Association of Temporal change in Body Mass Index with Sudden Cardiac Arrest in Diabetes Mellitus

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## COI Disclosure

Name of First Author:
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Background

- Body mass index (BMI) is the most common metric to assess individual's degree of obesity.

- Previous landmark studies on BMI have identified J-shaped association between BMI and mortality.

- Underweight and obesity are both associated with increased risk of overall mortality.

YG Kim et al. *J Clin Med*. 2023.12, 1045.

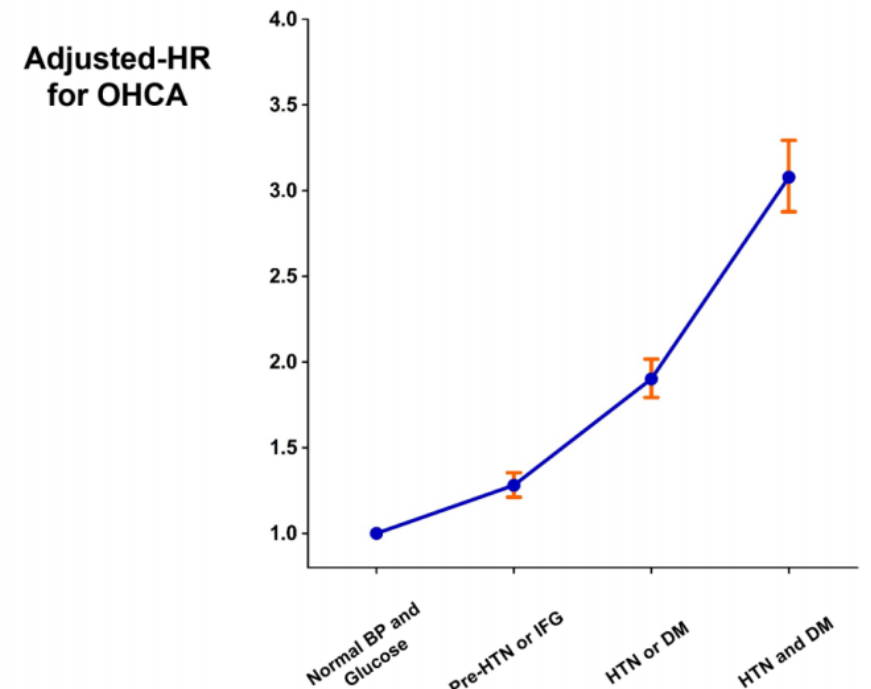Calle EE et al. *N Engl J Med*. 1999;341:1097-1105.
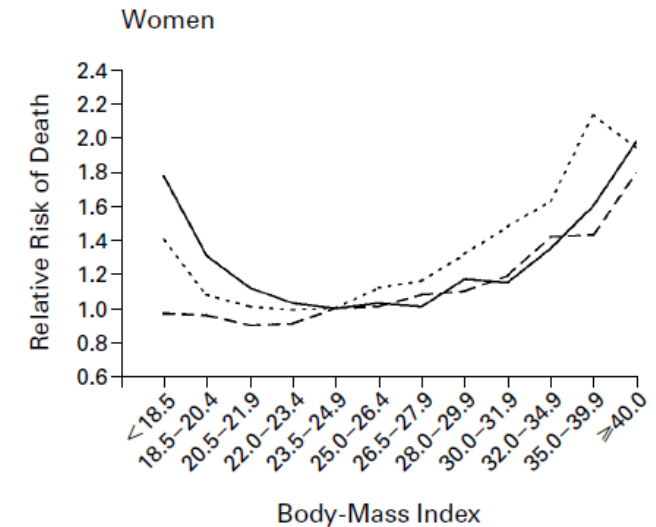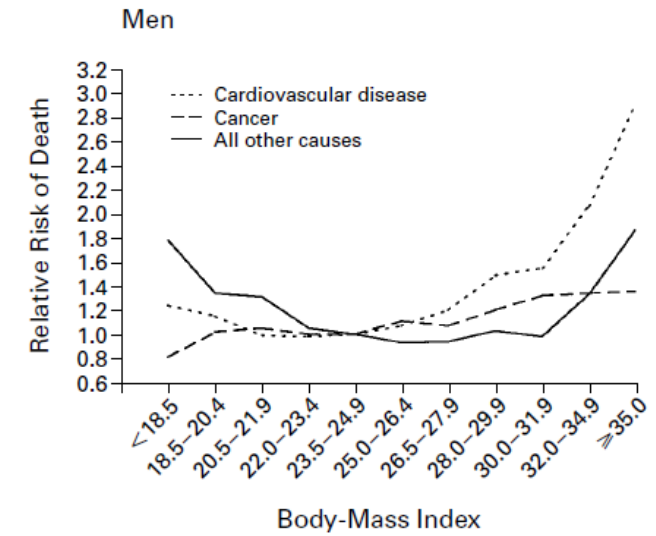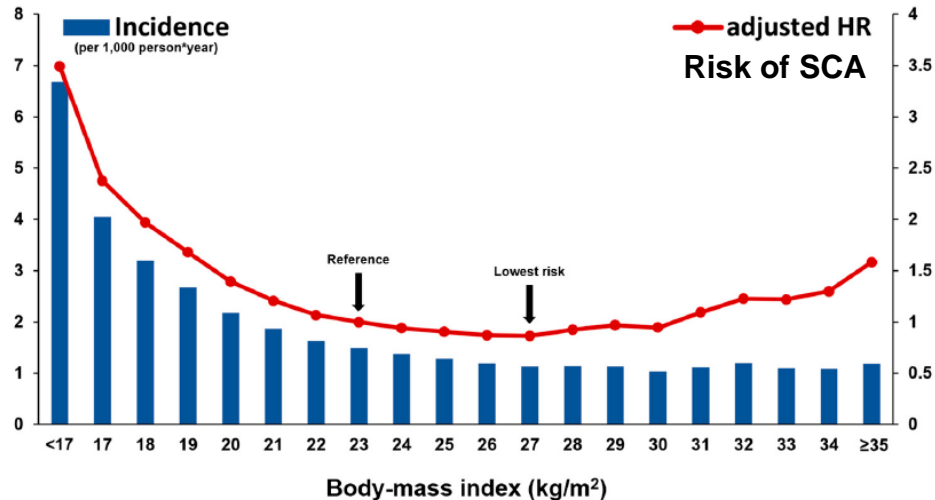
Background

