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Cost-effectiveness of a self-management and comprehensive training intervention in patients with type 2 diabetes up to 5 years of diagnosis in a specialized hospital in Mexico City

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ABSTRACT

Introduction To assess the cost-effectiveness of a multidisciplinary and comprehensive innovative diabetes care program (CAIPaDi) versus usual treatment in public health institutions.

Research design and methods Using a cost-effectiveness analysis, we compared the CAIPaDi program versus usual treatment given in Mexican public health institutions. The analysis was based on the IQVIA Core Diabetes Model, a validated simulation model used to estimate long-term clinical outcomes. Data were prospectively obtained from the CAIPaDi program and from public databases and published papers. Health outcomes were expressed in terms of life-years gained and quality-adjusted life years (QALYs). Health and economic outcomes were estimated from a public perspective and discounted at 5% per year over a 20-year horizon. Costs are reported in US dollars (US$) of 2019. A probabilistic sensitivity analysis was performed using life-years gained and QALYs.

Results The CAIPaDi costs on average US$559 (95% CI: −$879 to −$239) less than the usual treatment (95% CI: −$879 to −$239) and produced a difference in mean life-years gained (0.48, 95% CI: 0.45 to 0.52) and mean QALYs (1.43, 95% CI: 1.40 to 1.46). The cost-effectiveness ratio resulted in a saving per life-year gained of −US$1155 (95% CI: −$1962 to −$460). Mean differences in QALYs resulted in a saving per QALY of −US$735 (95% CI: −$1193 to −$305). Probabilistic sensitivity analysis proved the results are robust on both life-years gained and QALYs.

Conclusions CAIPaDi has a better cost-effectiveness ratio than the usual therapy in Mexican public health institutions.

Significance of this study

What is already known about this subject?

► Diabetes requires high costs of care, which are greatly increased by disabling complications.

What are the new findings?

► The CAIPaDi program is a comprehensive and multidisciplinary care model focused on the early stages of type 2 diabetes mellitus (T2DM) and based on patient training for the prevention of complications. This analysis proves that the model is cost-effective, in life-years gained and quality-adjusted life years (QALYs), compared with the usual therapy.

How might these results change the focus of research or clinical practice?

► The implementation of a comprehensive, multidisciplinary and preventive model can mitigate the economic impact of diabetes, prolong lifespan and improve quality of life.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a leading cause of disability and death in Mexico.[1] Among people living with T2DM in Mexico, nearly 20 000 amputations occur every year.[1] Additionally, more than 80 000 persons with T2DM progressed to renal failure and depend on replacement therapies to stay alive.[2] Mortality is high in patients between 35 and 74 years with diabetes, with risk ratios of 2.1 (95% CI 1.9 to 2.2) in patients undiagnosed and 3.0 (2.8 to 3.3) for patients with a previous diagnosis and HbA1c <9% and 5.2 (4.9 to 5.5) in those with HbA1c ≥9%.[3] In 2016, 105 574 persons died prematurely due to all types of diabetes, with an average age of 66.7 years old.[4] The impact of the T2DM is reflected not only in the high demand for healthcare services and medicines, but also in the patients' productivity level, which directly affects the family income. In a comprehensive

research exercise, the direct costs related to the healthcare resources utilization of T2DM in Mexico were estimated in 2013 as 1.1% of the gross domestic product (GDP) (about US$14 056 billion). Additionally, the indirect costs, those related to premature mortality and disability or handicap to contribute to the labor market, were estimated in 1.1% extra of the GDP (about US$14 359 billion).[5 6] (Exchange rate: average daily reported by Bank of Mexico for 2013 https://www.banxico.org.mx/tipcamb/main.do?page=tip&idioma=sp

It has been shown that, in all chronic diseases with multifactorial etiology, with various therapeutic alternatives and with great heterogeneity of complications, better results can be obtained in the patient when a multidisciplinary care team is formed.[7–9] For such teams to be effective, it is recommended to follow certain principles. Among them is the transmission of knowledge to the patient and developing skills for self-care. The team must include actions of education, cooperative and coordinated assistance based on guidelines or standardized procedures, with operational definitions and detailed descriptions of the interventions to be followed. All interventions used by the multidisciplinary team should seek to be simple, practical and easy to apply. The team members must be clear about their specific functions, which will be complementary. Tools should be implemented for auditing the actions that are carried out in order to reinforce those that give good results and correct areas of opportunity. A multidisciplinary diabetes team should include health professionals who are dedicated to the approach and resolution of medical or physical aspects, those dedicated to the emotional state, who promote favorable changes in lifestyle (diet and physical activity/exercise) and those dedicated to education about the disease. This approach to treating diabetes has been shown to increase the proportion of people who are better educated regarding their disease, achieving and maintaining goals for metabolic and blood pressure control, greater changes in their lifestyles, and improved well-being, mental health and quality of life in general. This produces a significant reduction in the personal and economic burden of the patient, his family and society in general.[10 11]

