ORIGINAL ARTICLE

Cost-effectiveness analysis of sensor-augmented pump therapy with low glucose-suspend in patients with type 1 diabetes mellitus and high risk of hypoglycemia in Spain

Ignacio Conget [a,*], Pilar Martín-Vaquero [b], Stéphane Roze [c], Isabel Elías [d], Cristina Pineda [d], María Álvarez [d], Alexis Delbaere [e], Francisco Javier Ampudia-Blasco [f]

[a] *Diabetes Unit, Department of Endocrinology and Nutrition, Hospital Clínic i Universitari de Barcelona, IDIBAPS, Barcelona, Spain*
[b] *Diabetes Unit, Clínica D-médical, Spain*
[c] *Heva Heor Sarl, 186 avenue Thiers, 69006 Lyon, France*
[d] *Health Economics & Outcomes Research, Medtronic Ibérica, S.A, Madrid, Spain*
[e] *Medtronic International Trading Sarl, Route du Molliau 31, 1131 Tolochenaz, Switzerland*
[f] *Diabetes Referral Unit, Endocrinology & Nutrition Department, Hospital Clínico Universitario, Valencia, Spain*

Abstract
Objective: To compare the cost-effectiveness of sensor-augmented pump therapy (SAP) [continuous subcutaneous insulin infusion (CSII) plus real-time continuous glucose monitoring (RT-CGM)] with low glucose suspend (MiniMed™ Veo™) and CSII alone in patients with type 1 diabetes mellitus (T1DM) at high risk of hypoglycemia in Spain.
Methods: The IQVIA CORE Diabetes Model was used to estimate healthcare outcomes as life-years gained (LYGs) and quality-adjusted life years (QALYs), and to project lifetime costs. Information about efficacy, resource utilization, and unit costs (€2016) was taken from published sources and validated by an expert panel. Analyses were performed from both the Spanish National Health System (NHS) perspective and the societal perspective.
Results: From the NHS perspective, SAP with low glucose suspend was associated to a €47,665 increase in direct healthcare costs and to increases of 0.19 LYGs and 1.88 QALYs, both discounted, which resulted in an incremental cost-effectiveness ratio (ICER) of €25,394/QALY.

---

* Corresponding author.
 E-mail address: iconget@clinic.cat (I. Conget).

From the societal perspective, SAP with low glucose suspend increased total costs (including direct and indirect healthcare costs) by €41,036, with a resultant ICER of €21,862/QALY. Considering the willingness-to-pay threshold of €30,000/QALY in Spain, SAP with low glucose suspend represents a cost-effective option from both the NHS and societal perspectives. Sensitivity analyses confirmed the robustness of the model.

Conclusions: From both the Spanish NHS perspective and the societal perspective, SAP with low glucose suspend is a cost-effective option for the treatment of T1DM patients at high risk of hypoglycemia.

Análisis coste-utilidad del sistema integrado con suspensión en hipoglucemia en pacientes con diabetes tipo 1 y alto riesgo de hipoglucemias en España

Resumen

Objetivo: Evaluar la relación coste-utilidad del sistema integrado (MiniMed® Veo®) con suspensión en hipoglucemia frente a la infusión subcutánea continua de insulina (ISCI) en el tratamiento de pacientes con diabetes tipo 1 (DM1) y alto riesgo de hipoglucemias en España.

Métodos: Se utilizó el modelo de diabetes IQVIA CORE para estimar los resultados en salud expresados como años de vida ganados (AVG) y años de vida ajustados por calidad (AVAC) y los costes a lo largo de la vida de los pacientes. La información sobre la eficacia, el consumo de recursos y los costes unitarios (2016 €) fue obtenida de fuentes publicadas y validadas por un panel de expertos. En el escenario principal se consideró la perspectiva del Sistema Nacional de Salud (SNS) y, en un escenario alternativo, la de la sociedad en general.

