

Table SI. Definitions of study variables^a

Variable	Codes	Data source
Cohort-defining variables		
Hospital-diagnosed atopic dermatitis in Danish-born individuals ^b	ICD-8: 691 ICD-10: DL20	The Danish National Patient Registry; The Medical Birth Registry
Outcome variables		
Hospital-diagnosed varicella ^c	ICD-8: 052; ICD-10: DB01, DG020A, DG051H, DG051K, DJ171A* In separate analyses of hospitalizations for varicella, we included all inpatient contacts with a duration of at least 1 days.	The Danish National Patient Registry
Herpes zoster^d		
Hospital-diagnosed herpes zoster	ICD-8: 053; ICD-10: DB02, DG051I, DG051M, DH031F, DH131M, DH165C, DH190D, DH192D, DH192J, DH220C, DH621B; In separate analyses of hospitalizations for zoster, we included all inpatient contacts with a duration of at least 1 days.	The Danish National Patient Registry
Antiviral treatment in general practice	A first-time antiviral prescription at age ≥ 40 for an antiviral drug used to treat zoster: ATC: J05AB01 (800 mg tablet doses of acyclovir in packages of 35 pills), J05AB011 (500 mg tablet doses of valacyclovir), J05AB09 (500 mg tablet doses of famciclovir)	The Danish National Prescription Registry

Censoring variables	Emigration or death	The Civil Registration System
Complications to varicella or zoster ^c		
Nervous system		
- Encephalitis, meningitis, myelitis	ICD-10: DA869, DA878, DA879, DA899, DG048, G049, DG051 For varicella also, ICD-10: DB010, DB011, DG051H For zoster also, ICD-10: DB020, DG051I, DB021	The Danish National Patient Registry
- Ataxia	ICD-10: DR27	The Danish National Patient Registry
- Afebrile seizures, status epilepticus	ICD-10: DR25, DG41, DR56 (excluding DR560)	The Danish National Patient Registry
- Febrile seizures	ICD-10: DR560	The Danish National Patient Registry
- Other: acute disseminated encephalomyelitis, hypertensive encephalopathy, stroke, arteritis cerebri, Reye's syndrome	ICD-10: DG369, DI674, DI61, DI63, DI64, DI677, DG937	The Danish National Patient Registry
- Peripheral nervous system: Guillain-Barré, facial nerve disorders, cranial nerve palsy, polyneuropathy, neuritis, neuralgia, radiculopathy	ICD-10: DG610, DG51 (excluding DG512), DG530, DG531, DG538, DM792 For zoster also, ICD-10: DB022	The Danish National Patient Registry
Bacterial complications		
- Infection of skin and soft tissue, including	ICD-10: DA46, DL00 (excluding DL009B), DL01, DL02, DL03, DL04, DL088	The Danish National Patient Registry

orbital cellulitis and necrotizing fasciitis	(excluding DL088C), DL089, DH050, DM726	
- Sepsis, septic shock, and toxic shock syndrome	ICD-10: DA40, DA41 (excluding DA413, DA414, DA415, DA419B), DA483, DR572, DR578A, DP369	The Danish National Patient Registry
- Septic arthritis, osteomyelitis, synovitis, tenosynovitis, myositis, spondylodiskitis	ICD-10: DM00 (excluding DM001), DM60 (excluding DM601 and DM602), DM65 (excluding DM652; DM653; DM654), DM86 (excluding DM863, DM864, DM865, DM866), DM462, DM463 (excluding DM463A), DM465	The Danish National Patient Registry
- Meningitis, intraspinal/-cranial abscess	ICD-10: DG002, DG003, DG009, DG060 (excluding DG061C, DG061G-L), DG061 (excluding DG061E-G)	The Danish National Patient Registry
- Endocarditis, myocarditis	ICD-10: DI33, DI400	The Danish National Patient Registry
- Pericarditis	ICD-10: DI301 (excluding DI301A and DI301E)	The Danish National Patient Registry
- Pneumonia (if specified as staphylococcal [possible hematological spread])	ICD-10: DJ152	The Danish National Patient Registry
- Bacterial infections of unspecified type or location, including bacteremia	ICD-10: DA488 (excluding DA488A), DA490, DA491, DA498, DA499, DB95 (excluding DB953)	The Danish National Patient Registry
- Antibiotic prescription (penicillins and other beta-lactam antibiotics, Macrolides, Quinolones)	ATC: J01C, J01D, J01F, J01M	The Danish National Prescription Registry
Immune-mediated (dermatological /		

