

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. *International Statistical Classification of Diseases 10th revision codes for cause of death*

Cause-specific deaths according to the organ system

Cause	Code
Infectious disease	A00–B99
Neoplasm/oncological disease	C00–D48
Endocrine disease	E00–E90
Intentional self-harm/psychiatric disease	F00–F99, X60–X84
Neurological disease	G00–G99
Cardiovascular disease	I00–I99
Respiratory disease	J00–J99
Gastrointestinal disease	K00–K93
Connective tissue disease	L00–M99
Urogenital disease	N00–O99

10 leading internal causes of death in patients with alopecia areata

Disease	Code
Lung cancer	C34
Hepatocellular carcinoma	C22
Gastric cancer	C16
Ischemic heart disease	I20, I21, I22, I23, I24, I25
Hemorrhagic stroke	I60, I61, I62
Pancreatic cancer	C25
Colon cancer	C18
Ischemic stroke	I63
Diabetes mellitus	E10, E11, E12, E13, E14
Pneumonia	J09, J10, J11, J12, J13, J14, J15, J16, J17, J18

eTable 2. Cox proportional-hazards models for estimating all-cause and cause-specific mortality risks in patients with alopecia areata and controls

Model	Covariates for adjustment											
	Income quartile	Location of residence	No. of household members	Self-reported personal history						Smoking status	Alcohol intake ^a	Stress
				Hypertension	Diabetes	Stroke	Heart disease	Liver disease	Malignancy			
Model 1 ^b (crude)	-	-	-	-	-	-	-	-	-	-	-	-
Model 2	○	○	○	-	-	-	-	-	-	-	-	-
Model 3	-	-	-	○	○	○	○	○	○	-	-	-
Model 4 ^c (fully-adjusted)	○	○	○	○	○	○	○	○	○	○	○	○

^a The product of the frequency (per week) and the amount (per drink).

^b Estimates in model 1 are presented as the crude hazard ratio and 95% confidence interval in the text.

^c Estimates in model 4 are presented as the adjusted hazard ratio and 95% confidence interval in the text.

eTable 3. All-cause and cause-specific mortality risks in patients with alopecia areata

Cause of death		No. of deaths		Model 1 ^a		Model 2		Model 3		Model 4 ^b	
		AA (73,107)	Control (731,070)	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
All cause		1,430	14,579	0.98	0.93 – 1.03	0.99	0.94 – 1.05	0.98	0.93 – 1.03	0.98	0.93 – 1.05
Cause-specific death according to systemic or organ disease	Infectious disease	34	316	1.08	0.76 – 1.54	1.05	0.73 – 1.52	1.07	0.75 – 1.52	0.97	0.66 – 1.44
	Oncological disease	579	5,978	0.97	0.89 – 1.06	0.98	0.90 – 1.07	0.97	0.89 – 1.06	0.96	0.88 – 1.05
	Endocrine disease	27	509	0.53	0.36 – 0.79	0.54	0.36 – 0.80	0.54	0.37 – 0.79	0.56	0.38 – 0.84
	Psychiatric disease	193	1,594	1.21	1.04 – 1.41	1.21	1.03 – 1.41	1.21	1.05 – 1.41	1.20	1.02 – 1.40
	Neurological disease	33	280	1.18	0.82 – 1.68	1.12	0.77 – 1.62	1.17	0.82 – 1.68	1.13	0.77 – 1.66
	Cardiovascular disease	269	2,627	1.02	0.90 – 1.16	1.05	0.93 – 1.20	1.02	0.90 – 1.15	1.07	0.94 – 1.22
	Respiratory disease	68	699	0.97	0.76 – 1.24	1.06	0.82 – 1.35	0.97	0.76 – 1.24	1.07	0.83 – 1.38
	Gastrointestinal disease	24	208	1.15	0.76 – 1.75	1.19	0.77 – 1.82	1.14	0.75 – 1.74	1.21	0.70 – 1.89
	Rheumatoid disease	9	78	1.11	0.56 – 2.21	1.17	0.59 – 2.32	1.12	0.57 – 2.22	1.26	0.64 – 2.52
Urogenital disease	12	195	0.62	0.35 – 1.11	0.65	0.37 – 1.17	0.62	0.35 – 1.11	0.64	0.35 – 1.18	
10 leading causes of death in patients with alopecia areata	Lung cancer	112	1,156	0.97	0.80 – 1.18	0.98	0.80 – 1.19	0.97	0.80 – 1.18	0.95	0.77 – 1.17
	Hepatocellular carcinoma	91	1,065	0.85	0.69 – 1.05	0.87	0.70 – 1.08	0.85	0.68 – 1.05	0.85	0.67 – 1.06
	Ischemic heart disease	79	713	1.11	0.88 – 1.40	1.10	0.87 – 1.40	1.10	0.88 – 1.39	1.11	0.87 – 1.42
	Gastric cancer	78	833	1.00	0.79 – 1.26	1.03	0.81 – 1.30	1.00	0.80 – 1.26	0.99	0.77 – 1.27
	Hemorrhagic stroke	53	505	1.05	0.79 – 1.39	1.11	0.83 – 1.47	1.06	0.80 – 1.40	1.07	0.79 – 1.44
	Pancreatic cancer	53	417	1.27	0.96 – 1.69	1.32	0.99 – 1.75	1.28	0.96 – 1.70	1.24	0.93 – 1.66
	Colon cancer	33	331	1.00	0.70 – 1.43	0.98	0.68 – 1.41	1.00	0.70 – 1.43	0.94	0.64 – 1.39
	Ischemic stroke	29	275	1.05	0.72 – 1.53	1.14	0.77 – 1.67	1.04	0.71 – 1.52	1.15	0.77 – 1.70
	Diabetes mellitus ^c	26	461	0.56	0.37 – 0.82	0.55	0.37 – 0.83	0.56	0.38 – 0.83	0.58	0.38 – 0.87
Pneumonia	23	298	0.77	0.51 – 1.18	0.85	0.55 – 1.28	0.78	0.51 – 1.18	0.85	0.54 – 1.32	