- Diabetes mellitus is an established risk factor for atherosclerotic cardiovascular disease and sudden cardiac arrest (SCA).

- Presence of diabetes mellitus as well as hyperglycemia has 1.7 to 3.2-fold increased risk of SCA.

Table 2 Association of diabetes status with out-of-hospital cardiac arrest

Diabetes status	Overall			No heart disease			Heart disease		
	Case/control	OR[a]	95% CI	Case/control	OR[a]	95% CI	Case/control	OR[a]	95% CI
No diabetes	1427/3145	1		553/1485	1		874/1860	1	
Borderline diabetes	148/237	1.24	0.98–1.57	38/68	1.53	0.99–2.34	110/169	1.09	0.82–1.45
Diabetes without microvscular disease	262/292	1.73	1.28–2.34	65/70	2.25	1.27–3.98	197/222	1.45	1.01–2.07
Diabetes with microvascular disease	203/126	2.66	1.84–3.85	41/27	3.35	1.66–6.74	162/99	2.32	1.50–3.61

Adjusted-HR for OHCA

Jouven et al. *Euro Heart J.* 2005. 26, 2142–2147

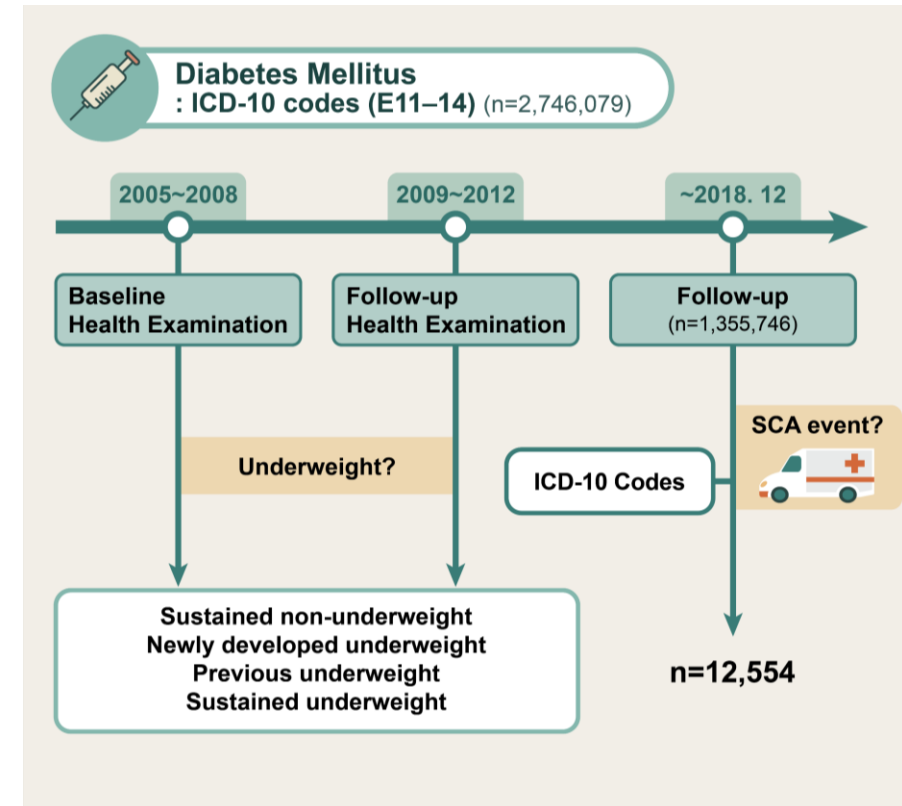YG Kim et al. *Sci Rep.* 2022. 12(1):12307

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Background

- Body weight status may be highly variable across time.

- Less is investigated about the temporal change of BMI with risk of SCA in diabetes mellitus.

- We aimed to investigate the association between SCA and temporal change in BMI in diabetes mellitus.

Methods

- This study is based on Korean National Health Insurance Service (K-NHIS) database.

