

Long-term cost-effectiveness analysis of once-weekly semaglutide versus dulaglutide in patients with type 2 diabetes with inadequate glycemic control in China

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SUPPLEMENTARY MATERIAL

Table S1: Baseline population characteristics

Characteristics	Value	Source
Demographics		
Age, years	55.67	SUSTAIN 7(2018) ^[1]
Diabetes duration, years	7.42	SUSTAIN 7(2018) ^[1]
Female, %	44.79	SUSTAIN 7(2018) ^[1]
Smoker, %	14.01	SUSTAIN 7(2018) ^[1]
Biomarkers		
HbA _{1c} , %	8.22	SUSTAIN 7(2018) ^[1]
SBP, mmHg	132.96	SUSTAIN 7(2018) ^[1]
TC, mg/dl	181.24 ^a	Johansen et.al(2019) ^[2]
HDL, mg/dl	44.82 ^a	Johansen et.al(2019) ^[2]
LDL, mg/dl	102.29 ^a	Johansen et.al(2019) ^[2]
TG, mg/dl	181.31 ^a	Johansen et.al(2019) ^[2]
BMI, kg/m ²	33.5	SUSTAIN 7(2018) ^[1]
HR, bpm	75.19	SUSTAIN 7(2018) ^[1]
WBC, 1x10 ⁶	7.39	SUSTAIN 7(2018) ^[1]
eGFR, mL/min/1.73m ²	97.2	SUSTAIN 7(2018) ^[1]
Risks of Complications at Baseline		
Background Retinopathy	2.9%	SUSTAIN 7(2018) ^[1]
Proliferative Retinopathy	0.0%	SUSTAIN 7(2018) ^[1]
Macular Edema	0.0%	SUSTAIN 7(2018) ^[1]
Proliferative Retinopathy & Macular Edema	0.0%	SUSTAIN 7(2018) ^[1]
Severe Visual Loss	0.3%	SUSTAIN 7(2018) ^[1]
Symptomatic Neuropathy	9.1%	SUSTAIN 7(2018) ^[1]
Peripheral Vascular Disease	0.7%	SUSTAIN 7(2018) ^[1]
Lower Extremity Amputation	0.4%	SUSTAIN 7(2018) ^[1]
Microalbuminuria	1.6%	SUSTAIN 7(2018) ^[1]
Macroalbuminuria	0.5%	SUSTAIN 7(2018) ^[1]
End Stage Renal Disease	0.0%	SUSTAIN 7(2018) ^[1]
Ischemic Heart Disease	14.5%	SUSTAIN 7(2018) ^[1]
First Myocardial Infarction	4.3%	SUSTAIN 7(2018) ^[1]
Subsequent Myocardial Infarction	0.0%	SUSTAIN 7(2018) ^[1]
First Stroke	2.2%	SUSTAIN 7(2018) ^[1]
Subsequent Stroke	0.0%	SUSTAIN 7(2018) ^[1]
Heart Failure	5.4%	SUSTAIN 7(2018) ^[1]

^a: Values have been converted from mg/dL to mmol/L by multiplying the mg/dL values with 0.0259 (TC, HDL, LDL) and 0.0113 (TG).

Table S2: Annual pharmacy costs

	Semaglutide 0.5 mg (CNY)	Semaglutide 1.0 mg (CNY)	Dulaglutide 1.5 mg (CNY)	insulin glargine (CNY)
Annual medication costs	6002.10	10035.99	7769.29	4221.67
Annual metformin costs	1482.63	1482.63	1482.63	1482.63
Annual needle costs	140.40	140.40	0 ^a	140.40
Total annual costs	7625.13	11659.02	9251.92	5844.70

^a: In China, needles were included in the dulaglutide packs, while it is not included in the semaglutide packs.

