

Real-world data-based health economic framework for drug value re-assessment to support clinical and policy decisions using glucose-lowering agents as an example

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Conflict of interest

- All authors have no conflict of interest to be disclosed.

Challenges for conducting real-world data (RWD)-based cost-effectiveness analyses (CEAs)

- Data
 - **Representativeness** and **comprehensiveness** for target populations
- Parameters (i.e., effectiveness, safety, costs, patient-reported outcomes e.g., health utility)
 - **Specific** to target populations/settings
 - **Valid** (minimize potential biases arisen from the use of RWD)
- Analyses (e.g., modeling simulation approaches)
 - **Applicability** to target populations/settings

Framework for RWD-based CEAs

- Step 1 (Pattern): Drug utilization pattern
 - Identify drug candidates (e.g., high healthcare spending)
- Step 2 (Parameters): Collect real-world parameters for CEAs
 - Effectiveness and safety associated with target treatments
 - Costs associated with modeled health states
 - Health utilities (i.e., penalties or decrements) associated with modeled health states
- Step 3 (Refine): Improve CEA methodology
- Step 4 (Analysis): Conduct RWD-based CEAs

Flow of this workshop (using glucose-lowering agents as an example)

- Topic 1 (Effectiveness/safety parameters):
Identify a study cohort of comparable treatment groups for generating reliable real-world evidence on comparative treatment effectiveness/safety (Chun-Ting Yang, MS)
- Topic 2 (Cost and utility parameters):
Estimate country/setting-specific health cost and utility parameters for better reflecting patient characteristics in target clinical settings (Shihchen Kuo, RPh, PhD)
- Topic 3 (CEAs):
Conduct cohort study-based and model-based simulation studies for analyzing the long-term health and economic outcomes (Zi-Yang Peng, MS)
- Q&A (for all presented topics)
- Exercise

How to estimate treatment effectiveness and safety with real-world population data

Chun-Ting Yang, MS

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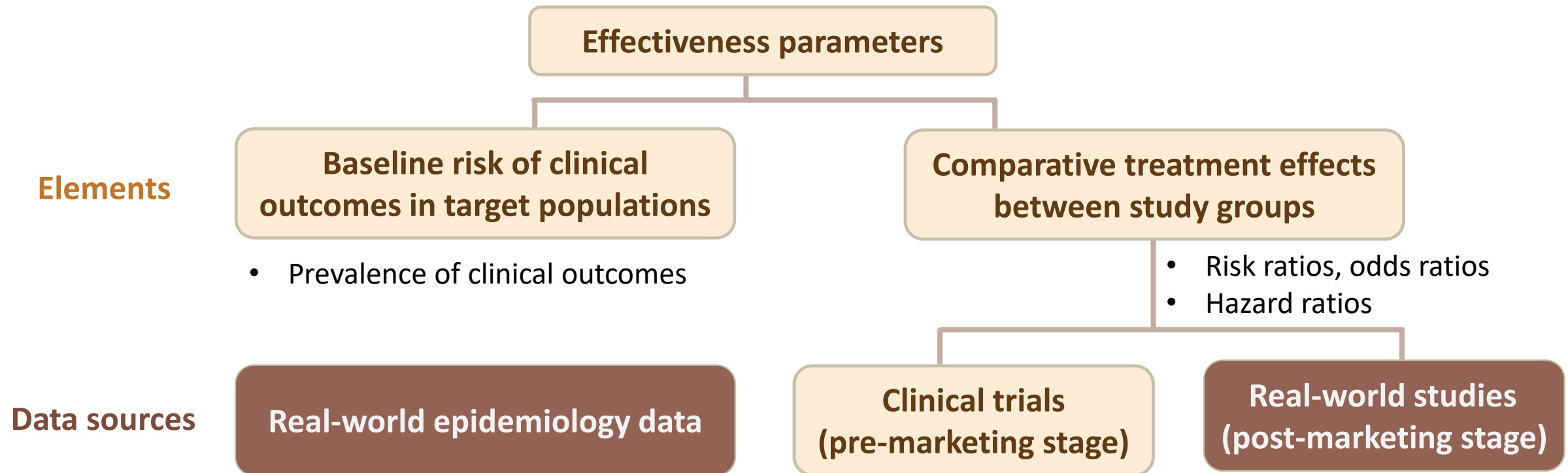
Tainan, Taiwan

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Outline

- Role of RWD in a CEA
- Methodological challenges of generating effective parameters using RWD
 - ✓ Our research experiences of obtaining valid effectiveness parameters using RWD
- Uniqueness of RWD as data sources in CEAs
 - ✓ Exploration of diversity and heterogeneity in health and economic outcomes
- Recap

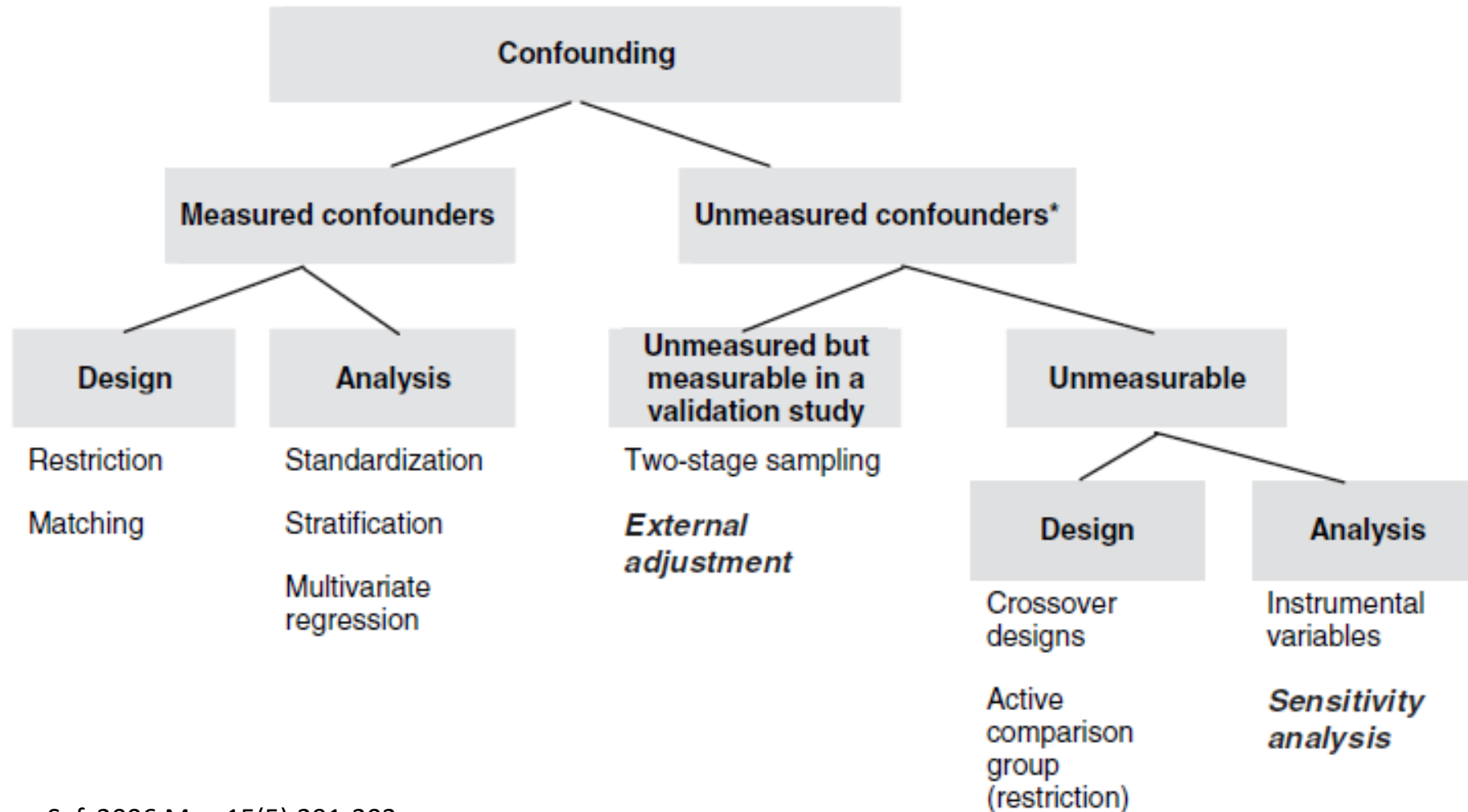
Effectiveness parameters derived from RWD in CEAs



What are RWD?