- Inclusion criteria
  1. Participants who underwent health examination from 2009 to 2012
  2. History of diabetes mellitus (ICD-10, E11-14)
  3. Those who had undergone prior health examination 4 years ago

- Participants were divided into 4 groups
  - Baseline body weight status + change during 4 years of f/u

- Primary outcome was defined as occurrence of SCA event during f/u.

Results

K-NHIS Database

Nationwide health medical examination (2009 – 2012)
- ICD-10 codes of diabetes mellitus (E11 - 14)
- n = 2,746,079

Exclusion
- Underage (age < 20 years-old) : n=390
- No data of previous health examination (4 years ago) : n=1,306,520
- Missing data: n=72,520
- Previously diagnosed SCA: n=439
- Death or SCA within one year of health examination: n=24,732

Sudden cardiac arrest (SCA)
- **Claimed ICD-10 codes or CPR at emergency system**
  - I46.0 (cardiac arrest with successful resuscitation)
  - I46.1 (sudden cardiac arrest)
  - I46.9 (cardiac arrest, cause unspecified)
  - I49.0 (ventricular fibrillation and flutter)
  - R96.0 (instantaneous death)
  - R96.1 (death occurring less than 24 hours from symptom onset)

Clinical follow-up
- Followed up until December 2018 : n=1,355,746
- Mean follow-up duration: 6.72 ± 1.54 years
- SCA cases : n=12,554

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Results : Baseline characteristics

	Sudden Cardiac Arrest		p-value
	No (n=1,343,192)	Yes (n=12,554)	
Age, years	58.5 ± 11.8	66.1 ± 10.5	<.001
Sex (Male)	831,429 (61.9%)	9,247 (73.7%)	<.001
Income, Lowest Quartile	237,085 (17.7%)	2,517 (20.1%)	<.001
Smoking			<.001
Non-smoker	750,205 (55.9%)	6,195 (49.4%)	
Ex-smoker	274,645 (20.5%)	2,951 (23.5%)	
Current smoker	318,342 (23.7%)	3,408 (27.2%)	
Drinking			<.001
Non-drinker	764,957 (57.0%)	7,892 (62.9%)	
Mild-drinker	455,134 (33.9%)	3,529 (28.1%)	
Heavy-drinker	123,101 (9.2%)	1,133 (9.0%)	
Regular exercise	301,338 (22.4%)	2,593 (20.7%)	<.001
Hypertension	773,548 (57.6%)	9,028 (71.9%)	<.001
Dyslipidemia	574,278 (42.8%)	5,336 (42.5%)	0.573

	Sudden Cardiac Arrest		p-value
	No (n=1,343,192)	Yes (n=12,554)	
Chronic kidney disease	152,581 (11.4%)	3,054 (24.3%)	<.001
Cardiovascular disease*	81,388 (6.1%)	1,400 (11.2%)	<.001
Diabetes mellitus Duration, ≥5 years	455,843 (33.9%)	6,298 (50.2%)	<.001
Use of insulin	113,012 (8.4%)	2,410 (19.2%)	<.001
Use of oral hypoglycemic agents, ≥ 3	201,549 (15.0%)	2,706 (21.6%)	<.001
Body mass index, kg/m2	25.0 ± 3.3	24.3 ± 3.6	<.001
Waist Circumference, cm	85.4 ± 8.4	86.0 ± 8.8	<.001
Systolic Blood Pressure, mmHg	128.7 ± 15.3	130.8 ± 17.2	<.001
Diastolic Blood Pressure, mmHg	78.8 ± 10.0	78.3 ± 10.9	<.001
Fasting glucose, mg/dL	141.6 ± 43.6	144.5 ± 54.3	<.001
Total cholesterol, mg/dL	194.7 ± 41.8	189.3 ± 44.3	<.001
HDL -cholesterol, mg/dL	51.7 ± 22.6	49.9 ± 22.1	<.001
LDL -cholesterol, mg/dL	110.2 ± 40.3	107.3 ± 42.6	<.001
Triglyceride, mg/dL	143.9 (143.8-144.1)	140.8 (139.5-142.2)	<.001

* Chronic kidney disease: eGFR <60 ml/min/1.73 m^2
**Cardiovascular disease: Previous diagnosis of myocardial infarction or stroke

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Results : Baseline characteristics