Table S3: Diabetic complications treatment costs*

State of complication	First year (CNY)	Subsequent years(CNY)	Source
Background cost	3,329	-	Xie et.al(2005) ^[3]
Background Retinopathy	15,663	902	He et.al(2019) ^[4]
Proliferative Retinopathy	15,663	902	He et.al(2019) ^[4]
Macular Edema	16,346	2,150	Wu et.al(2016) ^[5]
Proliferative Retinopathy & Macular Edema	32,009	3,052	He et.al(2019) ^[4] Wu et.al(2016) ^[5]
Severe Visual Loss	14,861	11,469	Deng et.al(2015) ^[6]
Symptomatic Neuropathy	18,656	7,158	Deng et.al(2015) ^[6]
Peripheral Vascular Disease	27,939	10,902	Wu et.al(2016) ^[5]
Lower Extremity Amputation	22,491	17,927	Wu et.al(2016) ^[5]
Microalbuminuria	200	200	Men et.al(2020) ^[7]
Macroalbuminuria	14,764	5,634	Deng et.al(2015) ^[6]
End Stage Renal Disease	157,451	126,632	Duan et.al(2020) ^[8]
Ischemic Heart Disease	48,158	8,597	Su et.al(2019) ^[9]
MI (first and second)	80,139	25,333	Deng et.al(2015) ^[6]
Stroke (first and second)	31,733	15,699	Su et.al(2019) ^[9]
Heart Failure	38,393	20,367	Su et.al(2019) ^[9]
Non-severe hypoglycemic event	874	0	Su et.al(2019) ^[9]
Severe hypoglycemic event	13,707	0	Su et.al(2019) ^[9]

*: The costs have been inflated to 2021 CNY through the Chinese healthcare consumer price index (CPI). The healthcare CPI from 2006 to 2021 was 100.2, 102.1, 102.2, 101.4, 103.3, 102.9, 101.7, 101.5, 101.7, 102.7, 103.8, 106.0, 104.3, 102.4, 101.8 and 100.4, respectively (last year = 100).

Table S4: Health state utilities applied in the analyses

Variables	Mean (S.E)	Source
Baseline HRQoL level	0.910 (0.008)	Pan et.al (2016) ^[10]
Background Retinopathy	-0.040 (0.004)	Clarke et.al(2002) ^[11]
Proliferative Retinopathy	-0.070 (0.007)	Johansen et.al(2019) ^[2]
Macular Edema	-0.040 (0.013)	Clarke et.al(2002) ^[11]
Proliferative Retinopathy & Macular Edema	-0.070 (0.015)	Pan et.al (2016) ^[10]
Severe Visual Loss	-0.074 (0.025)	Clarke et.al(2002) ^[11]
Symptomatic neuropathy	-0.084 (0.014)	Clarke et.al(2002) ^[11]
Peripheral Vascular Disease	-0.061 (0.015)	Beaudet et.al(2014) ^[12]
Lower Extremity Amputation Event	-0.280 (0.056)	Beaudet et.al(2014) ^[12]
History of Lower Extremity Amputation	-0.280 (0.056)	Beaudet et.al(2014) ^[12]
Microalbuminuria	0	Assumption
Macroalbuminuria	-0.048 (0.022)	Beaudet et.al(2014) ^[12]
End Stage Renal Disease	-0.263 (0.026)	Deng et.al (2015) ^[6]
Ischemic Heart Disease	-0.090 (0.018)	Clarke et.al(2002) ^[11]

First Myocardial Infarction Event	-0.055 (0.006)	Clarke et.al(2002) ^[11]
History of First Myocardial Infarction	-0.055 (0.007)	Clarke et.al(2002) ^[11]
Subsequent Myocardial Infarction Event	-0.0012 (0.001)	Pan et.al (2016) ^[10]
History of Subsequent Myocardial Infarction	-0.0012 (0.000)	Pan et.al (2016) ^[10]
First Stroke Event	-0.164 (0.030)	Clarke et.al(2002) ^[11]
History of First Stroke	-0.164 (0.031)	Clarke et.al(2002) ^[11]
Subsequent Stroke Event	-0.040 (0.004)	Johansen et.al(2019) ^[2]
History of Subsequent Stroke	-0.040 (0.004)	Johansen et.al(2019) ^[2]
Heart Failure	-0.108 (0.031)	Clarke et.al(2002) ^[11]
Per every 10 years increase in age	-0.024 (0.001)	Johansen et.al(2019) ^[2]
Female	-0.093 (0.009)	Johansen et.al(2019) ^[2]
Per every additional 10 years of diabetes	-0.016 (0.001)	Johansen et.al(2019) ^[2]
Per unit increase in BMI over 25	-0.006 (0.001)	Beaudet et.al(2014) ^[12]
Non-severe hypoglycemia	-0.014 (0.001)	Johansen et.al(2019) ^[2]
Severe hypoglycemia	-0.047 (0.005)	Johansen et.al(2019) ^[2]