According to the National Survey on Nutrition and Health 2018, 10.3% of adults older than age 20 years had a medical diagnosis of T2DM. Although 87.7% reported to receive at least one glucose-lowering agent, only 15.6% had at least one glycated hemoglobin (HbA1c) measurement, 20.9% had a foot examination and 4.7% had a microalbuminuria test during the year before.[12] However, quality of care is highly heterogeneous nationwide. This serious public health problem in general has been attended for years through a classic medical model in which fundamentally patients attend medical visits to receive drug prescriptions, with little information about their disease and with low commitment to self-care behaviors. There have been some efforts from different Mexican institutions to improve and innovate the healthcare model for diabetes, but until recently, they have published only one cost-effectiveness evaluation which found that a multidisciplinary healthcare model for patients with T2DM is cost-effective versus a 'conventional healthcare model'.[13] Also, there is similar experience in Argentina. Here, González *et al*[14] assessed the cost-effectiveness of education of people with T2DM over a year versus education and support delivered by trained peers with T2DM. They found that education through peers as a complement to control and provide treatment for the disease is cost-effective compared with traditional education. However, evidence is still scarce about the long-term outcomes in economic evaluations of public health interventions targeted to patients with T2DM relative to usual treatments in Mexico or in Latin American countries.

The Center of Comprehensive Care for the Patient with Diabetes (CAIPaDi—an acronym for its name in Spanish) is an innovative intervention designed to provide education to patients implemented by the National Institute of Medical Science and Nutrition Salvador Zubirán in Mexico City.[11 15] This report describes a cost-effectiveness analysis of the CAIPaDi program versus usual treatment in public health institutions. These results constitute a robust evaluation of a healthcare intervention tackling a complex disease, and shed some light on how cost-effectiveness evaluation of innovative interventions may improve the decision-making process in Mexico.

RESEARCH DESIGN AND METHODS

This study was an economic evaluation (cost-effectiveness analysis), comparing the long-term (20 years) health outcomes: life years (LYs) and quality-adjusted life years (QALYs) and the direct medical costs associated with the CAIPaDi program versus the conventional model of healthcare in Mexican public institutions for patients with T2DM using the robust, previously validated 'IQVIA Core Diabetes Model (IQVIA CDM)'. The structure, data inputs and validation of the IQVIA CDM have been published elsewhere.[16 17] Additionally, online supplemental appendix 1 includes information regarding the IQVIA CDM.

The CAIPaDi program

The study design for the CAIPaDi program has been described in detail elsewhere.[11] In summary, the CAIPaDi program is an intervention designed to provide education and empowerment techniques using simple low-cost interactive tools over a short period of time followed by at-distance support using internet or cell phone technology. The target population consists of patients with T2DM, aged 18–70 years, non-smokers, less than 5 years of diagnosis, and without disabling complications.

The intervention consists of a training of four initial 6-hour monthly visits followed by annual evaluations in the center with a continuous at-distance support system. The interventions are delivered in individualized or

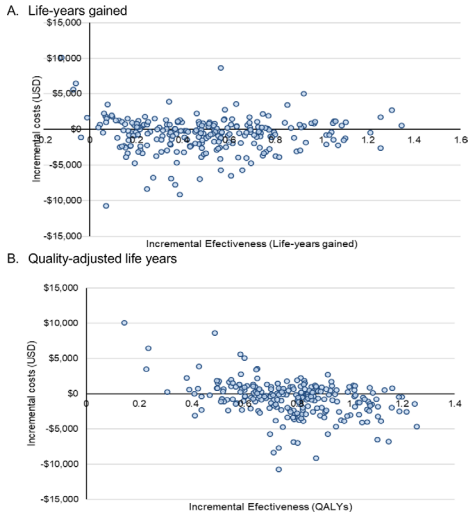

Figure 1 Scatter plot of incremental cost against incremental life-years and quality-adjusted life years (QALYs) for CAIPaDi versus usual treatment years. (A) Cost-effectiveness scatter plot of the life-years gained versus the incremental costs. (B) Cost-effectiveness scatter plot of the QALYs gained versus the incremental costs. Each point represents a sensitivity analysis run.

