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Real-World–Based Cost-Effectiveness of Lipid-Lowering Therapies for ASCVD Patients With High CV Risk in Taiwan

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INTRODUCTION

Cholesterol management is a cornerstone in the prevention of CV event

- Estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths. Of these deaths, 85% are due to heart attack and stroke.
- Previous studies have demonstrated lipid-lowering therapy is crucial for high-risk patients

Unmet medical need for statin intolerance and uncontrolled hypercholesterolemia patients with high CV risk

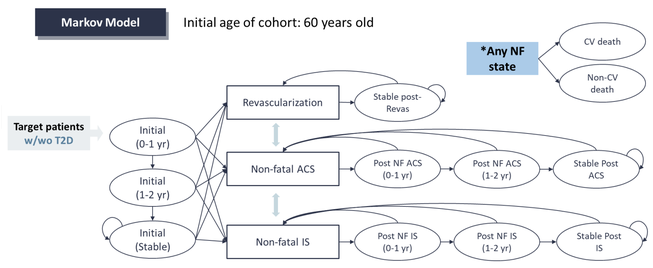
- In 2021, **29.11%** of patients with major CV event in prior 1 year and had LDL-c levels ≥100 mg/dL, with **8.65%** of them having LDL-c levels ≥135 mg/dL.
- A Real-World Data-Driven microsimulation model is important for Asian population

OBJECTIVE

Developing a **Real-World Data-Driven** microsimulation model for CVD patients to evaluate the long-term cost and effectiveness of different lipid-lowering therapies.

METHODS

A **lifetime microsimulation model** was developed based on the baseline characteristics of real-world cohort obtained from the National Health Insurance Research Database (NHIRD) in 2020-2022.



PICOs

Patient | Patient had major CV event in **prior 0-12 months**

Intervention & Comparator

High-intensity statin [Rosuvastatin 20-40 mg or Atorvastatin 40-80mg] **(hStatin)**
Ezetimibe 10 mg QD + high-intensity statin **(hS/Eze)**
PSCK9-i + high-intensity stain **(hS/P)**
PSCK9-i + Ezetimibe + high-intensity stain **(hS/Eze/P)**
Inclisiran + high-intensity stain **(hS/Inc)** [Out-of-pocket]

Outcomes | **Perspective:** healthcare payer | **Time Horizon:** Lifetime

- Life-yeas, Quality-adjusted Life-years, Direct medical costs, Incremental Cost-Effectiveness Ratio (ICER),
- Major CV event rate in 1 year, Non-fatal CV event in 1 year, CV death rate in 1 year

Treatment Effect

- The relative LDL-C reduction (table 3) was driven from published NMA study.
- **Formular to estimate the risk of CV events:**

Reference group (hS group)	1-EXP(-((-DM %*LN(1-CV event rate))-((1-DM %)*LN(1-CV event rate)))^(1+annual risk of CV event – NF event rate)^(model initial age - (DM %* initial age of cohort +(1-DM %)*initial age of cohort)*(RR of treatment effect^(mean LDL-C level of cohort (LDL-C >=100 mg/dL) *0.0259 - baseline LDL-C level of cohort (mg/dL) *0.0259))
Treatment group	1-EXP(-(-LN(1- transition probability of reference group)*RR of study drug^(baseline LDL-C level of cohort (mg/dL)*0.0259) – ((1- % of LDL-C reduction caused by study drug)* Target LDL-C level for treatment [set as <100 mg/dL]*0.0259))

Table 1. Baseline characteristic of patient with major CV event in prior 0-12 months

	Without DM (n=16,458)	With DM (n=14,098)
	mean (SD)	mean (SD)
Demographics		
Age	63.70 (13.22)	67.36 (11.13)
Male	12,870 (78.2)	9,742 (69.1)
Insured monthly salary, NT$		
<24000	3,945 (23.97)	3,583 (25.41)
24001-48200	10,031 (60.95)	8,709 (61.77)
48201-96600	1,960 (11.91)	1,460 (10.36)
>96601	522 (3.17)	346 (2.45)
Biological data		
LDL-C, mg/dL	112.90 (36.79)	94.46 (32.67)
HDL-C, mg/dL	44.25 (12.33)	42.86 (12.28)
TC, mg/dL	177.60 (41.57)	160.77 (39.86)
TG, mg/dL	139.47 (96.57)	159.55 (105.3)
AC, mg/dL	125.13 (50.17)	164.63 (67.81)
HbA1c, %	6.09 (1.26)	7.44 (1.61)
GPT, U/L	42.29 (113.08)	35.13 (97.71)
GOT, U/L	63.26 (224.11)	47.89 (200.78)
eGFR, mL/min/1.73m^2	76.55 (26.9)	63.49 (31.94)
BUN, mg/dL	21.65 (14.6)	29.20 (20.93)