Resultados: Bajo la perspectiva del SNS el tratamiento con el sistema integrado con suspensión en hipoglucemia se asoció con mayores costes sanitarios directos (47.665 €) y un incremento de 0,19 AVG y 1,88 AVAC, resultando en un ratio coste-utilidad incremental (RCUI) de 25.394 €/AVAC. Considerando la perspectiva de la sociedad, los costes totales (sanitarios directos e indirectos) se incrementaron en 41.036 €, siendo el RCUI resultante de 21.862 €/AVAC. Los análisis de sensibilidad confirmaron la robustez de los resultados en todos los escenarios evaluados.

Conclusión: Considerando el umbral de máxima disposición a pagar para España de 30.000 €/AVAC, el sistema integrado con suspensión en hipoglucemia representa una opción eficiente en comparación con la ISCI tanto desde la perspectiva del SNS como de la sociedad en su conjunto.

Introduction

Costs associated with the treatment of diabetes mellitus and its complications constitute a substantial proportion of total healthcare expenses in Spain. Thus, there is an urgent need for measures to achieve complete control of this disease and to prevent progression of the related complications1.[1] Optimal glycaemic control is associated with reduced chronic complications and consequently lower diabetes-related costs; however, approximately 75.8% of patients with type 1 diabetes mellitus (T1DM) are not reaching their glucose control target.[2]

Among patients with chronic poor glycaemic control and patients whose control escalation is limited by hypoglycaemia, continuous subcutaneous insulin infusion (CSII) therapy is usually more effective than multiple daily insulin injections (MDI). A Spanish study conducted over a five-year period revealed that CSII therapy can reduce hypoglycaemic events, and showed long-term maintenance of this clinical benefit without increasing glycosylated haemoglobin (HbA_{1c}) levels.[3] From an economic perspective, a budget impact analysis conducted in Spain demonstrates that the increased costs associated with CSII vs. MDI therapy in patients with T1DM and recurrent severe hypoglycaemia are completely counterbalanced by the reduction of severe hypoglycaemic events, with CSII even generating savings for the Spanish National Health System (NHS).[4]

Intensive insulin treatment needs frequent blood glucose testing to enable adequate adjustment of insulin dosing to achieve near-normoglycaemia in patients with T1DM.[5] However, intermittent blood glucose measurements do not provide information regarding the extent of fluctuations or the speed or and direction of the changes over time. Technological advances over the last 15 years have led to

Table 1 Baseline characteristics.[7]

Parameter	Value
Baseline age, mean (SD)	18.6 (11)
Female, %	50
Diabetes duration in years, mean (SD)	12 (8.9)
HbA$_{1c}$, % (SD)	7.5 (7.2–7.9)

SD, standard deviation.

the development of devices that provide continuous glucose monitoring (CGM), with information about glycaemic trends and different types of alarms (hyperglycaemia, hypoglycaemia, etc.).[6] Moreover, some of these systems can be combined with CSII therapy—enabling sensor-augmented pump therapy (SAP), in which low glucose suspend can be activated when blood glucose levels drop to a pre-set value (hypoglycaemia threshold). Overall, SAP with low glucose suspend therapy together with the treatment of diabetes-associated complications is more expensive than CSII, but is reportedly associated with reduced HbA$_{1c}$ levels and decreases in the number, duration, and severity of hypoglycaemia events compared to CSII.[7,8]

In the present study, we aimed to estimate the costs and healthcare outcomes of SAP with low glucose suspend vs. CSII alone for the treatment of T1DM patients at a high risk of hypoglycaemia in Spain.

Materials and methods

Model structure

The IQVIA CORE Diabetes Model has been validated and widely used to simulate diabetes development[9] enabling estimation of healthcare outcomes in life-years gained (LYG) and quality-adjusted life years (QALY), as well as life-long costs for T1DM patients at a high risk of severe hypoglycaemia. This model comprises 17 Markov sub-models that simulate the evolution of various diabetes-associated complications, such as angina, myocardial infarction, congestive heart failure, stroke, peripheral vascular disease, diabetic retinopathy, macular oedema, cataracts, hypoglycaemia, ketoacidosis, nephropathy, neuropathy, foot ulcers and amputation, pulmonary oedema, depression, and all-cause mortality.

