Real world risk of major outcomes for type 2 diabetes with stable coronary artery disease without prior MI or stroke and THEMIS-like patients using the SNDS French nationwide claims database

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Aims

- The THEMIS randomized trial showed a lower incidence of ischemic cardiovascular events but a higher incidence of major bleeding in ticagrelor plus aspirin group than in placebo plus aspirin group in patients with stable coronary artery disease and type 2 diabetes (CAD-T2M) without prior myocardial infarction (MI) or stroke (Steg et al, NEJM 2019).
- The objective was to estimate the incidence of major outcomes for patients with CAD-T2DM, without history of MI-stroke and, more specifically, for THEMIS-like patients in a real world setting.

Methods

Study design

Cohort study in the French nationwide claims database (SNDS, 86% of the 66 million people).

Data source

The SNDS database contains individual pseudonymised information from 66 million persons on:

- Gender, date of birth, area of residence, date of death;
- Long-term disease registration with associated ICD-10 codes for full insurance coverage (with start and end dates);
- Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs …;
- Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the date and duration of hospitalisation, medical procedures.

Study populations

- **CAD-T2DM population without prior MI-stroke**: all CAD-T2DM prevalent patients without MI-stroke within the 5-year history period identified on 1st January 2014, and followed for 2 years or until death in the database.
- **THEMIS-like population**: all patients of the previous population with specific criteria (≥ 50 years at index date, without renal failure with dialysis, cirrhosis/liver cancer history, intracranial/gastro-intestinal bleeding for the last 6 months, or anticoagulant/antiplatelet agent 2 months around index date).

Outcomes (primary diagnosis)

- Ischemic or unknown stroke;
- MI;
- Heart failure;
- Major bleeding* (associated diagnosis also considered) including Intracranial bleeding, haemorrhagic stroke, other critical organ or site bleeding, other bleeding, fatal bleeding ;
- All-cause death;
- Composite criterion: first event among stroke, MI, or death.

Data analysis

- Estimate of the prevalence proportion on 01/01/2014 with gender and 5-year age classes standardisation according to national 5INSEE) and European (Eurostat) statistics;
- Two-year cumulative incidence/probability of outcomes using Kaplan-Meier estimate (death, composite) or cumulative incidence function (CIF, other outcomes) to take into account death as competing risk.

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Results

- **Main characteristics of populations:** 258 260 patients in the CAD-T2DM population without prior MI-stroke and 64 334 in the THEMIS-like population were included, and presented similar main characteristics (**Table 1**).
- **French and European prevalence** (**Table 2**)
  - The THEMIS-like prevalence was estimated to be 1.53‰ French adults, representing about a quarter of CAD-T2DM patients without prior MI-stroke.
  - The prevalence was higher for men and increased with age in both populations.
  - This results was close to those found in the European population (1.50‰).
- **Two-year cumulative incidence / probability of outcomes** (**Figures 1 and 2**)

  For all patients, according to age, the two-year cumulative incidence/probability was:
  - Little higher for the CAD-T2DM population without prior MI-stroke than THEMIS-like population for ischemic or unknown stroke (1.7% vs. 5.5%) and MI (1.7% vs. 1.3%).
  - Clearly higher for the CAD-T2DM population without prior MI-stroke than THEMIS-like population for heart failure (9.5% vs. 5.3%), major organ specific bleeding (4.9% vs. 3.2%), all-cause death (13.6% vs. 9.7%), and the composite event (16.2% vs. 12.0%).

