

Rates of Cardiovascular Events Among Patients With Moderate-to-Severe Atopic Dermatitis: A Retrospective Cohort Study

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BACKGROUND

- Atopic dermatitis (AD) is a common chronic inflammatory skin disease characterized by intense itch, lesions, and dry skin that affects up to 10% of adults^{1,3}
- Previous reports suggest a relationship between AD and cardiovascular (CV) disease^{4,6}; however, incidence rates of CV events among patients with moderate-to-severe AD are unknown

OBJECTIVE

- To evaluate the incidence rates of CV events in patients with moderate-to-severe AD using data from a cohort of Kaiser Permanente Northern California (KPNC) health plan members

METHODS

Study Design and Patients

- This retrospective cohort study included adolescent and adult KPNC health plan members (≥12 years of age) with the following characteristics:
 - A clinical diagnosis of moderate-to-severe AD (defined as having an outpatient dermatologist-rendered visit coded with an ICD-9 code of 691.8 or an ICD-10 of L20 between January 1, 2007, and December 31, 2018)
 - Enrollment in the KPNC health plan at least 1 year before the study index date, which was defined as the first date at which an eligible patient filled a prescription for a topical or systemic agent or the first date at which a patient received phototherapy
- Moderate-to-severe disease was defined as disease necessitating topical therapy or phototherapy (moderate) or systemic treatment (severe) because of a diagnosis of AD
 - Adjudication was conducted by a board-certified dermatologist
 - Agreement of ≥80% between the cases identified by study parameters and dermatologist medical record review was deemed acceptable
- CV events (major adverse cardiovascular event [MACE], venous thrombotic event [VTE], deep vein thrombosis [DVT], and pulmonary embolism [PE]) were analyzed regardless of presumed causality, graded in terms of severity, and coded using the Medical Dictionary for Regulatory Activities (MedDRA)
 - MACE is a composite measure of CV death (including sudden cardiac death or death due to acute myocardial infarction, heart failure, stroke, CV procedures, CV hemorrhage, or other CV causes [ie, peripheral artery disease]), nonfatal myocardial infarction, nonfatal stroke of any classification, and nonfatal MACE cases requiring hospitalization

Statistical Analysis

- Incidence rates per 1000 person-years and 95% confidence limits were reported overall and by year of study index date and were analyzed separately in 2 age groups (≥12 to <18 years vs ≥18 years [adolescents vs adults]; and ≥12 to <65 vs ≥65 years [nonseniors vs seniors]), and by sex, race, ethnicity, and selected additional risk factors

RESULTS

Demographic and Baseline Characteristics

- The KPNC database included 34,405 health plan members with an AD diagnosis between 2007 and 2018, of which 8197 patients had moderate-to-severe AD and were included in this analysis
 - Adjudication of AD severity indicated that the definitions used to classify moderate and severe AD were acceptable (agreement for confirmed cases ≥80%)
- Demographic and baseline disease characteristics are summarized in **Table 1**