Treatment options and healthcare outcomes

Baseline characteristics were based on data from a randomized clinical trial8 that included patients with T1DM at a high risk of hypoglycaemia.[10] The mean patient age was 18.6 years, and 50% were females. The mean diabetes duration was 12 years, and the mean HbA$_{1c}$ level was 7.5% (Table 1). The rates of severe hypoglycaemic events after six months of treatment were 0 events/100 patients/month with SAP with low glucose suspend vs. 2.2 events/100 patients/month with CSII alone.

Perspective, reduction rate, and time-frame

The primary analysis was conducted from the perspective of the Spanish National Healthcare System (NHS), and thus considered direct healthcare costs. In an alternative analysis, we also assessed the societal perspective by including the indirect costs associated with T1DM. We employed a lifetime horizon, and applied an annual 3% reduction rate to both costs and healthcare outcomes.[10]

Resources used and cost per unit

The data regarding the utilized resources and unitary costs were obtained from various published sources,[11–20] and validated by a panel of experts. For intervention costs only, the incremental cost of SAP with low glucose suspend therapy relative to CSII therapy was applied. Costs were updated to €2016 using the relevant variation of the consumer price index (Table 2). In our analysis, we considered 70% sensor adherence, i.e. 43 sensors per year, each worn over a 6-day period.[21] For analysis from the societal perspective, we considered the average annual salary in Spain, the average ages of integration into working life and retirement, and the days of sick leave due to diabetes-associated complications.[22]

Quality of life

Health-related quality of life is incorporated into economic evaluations via estimation of QALY, based on the correction of survival in LYG, with a utility value representing the patient's subjective preference for certain health conditions. Here we considered utility values based on the published literature,[23–25] with a lower utility value assigned when a patient simultaneously presented multiple complications. Since the studied population had a high risk of hypoglycaemic events, we also considered the potential impact on quality of life due to reduced fear of hypoglycaemia in patients treated with SAP with low glucose suspend.[24,25]

Sensitivity analysis

We performed univariate and bivariate deterministic sensitivity analyses (SAs), along with a probabilistic SA to evaluate the impacts of certain parameters on the results. Univariate deterministic SAs were conducted to evaluate the impact associated with variations in the sensor adherence rate (80% and 90%), rate of severe hypoglycaemic events (2 events/100 patients/month with CSII vs 0 events/100 patients/month with SAP with low glucose suspend; 8 episodes/100 patients/month with CSII vs 0 with SAP with low glucose suspend), reduction rate (0% and 5%), cost of complications (±20%), time-frame of the analysis (10, 20, and 30 years), number of self-monitoring blood glucose tests, and average transmitter life (2 years). Bivariate deterministic SAs were performed to account for variations in both transmitter cost (10% and 20% reduction) and transmitter life (2 years). Probabilistic SA comprised 1000 Monte Carlo simulations, each including 1000 patients, with

Table 2 Costs of the management of diabetes and associated complications.