rheumatological / hematological)		
- Urticaria, erythema multiforme, erythema nodosum, cutaneous vasculitis	ICD-10: DL50, DL51, DL52, DL758, DL759	The Danish National Patient Registry
- Aseptic arthritis	ICD-10: DM015, DM018, DM028, DM029, DM036, DM13	The Danish National Patient Registry
- Hematological: Sickle cell crisis, thrombocytopenia (including idiopathic thrombocytopenic purpura), cryoglobulinemia, lymphangitis, disseminated intravascular coagulopathy, agranulocytosis, or need for transfusion	ICD-10: DD570, DD693, DD695, DD696, DD891, DD65, DD70 (excluding DD709A-D) or treatment code BOQA or BOUA0	The Danish National Patient Registry
Ocular / otological		
- Ocular (blepharitis, conjunctivitis, keratitis, scleritis/episcleritis, uveitis, iridocyclitis, retinal necrosis, opticus neuritis)	ICD-10: DH010, DH018, DH019, DH031, DH038, DH103, DH105, DH106, DH108, DH109, DH112, DH131, DH132, DB308 (excluding DB308A), DB309, DH150, DH151, DH160, DH17, DH165 (excluding DH165A, DH165B, DH165D-G), DH169, DH17, DH192 (excluding DH192A-C, DH192E-I, DH192K), DH200, DH208, DH209, DH30, DH44IE, DH220 (excluding DH220D-G), DH329 (excluding DH329C-E), DH33, DH46	The Danish National Patient Registry

	For zoster, also ICD-10: DB023, DH031F, DH131M, DH165C, DH190D, DH192D, DH192J, DH220C	
- Otological (external otitis, zoster oticus [for zoster])	ICD-10: DH621 For zoster, also ICD-10: H621B	The Danish National Patient Registry
Disseminated viral infection		
- Respiratory (fibrosis, including organizing pneumonia, diffuse alveolar damage and acute respiratory distress syndrome)	ICD-10: DJ128, DJ129, DJ171, DJ80, DJ841, DJ849 For varicella, also ICD-10: DB012	The Danish National Patient Registry
- Hepatitis/liver failure (unspecified/viral)	ICD-10: DK759A, DK720, DB178, DB179, DB19	The Danish National Patient Registry
- Glomerulonephritis (acute or unspecified) and nephrotic syndrome	ICD-10: DN00, DN01, DN04, DN05	The Danish National Patient Registry
- Pericarditis, viral	ICD-10: DI30 (excluding DI301A-D)	The Danish National Patient Registry
- Myocarditis, non-infectious	ICD-10: DI40 (excluding DI400 and DI408A)	The Danish National Patient Registry
- Orchitis	ICD-10: DN459 (excluding DN459D, DN459E)	The Danish National Patient Registry
- Pancreatitis, unspecified	ICD-10: DK859	The Danish National Patient Registry
- Unspecified disseminated	For zoster only, ICD-10: DB027	The Danish National Patient Registry
Other/unspecified complication		

- Other (dehydration, hypovolemia, nausea and vomiting)	ICD-10: DE86, DR571, DR11	The Danish National Patient Registry
- Unspecified ^e	For varicella, ICD-10: DB018 For zoster, ICD-10: DB028	The Danish National Patient Registry
Post-herpetic neuralgia	For zoster only. Defined as a diagnosis code for post-herpetic neuralgia in the Danish National Patient Registry (ICD-10: DG530) or a prescription for a drug used to treat post-herpetic neuralgia in the Danish National Prescription Registry within 90 to 365 days after the initial zoster event. According to Danish guidelines for the treatment of neuralgia, we included capsaicin (ATC: N01BX04), gabapentin (ATC: N02BF01, N03AX12), pregabalin (ATC: N02BF02; N03AX16), amitriptyline (ATC: N06AA09), nortriptyline (ATC: N06AA10), duloxetine (ATC: N06AX21), venlafaxine (ATC: N06AX16). We did not include those with a prescription for the agents in the year leading up to the zoster event in order not to misclassify other indications (e.g., baseline depression) as post-herpetic neuralgia. Previous prescriptions within the first 0–90 days after zoster were allowed though.	The Danish National Patient Registry and The Danish National Prescription Registry
Length of hospital stay for varicella or zoster	To account for potential transfer between hospital departments and hospitals, we considered an admission on the same day as a discharge to belong to the same hospital admission and the length of stay was computed as the time between first admission and the last discharge.	The Danish National Patient Registry