Table 1. Demographic and Baseline Characteristics

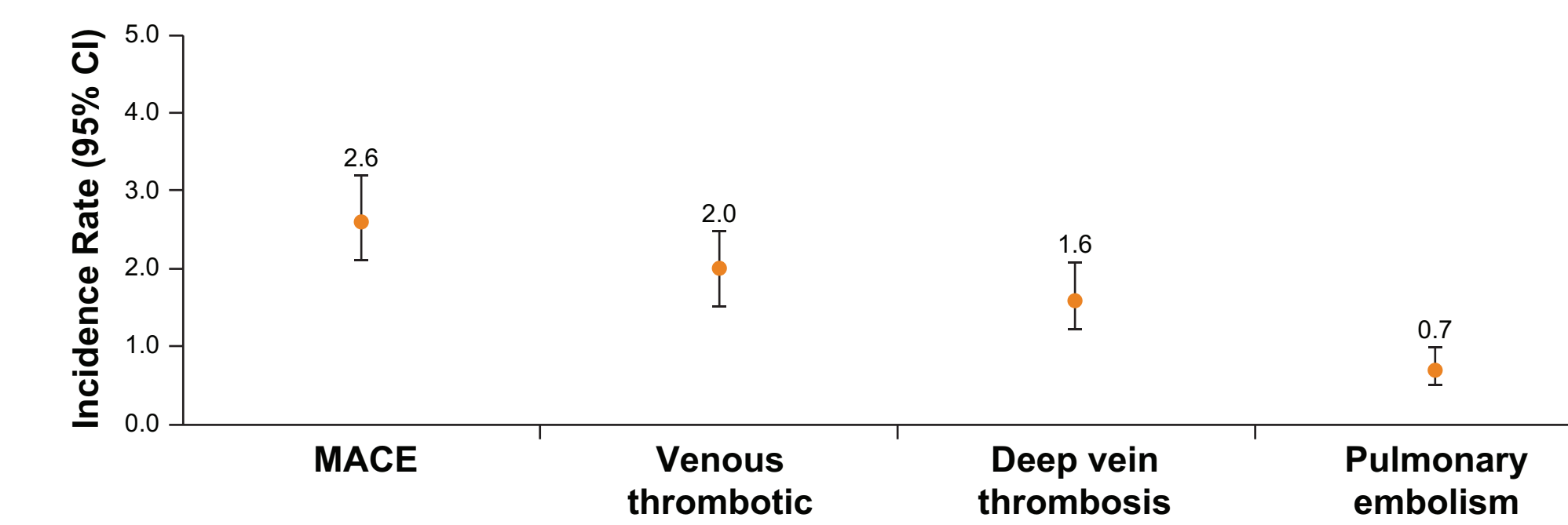
Characteristic	Patients N=8197
Age, mean (SD), y	39.4 (18.0)
≥12 to <18, n (%)	1147 (14.0)
≥18, n (%)	7050 (86.0)
<65, n (%)	7388 (90.1)
≥65, n (%)	809 (9.9)
Sex, n (%)	
Women	5229 (63.8)
Men	2966 (36.2)
Missing	2 (0.02)
Race, n (%)	
White	2779 (33.9)
Black	664 (8.1)
Asian	2916 (35.6)
Native American	32 (0.4)
Native Hawaiian or other Pacific Islander	91 (1.1)
Multiracial	468 (5.7)
Missing/other	1247 (15.2)
Ethnicity, n (%)	
Hispanic	1192 (14.5)
Non-Hispanic	3669 (44.8)
Missing	3336 (40.7)
AD severity, n (%)	
Moderate	7158 (87.3)
Severe	1039 (12.7)
BMI, n (%)	
<25 kg/m ²	3303 (40.3)
25 to <30 kg/m ²	2180 (26.6)
≥30 kg/m ²	1677 (20.5)
Missing	1037 (12.7)
Smoking, n (%)	
Yes/current	462 (5.6)
Quit/former	1085 (13.2)
Passive/secondhand	92 (1.1)
Never	4737 (57.8)
Missing	1821 (22.2)
Diabetes, n (%)	
Yes	443 (5.4)
No	7754 (94.6)

AD, atopic dermatitis; BMI, body mass index.

Incidence Rates of Cardiovascular Events in Patients With Moderate-to-Severe AD

- The CV event with the highest incidence rate in patients with AD per 1000 person-years was MACE, followed by VTE, DVT, and PE (**Figure 1**)

