The Risk of Venous Thromboembolism in Atopic Dermatitis: A Population-Based Cohort Study

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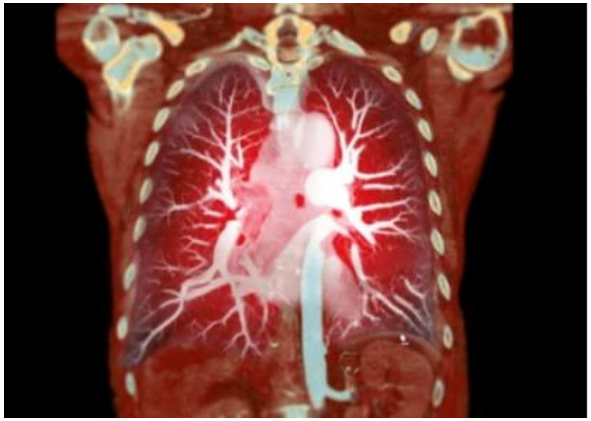
Disclosure

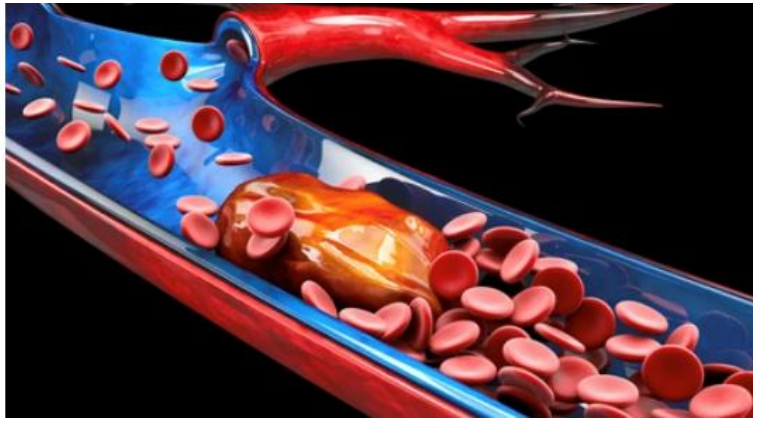
- Advisory board: ACO, Lilly, LEO, Almirall, Sanofi-Genzyme, Abbvie
- Lectures: ACO, Sanofi-Genzyme, Abbvie

Why Study VTE Risk in Atopic Dermatitis?

- JAK inhibitors: **VTE (venous thromboembolism)** risk warnings based on data from RA and other inflammatory diseases
- Baseline VTE (including PE, DVT) risk in AD remains unclear
- Prior studies have shown conflicting findings



Pulmonary embolism (PE)



Deep vein thrombosis (DVT)

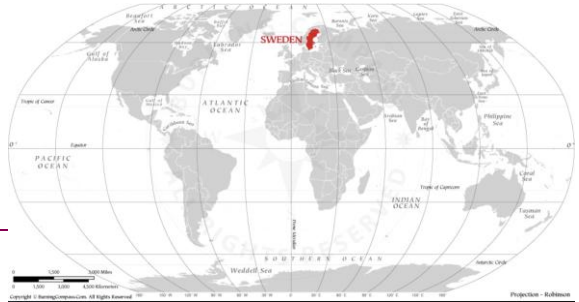
Aim of the study

- To investigate whether individuals with AD have a higher baseline risk of incident **venous thromboembolism (**VTE), including **deep vein thrombosis** (DVT) and **pulmonary embolism** (PE), compared with the general population