	Sustained non-underweight (n = 1,330,899)	Newly developed underweight (n = 10,270)	Previous underweight (n = 6,415)	Sustained underweight (n = 8,162)	p-value
Age, years	58.5 ± 11.7	63.0 ± 13.5	57.4 ± 15.4	58.5 ± 15.4	< 0.001
Sex (Male)	825,865 (62.1%)	5,759 (56.1%)	3,827 (59.7%)	5,225 (64.0%)	< 0.001
Income, Lowest Quartile	234,673 (17.6%)	2,046 (19.9%)	1,296 (20.2%)	1,587 (19.4%)	< 0.001
Smoking					< 0.001
Non-smoker	742,871 (55.8%)	5,932 (57.8%)	3,513 (54.8%)	4,084 (50.0%)	
Ex-smoker	274,040 (20.6%)	1,407 (13.7%)	1,053 (16.4%)	1,096 (13.4%)	
Current smoker	313,988 (23.6%)	2,931 (28.5%)	1,849 (28.8%)	2,982 (36.5%)	
Drinking					< 0.001
Non-drinker	757,270 (56.9%)	6,873 (66.9%)	3,861 (60.2%)	4,845 (59.4%)	
Mild-drinker	451,410 (33.9%)	2,583 (25.2%)	2,055 (32.0%)	2,615 (32.0%)	
Heavy-drinker	122,219 (9.2%)	814 (7.9%)	499 (7.8%)	702 (8.6%)	
Regular exercise	299,873 (22.5%)	1,731 (16.9%)	1,073 (16.7%)	1,254 (15.4%)	< 0.001
Hypertension	772,899 (58.1%)	4,456 (43.4%)	2,545 (39.7%)	2,676 (32.8%)	< 0.001
Dyslipidemia	573,712 (43.1%)	2,783 (27.1%)	1,633 (25.5%)	1,486 (18.2%)	< 0.001
Chronic kidney disease	152,772 (11.5%)	1,363 (13.3%)	735 (11.5%)	765 (9.4%)	< 0.001
Cardiovascular disease	81,117 (6.1%)	896 (8.7%)	373 (5.8%)	402 (4.9%)	< 0.001
Diabetes mellitus Duration, ≥ 5 years	453,736 (34.1%)	4,043 (39.4%)	1,962 (30.6%)	2,400 (29.4%)	< 0.001
Use of insulin	111,890 (8.4%)	1,638 (16.0%)	914 (14.3%)	980 (12.0%)	< 0.001
Use of oral hypoglycemic agents, ≥ 3	200,474 (15.1%)	1,925 (18.7%)	837 (13.1%)	1,019 (12.5%)	< 0.001
Body mass index, kg/m^2	25.1 ± 3.2	17.7 ± 0.8	20.1 ± 1.9	17.2 ± 1.0	< 0.001
Waist Circumference, cm	85.7 ± 8.2	71.2 ± 6.6	74.8 ± 6.9	68.8 ± 5.7	< 0.001
Systolic Blood Pressure, mmHg	128.8 ± 15.3	123.0 ± 17.2	124.5 ± 16.5	121.7 ± 16.8	< 0.001
Diastolic Blood Pressure, mmHg	78.8 ±10.0	75.2 ± 10.6	75.9 ± 10.3	74.9 ± 10.4	< 0.001
Fasting glucose, mg/dL	141.5 ± 43.5	148.2 ± 63.7	140.2 ± 43.8	144.0 ± 51.0	< 0.001
Total cholesterol, mg/dL	194.8 ± 41.9	183.9 ± 42.6	188.2 ± 40.0	182.0 ± 37.5	< 0.001
HDL -cholesterol, mg/dL	51.6 ± 22.5	58.4 ± 26.3	57.2 ± 25.0	61.0 ± 28.0	< 0.001
LDL -cholesterol, mg/dL	110.3 ± 40.3	102.6 ± 41.5	106.1 ± 37.7	100.0 ± 37.9	< 0.001
Triglyceride, mg/dL	144.8 (144.7 – 145.0)	102.3 (101.2 – 103.4)	110.4 (108.9 – 111.9)	95.6 (94.5 – 96.7)	< 0.001