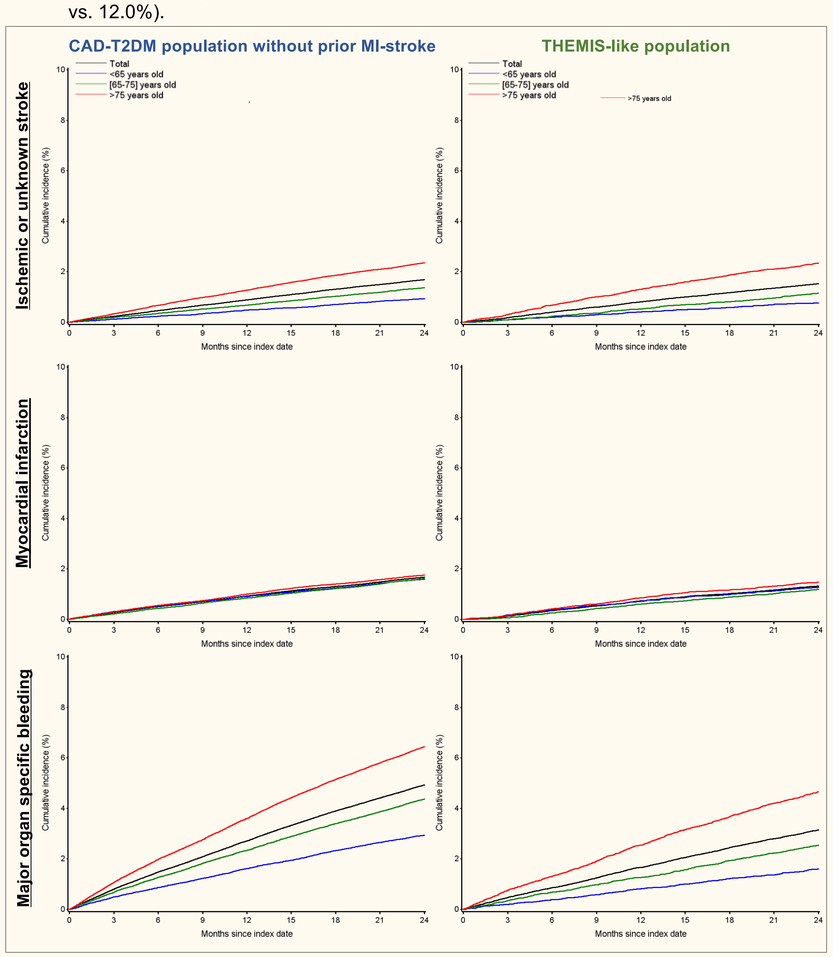

Figure 1. Cumulative incidence/probability of outcomes during two years of follow-up

Table 1. Main characteristics of the study populations at index date

	CAD-T2DM population without prior MI-stroke n = 258 260	THEMIS-like population n = 64 334
Male, n (%)	176 407 (68.3)	42 238 (65.7)
Median age (in years)	73.0	72.0
> 4 years of both CAD and T2DM diagnoses history, n (%)	67 040 (26.0)	16 346 (25.4)
History of hypertension, n (%)	204 943 (79.4)	48 554 (75.5)
History of diabetic complications, n (%)	101 419 (39.3)	20 301 (31.6)

Table 2. Estimated 2014 Prevalence of study populations for French and European adult populations*

	CAD-T2DM population without prior MI-stroke (‰)			THEMIS-like population (‰)		
	Men	Women	All	Men	Women	All
French adults (all) from INSEE	**8.96**	**3.63**	**6.17**	**2.14**	**0.98**	**1.53**
18-64 years	2.81	0.78	1.78	0.72	0.23	0.47
65-75 years	27.40	7.37	16.73	6.88	2.12	4.34
>75 years	40.61	16.46	25.45	8.70	4.18	5.86
European adults (all) from Eurostat	**8.74**	**3.51**	**6.04**	**2.09**	**0.95**	**1.50**
18-64 years	2.71	0.76	1.73	0.70	0.22	0.46
65-75 years	27.74	7.54	16.88	6.95	2.16	4.37
>75 years	40.54	16.20	25.38	8.71	4.11	5.84

* standardized to 2014 EU population

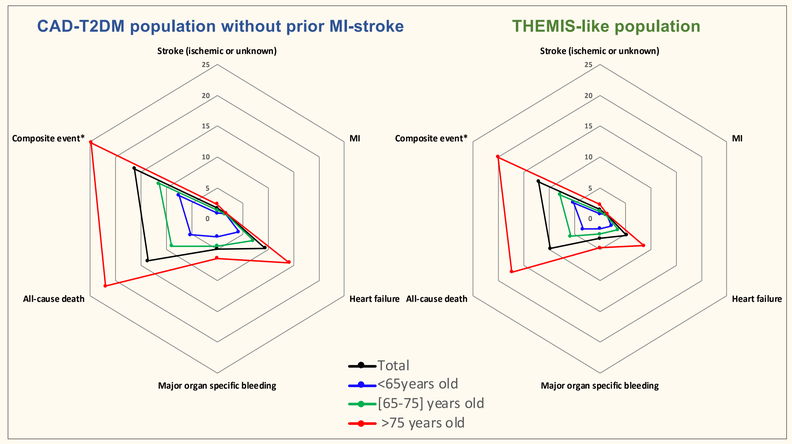

Figure 2. Cumulative incidence/probability of outcomes at two years of follow-up (%)

Conclusions

- In current French practice, the median age of the THEMIS-like population was 6 years older than in the THEMIS trial (i.e. 72 vs 66 years).
- The incidences observed in real world setting for THEMIS-like population after 2 years of follow-up were about double for the composite outcome (i.e. 12.0 vs 6,2%), triple for deaths (i.e. 9.7 vs 3,2%) and quadruple for major bleeding compared to TIMI major bleeding (i.e. 3,2% vs 0.8%) than those of the placebo arm of the THEMIS trial.

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