group sessions provided by nine specialized health professionals: endocrinology, ophthalmology/optometry, physical activity, nutrition, dentist, diabetes education, psychology, psychiatry and foot care.[11 15] Each session is 30 min long with the healthcare professionals. Group sessions are 45 min long. Every visit included the nine healthcare professional interventions in a face-to-face session held at the CAIPaDi center. Patients participated in individual or group sessions. Each intervention followed a procedure manual to standardize the sessions with all the patients. In the first visit, a complete assessment of the patient provides information required to adapt the treatment in an individualized form. The second visit, a problem-oriented evaluation, is performed so the changes in treatment and recommendations were done based on patient's characteristics. Visit 3 is oriented to identify barriers that impede the achievement of metabolic goals. The fourth visit reinforced the knowledge acquired in previous visits and established a program to follow for the next year. In annual evaluations (visits 5, 6 and 7), the barriers and their proposed solutions were reviewed. Every visit evaluates the abilities acquired previously and a structured examination was applied asking every patient to undertake activities related to self-care (daily foot check, glucose monitoring, toothbrushing, etc). In each visit and intervention, the strategies applied were directed to empower patients focusing on their needs, beliefs and resources. Blood samples are taken to evaluate HbA1c, lipid profile, and creatinine (Bio-Rad Variant II Turbo HbA1c Kit 2, with high-performance liquid chromatography method). Albumin/creatinine ratio (SYNCHRON CX system with colorimetric method) was used for screening diabetic nephropathy at baseline and annual visits. An ECG is also done in the first and annual evaluations. Body composition was assessed by bioimpedance (JAWON medical ioi353). Between annual visits, the patients were regularly checked by their personal physician. For this analysis, the diagnosis of anxiety and depression was established according to the validated questionnaire for anxiety and depression symptoms (Hospital Anxiety and Depression Scale).[18 19] Online supplemental appendix 2 and figure 1 shows a flow diagram of the structure of the program and sessions. In the CAIPaDi, a total of 2741 patients have been evaluated in the first visit. So far 2275 patients have reached the second visit, 1989 in the third visit, 1787 are in the fourth visit, 914 have reached visit 5 (first annual evaluation), 503 in visit 6 (second annual evaluation), and 238 patients have reached visit 7 (3 years of follow-up).

IQVIA CDM input parameters

Anonymized clinical records of the CAIPaDi patients were provided by the hospital. A detailed summary of the variables is shown in the online supplemental appendix 3. To avoid any overestimation of effectiveness from the intervention, we only considered data from the cohort of patients with the latest follow-up available (3 years, n=238).

The baseline characteristics of the patients for both arms in the analysis were assumed to be the same and were obtained from the CAIPaDi baseline patient characteristics (table 1).

For the effectiveness of the intervention arm (the CAIPaDi program), the model was populated using the anonymized patient record dataset; whereas for the reference group (standard model of healthcare), we selected a set of public reports that show the current landscape of the clinical condition of the patients with T2DM covered by the Mexican public healthcare institutions: the Mexican National Nutrition Survey 2018,[12] the demographic indicators from the National Institute of Statistics and Geography (INEGI)[4] and the pharmacological treatment effectiveness reported[20 21] (more information regarding the effectiveness of the treatments is presented in online supplemental appendix 4).

As the analysis was developed from a payer's perspective, only direct costs were taken into account: direct medical costs associated with the programs (CAIPaDi and standard healthcare model), diagnostics and imaging, and costs of complications (cardiovascular disease, kidney disease, ulcer, amputation, neuropathy and eye disease).

The cost of the CAIPaDi program in the first year was estimated at $2706, and for second and subsequent years at $582, and included the healthcare resources per visit. Whereas for the usual treatment, the cost per year was estimated in $210, and included only, in a conservative scenario, the pharmacological treatment recommended by the Mexican guidelines: metformin 1700 mg daily, glybenclamide 10 mg daily and Neutral Protamine Hagedorn insulin 0.4 UI/kg. Cost composition is detailed in the online supplemental appendix 5.

Table 1 Summary of clinical and demographic baseline characteristics

	Mean	SD
Patient demographics		
Age (years)	57.61	8.89
Duration of T2DM (years)	1.32	1.57
Percentage male	45	–
Baseline risk factors		
HbA1c (%)	7.65	2.18
Systolic blood pressure (mm Hg)	128.72	16.36
Total cholesterol (mg/dL)	194.73	44.55
HDL-c (mg/dL)	42.88	10.61
LDL-c (mg/dL)	114.06	42.64
Triglyceride (mg/dL)	206.05	144.99
Body mass index (kg/m^2)	29.17	4.40

N=238 patients who completed the 3-year evaluation.
HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus.