Covariables ^a		
Age at index date	Categories: 0–5, 6–9, 10–17, 18–40, 40+ years. Grouping chosen to capture age-dependent differences in incidence of atopic dermatitis (typically diagnosed in childhood, especially before age 6) and zoster (incidence increases sharply after age 40) with age.	
Sex	Categories: Female, Male	
Calendar period	Categories: 1982–1994, 1995–1999, 2000–2009, 2010–2013, 2014–2016.	
Atopic dermatitis severity	Categorized based on treatment in the year before varicella/zoster (or corresponding date for controls).	The Danish National Patient Registry and the Danish National Prescription Registry
Severe	Prescription for a systemic glucocorticoid or other immunosuppressant identified by procedure codes: “BNGA1” “BNGA2” “BNGA3” “BNGA4” “BOHJ18B8” “BWHB83” “BWHA115” “BOHJ20” “BOHJ22”) or ATC: L04AX01, L01BA01, L04AX03, L04AD01, L04AA06, D11AH05, H02AB (excluding inj. treatment)	The Danish National Patient Registry and the Danish National Prescription Registry
Moderate	Prescription for a topical corticosteroid or calcineurin inhibitor identified by ATC : D07, D11AH01, D11AH02	The Danish National Prescription Registry
Mild	Patients not classified as moderate or severe.	
Asthma	One asthma diagnosis or two asthma-related prescriptions ever before.	The Danish National Patient Registry and the
	ICD-8 : 493	

	ICD-10: DJ45; DJ46 ATC: R03	Danish National Prescription Registry
Rhinitis	ICD-8: 507; ICD-10: DJ30	The Danish National Patient Registry
Solid cancer	ICD-8: 140–199, 27559; ICD-10: DC00–DC80	The Danish Cancer Registry
Severe immunosuppression	Previous diagnosis ever or treatment within past 90 days for the codes below <i>Note: Excludes oral glucocorticoids and other immunosuppressants where atopic dermatitis may be the indication (considered in severity definition)</i>	
Human immunodeficiency virus infection	ICD-8: 079.83, Y4049, Y4149 ICD-10: DB20; DB21; DB22; DB23; DB24; DF024; DZ21	The Danish National Patient Registry
Lymphoma	ICD-8: 200; 201; 202 ICD-10: DC81; DC82; DC83; DC84; DC85; DC86; DC88; DC96	The Danish Cancer Registry
Leukemia	ICD-8: 204; 205; 206; 207 ICD-10: DC91; DC92; DC93; DC94; DC95	The Danish Cancer Registry
Myeloma	ICD-8: 203 ICD-10: DC90	The Danish Cancer Registry
Hematopoietic stem cell or bone marrow transplantation	ICD-8: None ICD-10: DT860; DZ948C; DZ948 if not DZ948A, DZ948B, DZ948C and if coded as a B-diagnosis or additional diagnosis together with one of the following A-diagnoses C770, C81–C96, D45–D47, D50–D85, D87–D89, T86.0, T86.0A, or T88.8N Procedure codes: BOQE; BOQF	The Danish National Patient Registry
Other cellular immune deficiency	ICD-8: 284.01; 284.02; 284.08; 284.09; 758.30	The Danish National Patient Registry