^a Estimates in model 1 are presented as the crude HR and 95% CI in the text.

^b Estimates in model 4 are presented as the adjusted HR and 95% CI in the text.

^c Type I diabetes (n = 1/487), type II diabetes (n = 335/487, HR 0.64, 95% CI 0.41–1.01), unspecified diabetes (n = 151/487, HR 0.35, 0.14–0.84)

Abbreviations: AA, alopecia areata; HR, hazard ratio; 95% CI, 95% confidence interval.

eTable 4. All-cause and cause-specific mortality risks in patients with alopecia totalis/universalis

Cause of death		No. of deaths		Model 1 ^a		Model 2		Model 3		Model 4 ^b	
		AT/AU (6,024)	Control (731,070)	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
All cause		130	14,579	1.03	0.87 – 1.23	1.05	0.88 – 1.26	1.04	0.87 – 1.23	1.06	0.88 – 1.27
Cause-specific death according to systemic or organ disease	Infectious disease	4	316	1.48	0.55 – 3.95	1.17	0.38 – 3.65	1.47	0.55 – 3.94	1.27	0.41 – 3.95
	Oncological disease	59	5,978	1.15	0.89 – 1.49	1.17	0.90 – 1.52	1.16	0.99 – 1.50	1.18	0.90 – 1.55
	Endocrine disease	-	509	-	-	-	-	-	-	-	-
	Psychiatric disease	25	1,594	1.85	1.25 – 2.75	1.90	1.27 – 2.84	1.86	1.25 – 2.76	1.93	1.28 – 2.92
	Neurological disease	3	280	1.23	0.40 – 3.84	1.28	0.41 – 3.99	1.24	0.40 – 3.87	1.42	0.45 – 4.42
	Cardiovascular disease	19	2,627	0.84	0.54 – 1.32	0.90	0.57 – 1.41	0.85	0.54 – 1.34	0.89	0.55 – 1.43
	Respiratory disease	4	699	0.70	0.26 – 1.87	0.76	0.28 – 2.02	0.70	0.26 – 1.88	0.84	0.32 – 2.25
	Gastrointestinal disease	2	208	1.03	0.87 – 1.23	1.05	0.88 – 1.26	1.04	0.87 – 1.23	1.06	0.88 – 1.27
	Rheumatoid disease	-	78	-	-	-	-	-	-	-	-
	Urogenital disease	1	195	0.59	0.08 – 4.21	0.62	0.09 – 4.41	0.60	0.08 – 4.29	0.71	0.10 – 5.09
10 leading causes of death in patients with alopecia areata	Lung cancer	21	1,156	2.16	1.41 – 3.33	2.17	1.39 – 3.37	2.17	1.41 – 3.33	2.08	1.30 – 3.31
	Hepatocellular carcinoma	8	1,065	0.88	0.44 – 1.77	0.94	0.47 – 1.88	0.89	0.44 – 1.78	1.03	0.51 – 2.06
	Ischemic heart disease	3	713	0.50	0.16 – 1.55	0.53	0.17 – 1.55	0.53	0.17 – 1.64	0.57	0.18 – 1.78
	Gastric cancer	6	833	1.40	0.65 – 3.01	1.49	0.69 – 3.19	1.41	0.66 – 3.02	1.39	0.65 – 2.97
	Hemorrhagic stroke	6	505	1.38	0.62 – 3.08	1.47	0.66 – 3.29	1.40	0.63 – 3.14	1.35	0.60 – 3.48
	Pancreatic cancer	5	417	1.38	0.57 – 3.33	1.42	0.59 – 3.44	1.38	0.57 – 3.34	1.35	0.55 – 3.24
	Colon cancer	4	331	1.42	0.53 – 3.80	1.47	0.55 – 3.94	1.42	0.53 – 3.80	1.37	0.51 – 3.70
	Ischemic stroke	-	275	-	-	-	-	-	-	-	-
	Diabetes mellitus	-	461	-	-	-	-	-	-	-	-
	Pneumonia	2	298	0.81	0.20 – 3.27	0.88	0.22 – 3.51	0.82	0.21 – 3.30	0.99	0.25 – 3.98