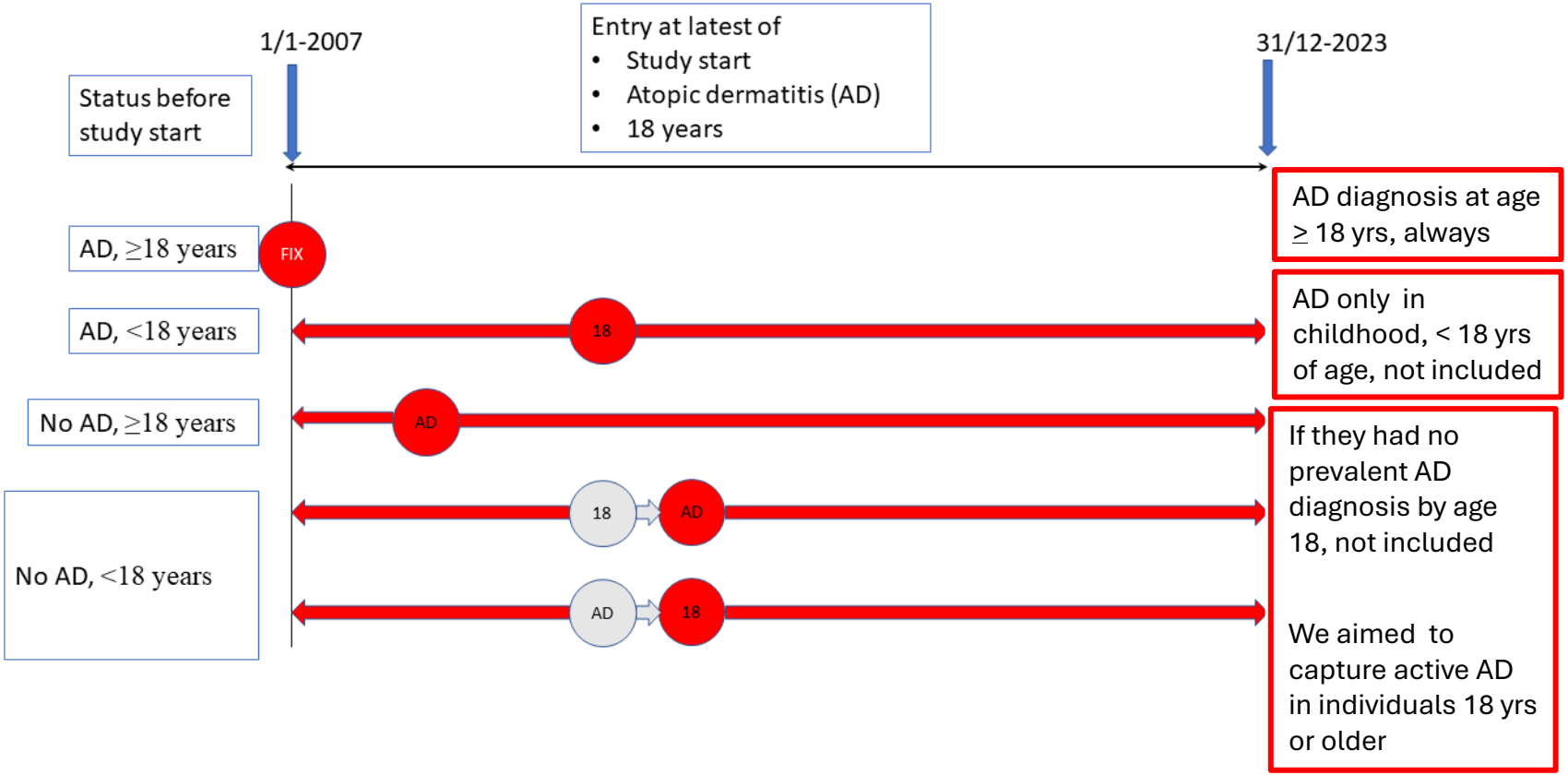
- To assess whether the risk varies by demographics and AD severity

Methods

- Nationwide register-based matched cohort study (Swedish national healthcare and population registers)
- Individuals diagnosed with AD, aged 18 years or older, starting from January 1, 2007 – December 31, 2023
- Matching: 1 AD: 5 non-AD Controls (Sex/Age)
- ◦ Exclusion: History of VTE