	ICD-10: DD611; DD612; DD613; DD618; DD619; DD81; DD820; DD821; DD821A; DD822; DD83	
Immune-modulating therapy	ATC: L01; L04; V02CA01; V02CA02 (except: L04AX01, L01BA01, L04AX03, L04AD01, L04AA06) Procedure codes: BOHJ; BWG; BWHA; BWHB (except: BWHB4, BWHB83, BWHA115, BOHJ20, BOHJ22) Or ATC ML01, ML04, MV02CA01, or MV02CA02 (except: ML04AX01, ML01BA01, ML04AX03, ML04AD01, ML04AA06) used as additional code in the Patient Registry	The Danish National Patient Registry and the Danish National Prescription Registry
Severe mood disorder	ICD-8: 296.09, 296.29, 296.99, 298.09, 300.49, 300.09, 300.19, 300.29, 295.79 ICD-10: DF00x3, DF01x3, DF02x3, DF0393, DF0632, DF064, DF1x54, DF204, DF25, DF32, DF33, DF341, DF40, DF41, DF43, DF3810, DF530, DO993B2, DO993B3	The Danish National Patient Registry and the Danish Psychiatric Central Research Registry
Education level	Based on information on the highest of attained education for mother or father (if available) for those aged below 22 years and patients own education level for those aged 22 or older. Categorized as: – Below lower secondary school if lower secondary school, upper secondary school or higher education was not completed – 1 Lower secondary education: AFSP1H or HOVEDOMRAADE_OVER = 10 or 29 AND HFAUDD 210, 1009, 1010, 1011, 1109, 1110, 1111 or 1209	The Population Education Registry

- 2 Upper secondary education: **AFSP1H** or **HOVEDOMRAADE_OVER** = 20, 25, 30, 35, or 39
- 3 Higher education: **AFSP1H** = 40, 50, 60, 65, or 70 or **HOVEDOMRAADE_OVER** = 40, 50, 60, 70, or 80

Abbreviations: ICD=International Classification of Disease; ATC=Anatomical Therapeutic Chemical Classification System

^a For all variables, all subcodes were included unless otherwise stated; all types of contacts (inpatient, outpatient, and emergency department), and primary and secondary diagnoses were considered. Note, that all ICD-10 codes carry the prefix “D”. Note that the Danish National Patient Registry does not contain information from general practitioners. However, in January 2014, the Capital Region (one of the five Danish regions) introduced a new hospital-based system for primary care patients seen out-of-hours, and consequently, these patients have been included in DNPR as outpatient contacts since.

^b The earliest date of admission or first outpatient appointment for AD served as the diagnosis date. We excluded those with an ICD-8 diagnosis recorded together with an additional (“modification”) code indicating that it is potentially an uncertain/unverified/working diagnosis (c_diagmod=1–7).

^c Excludes specific code for congenital varicella (ICD-10: DP358A). The date of diagnosis for varicella was defined as the date of admission or first outpatient or emergency department visit.

^d The date of diagnosis for zoster was defined as the date of admission, first outpatient or emergency department visit, or antiviral prescription for zoster, whichever came first

^e We limited the assessment of complications to varicella-zoster infections diagnosed since 1994 when the 10th revision of the International Classification of Diseases, with its greater level of detail, was introduced. When considering complications separately, patients could contribute to several categories.

^f Defined as being registered with an ICD-10 diagnosis of DB018 (varicella with other complication) or DB028 (zoster with other complication), respectively, and no other ICD-10 codes compatible with complications in the Danish National Patient Registry at the time of first hospital diagnosis for varicella.

^g We restricted the analysis of potential risk factors of interest to those with outcomes since 1 January 1996 to ensure at least one year of prescription history. We defined all covariables using information recorded up to the date of varicella or zoster (and the corresponding date for controls).

Table SII. Characteristics of patients with hospital-diagnosed AD. Values are numbers (percentages) unless stated otherwise