- Sources of RWD
 - ✓ Electronic health records
 - ✓ Administrative claims data
 - ✓ Product and disease registries
 - ✓ Others: patient-reported data in home-use settings, information collected from mobile devices
- Common epidemiologic and biostatistical challenges to the use of RWD
 - Data quality
 - **Identifying appropriate RWD sources** based on research questions, clinical knowledge, understanding of potential RWD sources
 - **Data management** (e.g., distribution, imputation)
 - Confounding bias (comparative studies)
 - **Rigorous study design and statistical analyses**

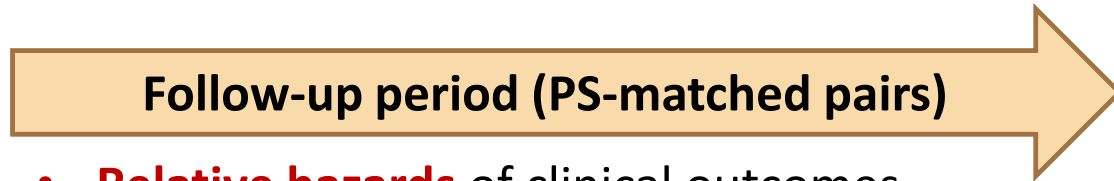
Solutions to control for confounders in comparative studies



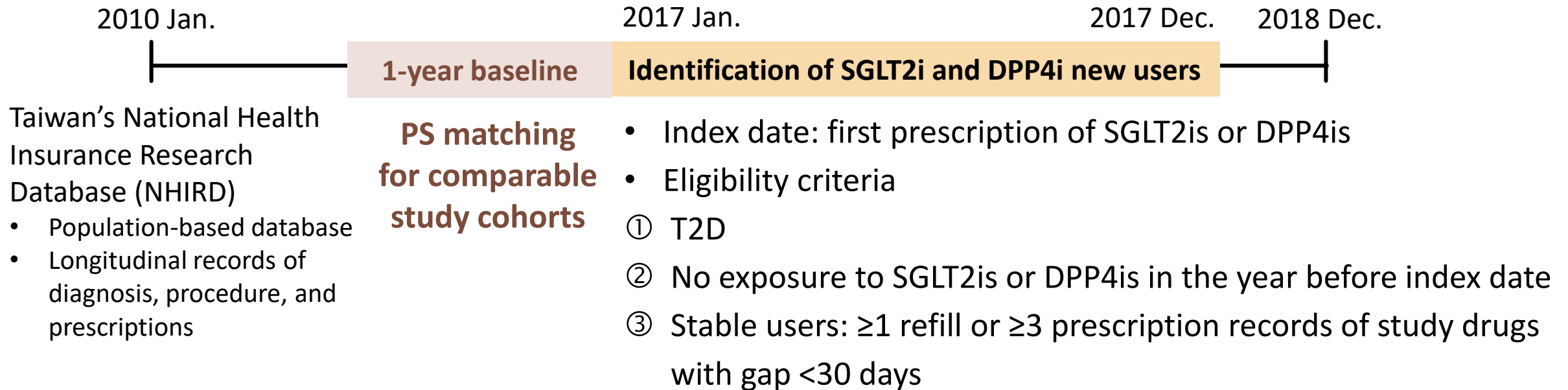
Incident new-user and active-comparator (INU-AC) design

- Commonly applied approaches nowadays
 - **Incident new-user design**
 - ✓ Avoid prevalent-user and survivor bias
 - **Active comparator design**
 - ✓ Minimize the confounding effects attributable to comparisons between users and non-users
 - ✓ Choice of active comparators based on knowledge of clinical domain and drug utilization pattern in usual practice
 - **Propensity score (PS) matching**
 - ✓ Enhance the between-group comparability

Case illustration: sodium-glucose cotransporter-2 inhibitors (SGLT2is) versus dipeptidyl peptidase-4 inhibitors (DPP4is) in type 2 diabetes (T2D)



- **Relative hazards** of clinical outcomes estimated by subdistributional hazard models



Limitations of the INU design and PS matching procedure?

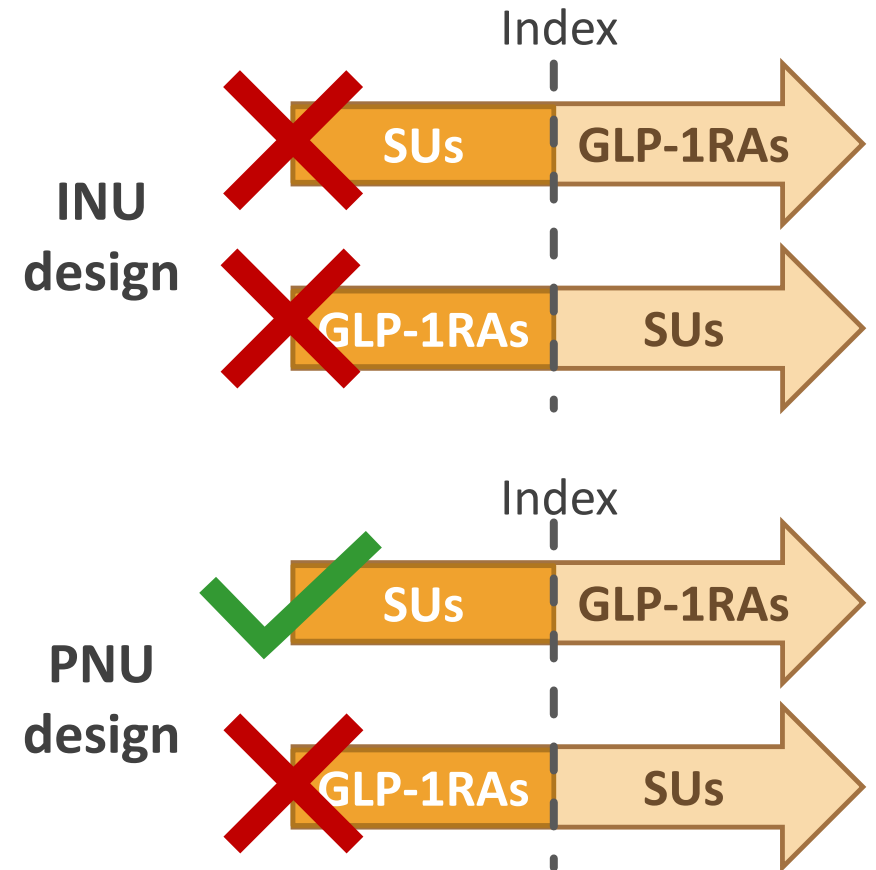
- Incident new users
 - Great loss of sample size when novel agents were compared with traditional medications
 - ✓ Glucagon-like peptide-1 receptor agonists (GLP-1RAs) versus sulfonylureas (SUs)¹
 - ✓ Non-vitamin K antagonist oral anticoagulants (NOACs) versus warfarin²
- PS matching
 - Only adjust for measured confounders
 - ✓ Residual confounding effects attributable to the lack of laboratory or behavior data in administrative claims database

1. Pharmacoepidemiol Drug Saf. 2017 Apr;26(4):459-468.

2. Drugs Real World Outcomes. 2019 Sep;6(3):93-104.

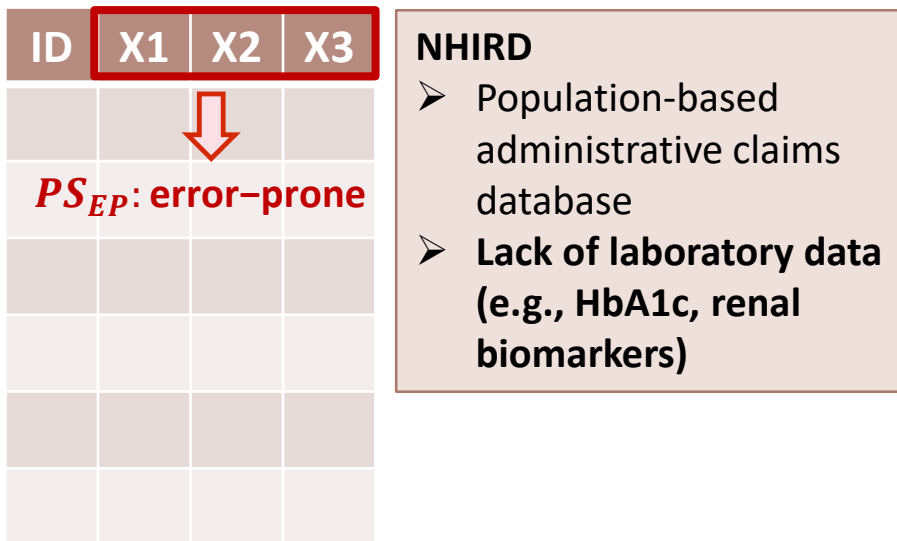
Case illustration: GLP-1RAs versus SUs in T2D populations

- **Prevalent new-user (PNU) design**
- **Multi-step matching algorithm**
 - ① Index date of study drug initiation (± 180 days)
 - ✓ Similar background of clinical practice settings
 - ② Previous utilization pattern of glucose-lowering agents (types and exposure period)
 - ✓ Diabetes severity and progression
 - ③ PS matching
 - ✓ PS measured by a comprehensive list of patient clinical characteristics



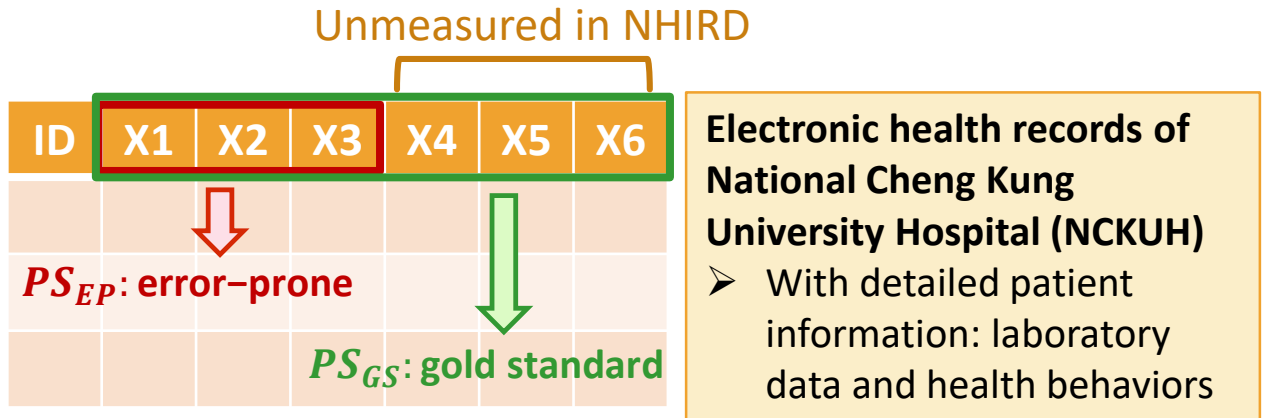
Case illustration: DPP4is versus SUs in T2D populations

