effectiveness analyses of diabetes interventions. Attempts were made to mitigate some of the inherent uncertainly around long-term projections through the use of a previously published and extensively validated model, as well as through conducting numerous sensitivity analyses to explore uncertainty in input parameters [34]. Our simulations were informed by clinical data from adults with T1D in Sweden and, hence, the findings may not be generalizable to wider populations. Future studies comparing smart insulin pens with standard care both in combination with CGMs are required to further validate that changes in glycemic control are a result of smart insulin pen use.

CONCLUSION

Our projections suggest that the introduction of smart insulin pens and their continued use over patients' lifetimes was likely to improve clinical outcomes at lower costs relative to standard of care without smart insulin pens in a Swedish T1D population. Use of smart insulin pens in this adult patient population is, therefore, likely to be a good use of healthcare resources in Sweden.

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