^a Estimates in model 1 are presented as the crude hazard ratio and 95% CI in the text.

^b Estimates in model 4 are presented as the adjusted hazard ratio and 95% CI in the text.

^c Subgroup analysis was limited due to lack of cause-specific mortality events in patients with alopecia totalis/universalis.

Abbreviations: AT/AU, alopecia totalis/universalis; HR, hazard ratio; 95% CI, 95% confidence interval.

eTable 5. All-cause and cause-specific mortality risks in patients with alopecia areata aged ≥65 years

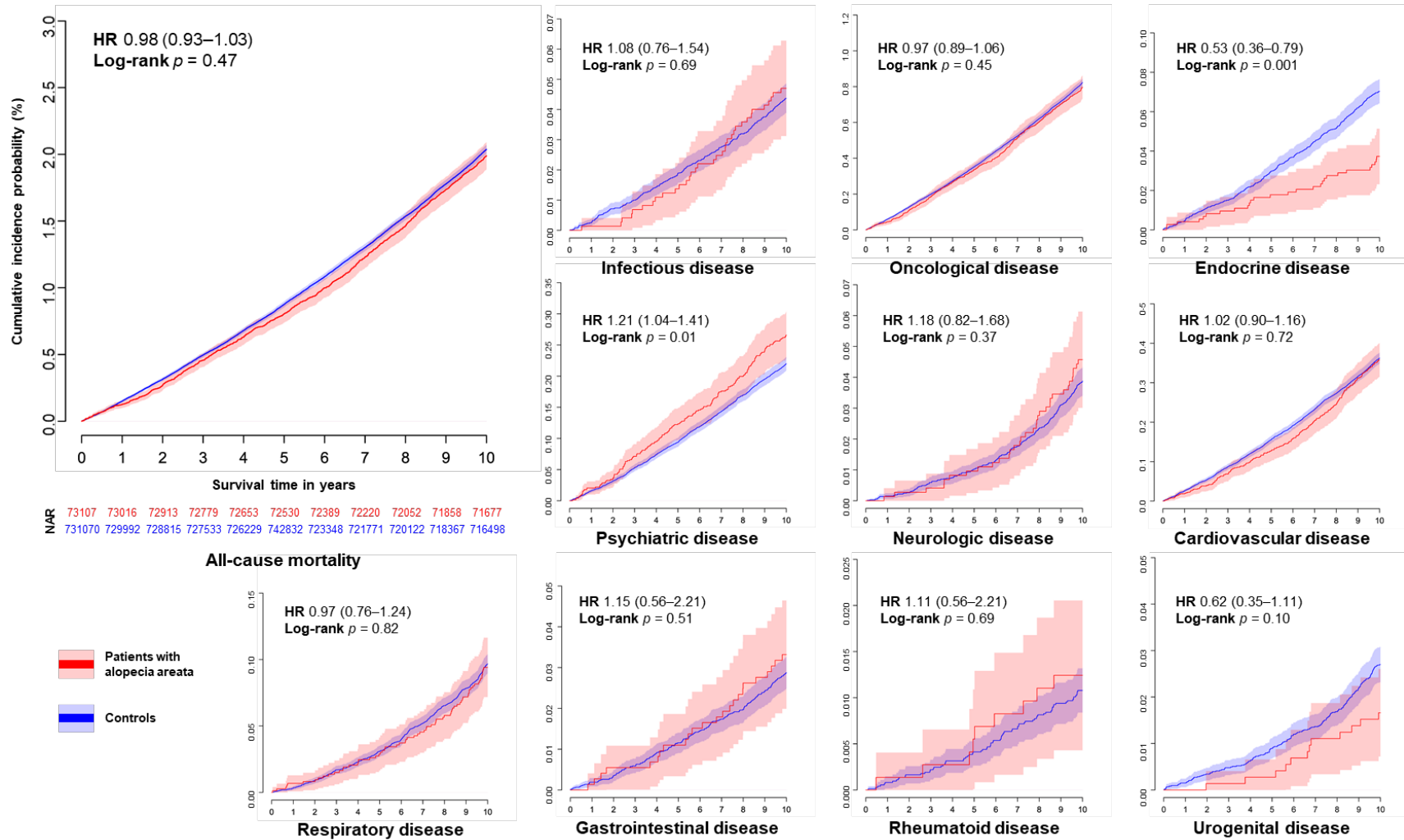
Cause of death		No. of deaths		Model 1		Model 2		Model 3		Model 4	
		AA (1,426)	Control (14,260)	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
All cause		317	3,183	0.97	0.87 – 1.09	0.99	0.88 – 1.11	0.96	0.86 – 1.08	0.98	0.87 – 1.11
Cause-specific death according to systemic or organ disease	Infectious disease	10	85	1.11	0.58 – 2.12	0.93	0.45 – 1.91	1.09	0.57 – 2.09	0.89	0.41 – 1.92
	Oncological disease	105	1,021	1.03	0.84 – 1.25	1.04	0.85 – 1.28	1.02	0.83 – 1.24	1.02	0.83 – 1.27
	Endocrine disease	6	154	0.39	0.17 – 0.88	0.37	0.16 – 0.83	0.36	0.16 – 0.82	0.37	0.16 – 0.84
	Psychiatric disease	12	147	0.80	0.44 – 1.43	0.86	0.48 – 1.56	0.79	0.44 – 1.42	0.84	0.46 – 1.56
	Neurological disease	15	97	1.58	0.92 – 2.67	1.40	0.79 – 2.49	1.59	0.93 – 2.73	1.43	0.78 – 2.60
	Cardiovascular disease	91	832	1.06	0.85 – 1.31	1.09	0.88 – 1.36	1.05	0.85 – 1.31	1.10	0.87 – 1.38
	Respiratory disease	31	343	0.91	0.63 – 1.32	1.00	0.70 – 1.45	0.92	0.64 – 1.32	1.01	0.69 – 1.48
	Gastrointestinal disease	11	91	1.22	0.59 – 2.53	1.23	0.59 – 2.56	1.19	0.57 – 2.47	1.27	0.58 – 2.77