Methods


1/1-2007
Entry at latest of
• Study start
• Atopic dermatitis (AD)
• 18 years
31/12-2023
Status before study start
AD, ≥18 years
FIX
AD, <18 years
18
No AD, ≥18 years
AD
No AD, <18 years
18
AD
AD
18
AD diagnosis at age ≥ 18 yrs, always
AD only in childhood, < 18 yrs of age, not included
If they had no prevalent AD diagnosis by age 18, not included
We aimed to capture active AD in individuals 18 yrs or older

Methods

- **Severe AD Criteria (Either/Or):**

Systemic Rx dupilumab, tralokinumab, JAK inhibitors, azathioprine, methotrexate, ciclosporin, or mycophenolate mofetil (1.5 yr look-back)

Hospitalization (Primary AD Dx, 5 yr look-back)

- **Non-Severe AD: Remaining Cases**
- Severity: Hierarchically Time-Varying

Very few patients received JAKi, and excluding these did not affect results that will be presented

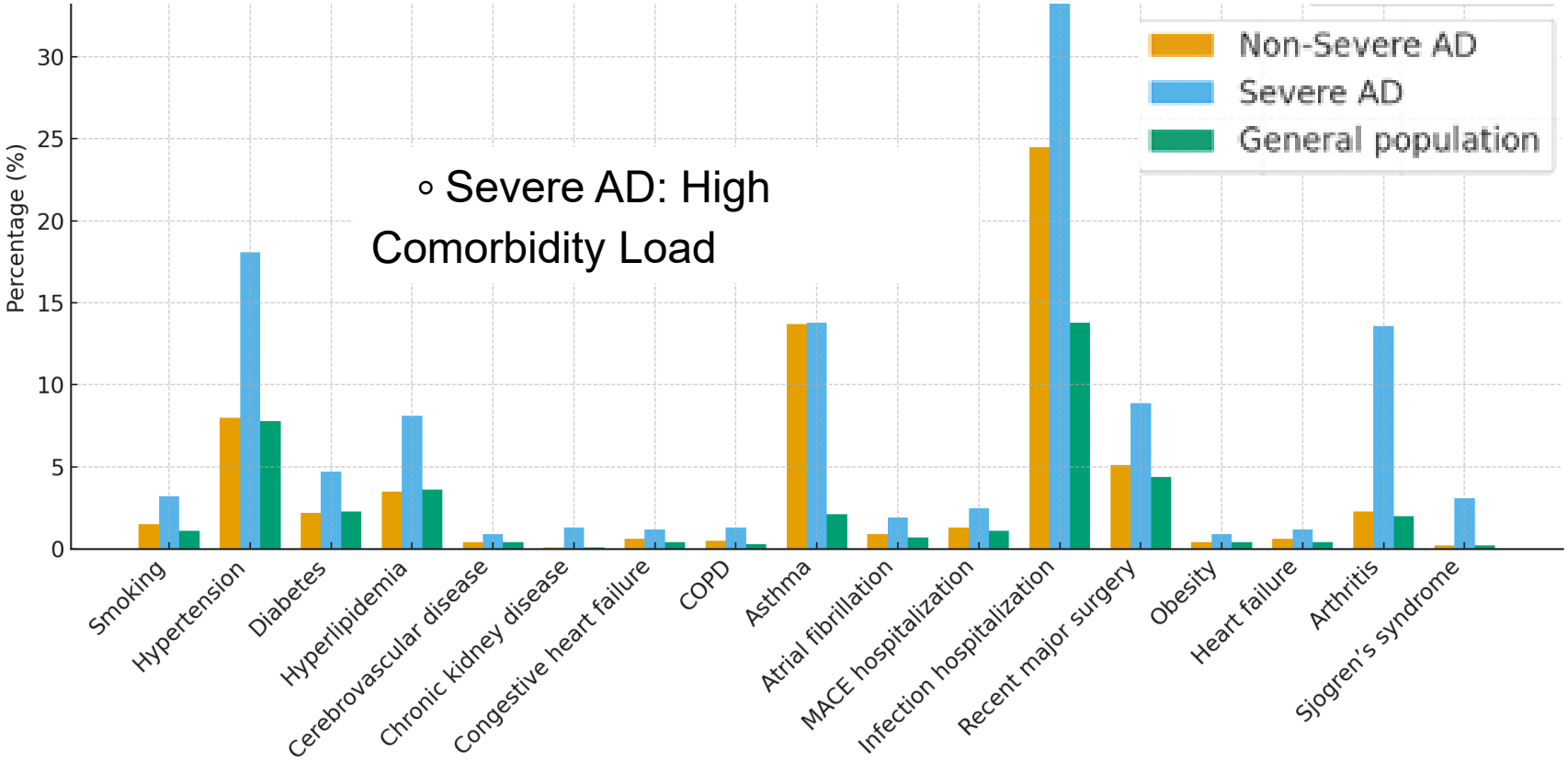
Result

Baseline differences: Severe AD had more comorbidities

- **Severe AD**: **Higher comorbidity burden**, Older (Mean 38.7 yrs)
- Total N: 210,492 AD Patients