	Without DM (n=16,45	With DM (n=14,098
	n (%)	n (%)
Comorbidity (yes)		
Hypertension	7,782 (47.28)	10,238 (72.62)
Hyperlipidemia	4,653 (28.27)	8,006 (56.79)
IHD	5,664 (34.41)	6,711 (47.6)
MI	737 (4.48)	892 (6.33)
ACS	1,846 (11.22)	1,799 (12.76)
Angina	1,578 (9.59)	1,502 (10.65)
HF	1,531 (9.3)	2,186 (15.51)
AF	618 (3.76)	657 (4.66)
Ischemic strokes	356 (2.16)	605 (4.29)
Hemorrhagic stroke	70 (0.43)	72 (0.51)
Transient ischemic attack	322 (1.96)	383 (2.72)
Stroke subsquence	192 (1.17)	310 (2.2)
COPD	791 (4.81)	706 (5.01)
Asthma	640 (3.89)	653 (4.63)
CKD stage 1	1,398 (8.49)	3,371 (23.91)
CKD stage 3	637 (3.87)	1,580 (11.21)
ESRD	625 (3.8)	1,648 (11.69)
Dialysis	136 (0.83)	420 (2.98)
Renal transplantation	21 (0.13)	32 (0.23)
Diabetic retinopathy	379 (2.3)	1,708 (12.12)
Diabetic neuropathy	11 (0.07)	1,223 (8.67)
Diabetic nephropathy	14 (0.09)	4,161 (29.51)
PVD	173 (1.05)	618 (4.38)
Cataract	1,247 (7.58)	2,739 (19.43)

	Without DM (n=16,45	With DM (n=14,098
	n (%)	n (%)
Current lipid-lowering agents (yes)		
Statin	14,770 (89.74)	12,519 (88.8)
High-intensity statin	6,574 (39.94)	4,360 (30.93)
Ezetimibe	3,990 (24.24)	3,475 (24.65)
PCSK9-i	23 (0.14)	11 (0.08)
Medication in prior 1 year (yes)		
Statin	5,182 (31.49)	9,277 (65.8)
Ezetimibe	732 (4.45)	1,433 (10.16)
Other lipid-lowering agents	5,801 (35.25)	10,623 (75.35)
OADs	0 (0)	12,589 (89.3)
Insulin	0 (0)	2,905 (20.61)
ACEI	530 (3.22)	835 (5.92)
ARB	6,141 (37.31)	9,098 (64.53)
Beta-blockers	5,470 (33.24)	7,357 (52.18)
Calcium-channel Blockers	6,003 (36.47)	7,948 (56.38)
Thiazides	263 (1.6)	418 (2.96)
Diuretics	974 (5.92)	2,113 (14.99)
Nitrates	2,710 (16.47)	3,634 (25.78)
Other antihypertensive drugs	1,018 (6.19)	1,832 (12.99)
Antiplatelet	6,074 (36.91)	8,692 (61.65)
Anticoagulants	533 (3.24)	639 (4.53)
Heparin	117 (0.71)	186 (1.32)

Table 2. CV event costs and follow-up cost of non-fatal event

Unit: €	Event cost and follow-up cost					
	n	mean	SE	median	Q1	Q3
Event-based cost						
NF-MI	2,114	2,445.17	71.95	2,022.19	1,480.66	2,506.60
UA	2,931	1,345.49	12.59	1,551.69	848.43	1,596.74
Revascularization	5,162	7,511.69	101.39	4,444.77	3,768.06	11,166.03
NF-IS	18,181	2,092.01	19.12	1,281.09	892.51	2,203.03
CV death	4,701	7,351.57	253.91	390.54	67.20	5,622.14
Follow-up cost: 1y						
MI	943	2,224.34	175.63	409.40	130.11	1,213.49
UA	714	1,082.30	95.84	247.11	70.11	741.94
Revascularization	429	11,021.32	565.00	6,315.14	4,034.80	13,194.17
IS	15,214	1,468.25	21.10	520.14	188.89	1,542.71
Follow-up cost: 2y						
MI	335	972.67	147.86	323.14	169.49	707.66
UA	280	693.30	62.57	287.43	135.83	771.99
Revascularization	264	9,187.45	747.23	4,889.23	3,773.87	9,136.99
IS	6,372	839.96	20.79	355.04	160.77	808.09

Table 3. % change relative to stain (as background therapy) from the NMA study

Versus	Mean difference	(95% CI)
Ezetimibe 10mg QD	-25.21%	(-28.87 – -21.55)
Alirocumab 75mg Q2W	-53.17%	(-56.61 - -49.73)
Evoloucumab 140mg Q2W	-64.55%	(-68.37 - -62.51)
PCSK9-I + Ezetimibe	-69.2%	
Inclisiran 300mg Q3M to Q6M	-50.17%	(-55.01 - -45.34)
Bempedoic acid 180mg QD	-8.36%	(-23.78 - -12.97)
Ezetimibe/Bempedoic	-37.90%	(-46.69 - -29.11)