- PS calibration techniques to adjust for imbalanced baseline characteristics between users of DPP4is and SUs



$$PS_{EP,NHIRD} = \Pr(E = 1 | X_1, X_2, X_3)$$

$$h[t|E, e(X)] = h_0[t] \exp\{\beta_E E + \beta_x e(X)\}$$



$$PS_{EP,NCKUH} = \Pr(E = 1 | X_1, X_2, X_3)$$

$$PS_{GS,NCKUH} = \Pr(E = 1 | X_1, X_2, X_3, X_4, X_5, X_6)$$

$$E [PS_{GS,NCKUH} | E, PS_{EP,NCKUH}] = \lambda_0 + \lambda_E E + \lambda_x (PS_{EP,NCKUH})$$

↓ Calibration adjustment

$$\textcircled{1} \beta^*_{E} = \beta_E - \lambda_E \frac{\beta_x}{\lambda_x} \quad \textcircled{2} \beta^*_{x} = \frac{\beta_x}{\lambda_x}$$

$$h[t|E, e(X_{GS})] = h_0[t] \exp\{\beta^*_{E} E + \beta^*_{x} e(X_{GS})\}$$

Other approaches

- Other PS techniques¹
 - High-dimensional PS matching
 - Weighting (Inverse probability of treatment weights, standardized mortality ratio weights)
 - PS fine stratification
- External adjustment: two-stage calibration
- Control outcome calibration approach²
- Instrumental variable analysis

Key concepts

- **Between-group comparability**
 - Choice of active comparators
 - Identification of comparable study cohorts
- **Balance between internal and external validity**

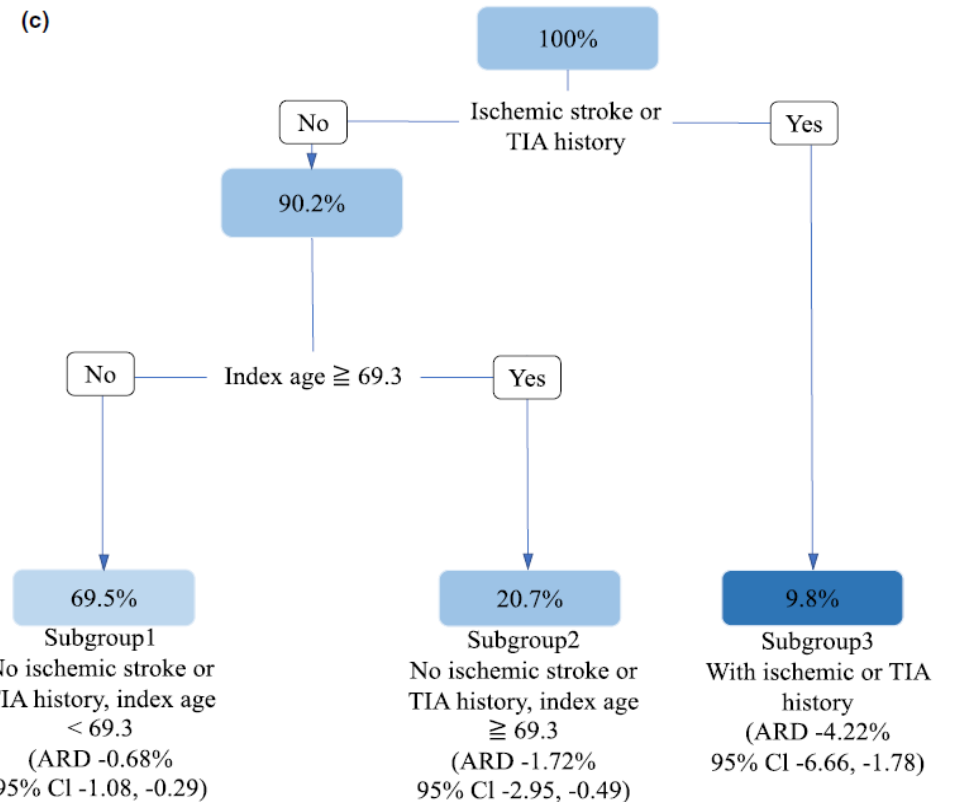
1. BMJ 2019;367:l5657

2. Am J Epidemiol. 2014 Mar 1; 179(5): 633–640.

Advantages of using RWD in treatment effectiveness research

- Ensure the **generalizability** of study findings to patients in usual practice settings
- Expansion of the treatment effectiveness and safety profile
- Explore **heterogeneous treatment effects** varied by patient characteristics
 - Identification of populations with enhanced benefit and risk
 - Personalized treatment strategies

Heterogeneous treatment effects of DPP4is versus SUs on cardiovascular outcomes



Recap

- RWD could be valuable resources for estimating treatment effectiveness and safety
- How to obtain reliable and valid estimates of treatment effects using RWD?
 - **Background knowledge with rigorous study design** based on
 - Real-world physician prescribing behavior, drug utilization pattern, and patient profile of target study populations
 - **Balance between internal and external validity**
 - Robustness of study findings confirmed by a series of **sensitivity analyses**
 - Intention-to-treat and as-treated scenario, modification of inclusion/exclusion criteria
- Exploration of **heterogeneity in treatment effects** across different patient characteristics
 - Supportive evidence for individualized medicine in clinical practice
 - Materials for further health and economic evaluations to optimize healthcare resource allocation

Thank you!

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Estimating healthcare costs and health utilities for people with type 2 diabetes using real-world data to support health economic analysis

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September 20, 2022 at ISPOR Asia Pacific 2022

Outline

- Why to estimate healthcare costs and health utilities for health economic analysis
- How to estimate healthcare costs and health utilities for health economic analysis
- Estimating healthcare costs associated with complications of T2D
- Valuing health states of people with T2D
- Recap

Why to estimate healthcare costs and health utilities for health economic analysis?

- Selecting strategies/options for comparison [*usually straightforward*]
- Determining the analysis perspective [*crucial, but usually straightforward*]
- Determining the time horizon [*crucial, but usually straightforward*]
- Determining the analysis scope [*crucial, easy to get wrong*]
- Measuring and valuing **costs (formal, informal, and non-healthcare sectors)** [*tedious*]
- Measuring and valuing **outcomes (e.g., quality-adjusted life years)** [*tedious*]
- Determining time preference/discount rate [*crucial, but usually straightforward*]
- Choosing the analytic method/model [*crucial, easy to get wrong*]
- Calculating the incremental cost-effectiveness ratio [*easy*]
- Accounting for uncertainty using sensitivity/scenario/subgroup analyses [*fun*]
- Interpreting analysis results [*tricky, hard*]

How to estimate healthcare costs and health utilities using RWD to support model-based simulation health economic analysis?

- Reliable estimates from **country-specific** and **population-specific** data
 - ✓ Sensitive to the cultural norms, availability of medical technologies, affordability and accessibility of medical services, medical practices, and healthcare systems
- Development of country-specific unit-cost catalogs as a key area for future exploration in cost-effectiveness research (by the Second Panel on Cost-Effectiveness in Health and Medicine)
- **Health claims** as the suitable data source to estimate **healthcare costs** because of the large sample size, wide coverage, and detailed cost data
- **Population-based surveys** as the suitable data source to estimate **health utilities** because of the national representativeness and diverse characteristics
- **Multivariable regression analysis** using cross-sectional or longitudinal data to form **an additive model** or **a multiplicative model** with adjustment for a wide range of demographic, socioeconomic, and clinical characteristics

Diabetes Care. 2012 Nov;35(11):2250-6.

Am J Manag Care. 2013 May;19(5):421-30.

Value Health. 2014 Jun;17(4):462-70.

Value Health. 2018 Jul;21(7):881-890.

Diabetes Care. 2018 May;41(5):971-978.

Med Decis Making. 2018 Oct;38(7):767-777.

Pharmacoeconomics. 2019 May;37(5):631-643.

Diabetes Care. 2021 Feb;44(2):381-389.