  - Severe AD Subgroup: 6 % (12,472 Patients)

	Atopic dermatitis cohort	Non-severe atopic dermatitis	Severe atopic dermatitis	General population
Total number of individuals	210,492	198,020	12,472	1,048,395
Age (years), mean (SD)	30.4 (17.4)	29.9 (17.1)	38.7 (19.3)	30.4 (17.3)

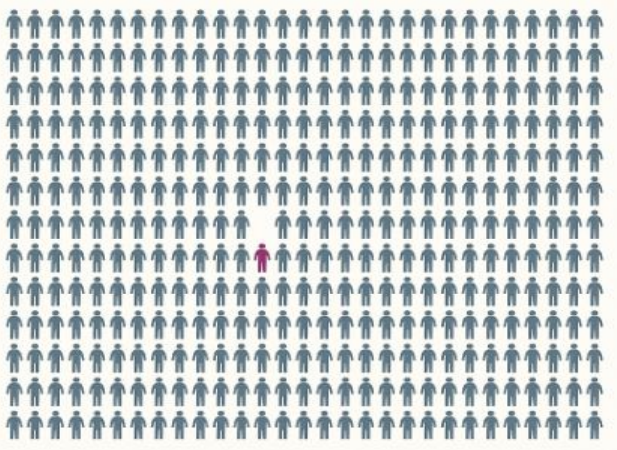
Baseline characteristics for patient in the AD population and the general population



VTE events rare and similar in AD and the general population

- Total VTE Events: 3,292 in AD Cohort
- IR per 1,000 person-years: 1.5 (AD cohort) vs 1.7 (general population)

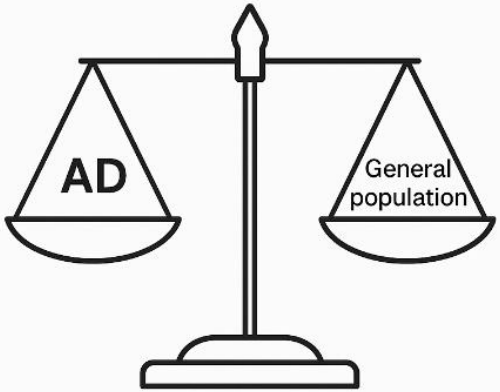
roughly 1-2 events per 1000 people/year



Overall VTE Risk in AD: Similar to the general population

- Adjusted HR (aHR)*: **1.04** (95% CI 1.01–1.09)

**Adjusted for comorbidities, medication, prothrombotic disorders and events e.g., factor V Leiden, prothrombin gene mutations, protein C, protein S, antithrombin deficiency, antiphospholipid syndrome, malignancy, surgery, infection hospitalization*