	€2016	References
Annual cost of treatment and diagnostic tests		
Statins	436.25	11
Aspirin	28.47	11
Angiotensin-converting enzyme (ACE)	142.34	11
Screening test for microalbuminuria/proteinuria	14.17	17
Interruption of ACE treatment due to adverse events	54.40	12
Eye examination	78.93	11
Screening test for diabetic foot	14.23	11
Non-conventional ulcer treatment	274.20	12
Antidepressants	38.34	Assumption
Cost of cardiovascular complications		
Myocardial infarction, first year since event	23,536.00	11
Myocardial infarction, subsequent years	948.00	11
Angina, first year since event	2517.97	13
Angina, subsequent years	532.01	13
Heart failure, first year since event	5557.66	14
Heart failure, subsequent years	1054.42	Assumption
Stroke, first year since event	6120.32	15
Stroke, subsequent years	2485.66	15
Fatal stroke	4142.09	11
Peripheral vascular disease, per event	7020.12	1
Cost of renal complications		
Haemodialysis, first year	38,242.12	16
Haemodialysis, subsequent years	35,389.64	16
Peritoneal dialysis, first year	29,374.18	16
Peritoneal dialysis, subsequent years	27,788.78	16
Renal transplant, first year	41,224.79	16
Renal transplant, subsequent years	6760.51	16
Cost of acute events		
Severe hypoglycaemia	3628.63	1
Ketoacidosis	4060.43	17
Oedema	38.34	18
Oedema follow-up	38.34	18
Cost of eye complications		
Treatment with laser	415.54	18
Cataract surgery	1287.35	18
Annual cataract follow-up	1163.67	Assumption
Blindness, first year	2405.35	20
Blindness, subsequent years	2405.35	20
Cost of neuropathy/ulcer/amputation		
Neuropathy, first year	3275.11	11
Lower limb amputation, first year since event	11,392.39	17
Amputation/prosthesis (event)	1927.75	18
Gangrene treatment	9499.44	17
Ulcer with infection	2440.78	19
Ulcer without infection	1394.38	19

simultaneous modification of the values of the parameters according to the normal and gamma distributions.

Results

In terms of disease burden, treatment with SAP with low glucose suspend was associated with increases of 0.19 in LYG and 1.88 in QALY, both discounted, compared to CSII alone. The use of SAP with low glucose suspend was also associated with a reduced cumulative incidence and delay to onset of diabetes-related complications. The most pronounced delay was for end stage renal disease, myocardial infarction and congestive heart failure. The mean onset of all complications was delayed by 0.33 years with SAP with low glucose suspend compared with CSII alone. Table 3 presents

Table 3 Analysis results.

	SAP	CSII
Time free of complications		
Proliferative retinopathy	30.80	30.46
Microalbuminuria	15.22	15.12
Proteinuria	33.04	32.67
End-stage renal failure	36.42	35.98
First ulcer	29.43	29.11
Amputation	34.67	34.27
Neuropathy	19.87	19.70
Peripheral vascular disease	35.50	35.10
Congestive heart failure	35.55	35.13
Angina	35.22	34.83
Myocardial infarction	35.74	35.31
Stroke	34.86	34.46
Cataracts	31.55	31.18
Macular oedema	22.72	22.54
Severe vision loss	27.22	26.98
LYG		
LYG	21.00	20.81
QALY		
QALY	13.11	11.23
Total costs (€2016)		
Total costs (€2016)	112,445	64,780
ICER (€/QALY)	NHS	Society
ICER (€/QALY)	25,394	21,862

QALY, quality-adjusted life years; LYG, life-years gained; CSII, continuous subcutaneous insulin infusion; ICER, incremental cost-effectiveness ratio; NHS, National Health System; SAP, sensor augmented pump.

the time free of complications, LYG, QALY, and total costs associated with both therapies and with the management of complications.

From the Spanish NHS perspective, direct healthcare costs were €47,665 higher for treatment with SAP with low glucose suspend compared to treatment with CSII alone (€112,445 vs. €64,780). All cost items associated with both therapy and management of various complications were higher in the case of SAP with low glucose suspend, with therapy costs having the greatest impact on total cost. The costs associated with complications were higher in the case of SAP with low glucose suspend treatment due to a ''survival paradox'' in which patients accrue direct costs and experience complications over a longer period of time owing to higher life expectancy. The incremental cost-effectiveness ratio (ICER) estimated from the Spanish NHS perspective was €25,394 per QALY gained.

From the societal perspective, total costs (direct and indirect) were increased by €41,036 with SAP with low glucose suspend compared to CSII therapy (€217,272 vs. €176,236), yielding an ICER of €21,862 per QALY gained. Therefore, SAP with low glucose suspend was associated with greater clinical benefits despite the higher costs relative to therapy with CSII alone. The generally accepted willingness-to-pay threshold in Spain is €30,000 per QALY[26]. Thus, these results indicate that SAP with low glucose suspend is a cost-effective option for T1DM patients at a high risk of hypoglycaemia, from both the Spanish NHS perspective and the societal perspective.