Estimating healthcare costs associated with complications of T2D

Health Care Costs Associated With Macrovascular, Microvascular, and Metabolic Complications of Type 2 Diabetes Across Time: Estimates From a Population-Based Cohort of More Than 0.8 Million Individuals With Up to 15 Years of Follow-up

Hsuan-Ying Chen,¹ Shihchen Kuo,² Pei-Fang Su,³ Jin-Shang Wu,^{4,5,6} and Huang-Tz Ou^{1,7,8}

Diabetes Care 2020;43:1732–1740 | <https://doi.org/10.2337/dc20-0072>

Research design, data source, and analytic methods

- Nationwide, population-based, longitudinal retrospective study
- Taiwan's NHIRD (1996-2013)
- 802,429 adults with newly-diagnosed T2D during 1999-2010 with follow-up until death or 12/31/2013
- Healthcare costs in 2017 U.S. dollars, including two aspects of medical costs from the healthcare sector perspective: 1) costs paid by the third-party payer (costs reimbursed by Taiwan's National Health Insurance [NHI] program) and 2) out-of-pocket costs paid by individuals (copayments by patients)
- Multivariable generalized estimating equation (GEE) model with a log-link function to estimate the log-transformed annual healthcare costs as a function of patient demographics, comorbidities, complications, and antidiabetic treatments
- Back-transformation of the coefficients and 95% confidence intervals from the GEE model to the ordinal scale using an exponential function to form the cost multipliers for each patient characteristic

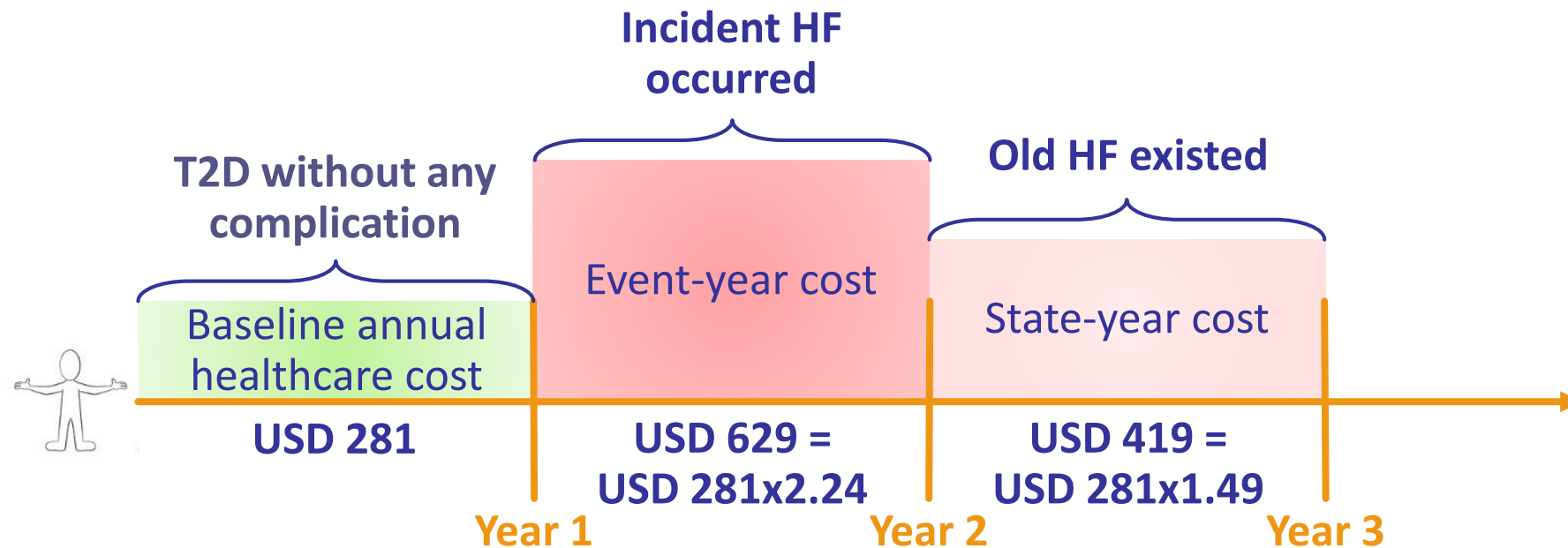
Results

Variable	Multiplier	95% CI	
Baseline annual health care cost (2017 U.S. \$), mean (95% CI)	281.21	279.25	283.21
Age at T2D diagnosis (years) (ref. <50)			
50–59	1.19	1.19	1.20
60–69	1.43	1.42	1.44
≥70	1.68	1.67	1.69
Diabetes duration (years) (ref. 1–4)			
≥5	0.85	0.84	0.85
Female (ref. male)	1.06	1.06	1.06
Comorbidity (ref. none)			
Hypertension	1.21	1.21	1.22
Hyperlipidemia	1.07	1.06	1.07
Liver disease	0.98	0.98	0.98
Cancer	1.04	1.04	1.05
Depression	1.81	1.80	1.82
Oral antidiabetic drug exposure (ref. none)	1.78	1.78	1.79
Injectable antidiabetic drug exposure (ref. none)	1.83	1.82	1.84

Variable	Multiplier	95% CI	
Complication (event year) (ref. none)			
Stroke	2.95	2.92	2.98
Myocardial infarction	2.53	2.48	2.58
Ischemic heart disease	2.51	2.49	2.53
Heart failure	2.24	2.21	2.27
Arteriosclerotic CVD	1.80	1.62	2.01
Arrhythmia	2.04	2.01	2.06
Nephropathy	1.49	1.48	1.50
Retinopathy	1.37	1.36	1.37
Neuropathy	1.41	1.40	1.41
Peripheral vascular disease	1.55	1.54	1.56
Hospitalized diabetic ketoacidosis	1.90	1.87	1.93
Hospitalized HHS	1.72	1.69	1.76
Hospitalized hypoglycemia	1.90	1.88	1.92
Complication (state year) (ref. none)			
Stroke	1.44	1.43	1.45
Myocardial infarction	1.18	1.16	1.20
Ischemic heart disease	1.32	1.31	1.33
Heart failure	1.49	1.47	1.51
Arteriosclerotic CVD	1.15	1.04	1.26
Arrhythmia	1.14	1.13	1.15
Nephropathy	1.18	1.18	1.19
Retinopathy	1.13	1.13	1.13
Neuropathy	1.13	1.13	1.13
Peripheral vascular disease	1.14	1.14	1.15
Death (ref. none)			
Fatal CVD	20.49	19.93	21.05
Other-cause death	16.42	16.20	16.64


Example of applying healthcare cost analysis results

- Baseline annual healthcare cost for a T2D man aged 45 years with 2 years of diabetes duration, and without comorbidities, complications, and antidiabetic treatments: USD 281 (in 2017 USD)
- Cost multiplier for heart failure (HF) in the event year: 2.24
- Cost multiplier for HF in state years: 1.49



Valuing health states of people with T2D

Valuing health states of people with type 2 diabetes: Analyses of the nationwide representative linked databases

Shihchen Kuo¹, Chun-Ting Yang^{2†}, Hsuan-Ying Chen^{2†}, Huang-Tz Ou^{2,3,4*} 

J Diabetes Investig 2021 Sep;12(9):1749-1758.