Absolut VTE risk: Expected Age Progression

- increased with age in the AD cohort and general population

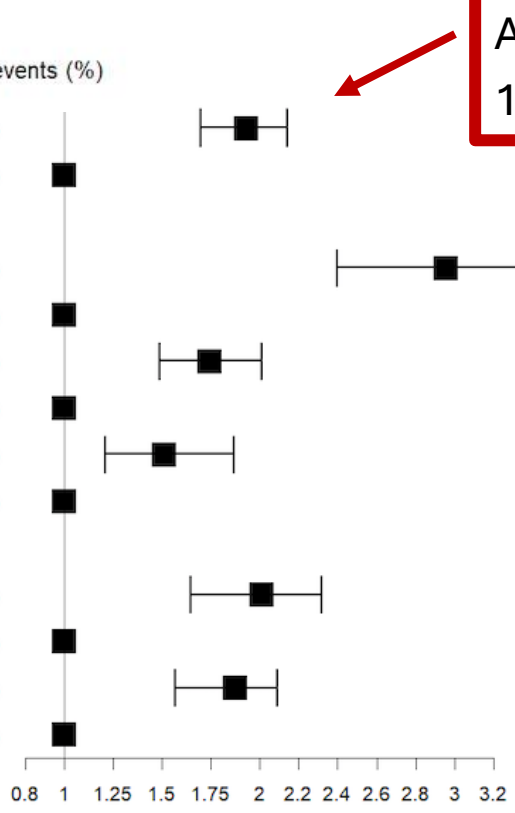
Severe AD IR (18-39 yrs): 2.1 per 1,000 person-years

Severe AD IR (65+ yrs): 10.5

- **Higher VTE incidence across all age groups in severe AD, exceeding matched controls**
- Non-severe AD: IR Matches Controls

Increased VTE Risk in Severe AD

Subgroup	Number of patients	Person-years at risk	VTE events (%)
Severe AD	12472	124528	483 (3.9)
General population	62026	621401	1281 (2.1)
Age			
Severe AD - 18-39	6983	70607	146 (2.1)
General population - 18-39	34792	339604	252 (0.7)
Severe AD - 40-64	3945	43055	223 (5.7)
General population - 40-64	19608	214418	652 (3.3)
Severe AD - 65+	1550	10866	114 (7.4)
General population - 65+	7626	53516	373 (4.9)
Sex			
Severe AD - Men	4982	48494	182 (3.7)
General population - Men	24691	242591	464 (1.9)
Severe AD - Women	7490	76034	301 (4)
General population - Women	37214	37881	817 (2.2)



aHR (Severe AD): **1.9** (95% CI 1.70–2.14)

all age groups *youngest group

Increased risk in both sexes

Increased VTE Risk in Severe AD

Youngest Group (18-39 yrs): Highest aHR

Subgroup	Number of patients	Person-years at risk	VTE events (%)
Severe AD - 18-39	6983	70607	146 (2.1)
General population - 18-39	34792	339604	252 (0.7)
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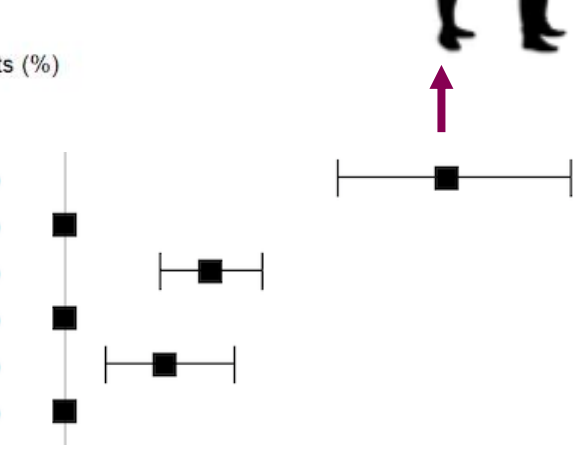