To present the most representative and updated costs of healthcare in Mexican institutions, only official sources were considered. The predominant sources of costs were: the Mexican Institute for Social Security (IMSS) diagnosis-related group data which include information about service costs and clinical pathways[22]; IMSS inpatient and outpatient unit costs[23]; direct costs due to acute adverse events estimated from a study of economic burden of T2DM in Mexico in 2013[5]; and finally, the unit cost of medications taken from the consolidated medicine purchasing data collected and published by IMSS in 2019.[24] All costs were updated to present value (2019) using the inflation rate calculator provided by the INEGI, if needed.[25]

Health outcomes were estimated as: LYs gained and QALYs using the IQVIA CDM to perform the cost-effectiveness analysis over a 20-year horizon. According to the Mexican institutional normative, a discounted rate of 5% was applied in this study.[26]

RESULTS

The CAIPaDi intervention was associated with an improvement of most of the key clinical outcomes from basal visit (visit 1) to a 3-year follow-up evaluation (visit 7) (table 2). Based on the clinical outcomes, the IQVIA CDM estimates a reduction in the incidence of eye, renal and cardiovascular diseases (including all the specific categories for each one of these), as well as the incidence of diabetic foot and depression. Moreover, a longer time alive and free of complications was estimated for the CAIPaDi participants (online supplemental appendices 6 and 7).

Costs

Table 3 provides a summary of the estimated differences between CAIPaDi and usual treatment in terms of use of resources. All costs are reported in US$, using the average

Table 2 Effect of CAIPaDi from visit 1 to visit 7 in diabetes control variables, October 2013 – August 2018

Variable	Parameter	Goal (%)	Basal (visit 1) Patients n=238 (%)	3-year follow-up (visit 7) Patients n=238 (%)	Change in percentage points
Glycated hemoglobin (%)	>9.0	≤15	50 (21)	21 (9)	−12
	7.0%–9.0	>60	62 (26)	62 (26)	0
	<7.0	>40	126 (53)	155 (65)	12
Blood pressure (mm Hg)	≥140/90	≤35	12 (4)	6 (3)	−2
	<130/80	>25	102 (43)	179 (7)	32
LDL-c (mg/dL)	≥130	≤37	76 (34)	40 (17)	−15
HDL-c (mg/dL)	<100		238 (100)	238 (100)	0
Triglyceride (mg/dL)	≤150	–	97 (41)	138 (58)	17
Albumin/creatinine ratio (mg/g)	<30	–	204 (86)	195 (82)	−4
BMI (kg/m^2)—normal	<25	–	38 (16)	47 (20)	4
Overweight	(25–29.9)	–	112 (47)	103 (43)	−4
Obesity level I	(30–34.9)	–	68 (29)	70 (29)	1
Obesity level II	(35–39.9)	–	14 (6)	18 (8)	2
Obesity level III	≥40	–	6 (3)	0 (0)	−3

Percentages may not add up to 100% due to rounding. The goal refers to the expected percentage of patients in the value defined in the parameter column.
All the clinical outcomes are not reported but they are available from the authors on request. There were no hospitalizations for severe hypoglycemia.
BMI, body mass index; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

Table 3 Comparison of direct medical costs between CAIPaDi and usual treatment over 20 years (2019 US$ prices)

Variable	Usual treatment (US$)	CAIPaDi (US$)
Treatment	38*	4734†
Diagnostics and imaging	87	1975
Complications		
Cardiovascular disease	5498	3832
Kidney disease	3701	1917
Ulcer/amputation/neuropathy	8154	4656
Eye disease	1341	1024
Total costs	18 819	18 138
Differential mean cost over 20 years, US$ (95% CI)	−681 (−995 to −366)	

Access to the estimation technical documentation is available from the authors on request.
US$–Mexican peso exchange rate=19.25739. Average of exchange rate from December 2018 to December 2019.
Source: Central Bank of Mexico.[6] Consulted: March 9, 2020.
*Includes only pharmacological treatment.
†Includes specialist visits, GP visits, facilitated meetings and use of at-distance support equipment.
GP, general practitioner.

exchange rate from December 2018 to December 2019 reported by the Central Bank of Mexico.[6] Overall, the discounted cost of the usual treatment of T2DM per patient in the public sector is approximately US$18 818 and US$18 138 in CAIPaDi. However, the saving of complication-related treatments and management ($7264) offset that additional cost. Moreover, the results show that the CAIPaDi saves an average of −US$681 (95% CI: −$995 to −$366) more than usual treatment, due to the decrease in diabetes complications.

Health and economic outcomes

Improvements in mean LYs gained and QALYs were projected over a 20-year time horizon (table 4). CAIPaDi patients were projected to gain on average 10.96 years (95% CI: 10.84 to 11.1) compared with 10.46 years (95% CI: 10.30 to 10.62) for patients receiving usual treatment. The mean QALYs were 6.84 (95% CI: 6.71 to 6.96) vs 6.06 (95% CI: 5.92 to 6.19) for usual treatment. This means that the CAIPaDi intervention produced a gain in mean LYs of 0.50 (95% CI 0.46 to 0.54) and QALYs of 0.78 (95% CI 0.75 to 0.80).