Research design, data source, and analytic methods

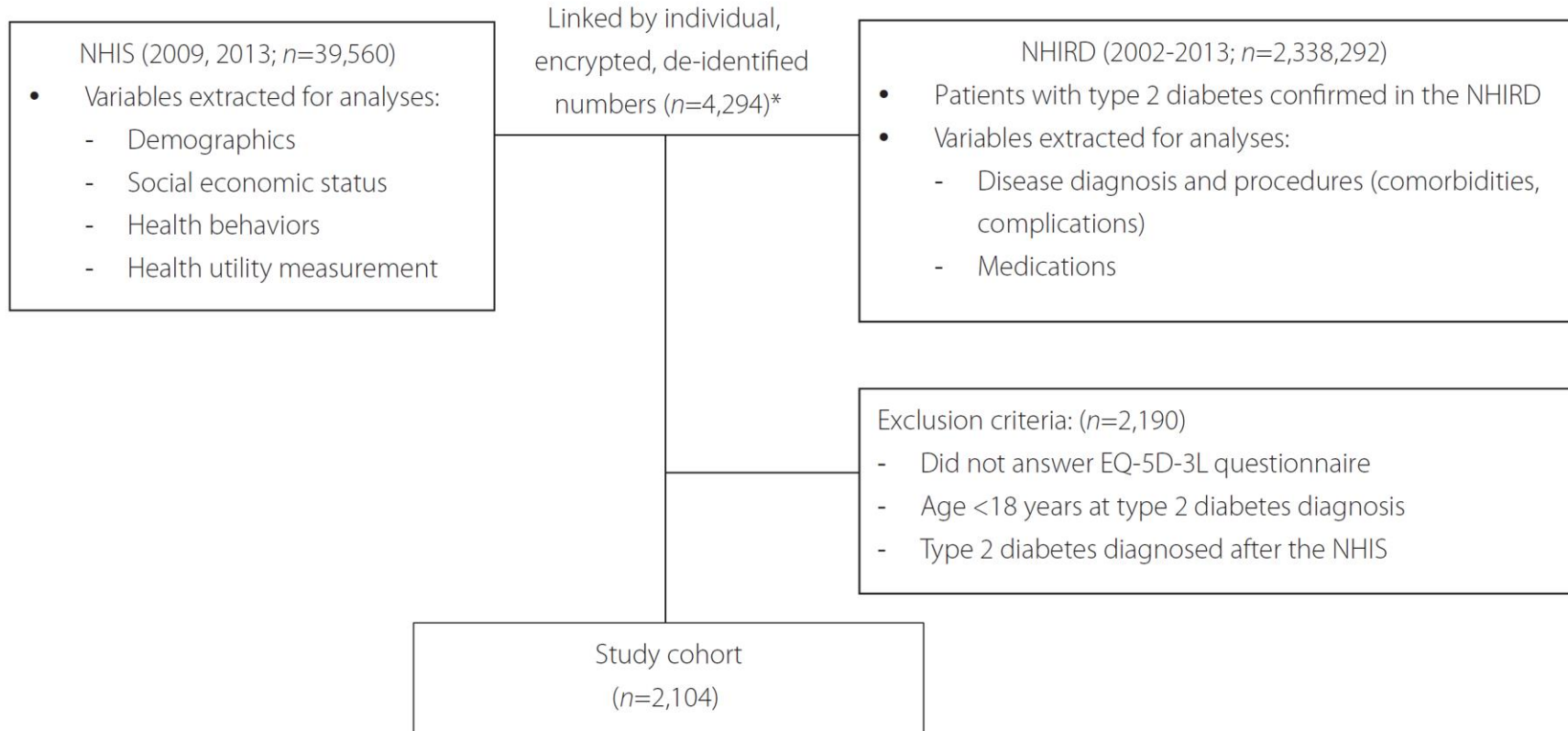


Figure 1 | Illustration of the database linking and study cohort identification. *The National Health Insurance Survey (NHIS) examines health status, health behaviors and healthcare utilization in a nationally representative sample of the entire population in Taiwan every 4 years since 2001. The National Health Insurance Research Database (NHIRD) comprises individual longitudinal medical records and claims from almost 23 million beneficiaries in Taiwan’s National Health Insurance program. The estimated prevalence of diagnosed type 2 diabetes in people aged 20–79 years during 2009–2014 in Taiwan was approximately 8.4–10.1% (*J Formos Med Assoc* 2019;118[Suppl 2]:S66–S73). EQ-5D-3L, EuroQol-5 dimensions-3 levels.

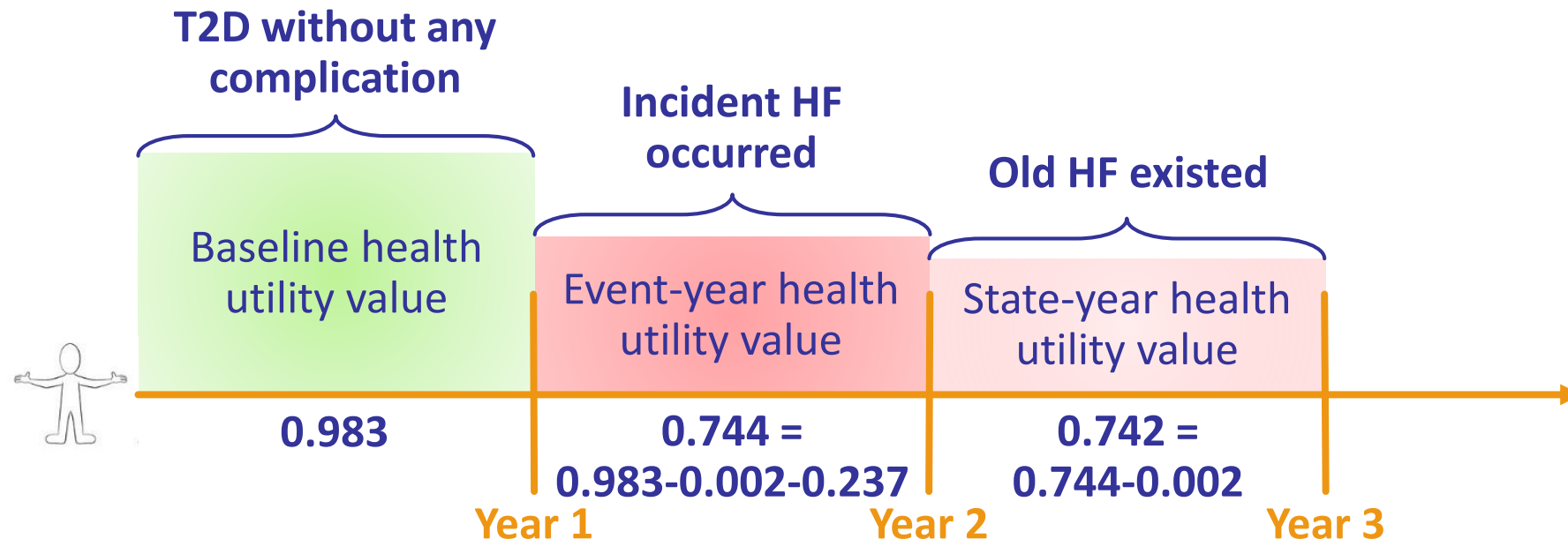
Results

Patient characteristics	OLS	
	Estimated coefficients	Standard errors
Intercept	0.983	0.014
Sex (ref: male)		
Female	−0.038	0.012
Age, years (per year greater; centered at 62)	−0.002	0.001
Marital status (ref.: single/married)		
Divorced	−0.034	0.025
Widowed	−0.039	0.018
Employment status (ref: ever/currently employed)		
Never worked	−0.043	0.028
Monthly household income (ref.: ≥NT\$70,000)		
NT\$30,000–NT\$69,000	−0.023	0.016
<NT\$30,000	−0.074	0.016
BMI, kg/m ² (ref.: BMI ≥18.5)		
Underweight (BMI <18.5)	−0.184	0.041
Comorbidities (ref.: no comorbidity)		
Depression	−0.101	0.017
Connective tissue disease	−0.067	0.020

Patient characteristics	OLS	
	Estimated coefficients	Standard errors
Diabetes-related complications (ref.: no complication)		
Cerebrovascular disease		
TIA or stroke	−0.078	0.022
Stroke with residual deficits	−0.266	0.041
Coronary heart disease		
PTCA or CABG	−0.093	0.048
Other coronary heart disease	−0.185	0.076
Heart failure	−0.237	0.030
Neuropathy		
Other neuropathy	−0.043	0.026
Polyneuropathy	−0.055	0.033
Diabetic neuropathy	−0.062	0.018
ESRD with dialysis/kidney transplant	−0.148	0.050
Amputation	−0.288	0.079
Diabetes treatment (ref.: none or oral therapy only)		
Injectable therapy	−0.058	0.020

Example of applying health utility analysis results

- Health utility value for a 62-year-old man with T2D, a monthly household income of NTD 70,000, a BMI of 25 kg/m², and being married, currently worked, treated with only oral glucose-lowering therapy, and without comorbidities and diabetes complications: 0.983
- Penalty of health utility for aging (per year greater; centered at 62): -0.002
- Penalty of health utility for developing HF: -0.237



Recap

- Characteristics of the most suitable data source for estimating healthcare costs and health utilities to support health economic analysis in real-world settings:
 - ✓ Accurate and valid
 - ✓ Country-specific and population-specific
 - ✓ Broadly applicable and population-based (representativeness)
 - ✓ Large sample size with variations in demographic and socioeconomic characteristics, comorbidities, complications, and treatments (diverseness)
 - ✓ Longitudinal data with sufficient follow-up period
- Statistical methods for analyzing healthcare costs and health utilities:
 - ✓ Crude/unadjusted data analysis (mean, median)
 - ✓ Regression analysis

Thank you!

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How to conduct cost-effectiveness studies using real-world data: methodologies, interpretations and implications

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Outline

- Roadmap of conducting RWD-based CEAs
- How RWD-based CEAs support decision-making and facilitate resource allocation?
- Clinical and policy implications from RWD-based CEAs
- Recap

Roadmap of conducting RWD-based CEAs

Step 1: Identification of “**drug candidates**” for optimizing their usage

Step 2: Construction and validation of **localized and clinical-oriented** economic model

Step 3: Input of **effectiveness** parameters derived from NHIRD

Step 4: Input of **healthcare costs and health utility** parameters derived from NHIRD

Step 5: Economic simulation and **result interpretation**

Roadmap of conducting RWD-based CEAs

Step 1: identification of “drug candidates” for optimizing their usage

- What are the characteristics of potential drug candidates?

Drug candidates under real-world practice:¹

① Value-based assessment²

✓ **With less benefits** (i.e., unsafe, ineffective, costly, or replaceable)

✓ **With more benefits** (i.e., more effective)

