

Appendix S1

SUPPLEMENTARY METHODS

Pertaining data analysis

- Productivity was proxied by earnings: gross earnings consist of: salary (including: taxable and non-taxable salary, fringe benefits, severance payments, value of stock options and sickness benefits paid by the employer), net profits from self-employed business and other taxable income (including fees from lectures and consulting business).
- A common approach to estimating the cost associated with a disease or an intervention in a population-based study is to compare the patients' and reference individuals' mean costs in year t minus their mean costs in the year leading up to the patients receiving their diagnosis. This approach considers both the costs before the index date and the costs of individuals without the disease and thus provides an estimate of the costs attributable to the disease (difference-in-difference approach).

Appendix S2

SUPPLEMENTARY RESULTS

Effect on gross earnings

Lifetime earnings loss was calculated as the average earning loss among patients compared with reference individuals from age 18 years to age 65 years. Before the index date the average earning loss was EUR 90, while it was EUR 1,331 per year from the index date until retirement.

Discussion

Management and treatment of patients with moderate-to-severe atopic dermatitis (AD) in Denmark is associated with an attributable yearly cost of AD to the healthcare sector of EUR 5.6 million, calculated as the average yearly attributable healthcare cost in year 1 to year 5 for the 2018 prevalent population of 4,999 patients with moderate-to-severe AD.

This is well illustrated by the average patient in this sample having the first AD-related hospital contact at age 35 years and imposing attributable healthcare costs of almost EUR 55,400 during adulthood, from 18–65 years of age; calculated as the average attributable lifetime healthcare cost including costs of prescription medicines of an average of EUR 757 in ages 18–34 years, EUR 3,596 in the year of diagnosis of AD (age 35 years) and an average of EUR 1,298 in the years from age 36–65 years.

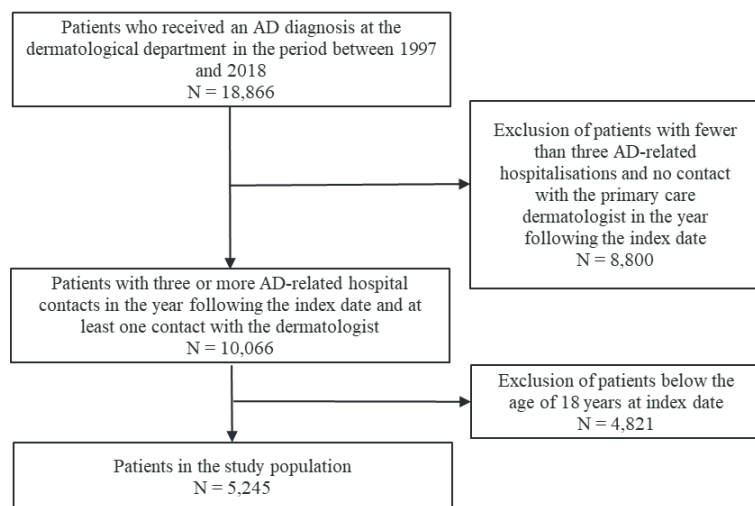


Fig. S1. Inclusion process for the study population. Specifically, the figure presents the remaining number of patients in the sample after each of the exclusion criteria was applied (*left*) as well as the number of patients excluded due to each of the exclusion criteria (*right*). AD: atopic dermatitis.

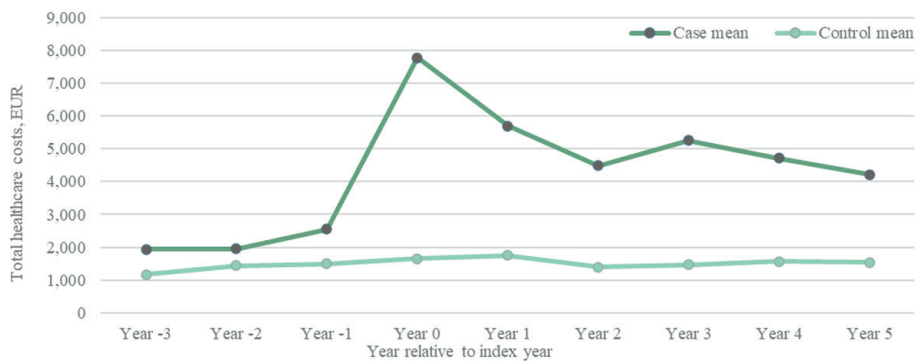


Fig. S2. Mean individual healthcare costs for patients with 3 or more atopic dermatitis (AD) contacts per year in the first 4 years after the index date and reference individuals per year relative to index date, in Euros (EUR).