Sensitivity analysis results

The results of the various conducted SAs confirmed the robustness of the model. The following parameters modified in the deterministic SA showed the greatest impact on the base case results: change in the number of severe hypoglycaemia events, treatment adherence, and the simul-
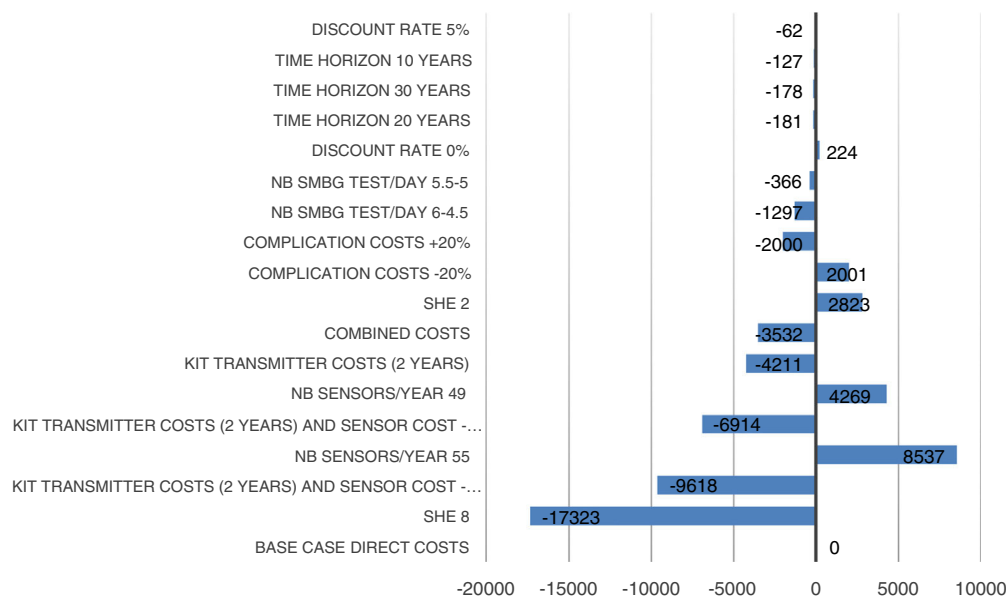
Figure 1 Deterministic sensitivity analysis results represented as a tornado diagram. NB, number; SMBG, self-monitoring blood glucose; SHE, severe hypoglycaemia event.
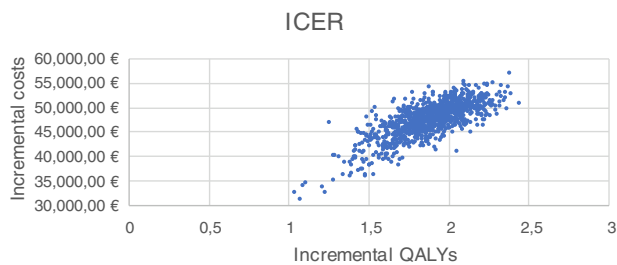
Figure 2 Cost-effectiveness plane, showing the 1000 ICER Monte Carlo simulations. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years.
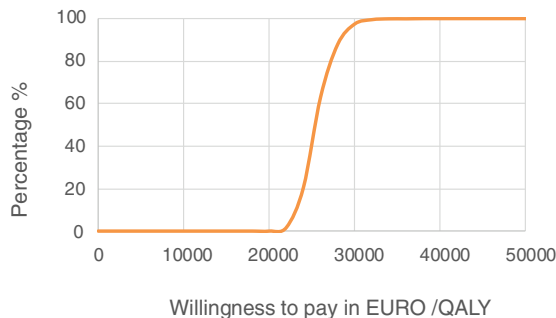
Figure 3 Cost-effectiveness acceptability curve SAP versus CSII. CSII, continuous subcutaneous insulin infusion; QALY, quality-adjusted life years; SAP, sensor-augmented pump.

taneous variation in the transmitter cost plus the transmitter lasting longer. Fig. 1 shows the results of the sensitivity analysis. The probabilistic SA was represented via the cost-effectiveness plane, with each point representing the ICER value of every 1000 Monte Carlo simulations conducted (Fig. 2). Of these 1000 simulations, 97.5% were below the €30,000 per QALY threshold[26] (Fig. 3).