Table S5: Cumulative incidence of diabetes-related complications

Cumulative incidence, %	OW Semaglutide 0.5mg	OW Semaglutide 1.0mg	Dulaglutide 1.5mg
Mortality			
Overall Mortality	95.31	94.88	95.55
Cardiovascular Event Mortality (Myocardial Infarction & Stroke)	20.03	19.51	20.34
Microvascular Complications			
Eye Disease			
Background Retinopathy	41.43	36.56	43.93
Proliferative Retinopathy	5.23	4.19	5.80
Macular Edema	20.61	17.76	22.12
Proliferative Retinopathy & Macular Edema	5.36	4.03	6.14
Severe Visual Loss	5.00	4.13	5.50
Lower Extremity Disease			
Symptomatic Neuropathy	10.01	8.73	10.70
Peripheral Vascular Disease	31.48	31.92	31.22
Lower Extremity Amputation	21.45	20.78	21.80
Kidney Disease			

Microalbuminuria	40.60	38.03	41.89
Macroalbuminuria	23.97	20.72	25.66
End Stage Renal Disease	9.24	7.71	10.07
Macrovascular Complications			
Ischemic Heart Disease	14.32	14.23	14.35
Myocardial Infarction			
First Myocardial Infarction	22.39	21.78	22.75
Second or Subsequent Myocardial Infarction	5.09	5.08	5.26
Stroke			
First Stroke	9.61	9.17	9.79
Second or Subsequent Stroke	2.93	2.85	2.97
Heart Failure	8.01	7.80	8.46
Cardiovascular Disease (Myocardial Infarction & Stroke)	29.41	28.52	29.88

Table S6: CHEERS checklist 2022^[13]

Section/topic	Item No	Guidance for reporting	Reported in section
Title			
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title
Abstract			
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Introduction
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Not report
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methods, Table S1
Setting and location	6	Provide relevant contextual information that may influence findings.	Introduction
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Introduction
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Introduction
Time horizon	9	State the time horizon for the study and why appropriate.	Methods
Discount rate	10	Report the discount rate(s) and reason chosen.	Methods
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methods
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Methods

Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Methods
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Methods
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methods, Table S2-3
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Methods
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methods
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Not applicable
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Not applicable
Characterizing uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Results, Discussion
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Not applicable
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Table 1, Table S1-4
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Results, Table 2
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Results, Table 3
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study.	Not applicable
Discussion			
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Discussion
Other relevant information			

Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis.	Funding
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Conflicts of interest

Table S7: Impact inventory

Sector	Type of Impact	From Health Care Sector Perspective	Notes
Formal Health Care Sector			
Health	Health outcomes (effects)		
	Longevity effects	√	Discounted life expectancy was simulated
	Health-related quality-of-life effects	√	Discounted quality-adjusted life expectancy was simulated
	Cumulative incidence of microvascular complications	√	Cumulative incidence of diabetes-related complications was simulated
	Cumulative incidence of macrovascular complications	√	
	Medical costs		
	Paid for by third-party payers	√	Costs paid by payer and patient were collected and calculated together
	Paid for by patients out-of-pocket	√	Lifetime drug cost and needle cost were collected
	Future related medical costs (payers and patients)	√	Lifetime treatment costs of complications and hypoglycemia were collected
	Future unrelated medical costs (payers and patients)	√	
Informal Health Care Sector			
Health	Patient-time costs	NA	
	Unpaid caregiver-time costs	NA	
	Transportation costs	NA	
Non-Health Care Sectors			
Productivity	Labor market earnings lost	NA	
	Cost of unpaid lost productivity due to illness	NA	
	Cost of uncompensated household production	NA	
Consumption	Future consumption unrelated to health	NA	
Social Services	Cost of social services as part of intervention	NA	
Legal or Criminal Justice	Number of crimes related to intervention	NA	
	Cost of crimes related to intervention	NA	
Education	Impact of intervention on educational achievement of population	NA	
Housing	Cost of intervention on home improvements (eg, removing lead paint)	NA	

Environment	Production of toxic waste pollution by intervention	NA
Other (specify)	Other impacts	NA

*: Table adapted from impact inventory template suggested by Second Panel on Cost-Effectiveness in Health and Medicine ^[14]. NA indicates not applicable.

Reference

1. Pratley RE, Aroda VR, Lingvay I, et al. Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. *Lancet Diabetes Endocrinol.* 2018;6(4):275-86.
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