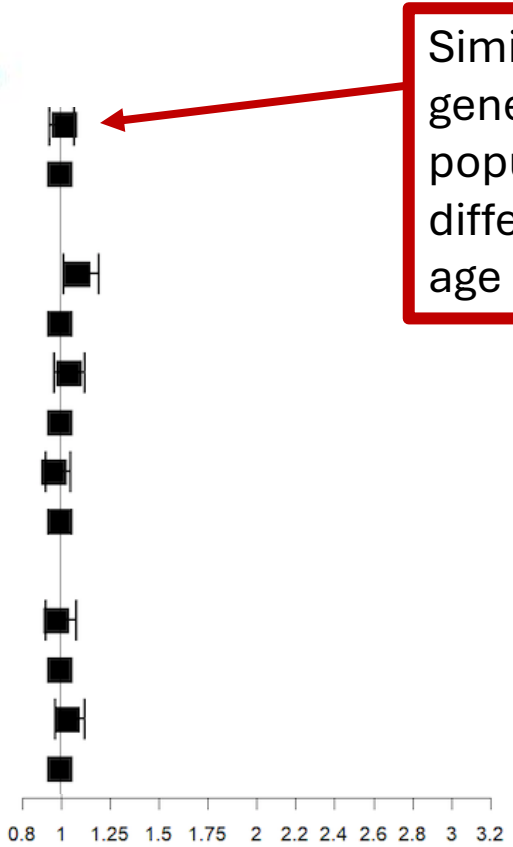
Severe AD (18-39 yrs) aHR: 2.95 (95% CI 2.40–3.59)

Not previously reported

Small absolute risk difference

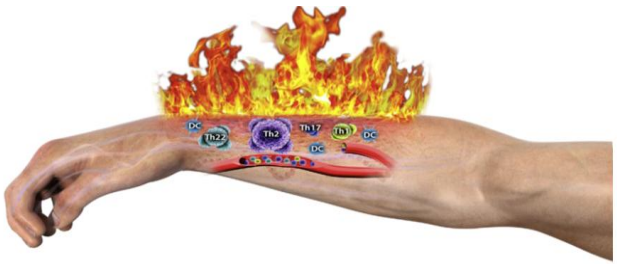
No increased VTE Risk in Non-Severe AD

Subgroup	Number of patients	Person-years at risk	VTE events (%)
Non-severe AD	198020	1799145	2809 (1.4)
General population	986369	8959221	12952 (1.3)
Age			
Non-severe AD - 18-39	151885	1341986	1055 (0.7)
General population - 18-39	758044	6326867	4504 (0.6)
Non-severe AD - 40-64	33345	363543	1079 (3.2)
General population - 40-64	165437	1803001	4983 (3)
Non-severe AD - 65+	12909	93616	675 (5.2)
General population - 65+	62888	460064	3304 (5.3)
Sex			
Non-severe AD - Men	80646	67783	988 (1.2)
General population - Men	403790	3383017	4622 (1.1)
Non-severe AD - Women	117374	1121316	1821 (1.6)
General population - Women	584234	5576204	8330 (1.4)



Similar to general population; no differences by age or sex

Discussion: Potential Mechanisms Linking severe AD to DVT Risk



- Remains unclear, but appears multifactorial
- Chronic systemic inflammation (pro-thrombotic) in severe AD ?
- Severe AD: High burden of conventional risk factors (we adjusted for major VTE risk factors) cumulative effects or unmeasured factors ?
- Lifestyle: immobility / sedentary behavior

[Brunner, Leung et al, Ann Allergy Asthma Immunol 2018]

Study Strengths and Limitations

- **Strengths:**

High quality, population-based registers

Large sample size (robust subgroups)

- **Limitations:**

No primary care data of AD (but AD cases come from specialist care, high validity of the diagnosis)
Severity defined by proxies (Rx/Hospitalization)
Residual confounding from unmeasured lifestyle factors

Conclusion

Overall Risk: No general increase VTE risk in AD

Severe AD approximately 2x VTE risk (aHR 1.93)

Highest relative risk in youngest adults (aHR 2.95)

Highlights the need to identify high-risk subgroups when assessing VTE risk

Thank you! To my colleagues in the epidemiological team at the Centre for Pharmacoepidemiology (CPE) at Karolinska Institutet, Sweden



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