Discussion

In this study, we performed analyses among adults in Spain with T1DM, who had a past history and a high risk of hypoglycaemia. This was the first study in this setting to evaluate the costs and healthcare outcomes of intensive treatment using SAP with low glucose suspend versus CSII therapy alone, which are two insulin therapies currently employed in clinical practice in Spain. Our analysis revealed that SAP with low glucose suspend was a cost-effective option for treatment of these patients relative to treatment with CSII alone, from both the NHS perspective and the societal perspective (even more cost-effective from the second one). This finding is in line with the results of previous economic evaluation studies conducted in different countries, including the United Kingdom,[27] Sweden.[28] and France,[29] which also suggest that SAP with low glucose suspend can be considered a cost-effective treatment option compared to CSII alone, from both the societal perspective and the health system perspective in each country.

Compared to other European countries, in Spain CSII therapy is less commonly used—reportedly, in less than 5% of T1DM patients.[2] This is mainly, although not exclusively, due to economic reasons based on the device purchase price. In

this setting, the use of CGM is even more restricted. The Spanish Diabetes Association Working Group on Diabetes and Technology recently published a consensus document based on scientific evidence, presenting the main indications for CGM use and analysing specific cases that warrant consideration of public funding for real-time CGM plus CSII.[6] These cases include patients with a high risk of recurrent severe, non-severe, or nocturnal hypoglycaemia, and patients with hypoglycaemia unawareness resulting in a disabling situation, since hypoglycaemia contributes to poor glycaemic control and commonly recurring hypoglycaemia may cause depression, fatigue, and anxiety, as well as fear of hypoglycaemia, which has a negative impact on the patient's quality of life. Moreover, prolonged hypoglycaemia over time can cause cognitive problems, convulsions, and even death. Additionally, hypoglycaemic events can constitute a major cost for the NHS, making prevention especially important.[30] The use of CSII and SAP with low glucose suspend both enable improved glycaemic control in patients, and reduce the number and severity of hypoglycaemic events.[3,7,8] Notably, SAP with low glucose suspend is reportedly more effective than CSII alone.[7,8] Lastly, the recent consensus document mentions numerous countries that already fund RT-CGM in specific situations and criteria relevant for each setting are consistent across Europe.[6]

This study has several limitations, starting with the theoretical nature of modelling, which is sometimes not representative of standard clinical practice. Another limitation of this study is that the patient baseline characteristics and efficacy data were obtained from a cohort of Australian patients with hypoglycaemia unawareness and HbA$_{1c}$ levels of ≤8.5%.[8] Additionally, the effectiveness data obtained from that study were collected after only 6 months of follow-up[8] and data were obtained with a mean sensor wear of 70%. A sensor use below this figure may preclude cost-effectiveness results. These limitations may reduce the generalizability of the findings. Moreover, our present analysis did not consider the extra costs required to train patients in SAP therapy vs. CSII therapy. It must also be emphasized that the efficacy data used in our analysis was for the previous pump model (MiniMed™ Veo™) rather than the model currently available on the market (MiniMed™ 640G). The prior model does not include the option of predictive low glucose suspend due to hypoglycaemia. However, based on both clinical evidence published to date and clinical experience, it can be suggested that the results would be even more favourable if the predictive low glucose suspend feature had been included.[3]

Conclusions

The outcomes of our present analysis reveal that SAP with low glucose suspend was associated with greater clinical benefits than CSII alone. Despite the greater costs of SAP, it is undoubtedly a cost-effective alternative[26] for the treatment of T1DM patients at high risk of hypoglycaemia from both the Spanish NHS perspective and the societal perspective.

