# Long-term Cost-effectiveness of Subcutaneous Once-weekly Semaglutide Versus Polyethylene Glycol Loxenatide for Treatment of Type 2 Diabetes Mellitus in China

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## INTRODUCTION

- Once-weekly (OW) subcutaneous semaglutide is an injectable glucagon-like peptide-1 (GLP-1) analogue, the efficacy of which has been shown in the Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes (SUSTAIN) trial program that comprises ten reported phase 3 global clinical trials[1-10].
- OW semaglutide (Ozempic®; Novo Nordisk, Denmark) has been included in the National Reimbursement Drug List in China, while evidence of the long-term cost-effectiveness between OW semaglutide and China's domestic OW GLP-1RA is limited.

## OBJECTIVE

- To assess the long-term cost-effectiveness of OW semaglutide 0.5mg and 1.0mg versus polyethylene glycol loxenatide (PEG-loxenatide) 0.2mg among patients with type 2 diabetes uncontrolled on metformin monotherapy in China.

## METHODS

- The Swedish Institute of Health Economics Diabetes Cohort Model (IHE-DCM) was used to evaluate the long-term cost and health outcomes of OW semaglutide and PEG-loxenatide. Analysis was conducted from the perspective of Chinese healthcare system over a time horizon of 40 years.
- Baseline demographic characteristics: HbA1c, BMI, and eGFR were derived from the SUSTAIN China clinical trial. A network meta-analysis was conducted to obtain comparative treatment effects of OW semaglutide and PEG-loxenatide based on two phase 3a clinical trials. Pharmaceutical costs were sourced from the national bidding price in China. Costs of complications and utilities associated with diabetes and related complications were derived from published sources. Costs were expressed in 2021 China Yuan (CNY). Clinical and economic outcomes were discounted at a rate of 5% annually.
- Key model assumptions: (1) patients were assumed to initiate treatment with either OW semaglutide or PEG-loxenatide and then switch to basal insulin after three years ; (2)$HbA_{1c}$ was assumed to increase annually at a rate of 0.14% according to data in the study of Kahn SE, et al[11]; (3) UKPDS 82 risk equations were applied to simulate the mortality. Risk equations sourced from the Swedish National Diabetes Register (NDR) were employed to predict the incidence of macrovascular complications.
- The base case result was evaluated through one-way sensitivity analysis and probabilistic sensitivity analysis.

## RESULTS

- Over a timeframe of 40 years, both doses of OW semaglutide were associated with lower cumulative incidences of micro-and macrovascular complications and mortality. (Table 1).
- Compared with PEG-loxenatide 0.2mg, OW semaglutide 0.5mg and 1.0mg were associated with improvements in discounted life expectancy of 0.08 and 0.12 years, respectively, and discounted quality-adjusted life expectancy of 0.16 and 0.22 QALYs, respectively (Table 2).
- Clinical benefits were achieved at reduced costs, with lifetime total cost savings of 19,309 CNY with OW semaglutide 0.5mg and savings of 10,179 CNY with OW semaglutide 1.0mg, resulting from the reduction of diabetes-related complications (Table 2).
- Sensitivity analysis verified the robustness of the base case result (Table 3). At a willingness-to-pay threshold of 1x GDP per capita (CNY 80,976) per QALY gained, the probabilities of being cost-effective for OW semaglutide 0.5mg and 1.0mg relative to PEG-loxenatide 0.2mg were both of 100% (Figure 1).

**Table 1. Cumulative Incidence of Micro- and Macrovascular Complications and Mortality**

| Item | OW semaglutide 0.5mg | OW semaglutide 1.0mg | PEG-loxenatide 0.2mg |
|---|---|---|---|
| **Mortality** | | | |
| Overall Mortality | 96.04% | 95.78% | 96.54% |
| Cardiovascular Event Mortality | 29.05% | 28.32% | 29.86% |
| **Microvascular Complications** | | | |
| **Eye Disease** | | | |
| Background Retinopathy | 30.89% | 29.36% | 35.30% |
| Proliferative Retinopathy | 3.24% | 2.98% | 4.06% |
| Macular Edema | 17.16% | 16.42% | 19.37% |
| Proliferative Retinopathy & Macular Edema | 2.77% | 2.51% | 3.60% |
| Severe Visual Loss | 4.60% | 4.41% | 5.21% |
| **Lower Extremity Disease** | | | |
| Symptomatic Neuropathy | 5.88% | 5.60% | 6.69% |
| Peripheral Vascular Disease | 28.36% | 28.53% | 27.96% |
| Lower Extremity Amputation | 29.45% | 29.40% | 29.71% |
| **Kidney Disease** | | | |
| Microalbuminuria | 23.44% | 22.85% | 25.12% |
| Macroalbuminuria | 13.86% | 13.14% | 15.97% |
| End Stage Renal Disease | 7.26% | 6.97% | 8.16% |
| **Macrovascular Complications** | | | |
| Ischemic Heart Disease | 19.83% | 19.51% | 20.57% |
| Myocardial Infarction | | | |
| First Myocardial Infarction | 28.16% | 27.19% | 29.30% |
| Second or Subsequent Myocardial Infarction | 6.57% | 6.30% | 6.82% |
| Stroke | | | |
| First Stroke | 22.25% | 22.05% | 23.29% |
| Second or Subsequent Stroke | 7.48% | 7.42% | 7.78% |
| Heart Failure | 30.94% | 30.22% | 33.27% |
| Cardiovascular Disease (Myocardial Infarction & Stroke) | 44.63% | 43.70% | 46.26% |