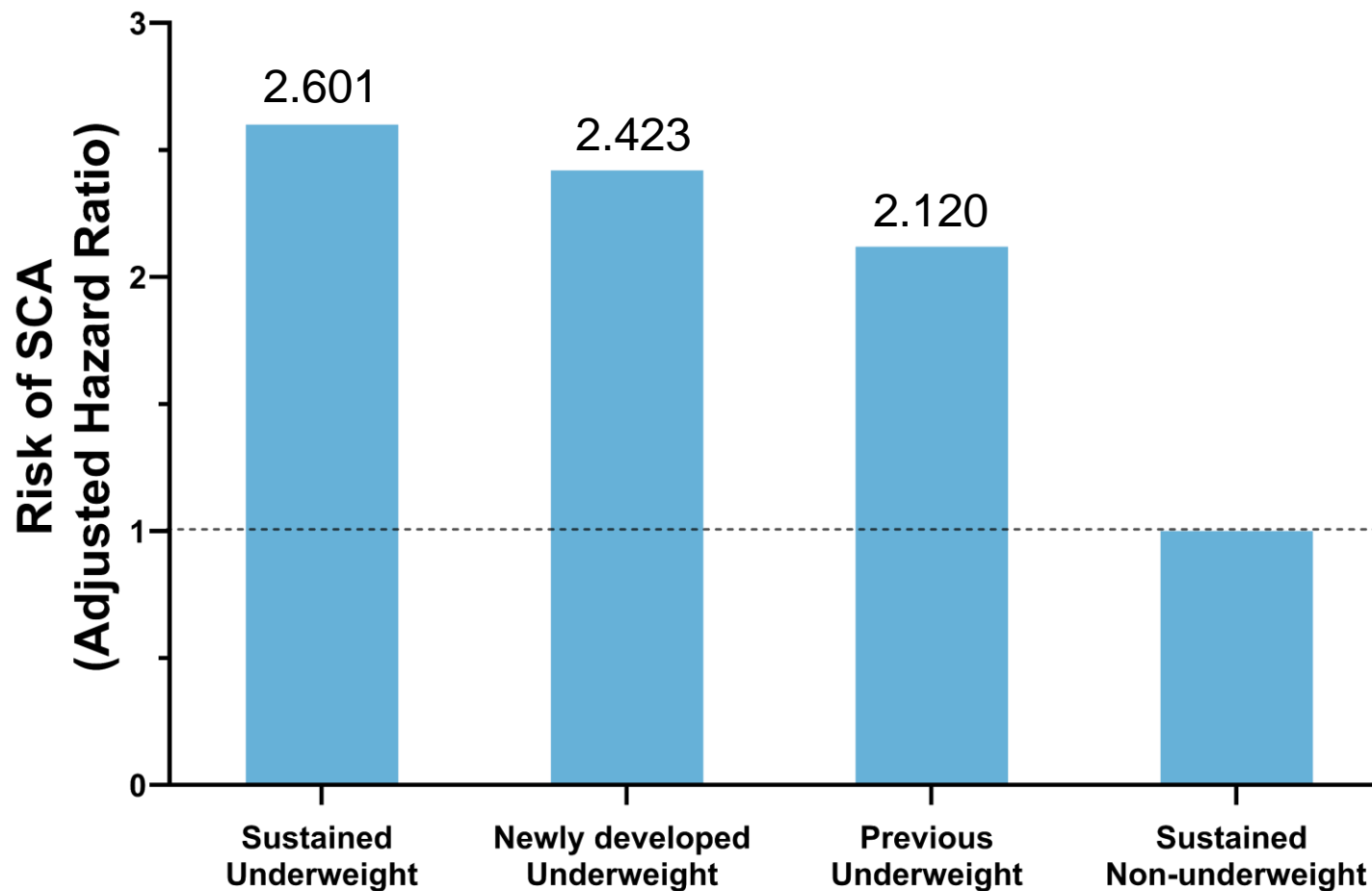# Results : Cumulative incidence of SCA
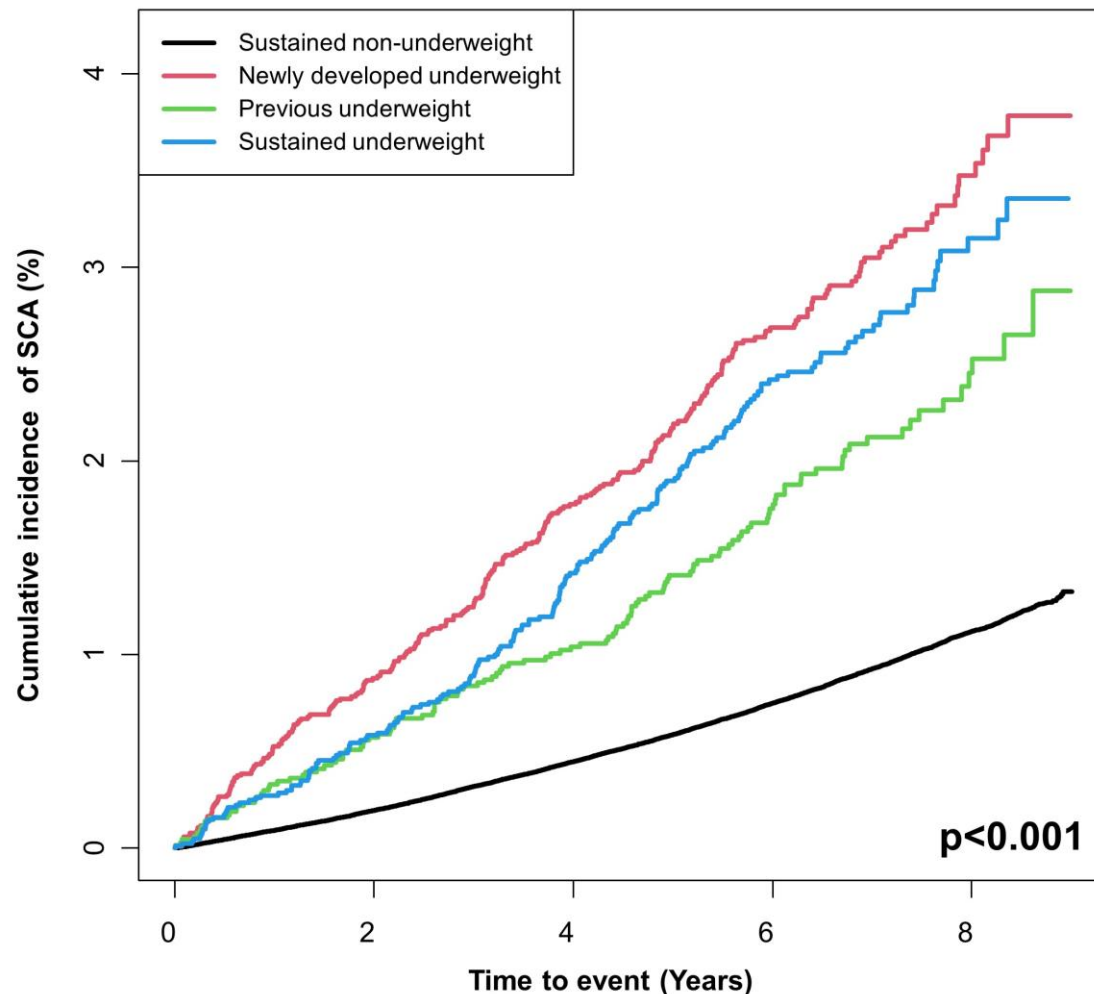