CAIPaDi has a higher efficacy and lower associated costs. The benefit of the program is assessed in terms of the generated incremental cost-effectiveness ratio (ICER). Mean differences in cost and LYs gained as well as QALYs showed a dominance of CAIPaDi versus usual treatment.

Sensitivity analyses

We conducted a probabilistic sensitivity analysis that allowed us to quantify the level of confidence in the output of the model in relation to the uncertainty in the inputs required by the IQVIA CDM. The model was estimated 1000 times to generate outputs of both discounted costs and health outcomes. Figure 1 shows the scatter plot of the incremental cost against both LYs gained and QALYs for the intervention and for the usual treatment. In both scatter plots, around 60% are located exclusively within the lower-right quadrant of the cost-effectiveness plane, indicating that CAIPaDi is projected to be a dominant intervention, associated with an increased efficacy and savings in costs.

In order to evaluate the specific contribution of each CAIPaDi component in the glycemic control, a scenario sensitivity analysis was performed. The scenario without nutrition intervention resulted in a total of 10.9 LYs and 6.75 QALYs, representing a decrease of −0.06 LYs and −0.08 QALYs from the base case, while the scenario

Table 4 Summary of health and economic outcomes over 20 years

Variable	Usual treatment (95% CI)	CAIPaDi (95% CI)
Health outcomes		
Life expectancy (life-years gained)	10.47 (10.30 to 10.62)	10.96 (10.84 to 11.1)
Differential life-years gained	0.50 (0.46 to 0.54)	
QALYs	6.06 (5.92 to 6.19)	6.84 (6.71 to 6.96)
Differential QALYs	0.78 (0.75 to 0.80)	
Cost		
20-year direct medical cost	$18 819 ($16 731 to $19 545)	$18 138 ($17 349 to $20 045)
Differential direct medical cost	−$681 (−$995 to −$366)	
Cost-effectiveness		
ICER based on life expectancy (95% CI)	−$13 565 per life year gained (−$1843 to −$789)	
ICER based on QALYs (95% CI)	−$874 per QALY gained (−$1238 to −$486)	

ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years.

without psychiatric intervention resulted in a total of 10.88 LYs gained and 6.72 QALYs for the CAIPaDi; this represents a decrease of −0.088 LYs and −0.12 QALYs, which lead to an increase of the ICER of the CAIPaDi without psychiatric intervention versus the usual treatment to US$3250 per LY gained and US$2009 per QALY. Even with this increase in the ICER, the CAIPaDi is still a cost-effective alternative. These results set a guideline for future analysis within the CAIPaDi program.

DISCUSSION

Patient training for self-management and the multidisciplinary healthcare attention are acknowledged as two significant complements to diabetes medical treatment. Nevertheless, to implement an attention model that includes these two components may be difficult due to budget limitations. The CAIPaDi program was designed to offer, at the same place, in the same visit and in a coordinated way, a comprehensive attention provided by specialists. It avoids multiple visits and assures the implementation of preventive and therapeutic actions. As a result, it reduces cost and increases the effectiveness of the management protocol, resulting in a dominant alternative compared with the usual treatment.

This report shows that a comprehensive program like CAIPaDi is an efficient investment in health. The results of the analysis, using the CDM, demonstrate that CAIPaDi provides better clinical results in all measured variables. The HbA1c, blood pressure, low-density lipoprotein cholesterol, triglycerides, and weight reductions contribute to improve the patients' conditions in the middle term. In a cascade effect, the risks of cardiovascular, renal, and ophthalmologic diseases and diabetic foot, as well as depression, will be reduced; and this reduction in the risk of complications reduces the costs associated with them as well, resulting in lower total costs than the usual treatment. In the long term, the health consequences are not only a longer life expectancy than the usual treatment for T2DM, but a higher quality life expectancy, free of diabetes complications for the patient and savings due to avoiding complication events for the healthcare system, even if the costs associated with the intervention are higher than the usual treatment.

The model's base case results were confirmed by the probabilistic sensitivity analysis. This analysis was consistent with both health results, LYs gained and QALYs, and also with the associated costs. Thus, more than half of the potential results were placed as better health results and with lower costs. That is, the model estimates that CAIPaDi is a dominant alternative. In consequence, a health intervention like this seems to be an efficient investment for public healthcare institutions, and particularly it seems to be recommendable to expand the nutrition and psychiatric professionals' participation. The difference in treatment and management costs reflects the need for more healthcare professionals, facilitator's interventions and use of at-distance support equipment included in the CAIPaDi.