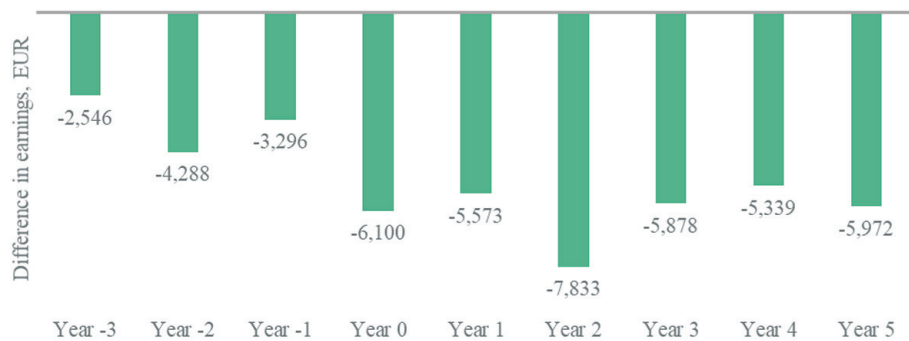


Fig. S3. Difference in gross earnings between patients with 3 or more atopic dermatitis (AD) contacts per year in the first 4 years after the index date and reference individuals per year relative to index year, in Euros (EUR).

Table SI. Mean individual healthcare costs per year relative to index date, in Euro (EUR)

Healthcare costs	Year -3	Year -2	Year -1	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5
Patients , mean (SD)	1,870 (4,304)	1,986 (4,606)	2,491 (5,713)	4,930 (6,813)	2,756 (5,580)	2,725 (8,722)	2,693 (7,004)	2,635 (9,543)	2,460 (7,076)
Patients	5,046	5,245	5,245	5,245	5,163	4,970	4,738	4,484	4,163
Reference individuals , mean (SD)	1,364 (2,484)	1,495 (2,939)	1,611 (2,773)	1,572 (3,078)	1,612 (3,418)	1,491 (2,462)	1,517 (2,919)	1,537 (2,496)	1,510 (2,223)
Number	15,077	15,656	15,656	15,656	15,410	14,831	14,135	13,373	12,410
Difference between patients and reference individuals	506	491	879	3,359	1,143	1,233	1,175	1,098	950
SD	(90)	(96)	(108)	(123)	(106)	(147)	(123)	(161)	(123)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

The table presents the mean and standard deviations (SD) of healthcare costs in the selected sample of patients and in the matched sample of reference individuals in each year relative to the index date. In addition, the table presents the difference in mean healthcare costs between the selected sample of patients and the matched reference individuals. Last, the table presents the *p*-value of a *t*-test for the difference between the healthcare costs in the selected sample of patients and the healthcare costs in the matched sample of reference individuals.

Table SII. Mean individual costs for prescription medicines, in Euro (EUR)

Costs	Year -3	Year -2	Year -1	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5
All prescription medicines									
Patients	239	256	336	408	363	368	379	376	389
Reference individuals	138	142	156	170	179	183	195	210	218
Difference	(101)***	(114)***	(180)***	(237)***	(183)***	(184)***	(185)***	(166)***	(171)***
Antibiotics for topical use and corticosteroids									
Patients	4	6	11	32	23	19	16	15	14
Reference individuals	0	0	0	1	1	1	1	1	1
Difference	(3)***	(5)***	(10)***	(31)***	(22)***	(19)***	(15)***	(14)***	(13)***
Other dermatological preparations									
Patients	28	42	80	237	172	144	117	111	103
Reference individuals	3	3	4	4	5	5	6	8	9
Difference	(26)***	(39)***	(76)***	(232)***	(168)***	(139)***	(111)***	(103)***	(94)***
Other prescription medicines									
Patients	208	219	262	293	292	305	321	320	337
Reference individuals	136	140	154	168	177	181	192	207	215
Difference	(72)***	(79)***	(107)***	(125)***	(115)***	(124)***	(129)***	(113)***	(122)***

The table presents the total mean cost of prescription medicines, as well as the cost of prescription medicines divided into 3 drug classes: antibiotics for topical use and corticosteroids (including antibiotics for topical use, Anatomical Therapeutic Chemical (ATC)-code D06A and sub-levels; corticosteroids, ATC-code D07 and sub-levels; tacrolimus, ATC-code D11AH01; and pimecrolimus, ATC-code D11AH02), other dermatological preparations (including cyclosporine, ATC-code L04AD01; azathioprine, ATC-code L04AX01; methotrexate, ATC-code L04AX03; prednisolone, ATC-code H02AB06; and mycophenolic acid, ATC-code L04AA06), and other prescription medicines. The mean cost of prescription medicines is shown for patients with moderate-to-severe AD (patients) and for their matched reference individuals in each year relative to the index date. The differences between patients and reference individuals are shown in parentheses, significant at *10%, **5%, ***1%.