RESULTS

Table 5. Base-case results

	Cost(€)	△Cost	LY	△LY	QALY	△QALY	ICER per QALY gained	GDP per capita in 2024
High-intensity Statin	67,085		19.01		9.33			
hStatin/Ezetimibe	62,318	-4,767	19.96	0.949	9.69	0.359	**Dominance**	
hStatin/Ezetimibe/PCSK9-i	78,736	11,651	21.80	2.791	10.20	0.869	**13,412**	0.43
hStatin/PCSK9-i	97,272	30,188	22.43	3.424	10.44	1.113	**27,125**	0.87
hStatin/Inclrisran	99,576	32,492	22.04	3.034	10.27	0.943	**34,469**	1.10

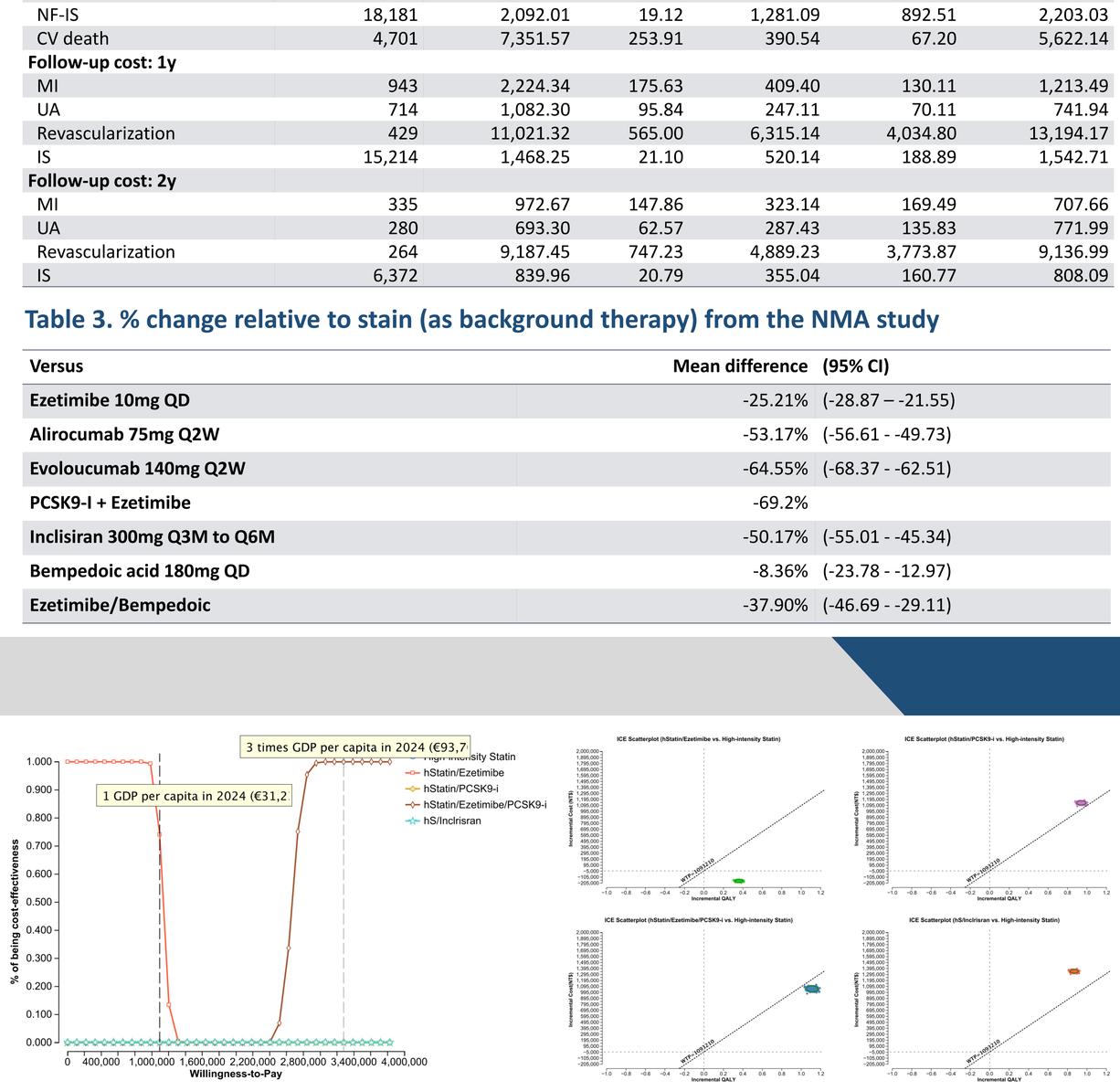


Figure 1. Cost-Effectiveness Acceptability Cure (CEAC) and CE scatter plot

CONCLUSIONS

- Under the existing data, aggressive lipid-lower therapies may be deemed a **cost-effective option (~1.4*GDP per capita)** for patients who, despite receiving statin, **fail to attain the target LDL-C levels (specifically, LDL-C ≥100 mg/dL)**.
- All results from the RWD-based model reported higher ICER values than those from the RCT-based model.
- RWD could be used while developing a CE model and demonstrate the value of combination therapy.

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CONFLICTS OF INTEREST

No conflict of interest to be disclosed.

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