Evidence suggests that programs run by peers are efficient assisting in managing metabolic parameters of patients with diabetes. A meta-analysis developed by Teljeur *et al*[27] suggests that self-management support education programs may be cost-effective. Moreover, Gilmer *et al*[28] recently found that two technology-enhanced diabetes programs were cost-effective under a time horizon of 15–20 years in Mexico. Comparison of our results against other international programs is limited by the differential effect of local costs and access to care.

It is important to point out the model applied here has some limitations that need to be considered when assessing its relative generalizability. First, as all long-term models, it relies on projected clinical outcomes, in this case after a 3-year follow-up. The IQVIA CDM comprises simulations using predictive equations, and for the long-term follow-up this may have underestimated or overestimated some of the health gains associated with patients' self-management skills acquired from the CAIPaDi program. Differences in utility over 20 years would influence life expectancy and QALYs that we are not able to predict. However, the IQVIA CDM is a widely published and validated model that has been used to estimate long-term clinical outcomes in T2DM within many contexts and comparing different healthcare technologies.[29]

On the other hand, it is important to consider that the perspective of this analysis was from a public health service and only considers direct medical costs for both interventions. Hence, this analysis does not include discounted indirect costs or additional benefits, and this may have had an effect of subestimation of the total costs and, therefore, a bias on the estimated ICER, which could be even better.

Given the beneficial results in the indicators of metabolic control, quality of care, in cost–benefit, and years of quality of life gained, it will be presented to stakeholders and policymakers in health to evaluate the extrapolation and implementation in a greater number of centers. It is also important to show this evidence so that the model can be applied in other chronic diseases.

In summary, the CAIPaDi program is a cost-effective intervention that provides additional benefits and long-term saving over the usual care provided in the Mexican public health institutions.

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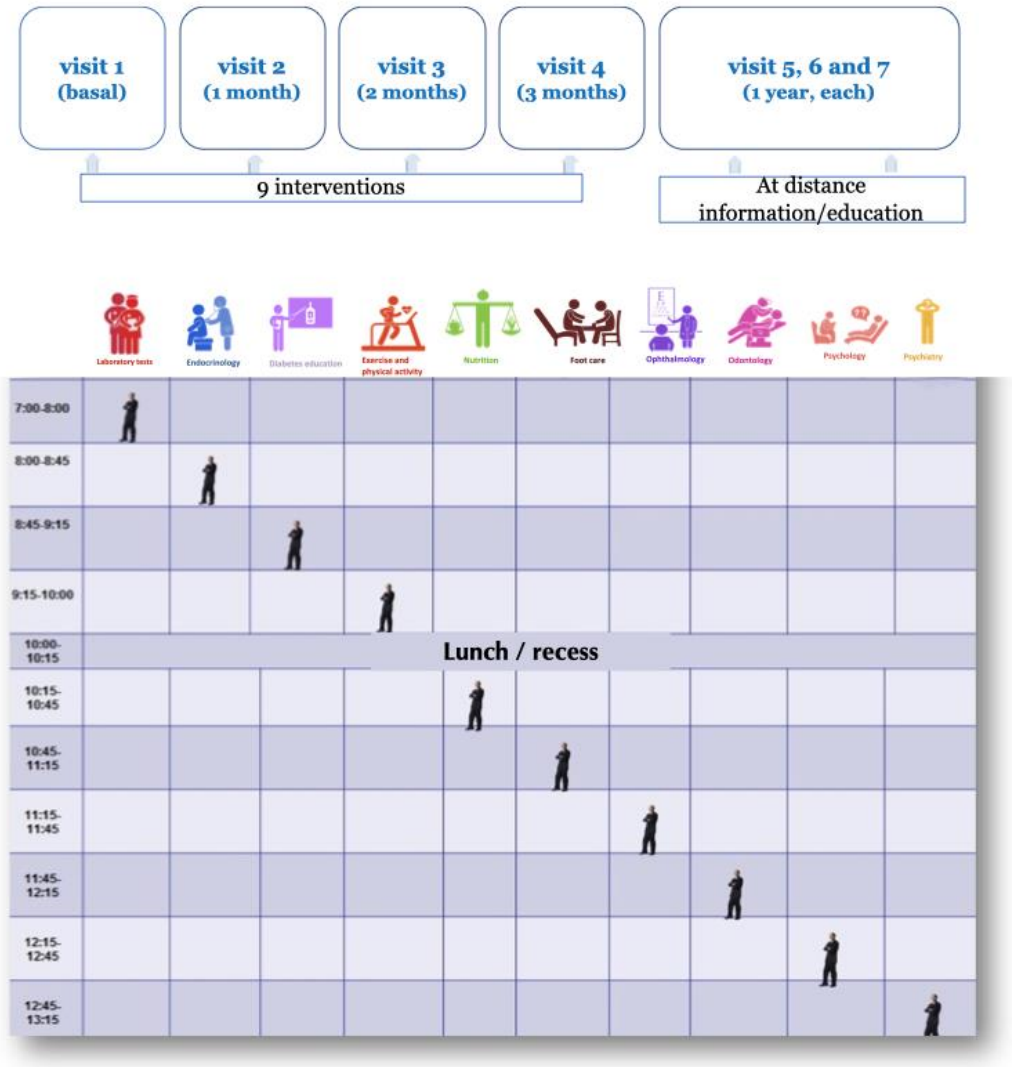
Appendix 1.