- **Incidence rate**
- Newly developed underweight = 4.45
- Sustained underweight = 3.90
- Previous underweight = 3.03
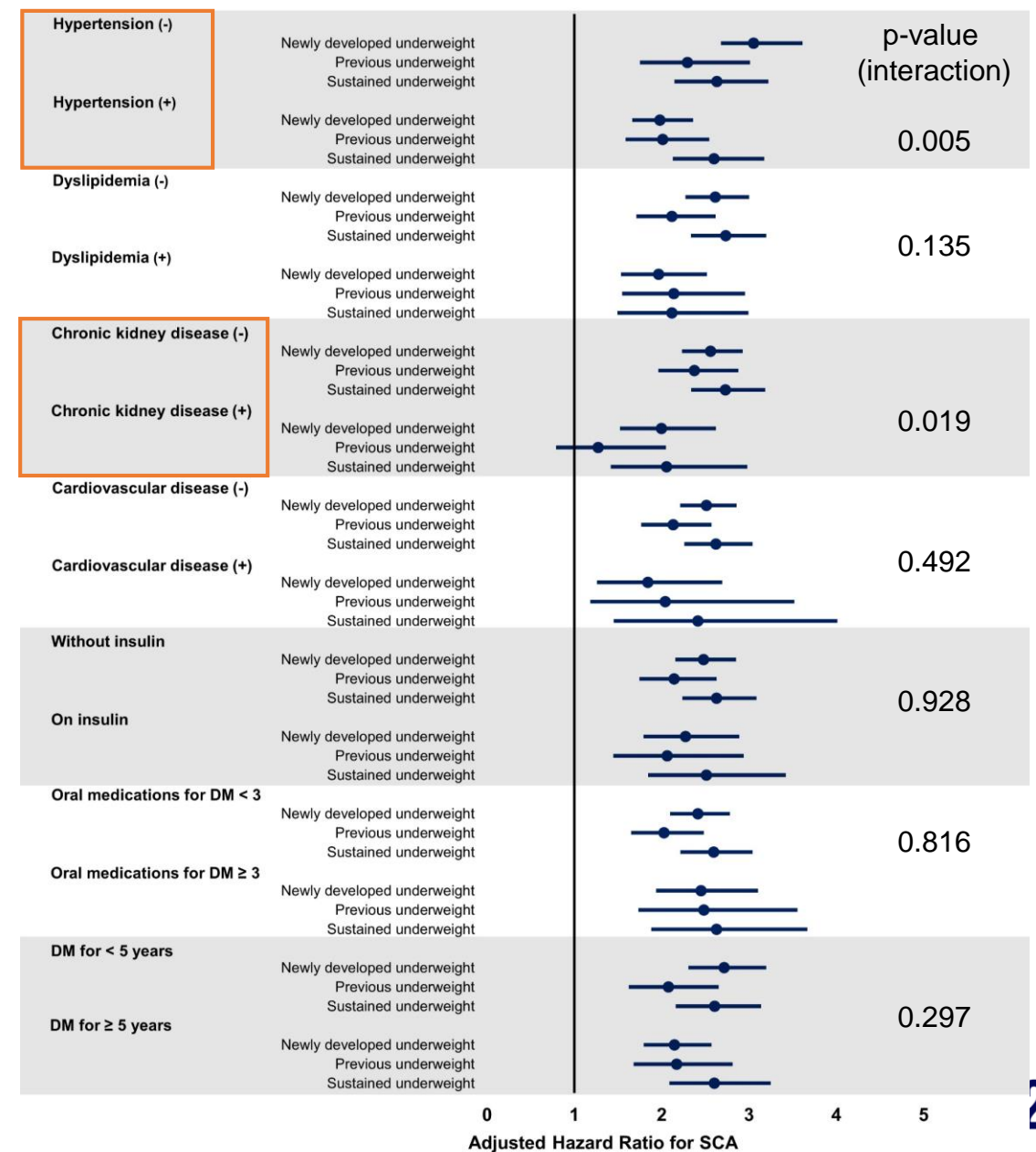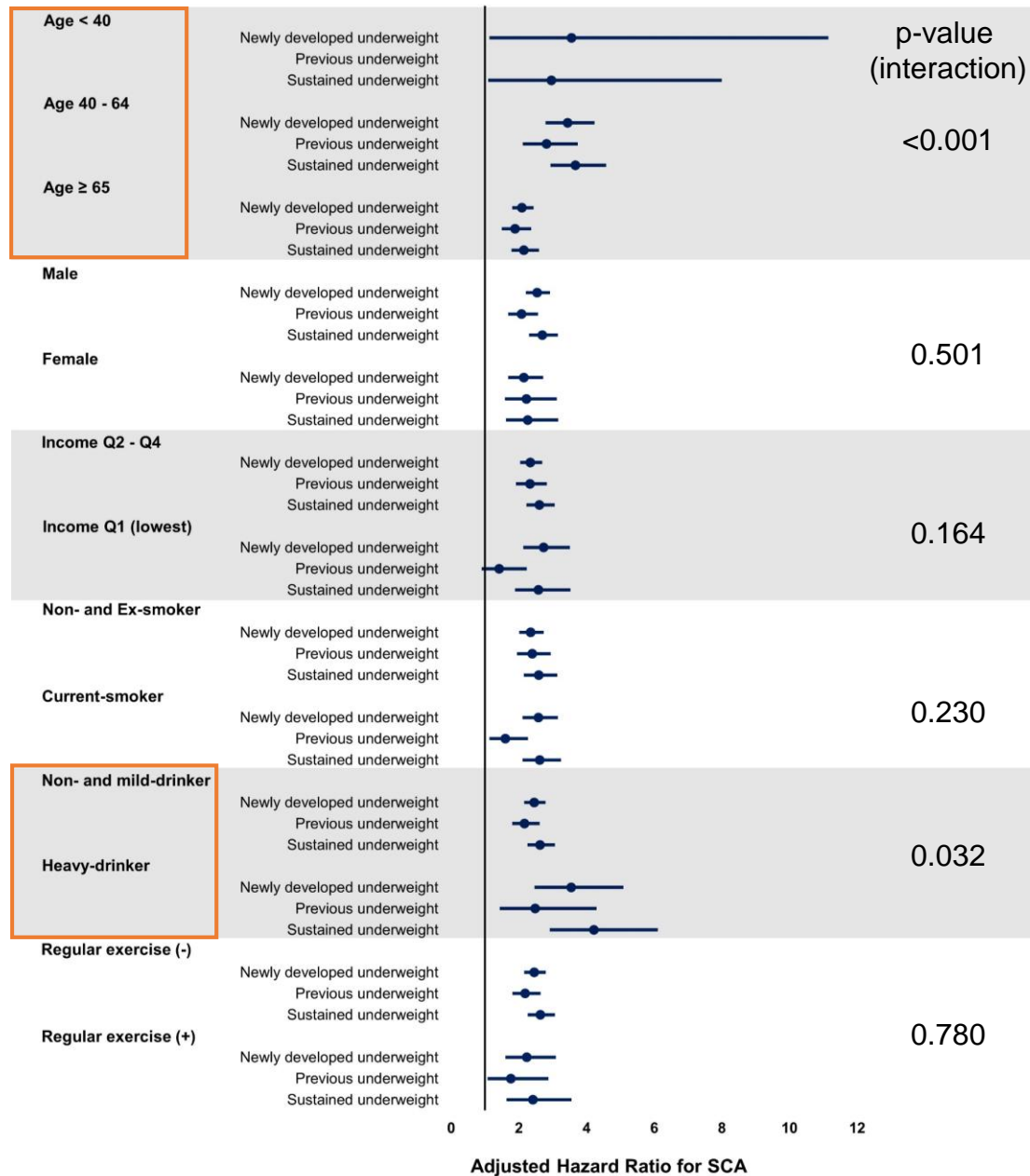- Sustained non-underweight = 1.34