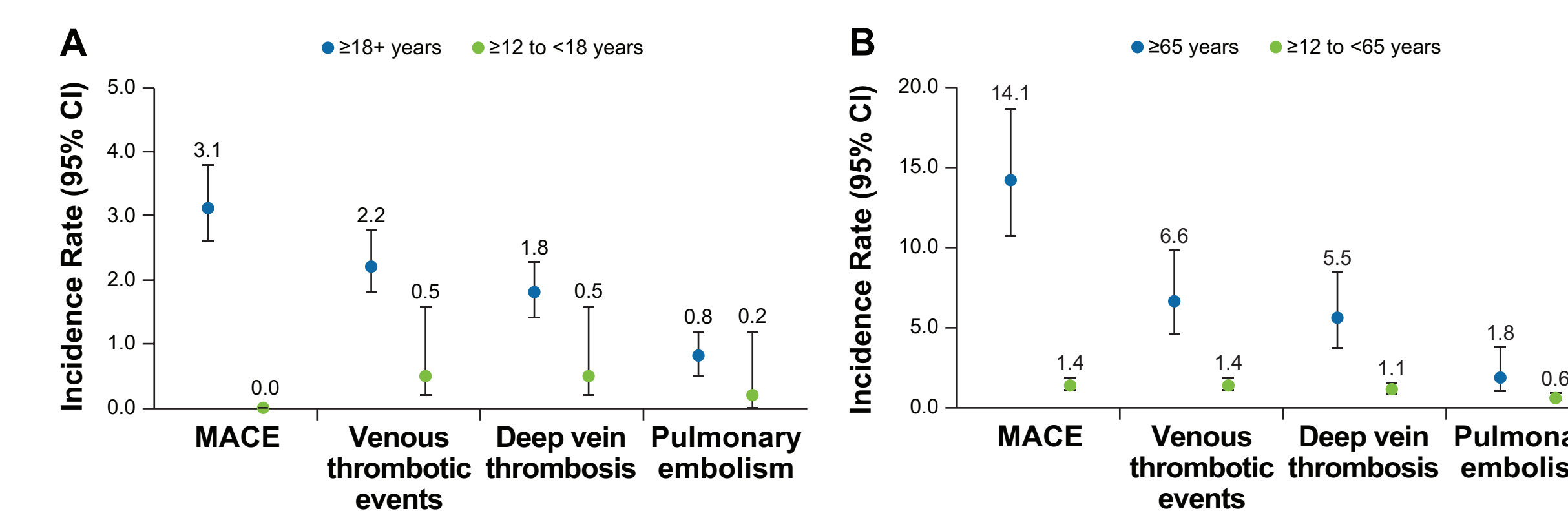
Figure 1. Incidence Rates per 1000 Person-Years of Cardiovascular Events Among Patients With Moderate-to-Severe AD



AD, atopic dermatitis; MACE, major adverse cardiovascular event.

- For all CV events, incidence rates were lower for adolescents than for adults (**Figure 2A**), with nonoverlapping 95% CIs for MACE and VTE
- Similarly, incidence rates were lower in nonseniors than seniors (**Figure 2B**), with nonoverlapping 95% CIs for all CV events