Conflicts of interest

This study was funded by Medtronic. I Conget, FJ Ampudia-Blasco, and P Martín-Vaquero disclose receipt of financial

References

1. Crespo C, Brosa M, Soria-Juanc A, Lopez-Alba A, López-Martínez N, Soria B. Direct cost of diabetes mellitus and its complications in Spain (SECCAID Study: Spain estimated cost Ciberdem-Cabimer in Diabetes). Av Diabetol. 2013;29:182–9.

2. Martín-Vaquero P, Martínez-Brocca MA, García-López JM. Grupo de Trabajo de Nuevas Tecnologías de la Sociedad Española; Grupo de Diabetes de la Sociedad Española de Endocrinología y Nutrición; Sociedad Española de Endocrinología Pediátrica Position statement on efficiency of technologies for diabetes management. Endocrinol Nutr. 2014;61:e45–63.

3. Pickup JC. Insulin pumps. Diabetes Technol Ther. 2017;19:S19–26.

4. Giménez M, Elías I, Álvarez M, Quirós C, Conget I. Budget impact of continuous subcutaneous insulin infusion therapy in patients with type 1 diabetes who experience severe recurrent hypoglycemic episodes in Spain. Endocrinol Diabetes Nutr. 2017;64:377–83.

5. The Diabetes Control, Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329:977–86.

6. Giménez M, Díaz-Soto G, Andía V, Ruíz de Adana MS, García-Cuartero B, Rigla M, et al. en nombre del Grupo de Tecnologías Aplicadas a la Diabetes de la SED y de la SEEP SED-SEEP Consensus document on the use of continuous glucose monitoring in Spain. Endocrinol Diabetes Nutr. 2017, pii:S2530-0164(17)30122-2.

7. Battelino T, Conget I, Olsen B, Schütz-Fuhrmann I, Hommel E, Hoogma R, et al. The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. Diabetologia. 2012;55:3155–62.

8. Ly TT, Nicholas JA, Retterath A, Lim EM, Davis EA, Jones TW. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. JAMA. 2013;310:1240–7.

9. McEwan P, Foos V, Palmer JL, Lamotte M, Lloyd A, Grant D. Validation of the IMS CORE Diabetes Model. Value Health. 2014;17:714–24.

10. López Bastida J, Oliva J, Antoñanzas F, García-AltésA, Gisbert R, Mar J, et al. Propuesta de guía para la evaluación económica aplicada a las tecnologías sanitarias. Gac Sanit. 2010;24, 154-70.13.

11. Ray JA, Valentine WJ, Secnik K, Oglesby AK, Cordony A, Gordois A, et al. Review of the cost of diabetes complications in Australia, Canada, France, Germany Italy and Spain. Curr Med Res Opin. 2005;21:1617–29.

12. Fonseca T, Clegg J, Caputo G, Norrbacka K, Dilla T, Alvarez M. The cost-effectiveness of exenatide once weekly compared with exenatide twice daily and insulin glargine for the treatment of patients with type two diabetes and body mass index ≥30 kg/m(2) in Spain. J Med Econ. 2013;16:926–38.

13. Schwander B, Gradl B, Zöllner Y, Lindgren P, Diener HC, Lüders S, et al. Cost-utility analysis of eprosartan compared to enalapril in primary prevention and nitrendipine in secondary prevention in Europe—the HEALTH model. Value Health. 2009;12:857–71.

14. Delgado JF, Oliva J, Llano M, Pascual-Figal D, Grillo JJ, Comín-Colet J, et al. Health care and multiple care costs in the treatment of patients with symptomatic chronic heart failure in Spain. Rev Esp Cardiol (Engl Ed). 2014;67:643–50.