② Utilization scanning and review³

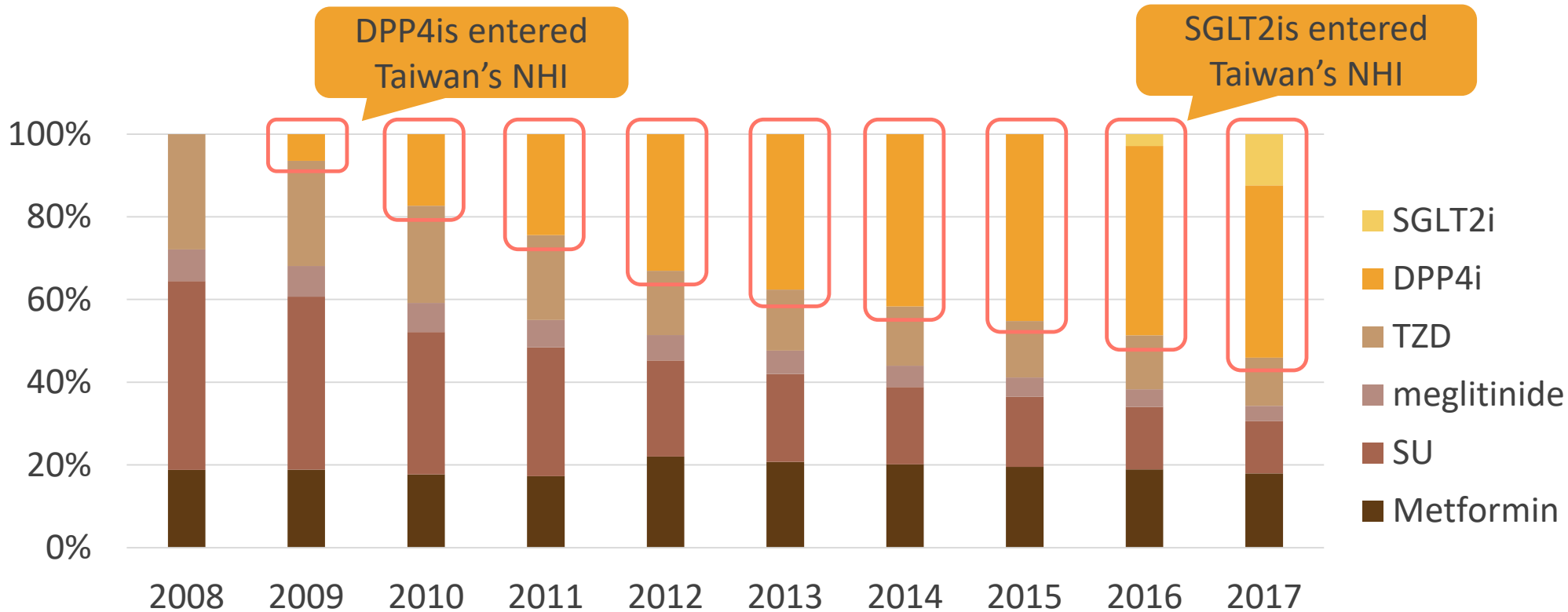
1.Int J Technol Assess Health Care. 2020 Jun;36(3):262-269.

2.Choosing wisely in Canada.

3.Pharmaceutical Benefits Advisory Committee in Australia.

Roadmap of conducting RWD-based CEAs

Step 1: identification of “drug candidates” for optimizing their usage



- ① **Increasing utilization/expenditures of new generation oral GLAs** (i.e., DPP4is and SGLT2is) over time since their entry of NHI
- ② New generation GLAs accounted for **over 50% of total oral GLA expenditure** in 2017

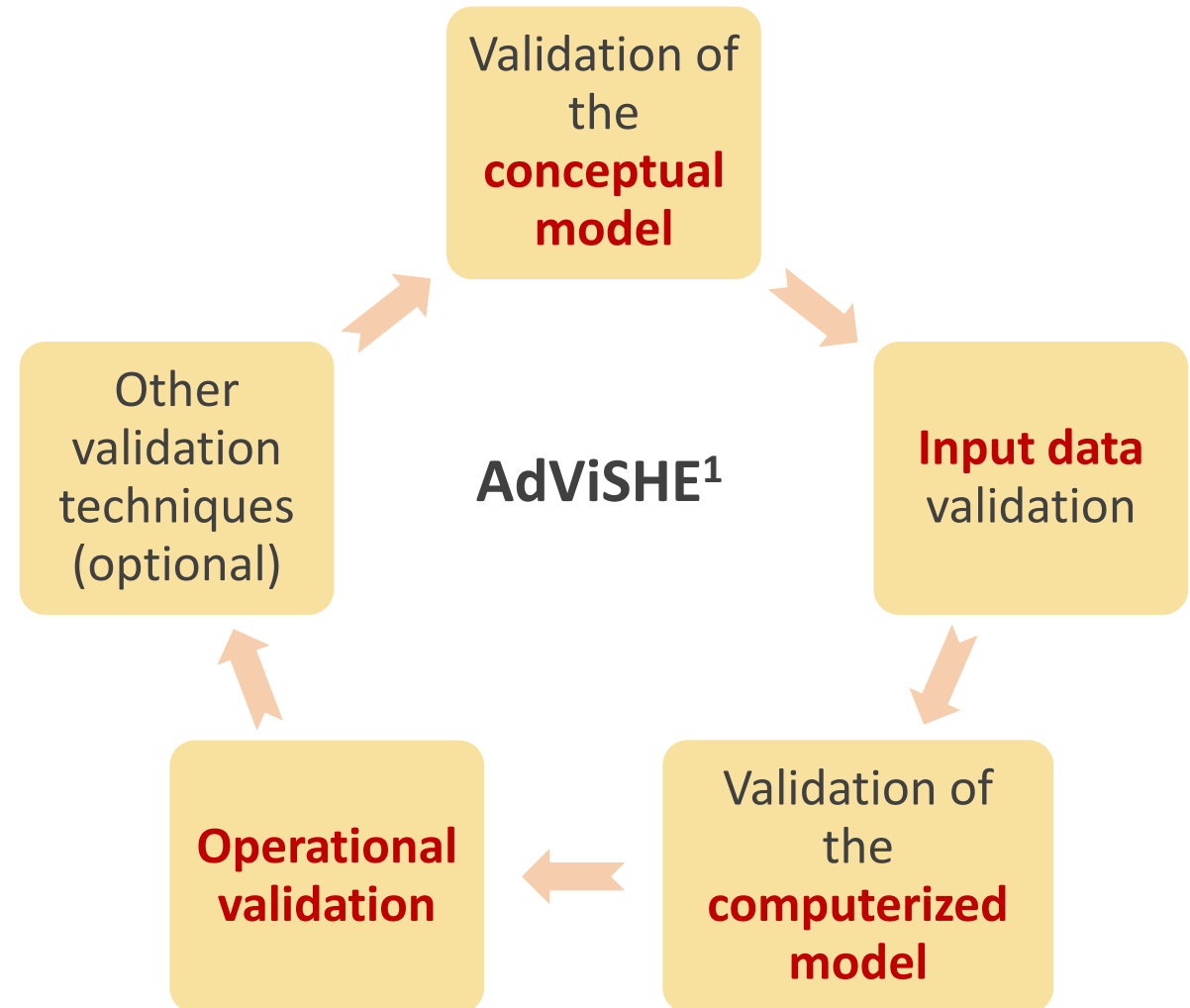
Roadmap of conducting RWD-based CEAs

Step 2: Construction and validation of localized and clinical-oriented economic model

- Trade off between **model validation** and **scarce resources** (i.e., time and money) in real-world setting¹

⇒ **Practical tool for model validation without large time or money consumption:**

Assessment of the Validation Status of Health-Economic decision models (AdViSHE)¹



Roadmap of conducting RWD-based CEAs

Step 2: Construction and validation of localized and clinical-oriented economic model

Construction

- ① Consider the **disease progression** of T2D in Taiwan
- ② Identify the **clinical meaningful** health states of T2D
- ③ **Adapt existing model structure** for reflecting the local and clinical situation in Taiwan

Macrovascular diseases¹

(mean 5 years after T2D diagnosis)



Stroke/ Myocardial infarction/ Heart failure/
cardiovascular death/ All-cause death¹

(event-year costs: USD 7,166 to 14,642)

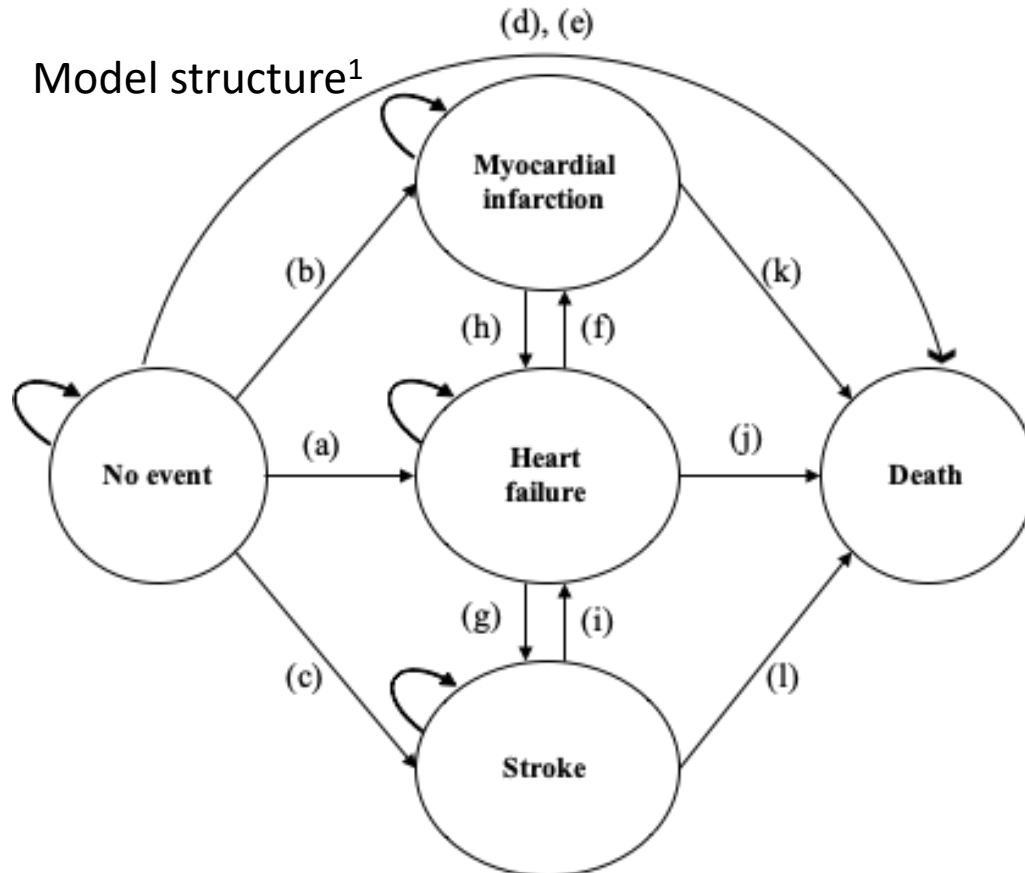


United Kingdom Prospective Diabetes Study (UKPDS),
CORE model, Cardiff model

Roadmap of conducting RWD-based CEA

Step 2: Construction and validation of localized and clinical-oriented economic model