Table SIII. Mean individual healthcare utilization by type of contact

Healthcare utilization	Year -3	Year -2	Year -1	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5
AD-related inpatient hospitalizations									
Patients	-	-	-	0.14	0.04	0.02	0.02	0.02	0.01
Reference individuals	-	-	-	-	-	-	-	-	-
Difference				(0.14)***	(0.04)***	(0.02)***	(0.02)***	(0.02)***	(0.01)***
Non-AD-related inpatient hospitalizations									
Patients	0.50	0.50	0.54	0.52	0.50	0.50	0.52	0.50	0.50
Reference individuals	0.40	0.41	0.44	0.41	0.39	0.38	0.40	0.39	0.39
Difference	(0.10)***	(0.09)***	(0.10)***	(0.11)***	(0.10)***	(0.12)***	(0.13)***	(0.11)***	(0.11)***
AD-related outpatient contacts									
Patients	-	-	-	8.78	1.98	1.29	1.08	0.79	0.66
Reference individuals	-	-	-	-	-	-	-	-	-
Difference				(8.78)***	(1.98)***	(1.29)***	(1.08)***	(0.79)***	(0.66)***
Non-AD-related outpatient contacts									
Patients	1.68	1.85	2.15	2.12	2.19	2.20	2.30	2.35	2.31
Reference individuals	1.12	1.26	1.32	1.36	1.41	1.41	1.43	1.48	1.44
Difference	(0.56)***	(0.59)***	(0.83)***	(0.76)***	(0.77)***	(0.79)***	(0.87)***	(0.87)***	(0.87)***
Dermatologist visits									
Patients	2.17	2.77	6.54	1.77	1.15	1.19	1.34	1.25	1.07
Reference individuals	0.27	0.27	0.25	0.25	0.29	0.28	0.28	0.25	0.27
Difference	(1.90)***	(2.50)***	(6.29)***	(1.51)***	(0.87)***	(0.92)***	(1.06)***	(1.00)***	(0.80)***

The table presents mean healthcare utilization in each of the 5 defined categories of healthcare services for patients with moderate-to-severe atopic dermatitis (AD) (patients) and for their matched reference individuals in each year relative to the index date. The differences between patients and reference individuals are shown in parentheses, significant at *10%, **5%, ***1%.

Table SIV. Mean individual healthcare costs by cost category, in Euros (EUR)

Costs	Year -3	Year -2	Year -1	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5
AD-related inpatient hospitalizations									
Patients	-	-	-	617	164	89	85	87	78
Reference individuals	-	-	-	-	-	-	-	-	-
Difference				(617)***	(164)***	(89)***	(85)***	(87)***	(78)***
Non-AD-related inpatient hospitalizations									
Patients	738	721	865	855	803	953	1,024	1,031	931
Reference individuals	603	670	747	707	744	625	674	661	656
Difference	(136)***	(50)***	(118)***	(147)***	(60)***	(328)***	(350)***	(369)***	(275)***
AD-related outpatient contacts									
Patients	-	-	-	1,975	486	316	270	193	162
Reference individuals	-	-	-	-	-	-	-	-	-
Difference				(1,975)***	(486)***	(316)***	(270)***	(193)***	(162)***
Non-AD-related outpatient contacts									
Patients	668	756	936	1,012	859	920	865	885	841
Reference individuals	451	507	540	540	540	530	505	529	507
Difference	(217)***	(249)***	(396)***	(472)***	(319)***	(389)***	(359)***	(355)***	(333)***
Dermatologist visits									
Patients	75	96	221	55	40	41	48	47	40
Reference individuals	12	11	11	11	12	12	12	11	12
Difference	(63)***	(85)***	(210)***	(44)***	(28)***	(29)***	(37)***	(35)***	(28)***
Other primary sector costs									
Patients	388	413	467	416	404	406	400	393	408
Reference individuals	298	306	314	314	316	324	326	335	335
Difference	(90)***	(107)***	(153)***	(102)***	(87)***	(82)***	(74)***	(58)***	(74)***

The table presents mean healthcare costs in each of the 6 cost categories for patients with moderate-to-severe atopic dermatitis (AD) (patients) and for their matched reference individuals in each year relative to the index date. The differences between patients and reference individuals are shown in parentheses, significant at *10%, **5%, ***1%.