15. Lopez-Bastida J, Oliva Moreno J, WorbesCerezo M, Perestelo Perez L, Serrano-Aguilar P, Montón-Álvarez F. Social and economic costs and health-related quality of life in stroke survivors in the Canary Islands Spain. BMC Health Serv Res. 2012;12:315.

16. Villa G, Rodríguez-Carmona A, Fernández-Ortiz L, Cuervo J, Rebollo P, Otero A, et al. Cost analysis of the Spanish renal replacement therapy programme. Nephrol Dial Transplant. 2011;26:3709–14.

17. CongetDonlo I, Serrano Contreras D, Rodríguez Barrios JM, Levy Mizrahil, CastellAbat C, Roze S. Análisis coste-utilidad de las bombas de ultipl frente a múltiples dosis diarias en pacientes con diabetes mellitus tipo 1 en España. Rev Esp Salud Publica. 2006;80:679–95.

18. Portal estadístico. Ministerio de Sanidad, Servicio Sociales e Igualdad. Available at: http://pestadistico.inteligenciadegestion.msssi.es/publicoSNS/comun/Default Publico.aspx [accessed September 2016].

19. eSalud. Información económica del sector sanitario. Available at: http://www.oblikue.com/bddcostes/ [accessed September 2016].

20. Informe sobre la ceguera en España. Available at: http://www.fundacionretinaplus.es/images/documentos/Informe_Ceguera.pdf.

21. Hommel E, Olsen B, Battelino T, Conget I, Schütz-Fuhrmann I, Hoogma R, et al. Impact of continuous glucose monitoring on quality of life, treatment satisfaction, and use of medical care resources: analyses from the SWITCH study. Acta Diabetol. 2014;51:845–51.

22. Sørensen J, PlougUffe Jon. The cost of diabetes-related complications: registry-based analysis of days absent from work. Econ Res Int. 2013;2013:e618039.

23. Beaudet A, Clegg J, Thuresson P-O, Lloyd A, McEwan P. Review of utility values for economic modeling in type 2 diabetes. Value Health J Int Soc Pharmacoeconomics Outcomes Res. 2014;17:462–70.

24. Nørgaard K, Scaramuzza A, Bratina N, LalićNM, Jarosz-Chobot P, Kocsis G, et al. Routine sensor-augmented pump therapy in type 1 diabetes: the INTERPRET study. Diabetes Technol Ther. 2013;15:273–80.

25. Currie CJ, Morgan CL, Poole CD, Sharplin P, Lammert M, McEwan P. Multivariate models of health-related utility and the fear of hypoglycaemia in people with diabetes. Curr Med Res Opin. 2006;22:1523–34.

26. Sacristán JA, Oliva J, Del Llano J, Prieto L, Pinto JL. ¿Qué es una tecnología eficiente en España? Gac Sanit. 2002;16:334–43.

27. Roze S, Smith-Palmer J, Valentine WJ, Cook M, Jethwa M, de Portu S, et al. Long-term health economic benefits of sensor-augmented pump therapy vs continuous subcutaneous insulin infusion alone in type 1 diabetes: a U.K. perspective. J Med Econ. 2016;19:236–42.

28. Jendle J, Smith-Palmer J, Delbaere A, de Portu S, Papo N, Valentine W, et al. Cost-effectiveness analysis of sensor-augmented insulin pump therapy with automated insulin suspension versus standard insulin pump therapy in patients with type 1 diabetes in Sweden. Diabetes Ther. 2017;8:1015–30.

29. Roze S, Smith-Palmer J, Valentine W, Payet V, de Portu S, Papo N, et al. Cost-effectiveness of sensor-augmented pump therapy with low glucose suspend versus standard insulin pump therapy in two different patient populations with type 1 diabetes in France. Diabetes Technol Ther. 2016;18:75–84.

30. Brito-Sanfiel M, Diago-Cabezudo J, Calderon A. Economic impact of hypoglycemia on healthcare in Spain. Expert Rev Pharmacoecon Outcomes Res. 2010;10:649–60.