The IQVIA Core Diabetes Model (IQVIA CDM) is a computer simulation model designed to assess the lifetime health outcomes and economic consequences of interventions in T1DM or T2DM. It projects outcomes for populations making HbA1c-dependent adjustments for the risks of diabetes complications, taking into account baseline cohort characteristics and past history of complications, current and future diabetes management and concomitant medications, screening strategies, and changes in physiological parameters over time. It is structured by 17 interdependent Markov sub-models that simulate a wide group of acute, chronic, micro and macrovascular diabetes complications, in addition to non-specific mortality. The model is a fixed-time increment (annual) stochastic simulations with each sub-model using time, state, and diabetes type dependent probabilities. Monte-Carlo simulations, of both the 1st and 2nd order, are performed at the individual patient level using tracker variables to accommodate complex interactions between individual complications sub-models. The IQVIA CDM uses separate transition probabilities and management strategies for T1DM and T2DM, and source data for model parameters are obtained from a broad range of published clinical and epidemiological studies. The predominant sources of data are the Diabetes Control and Complications Trial (DCCT) and Framingham studies for T1DM and UKPDS studies for T2DM. The results provided are therefore a de facto Probabilistic Sensitivity Analysis (PSA). The IQVIA CDM allows the estimation of direct and indirect costs; adjust for quality of life and allows users to

Hernández-Jiménez S, *et al. BMJ Open Diab Res Care* 2021; 9:e002097. doi: 10.1136/bmjdrc-2020-002097

perform cost-effectiveness and cost-utility analysis. The IQVIA CDM has been validated against 66 published studies.

Appendix 2.



Appendix 3.

Input variables to measure clinical efficacy of CAIPaDi, baseline characteristics and complications, ***October 2013 – August 2018***

	Mean	**Standard Deviation**
Patient demographics		
Age (years)	57.61	8.89
Duration of T2DMType 2 Diabetes Mellitus (years)	1.32	1.57
Percentage male	45%	
Baseline risk factors		
HbA1c (%)	7.65	2.18
Systolic blood pressure (mmHg)	128.72	16.36
Total cholesterol (mg/dl)	194.73	44.55
c-HDL (mg/dl)	42.88	10.61
c-LDL (mg/dl)	114.06	42.64
Triglyceride (mg/dl)	206.05	144.99
Body Mass Index (kg/m2)	29.17	4.40
Smokers (%)	0	
Cigarettes / day	-	
Alcohol consumption (oz/week)	0	
	Percentage	
Race (%)		
Hispanic	100	
Baseline CVD complications (%)		
Myocardial infarction	0	
Angina	0	
Peripheral vascular disease	0	
Stroke	0	
Congestive heart failure	0	
Atrial fibrillation	0	
Left ventricular hypertrophy	0	
Baseline renal complications (%)		
Microalbuminuria	0	
Macroalbuminuria	0	
End-Stage Renal Disease	0	
Baseline ophthalmologic complications (%)		
Non-proliferative diabetic retinopathy	0	
Proliferative diabetic retinopathy	0	
Severe vision loss	0	
Macular edema	0	
Cataract (%)	63.87	
Baseline foot ulcer complications (%)		
Uninfected ulcer	2.52	
Infected ulcer	0	
Healed ulcer	0	

History of amputation	0	
Baseline neuropathy (%)	1.0	
Baseline depression (%)	15.55	

HbA1c, glycated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein.

Appendix 4.

Treatment effectiveness

	Mean	Standard Deviation
HbA1c first year reduction (% HbA1c)		
CAIPaDi[1]	-0.94	1.95
Metformin monotherapy (13)	-0.22	0.08
Metformin + Glybenclamide (14)	-1.1	0.21
Insulin NPH + Metformin (14)	-1.5	1.1

[1] Data obtained from the participants' health records

Appendix 5.