Characteristic	Varicella analysis	Zoster analysis
Total	46,875 (100.0)	47,081 (100.0)
Median age (IQR) at first AD diagnosis, years	5.8 (1.7–21.0)	5.8 (1.7–21.0)
Age group at first AD diagnosis, years		
0–5	23,724 (50.6)	23,843 (50.6)
6–9	4,410 (9.4)	4,436 (9.4)
10–17	5,071 (10.8)	5,096 (10.8)
18–40	9,322–9,327 (19.9) ^a	9,357 (19.9)
≥40	4,344–4,348 (9.3) ^a	4,349 (9.2)
Sex		
Women	23,762 (50.7)	23,860 (50.7)
Men	23,113 (49.3)	23,221 (49.3)
Setting for first AD diagnosis		
Inpatient	14,547 (31.0)	14,592 (31.0)
Outpatient clinic or emergency department	32,328 (69.0)	32,489 (69.0)
Calendar period of index date		
1979–1994	11,306 (24.1)	11,342 (24.1)
1995–1999	7,966 (17.0)	7,990 (17.0)
2000–2009	14,931 (31.9)	15,014 (31.9)
2010–2013	7,194 (15.3)	7,229 (15.4)
2014–2016	5,478 (11.7)	5,506 (11.7)
Median age (IQR) at end of follow-up, years ^b	25.4 (15.3–39.6)	25.4 (15.4–39.5)
Age group at end of follow-up, years ^b		
0–5	3,106 (6.6)	2,990 (6.4)
6–9	3,619 (7.7)	3,651 (7.8)
10–17	7,876 (16.8)	7,960 (16.9)
18–39	20,831 (44.4)	21,033 (44.7)
≥40	11,443 (24.4)	11,447 (24.3)
Median duration of follow-up (IQR) ^b , days	5,189 (2,369–7,942)	5,155 (2,363–7,906)
Years of follow-up ^b		
0 to <1	309 (0.7)	285 (0.6)

1 to <5	8,671 (18.5)	8,758 (18.6)
5 to <10	8,268 (17.6)	8,356 (17.7)
10 to <20	15,378 (32.8)	15,523 (33.0)
>20	14,249 (30.4)	14,159 (30.1)
Reasons for end of follow-up ^b		
Outcome	209 (0.4)	1,075 (2.3)
Study end date	44,281 (94.5)	43,682 (92.8)
Death	1,419 (3.0)	1,349 (2.9)
Emigration	966 (2.1)	975 (2.1)

Abbreviations: AD: atopic dermatitis; IQR: interquartile range

^a Masked to prevent identification of individuals through cross-examination of tables, per rules by Statistics Denmark

^b In analysis of hospital diagnoses varicella and any zoster, respectively.

Table SIII. Cumulative incidence proportion of varicella^a and zoster in people with hospital-diagnosed AD, by time since diagnosis^a

Varicella		
Time since AD diagnosis	Any hospital diagnosis^b	Hospitalizations
1 year	0.0039 (0.0032–0.0048)	0.0025 (0.0019–0.0032)
2 years	0.0060 (0.0051–0.0071)	0.0036 (0.0029–0.0044)
3 years	0.0067 (0.0057–0.0078)	0.0040 (0.0033–0.0049)
4 years	0.0073 (0.0063–0.0084)	0.0043 (0.0035–0.0052)
5 years	0.0080 (0.0069–0.0092)	0.0046 (0.0038–0.0055)
10 years	0.0085 (0.0074–0.0098)	0.0048 (0.0040–0.0058)
Zoster		
Time since AD diagnosis	Any hospital diagnosis^c	Hospitalizations
1 year	0.0017 (0.0013–0.0021)	0.0002 (0.0001–0.0003)
5 years	0.0055 (0.0049–0.0063)	0.0006 (0.0004–0.0009)
10 years	0.0106 (0.0096–0.0116)	0.0008 (0.0006–0.0012)
15 years	0.0173 (0.0159–0.0188)	0.0011 (0.0008–0.0015)
20 years	0.0267 (0.0248–0.0288)	0.0013 (0.0009–0.0018)
25 years	0.0377 (0.0350–0.0406)	0.0015 (0.0011–0.0021)
30 years	0.0510 (0.0472–0.0550)	0.0021 (0.0014–0.0030)
35 years	0.0728 (0.0666–0.0793)	0.0021 (0.0014–0.0030)

Abbreviations: AD: atopic dermatitis

^a Varicella analyses were restricted to patients aged below 6 years at time of first AD diagnosis because of few events in older age groups

^b Including inpatient, hospital outpatient, and emergency department diagnoses

^c Including inpatient, hospital outpatient, and emergency department diagnoses and patients identified by antiviral prescriptions used for treatment of zoster.

