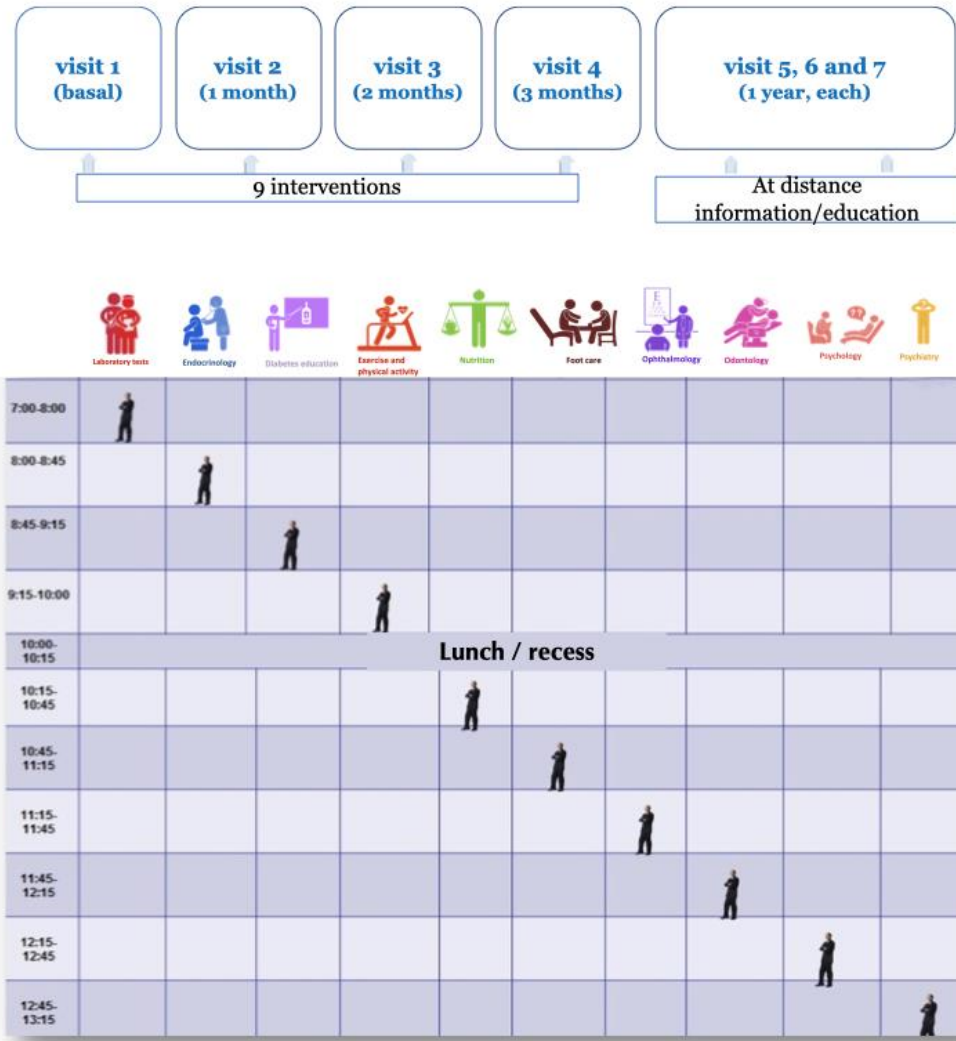


## Appendix 1.

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

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
<b>Patient demographics</b>		
Age (years)	57.61	8.89
Duration of T2DM Type 2 Diabetes Mellitus (years)	1.32	1.57
Percentage male	45%	
<b>Baseline risk factors</b>		
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/m <sup>2</sup> )	29.17	4.40
Smokers (%)	0	
Cigarettes / day	-	
Alcohol consumption (oz/week)	0	
	<b>Percentage</b>	
<b>Race (%)</b>		
Hispanic	100	
<b>Baseline CVD complications (%)</b>		
Myocardial infarction	0	
Angina	0	
Peripheral vascular disease	0	
Stroke	0	
Congestive heart failure	0	
Atrial fibrillation	0	
Left ventricular hypertrophy	0	
<b>Baseline renal complications (%)</b>		
Microalbuminuria	0	
Macroalbuminuria	0	
End-Stage Renal Disease	0	
<b>Baseline ophthalmologic complications (%)</b>		
Non-proliferative diabetic retinopathy	0	
Proliferative diabetic retinopathy	0	
Severe vision loss	0	
Macular edema	0	
Cataract (%)	63.87	
<b>Baseline foot ulcer complications (%)</b>		
Uninfected ulcer	2.52	
Infected ulcer	0	
Healed ulcer	0	

History of amputation	0	
<b>Baseline neuropathy (%)</b>	1.0	
<b>Baseline depression (%)</b>	15.55	

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

## Appendix 4.

*Treatment effectiveness*

	<b>Mean</b>	<b>Standard Deviation</b>
<b>HbA1c first year reduction (% HbA1c)</b>		
CAIPaDi <sup>†</sup>	-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

<sup>†</sup> 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 inpatient and outpatient costs (23)

## Healthcare resources utilization in the CAIPaDi per year and visit

Healthcare Resource	1st Year					2nd year and plus
	1	2	3	4	5	6+
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
Metformin + 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)
<b>Eye Disease</b>		
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)
<b>Renal Disease</b>		
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)
<b>Ulcer</b>		
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)
<b>CVD complications</b>		
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)
<b>Depression</b>		
Depression episode (%)	75.31 (69.08-81.54)	74.06 (68.03-80.11)