Results : Adjusted SCA risk

Adjusted for age, sex, income, smoking status, alcohol consumption status, regular exercise, hypertension, dyslipidemia, chronic kidney disease, cardiovascular disease, fasting glucose, duration of diabetes mellitus, use of insulin, and use of multiple (≥ 3) oral hypoglycemic agent.
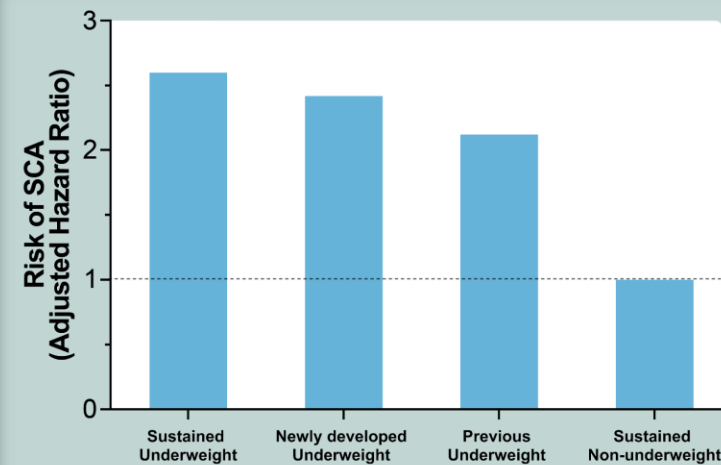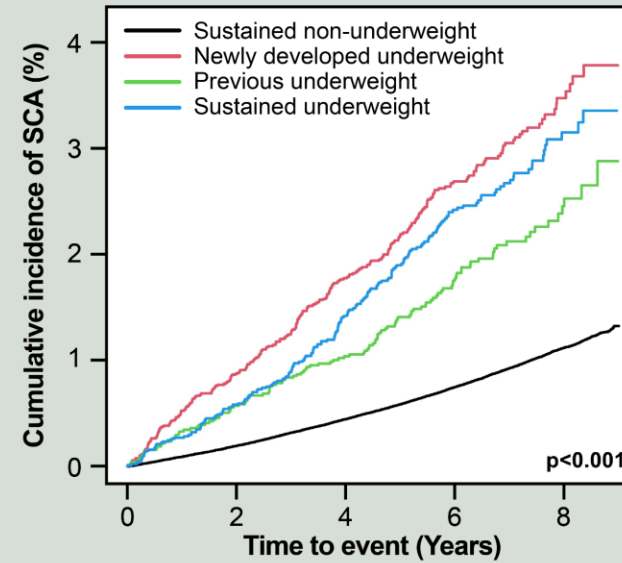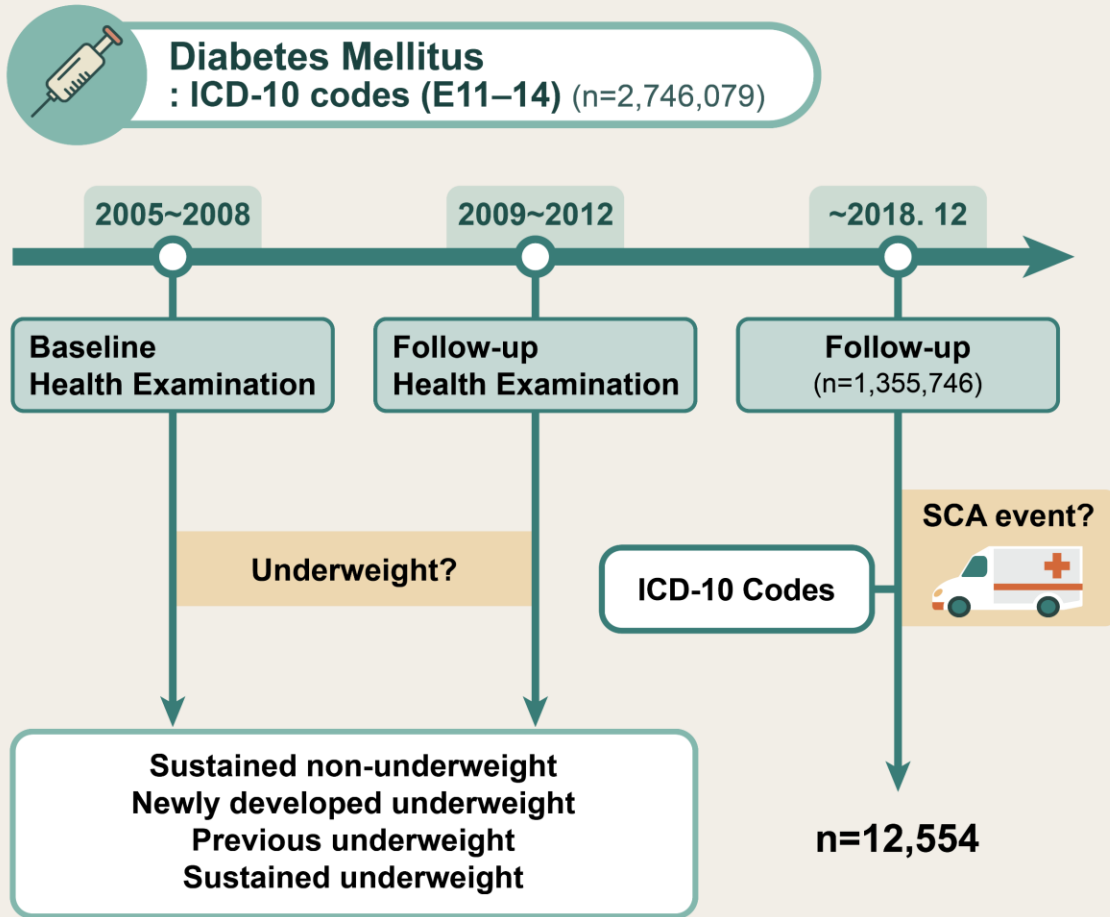
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Results : Subgroup analysis

Discussion

Korean National Health Insurance Service (K-NHIS) Database

Diabetes Mellitus
: ICD-10 codes (E11–14) (n=2,746,079)

2005~2008 — Baseline Health Examination
2009~2012 — Follow-up Health Examination
~2018. 12 — Follow-up (n=1,355,746)

Underweight?

SCA event?

ICD-10 Codes

Sustained non-underweight
Newly developed underweight
Previous underweight
Sustained underweight

n=12,554

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Discussion : Mechanisms

1. Patients with underweight exhibit decreased physiologic capacity and fat reserve.
   - They may be more vulnerable to increase of metabolic demand (i.e, acute inflammation, critically ill condition).

2. Patients in underweight – may represent those with progressed diabetes mellitus.

3. Decrease of bodyweight may be caused by external condition.
   - Malignancy, heart failure, respiratory disease, or systemic inflammatory disease.

Conclusion

- Underweight is associated with more than 2-fold increased risk of SCA in diabetes population.

- Persistent underweight as well as dynamic decrease of body weight are both significantly associated with increased risk of SCA, and recovery from underweight do not overcome the risk of SCA.

- In patient with diabetes mellitus and underweight at any time period, appropriate recognition, modification of relevant conditions, and serial monitoring of body weight status is needed.