Table SIV. Cumulative incidence proportion (95% confidence interval) of any zoster diagnosis^a in people with AD with the start of follow-up delayed until (a) age 18, (b) age 40, and (c) age 50, in patients who were alive and event-free by that age (landmark analysis)

(a) Age 18	
Year of / Age at follow-up	Cumulative incidence proportion
1 year / age 19	NA ^b
5 years / age 23	0.0006 (0.0003–0.0011)
10 years / age 28	0.0013 (0.0007–0.0021)
15 years / age 33	0.0029 (0.0019–0.0043)
20 years / age 38	0.0040 (0.0027–0.0059)
25 years / age 43	0.0431 (0.0337–0.0541)
30 years / age 48	0.1050 (0.0836–0.1291)
35 years / age 53	0.1834 (0.1229–0.2535)
(b) Age 40	
Year of / Age at follow-up	Cumulative incidence proportion
1 year / age 41	0.0171 (0.0142–0.0204)
5 years / age 45	0.0524 (0.0468–0.0584)
10 years / age 50	0.0999 (0.0908–0.1095)
15 years / age 55	0.1529 (0.1391–0.1672)
20 years / age 60	0.1754 (0.1585–0.1931)
25 years / age 65	0.2103 (0.1828–0.2391)
30 years / age 70	0.2623 (0.2131–0.3140)
35 years / age 75	0.4176 (0.1850–0.6365)
(c) Age 50	
Year of / Age at follow-up	Cumulative incidence proportion
1 year / age 51	0.0088 (0.0060–0.0124)
5 years / age 55	0.0490 (0.0410–0.0580)
10 years / age 60	0.0848 (0.0727–0.0981)
15 years / age 65	0.1289 (0.1094–0.1500)
20 years / age 70	0.1795 (0.1469–0.2147)
25 years / age 75	0.2276 (0.1727–0.2871)
30 years / age 80	0.2474 (0.1823–0.3177)
35 years / age 85	NA ^b

Abbreviations: AD: atopic dermatitis

^a Including inpatient, hospital outpatient, and emergency department diagnoses and patients identified by antiviral prescriptions used for treatment of zoster.

^b Masked to preserve anonymity per rules by Statistics Denmark.

Table SV. Association between patient characteristics and risk of herpes zoster in people with hospital-diagnosed AD^a

	Zoster cases n (%)	Controls n (%)	ORs (95% CI)	
			Unadjusted ^b	Adjusted ^c
Total	589	589		
Severity of AD				
Mild	221 (37.5)	291 (49.4)	Ref.	Ref.
Moderate	243 (41.3)	217 (36.8)	1.10 (0.93–1.31)	1.11 (0.93–1.32)
Severe	125 (21.2)	81 (13.8)	1.40 (1.13–1.73)	1.36 (1.09–1.70)
Asthma				
No	297 (50.4)	339 (57.6)	Ref.	Ref.
Yes	292 (49.6)	250 (42.4)	1.12 (1.00–1.26)	1.13 (1.00–1.28)
Rhinitis				
No	483 (82.0)	462 (78.4)	Ref.	Ref.
Yes	106 (18.0)	127 (21.6)	0.91 (0.79–1.05)	0.85 (0.73–0.99)
Solid cancer				
No	589 (100)	589 (100)	Ref.	Ref.
Yes	–	–	–	–
Mood disorder				
No	557 (94.6)	561 (95.2)	Ref.	Ref.
Yes	32 (5.4)	28 (4.8)	0.98 (0.77–1.26)	0.92 (0.70–1.20)
Severe immunosuppression				
No	533 (90.5)	560 (95.1)	Ref.	Ref.
Yes	56 (9.5)	29 (4.9)	1.63 (1.26–2.11)	1.51 (1.16–1.97)
Education level				
Below lower secondary education	78 (13.2)	108 (18.3)	0.81 (0.61–1.08)	0.78 (0.58–1.06)
Lower secondary education	39 (6.6)	56 (9.5)	Ref.	Ref.
Upper secondary education	238 (40.4)	252 (42.8)	0.97 (0.80–1.19)	0.97 (0.79–1.19)
Higher education	234 (39.7)	173 (29.4)	1.17 (0.96–1.43)	1.22 (0.99–1.51)

Abbreviations: AD: atopic dermatitis; CI: confidence interval; OR: odds ratio

^a Analysis restricted to outcomes after 1995 to ensure ≥ 1 year of prescription history for defining variables.

^b Accounts for matching factors

^c Adjusts additionally for the other factors in the table