Model structure¹



Validation using AdViSHE tool²

- ① Validation of the conceptual model:
face validity by clinicians and cross validity with other models
- ② Input data validation:
ensure that input real-world data is valid
- ③ Validation of the computerized model:
test the model with external data (e.g., literature review) and also extreme values
- ④ Operational validation:
validate the model outcomes after input our data
- ⑤ Other validation techniques (optional)

1. Diabetes Obes Metab. 2022 Jul;24(7):1328-1337.

2. Pharmacoeconomics. 2016 Apr;34(4):349-361.

How RWD-based CEAs support decision-making and facilitate resource allocation?

- Strengths of conducting RWD-based CEAs

Unanswered questions

Diverse patient population

Focus on **clinically important** problem

Narrow down and define an answerable research question

Whether **CV benefits** of SGLT2is could make them an **economically reasonable alternative**, compared with DPP4is, among Taiwanese T2D patients with established **cardiovascular diseases (CVDs)**?

Model and study cohorts' assumptions

- How we make assumptions on study model and SGLT2i and DPP4i users' baseline characteristics (e.g., demographics or disease status)?

Reflect to research question

Availability of data source

Previous studies and preliminary research

Model

- Yearly cycle
- Time horizon: 10 years
- Discounting rate: 3% for effectiveness and cost

Patients' characteristic at cohort entry¹

- 55 years old with T2D duration of 8 years
- With CVD history

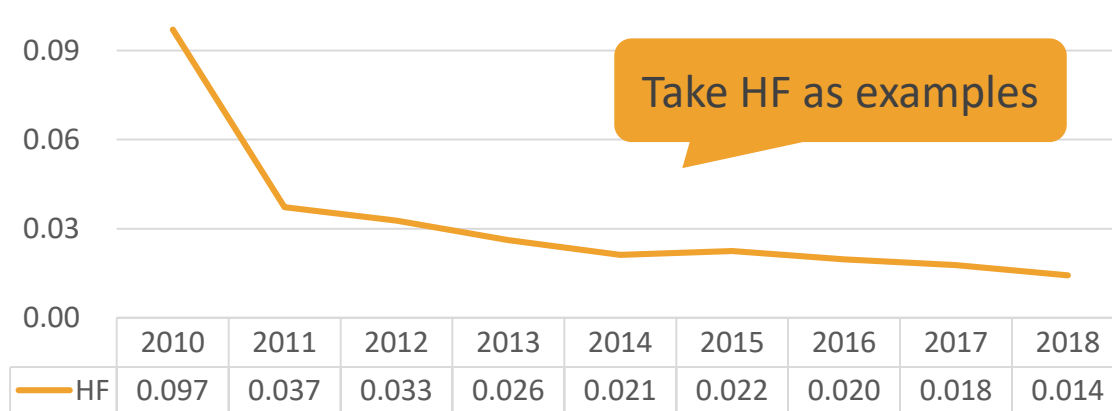
Roadmap of conducting RWD-based CEAs

Step 3: Input of effectiveness parameters derived from NHIRD

- Estimate the treatment arms' yearly transition probabilities (TPs) between health states over time in NHIRD

DPP4is arm

- Identify new DPP4i users in 2010 and followed up them until 2018



SGLT2is arm

Analytical issues of new technology (e.g., SGLT2is) in claims data

- Limited follow-up period in NHIRD
- Absence of time-varying TPs

Solutions ⇨ assume constant value after the last estimate of TPs (?)

Problems ⇨ make CEA outcomes uncertain

Roadmap of conducting RWD-based CEAs

Step 4: Input of healthcare costs and health utility parameters derived from NHIRD

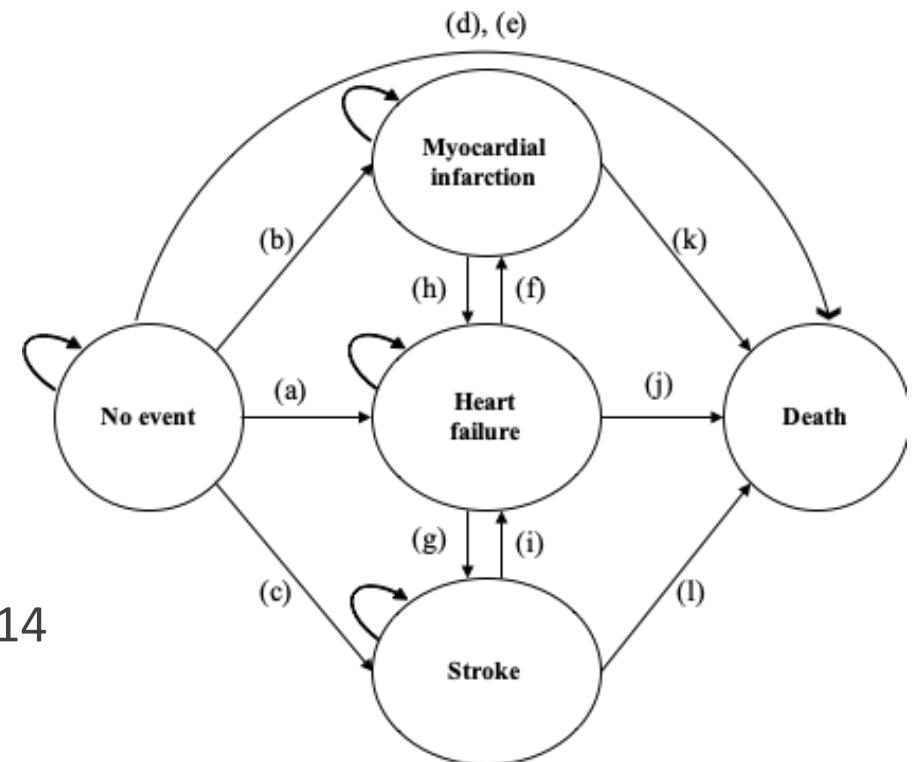
- Apply the **cost multipliers¹/ utility penalty² of given health state** to obtain the adjusted healthcare costs and health utility parameters
- Take pathway (a) as example

Healthcare costs in event year: **USD 624*****2.24**=USD 1,397.76



Health utility in event year: **0.798**-**0.237**=0.561

Annual drug acquisition costs: SGLT2is: USD 384; DPP4is: USD 214



1. Diabetes Care. 2020 Aug;43(8):1732-1740.

2. J Diabetes Investig. 2021 Sep;12(9):1749-1758.

Roadmap of conducting RWD-based CEAs

Step 5: Economic simulation and result interpretation

- Base-case analysis:
 - ✓ Cohort: T2D with CVD history
 - ✓ Time horizon: 10 years
 - ✓ Perspective: healthcare sectors
- One-way sensitivity analysis
- Probabilistic sensitivity analysis (PSA)
- Willingness-to-pay: USD 30,038 to 90,114 (one to three times of Taiwan's gross domestic product [GDP] per capita)
- Software: TreeAge

Values for conducting sensitivity analyses

■ **Scenario analysis**

Prolong or shorten time horizon:

Evaluate impact of length of medication use on CEA results

■ **Subgroup analyses**

Target the patients who have been excluded from/under-presented in trials:

Evaluate cost-effectiveness of SGLT2is versus DPP4is among specific populations

■ **Break-even point analysis**

Vary annual drug acquisition costs by 10-50%:

Determine value-based pricing of SGLT2is

Roadmap of conducting RWD-based CEAs

Step 5: Economic simulation and result interpretation

	Quality adjusted life years (QALYs)			Costs (USD)			Incremental cost-effectiveness ratio (USD per QALY gained)	Probability of being highly cost-effective for SGLT2is vs. DPP4is in PSA
	SGLT2is	DPP4is	Incremental	SGLT2is	DPP4is	Incremental		
<i>Base-case analyses (10-year simulation)</i>								
T2D with CVD history	6.492	6.294	0.198	11,306	10,661	644	3,244.07	100.0%

Interpretations:

Over a 10-year simulation based on real-world data, the use of SGLT2is versus DPP4is was highly cost-effective among T2D patients with CVD history.

Willingness-to-pay: USD 30,038 to 90,114 (one to three times of Taiwan's GDP per capita)

Roadmap of conducting RWD-based CEAs

Step 5: Economic simulation and result interpretation

	Quality adjusted life years (QALYs)			Costs (USD)			Incremental cost-effectiveness ratio (USD per QALY gained)	Probability of being highly cost-effective for SGLT2is vs. DPP4is in PSA
	SGLT2is	DPP4is	Incremental	SGLT2is	DPP4is	Incremental		
<i>Base-case analyses (10-year simulation)</i>								
T2D with CVD history							3,244.07	100.0%
<i>Scenario analyses</i>								
T2D with CVD history								
1-year simulation							7,659.27	85.6%
2-year simulation							4,383.65	99.0%
3-year simulation							4,281.99	99.8%
5-year simulation							3,797.91	100.0%
20-year simulation							2,700.90	100.0%
30-year simulation							2,541.73	100.0%

Interpretations:
Longer length of SGLT2i use, a greater economic benefit it will generate.