**Table 2. Base Case Results**

| Health Outcomes | OW semaglutide 0.5mg +metformin | PEG-loxenatide 0.2mg+metformin | Incremental |
|---|---|---|---|
| Life years (year) | 13.16 | 13.08 | 0.08 |
| QALYs | 7.85 | 7.69 | 0.16 |
| Total direct medical cost (CNY) | 322,489 | 341,798 | -19,309 |
| Treatment Cost | 114,775 | 124,353 | -9,578 |
| Microvascular Cost | 126,394 | 131,536 | -5,142 |
| Macrovascular Cost | 81,320 | 85,909 | -4,589 |
| ICER (CNY/QALY gained) | - | - | Dominant |

| Health Outcomes | OW semaglutide 1.0mg +metformin | PEG-loxenatide 0.2mg+metformin | Incremental |
|---|---|---|---|
| Life years (year) | 13.19 | 13.08 | 0.12 |
| QALYs | 7.91 | 7.69 | 0.22 |
| Total direct medical cost (CNY) | 331,619 | 341,798 | -10,179 |
| Treatment Cost | 127,105 | 124,353 | 2,752 |
| Microvascular Cost | 124,845 | 131,536 | -6,691 |
| Macrovascular Cost | 79,670 | 85,909 | -6,239 |
| ICER (CNY/QALY gained) | - | - | Dominant |

**Table 3. Results of One-way Sensitivity Analyses**

| Analysis | ICER (OW semaglutide 0.5mg VS. PEG-loxenatide 0.2mg） | ICER (OW semaglutide 1.0mg VS. PEG-loxenatide 0.2mg) |
|---|---|---|
| Base case | Dominant | Dominant |
| 30-year time horizon | Dominant | Dominant |
| 0% discount rates | Dominant | Dominant |
| 8% discount rates | Dominant | Dominant |
| Annual drift in $HbA_{1c}$ 0.1% | Dominant | Dominant |
| Annual drift in $HbA_{1c}$ 0.2% | Dominant | Dominant |
| HbA1c drift using UKPDS progression | Dominant | Dominant |
| Upper 95% CI of HbA1c estimated treatment difference | Dominant | Dominant |
| Lower 95% CI of HbA1c estimated treatment difference | Dominant | Dominant |
| Upper 95% CI of BMI estimated treatment difference | Dominant | Dominant |
| Lower 95% CI of BMI estimated treatment difference | Dominant | Dominant |
| $HbA_{1c}$ threshold 7% | Dominant | 7,400 |
| UKPDS 68 risk equations applied | Dominant | Dominant |
| Deng et al.[12]BMI disutility applied | Dominant | Dominant |

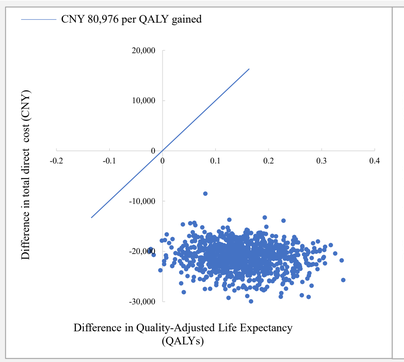


**Figure 1(a). Probabilistic sensitivity analyses scatter plot. CNY 2021 RMB, QALY quality-adjusted life-year (OW semaglutide 0.5mg VS. FEG-Loxenatide 0.2mg)**

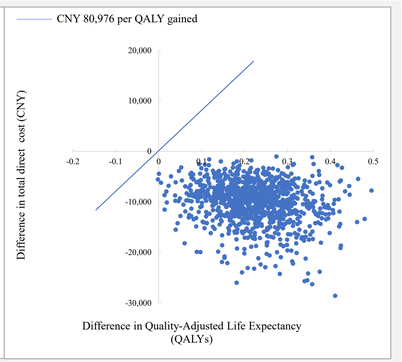


**Figure 1(b). Probabilistic sensitivity analyses scatter plot. CNY 2021 RMB, QALY quality-adjusted life-year (OW semaglutide 1.0mg VS. FEG-Loxenatide 0.2mg)**

## CONCLUSIONS

This study showed that OW semaglutide 0.5mg and OW semaglutide 1.0mg were estimated to be dominant (more effective and less costly) versus PEG-loxenatide 0.2mg in patients with type 2 diabetes uncontrolled on metformin monotherapy in China.

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