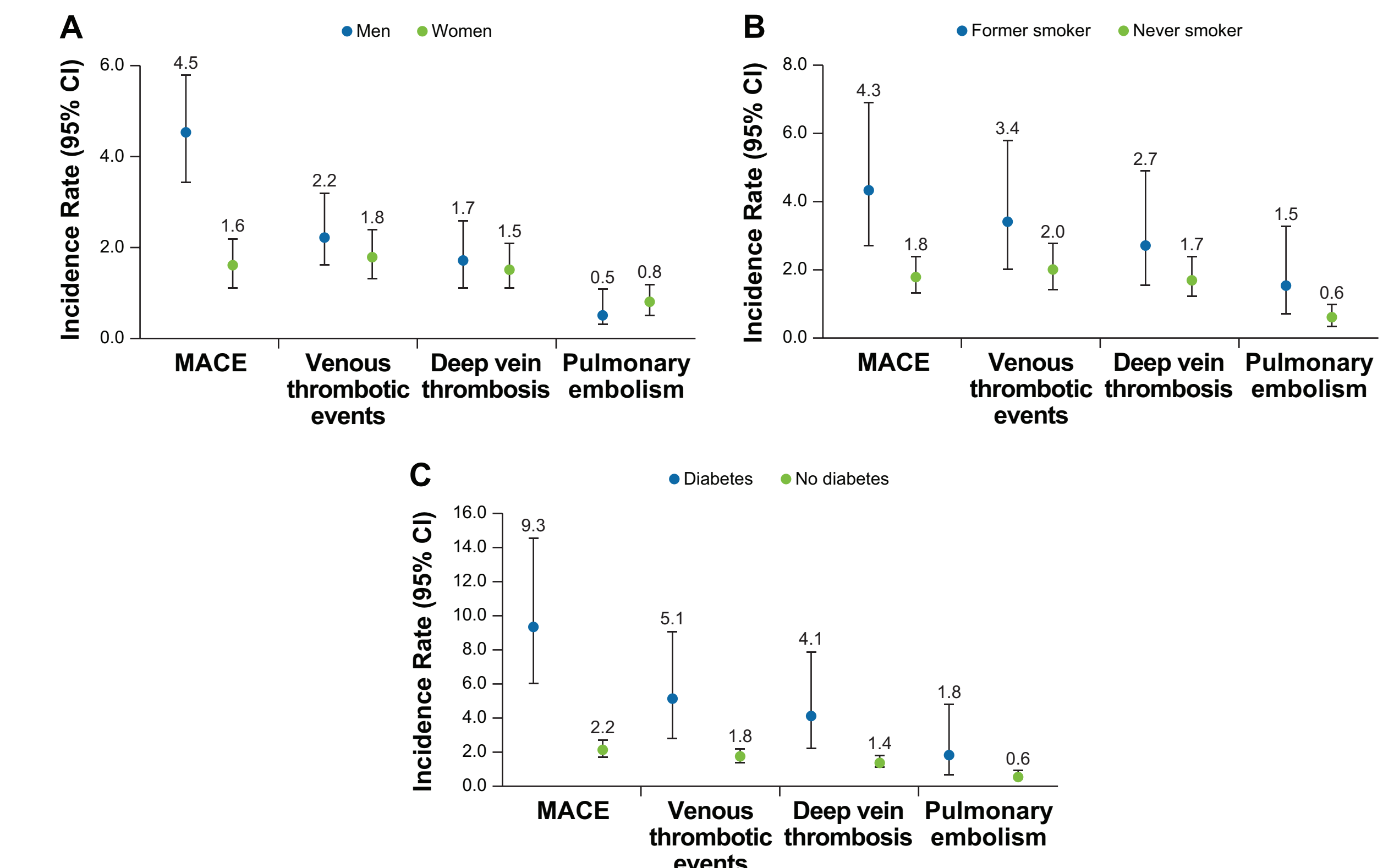
Figure 2. Incidence Rates per 1000 Person-Years of Cardiovascular Events Among (A) Adults and Adolescents and (B) Seniors and Nonseniors With Moderate-to-Severe AD



AD, atopic dermatitis; MACE, major adverse cardiovascular event.

- MACE incidence rates were higher (with nonoverlapping 95% CIs) among men than women (**Figure 3A**), former smokers than never smokers (**Figure 3B**), and those with diabetes than those without diabetes (**Figure 3C**)
 - Incidence rates for VTE and DVT were also higher (with nonoverlapping 95% CIs) among AD patients with diabetes (**Figure 3C**)

Figure 3. Incidence Rates per 1000 Person-Years of Cardiovascular Events Among Patients With Moderate-to-Severe AD for (A) Men and Women, (B) Former Smokers and Never Smokers, and (C) Members With Diabetes and Without Diabetes



AD, atopic dermatitis; MACE, major adverse cardiovascular events.

CONCLUSION

- In patients with moderate-to-severe AD who are representative of those with access to healthcare in the United States, the CV event with the highest incidence rate was MACE, followed by VTE, DVT, and PE
 - The MACE incidence rates per 1000 person-years were higher for those aged ≥65 years, men, those with diabetes, and former smokers
- This study is one of the first to report CV event incidence rates for patients with moderate-to-severe AD, providing valuable information for ongoing clinical trials in this patient population

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