Healthcare Resources Unitary costs

Healthcare Resource	Unitary costs (2019 USD)
Laboratory study	$5.87
Electrocardiogram	$26.54
Bioimpedance	$28.35
Endocrinology visit	$70.57
Ophthalmology visit	$70.57
Physical activity	$40.66
Nutritionist visit	$40.66
Dentist visit	$43.20
Diabetes education session	$40.66
Psychology session	$63.46
Psychiatrist visit	$70.57
Foot Care	$22.23
General Practitioner visit	$40.66

Source: IMSS impatient and outpatient costs (23)

Healthcare resources utilization in the CAIPaDi per year and visit

Healthcare Resource	1st Year					2nd year and plus
Visit	1	2	3	4	5	6+
Laboratory study	4	4	4	4	4	4
Electrocardiogram	1	0	0	0	1	1
Bioimpedance	1	1	1	1	1	1
Endocrinology visit	1	1	1	1	1	1
Ophthalmology visit	1	1	1	1	1	1
Physical activity	1	1	1	1	1	1
Nutritionist visit	1	1	1	1	1	1
Dentist visit	1	1	1	1	1	1
Diabetes education session	1	1	1	1	1	1
Psychology session	1	1	1	1	1	1
Psychiatrist visit	1	1	1	1	1	1
Foot Care	1	1	1	1	1	1
General Practitioner visit	1	0	0	0	1	1

CAIPaDi costs per year

CAIPaDi Cost	1st Year	2nd year and plus
Total Cost (2019 USD)	$2,706	$582

Usual treatment daily cost

Treatment and presentation	Unitary Cost (per mg or UI) (24)	Average daily dose (mg or UI) (REF)	Average Daily cost (2019 USD)
Metformin 850mg	$0.000011	1700	$0.019213
Glybenclamide 5mg	$0.000939	10	$0.009389
NPH Insulin 100 UI	$0.016378	30.96	$0.507067

(24) Consolidated medicine purchase IMSS 2019; (REF) Mexican Guideline

Usual treatment per year

Usual Treatment algorithm	1st Year	2nd year and plus
Metformin	$7.01	$7.01
Metfromin + Glybenclamide	$10.44	$10.44

Metformin + Insulin NPH	$192.09	$192.09
Total Cost (2019 USD)	$209.54	$209.54

Appendix 6

Time alive and free of complications of the CAIPaDi vs. usual treatment

Time alive and free of complications [in years]		
	Usual Treatment	CAIPaDi
Any complications	2.71	3.83
Non-proliferative retinopathy	13.48	15.46
Proliferative retinopathy	15.75	16.91
Microalbuminuria	12.99	14.59
Macroalbuminuria	14.89	16.44
End-Stage Renal Disease	15.74	16.85
1st Ulcer	13.84	16.13
Amputation	15.62	16.9
Neuropathy	11.28	13.84
Peripheral Vascular Disease	15.41	16.53
Congestive Heart Failure	15.43	16.51
Angina	15.19	16.18
Myocardial Infarction	15.3	16.54
Stroke	15.59	16.72
Cataract	6.04	6.37
Macular Edema	14.67	16.08
Severe Loss of Vision	15.51	16.77

Appendix 7.

Cumulative incidence of the main T2DM complications estimated in the time horizon

Cumulative incidence of main T2DM complications	Usual Treatment (95% IC)	CAIPaDi (95% IC)
Eye Disease		
Background Retinopathy	29.37 (27.91-30.83)	17.28 (15.3-19.26)
Proliferative Diabetic Retinopathy	5.32 (4.67-5.96)	1.73 (1.16-2.92)
Macular Edema	16.67 (15.71-17.63)	11.2 (9.74-12.65)
Severe Vision Loss	9.04 (8.25-9.82)	4.08 (3.39-4.76)
Cataract	10.72 (10.40-11.05)	8.24 (7.78-8.77)
Renal Disease		
Microalbuminuria	35.42 (33.67-37.18)	27.39 (24.8-30.03)
Gros Proteinuria	18.93 (17.18-20.70)	9.74 (7.53-11.95)
End-stage renal disease	8.35 (6.97-9.73)	4.64 (2.97-6.30)
Ulcer		
Ulcer	28.68 (27.34-30.03)	8.05 (7.0-9.1)
Amputation ulcer	46.6 (9.37-11.69)	2.61 (1.84-3.39)
Neuropathy	10.53 (53.25-56.50)	36.58 (33.89-39.26)
CVD complications		
Congestive heart failure	12.28 (11.46-13.15)	9.39 (8.60-10.17)
Peripheral vascular disease	9.55 (9.06-10.04)	7.23 (6.56-7.89)
Angina	11.8 (11.06-12.53)	10.49 (9.65-11.32)
Stroke	10.36 (8.94-10.52)	5.83 (5.15-6.51)
Myocardial infarction	9.73 (23.94-27.43)	15.64 (14.23-17.06)
Depression		
Depression episode (%)	75.31 (69.08-81.54)	74.06 (68.03-80.11)