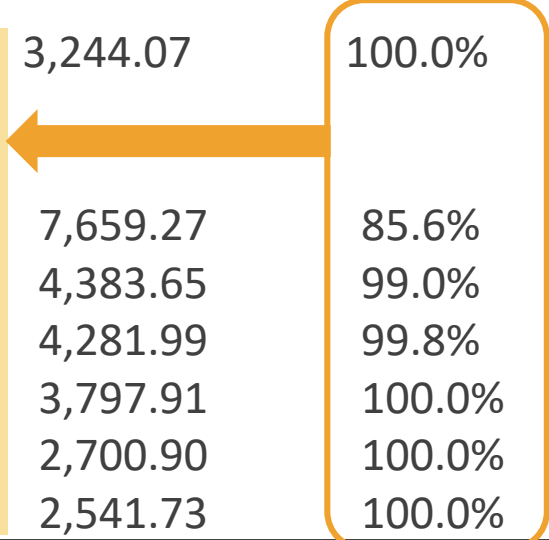
Willingness-to-pay: USD 30,038 to 90,114 (one to three times of Taiwan's GDP per capita)

Roadmap of conducting RWD-based CEAs

Step 5: Economic simulation and result interpretation

	Quality adjusted life years (QALYs)			Costs (USD)			Incremental cost-effectiveness ratio (USD per QALY gained)	Probability of being highly cost-effective for SGLT2is vs. DPP4is in PSA
	SGLT2is	DPP4is	Incremental	SGLT2is	DPP4is	Incremental		
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30-year simulation							2,541.73	100.0%

Interpretations:
SGLT2i therapies were a highly cost-effective alternatives to DPP4i therapies with consideration of the data uncertainty across analyses.

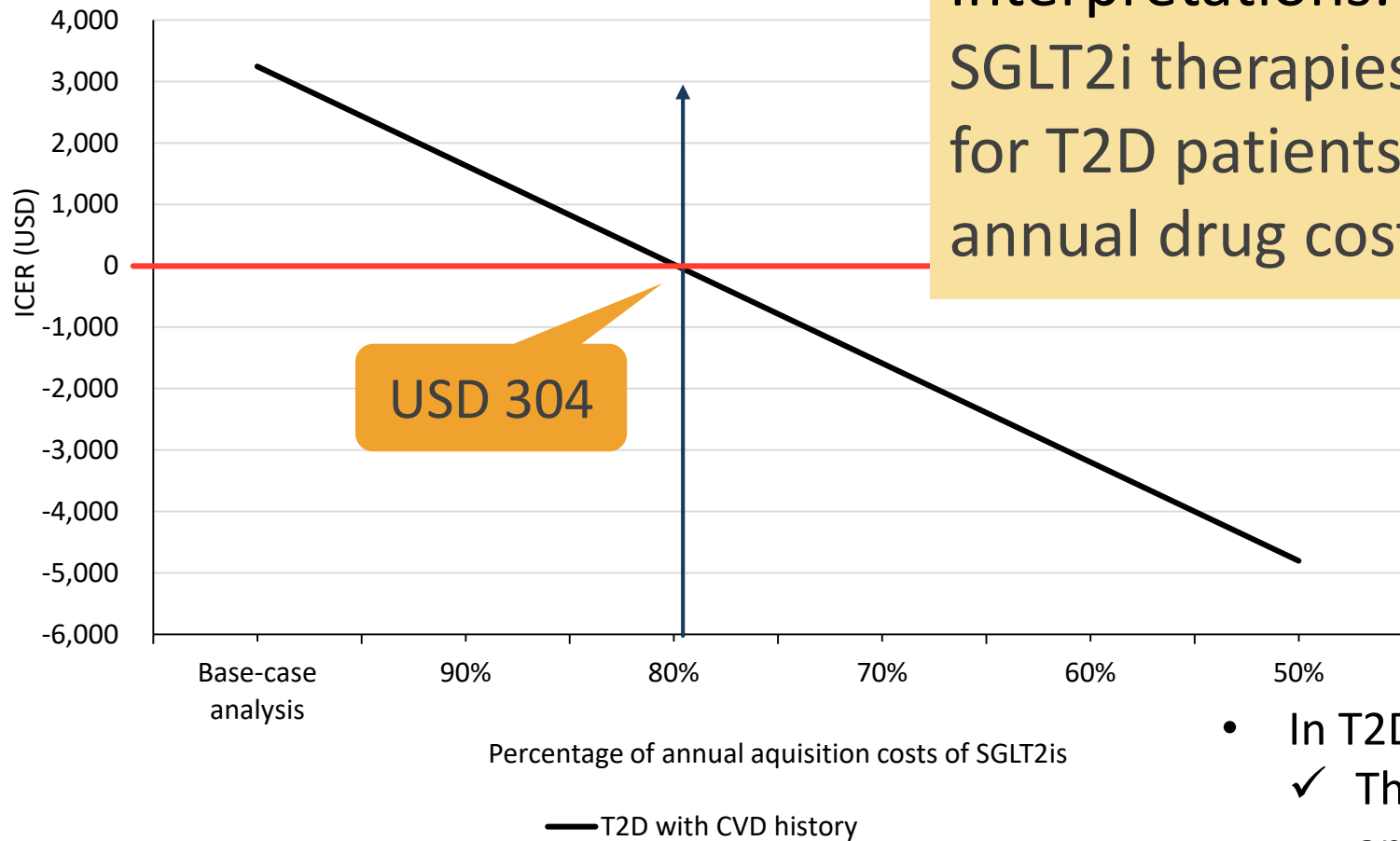


Willingness-to-pay: USD 30,038 to 90,114 (one to three times of Taiwan's GDP per capita)

Roadmap of conducting RWD-based CEAs

Step 5: Economic simulation and result interpretation

Interpretations:
SGLT2i therapies became cost-saving options for T2D patients with CVD history, when the annual drug costs was lower than USD 304.



- In T2D patients with CVD history
 - ✓ The break-even point went to around **79%** of annual drug costs for SGLT2is

Clinical and policy implications from RWD-based CEAs

- Clinical implications
 - ✓ Promote new technology use (e.g., SGLT2i therapies)
 - ✓ Prioritize new technology (e.g., SGLT2i therapies) for patient populations who may benefit most clinically and economically
- Policy implications
 - ✓ Tailor reimbursement policy for new technology (e.g., SGLT2i therapies)
 - ✓ Determine value-based pricing of new technology (e.g., SGLT2i therapies)

Recap

- Step-by-step approach for conducting RWD-based CEAs
- Strengths of using RWD to conduct CEAs
 - ✓ Answer unanswered questions/ focus on specific patient population and clinically important problem
- Values of performing sensitivity analyses in RWD-based CEAs
 - ✓ Scenario analysis/ subgroup analysis/ break-even point analysis
- Findings of RWD-based CEAs to inform clinical and policy decision-makings
 - ✓ From clinical perspective: promote and prioritize drug use
 - ✓ From policy perspective: tailor reimbursement policy/ determine value-based pricing

Thank you!

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Questions for discussion

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Chun-Ting Yang, MS.
Shihchen Kuo, RPh, PhD
Zi-Yang Peng, MS.

Exercise

Huang-Tz Ou, PhD.

Chun-Ting Yang, MS.

Shihchen Kuo, RPh, PhD

Zi-Yang Peng, MS.

September 20, 2022 at ISPOR Asia Pacific 2022

Estimate treatment effectiveness and safety for RWD-based CEAs

- What characteristics (key aspects) of RWD sources should be considered while evaluating the quality of RWD? ¹
 - Who collected the data (e.g., physicians or administrators...)?
 - How and why is the data being collected (e.g., prospectively or retrospectively)
 - For how long has data been collected?
 - Has the data source been used for research in the past?
 - What validation checking is undertaken during and after data collection?

- How to account for varying treatment effect beyond time periods of clinical studies that will be used as effectiveness parameters for long-term simulation in CEAs? ^{2,3}

1: Pharmacoepidemiol Drug Saf. 2020 Oct;29(10):1316-1318.

2: J Med Econ. 2019 Mar;22(3):205-214. 3: BMJMED 2022;1:e000094.

Estimating healthcare costs and health utilities for RWD-based CEAs

- What are the characteristics of the most suitable data source for estimating healthcare costs and health utilities to support real-world health economic analysis?
- What statistical methods could be used to analyze healthcare cost and health utility data?

Conducting RWD-based CEAs

- How does AdViSHE tool help to validate the economic model? Please explain briefly.
- How do we address the uncertainty of not including other health states which may be of clinical interest?
 - Other health states such as kidney diseases or drug-related hypoglycemia were not specified in the CVD-driven modeling CEAs (in our example)
- How can the results of RWD-based CEAs be used to support decision-making and facilitate resource allocation? Any real-world cases
 - e.g., clinical treatment selection, reimbursement policy decision

Thanks for your attention!

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