	Rheumatoid disease	3	26	1.05	0.32 – 3.42	1.12	0.34 – 3.70	1.03	0.32 – 3.38	1.19	0.36 – 3.94
	Urogenital disease	7	69	1.00	0.46 – 2.17	1.01	0.47 – 2.20	0.98	0.45 – 2.13	0.97	0.42 – 2.23
10 leading causes of death in patients with alopecia areata	Lung cancer	27	237	0.72	0.44 – 1.17	0.73	0.44 – 1.20	0.72	0.44 – 1.18	0.64	0.37 – 1.12
	Hepatocellular carcinoma	10	101	0.74	0.32 – 1.68	0.77	0.34 – 1.77	0.73	0.32 – 1.66	0.66	0.27 – 1.64
	Ischemic heart disease	23	166	1.32	0.86 – 2.03	1.27	0.81 – 2.00	1.31	0.85 – 2.02	1.26	0.79 – 2.00
	Gastric cancer	11	154	0.73	0.40 – 1.35	0.69	0.36 – 1.30	0.73	0.40 – 1.34	0.60	0.29 – 1.23
	Hemorrhagic stroke	11	100	1.08	0.58 – 2.00	1.16	0.62 – 2.16	1.07	0.58 – 1.99	1.05	0.53 – 2.09
	Pancreatic cancer	9	68	1.31	0.66 – 2.61	1.34	0.67 – 2.68	1.31	0.66 – 2.60	1.47	0.73 – 2.94
	Colon cancer	12	72	1.62	0.88 – 2.96	1.62	0.88 – 2.98	1.62	0.89 – 2.97	1.46	0.75 – 2.83
	Ischemic stroke	11	145	0.76	0.41 – 1.39	0.79	0.42 – 1.50	0.75	0.41 – 1.38	0.84	0.44 – 1.60
	Diabetes mellitus	6	141	0.41	0.18 – 0.93	0.39	0.17 – 0.87	0.39	0.17 – 0.87	0.39	0.17 – 0.87
	Pneumonia	10	151	0.68	0.36 – 1.28	0.73	0.39 – 1.39	0.68	0.36 – 1.29	0.65	0.32 – 1.32

Abbreviations: AA, alopecia areata; HR, hazard ratio; 95% CI, 95% confidence interval.

eFigure 1. Cumulative incidence functions for all-cause and cause-specific mortality in patients with alopecia areata

Cumulative incidence functions for each cause of death in patients with alopecia areata (red color) and controls (blue color), and NAR in each year of follow-up.

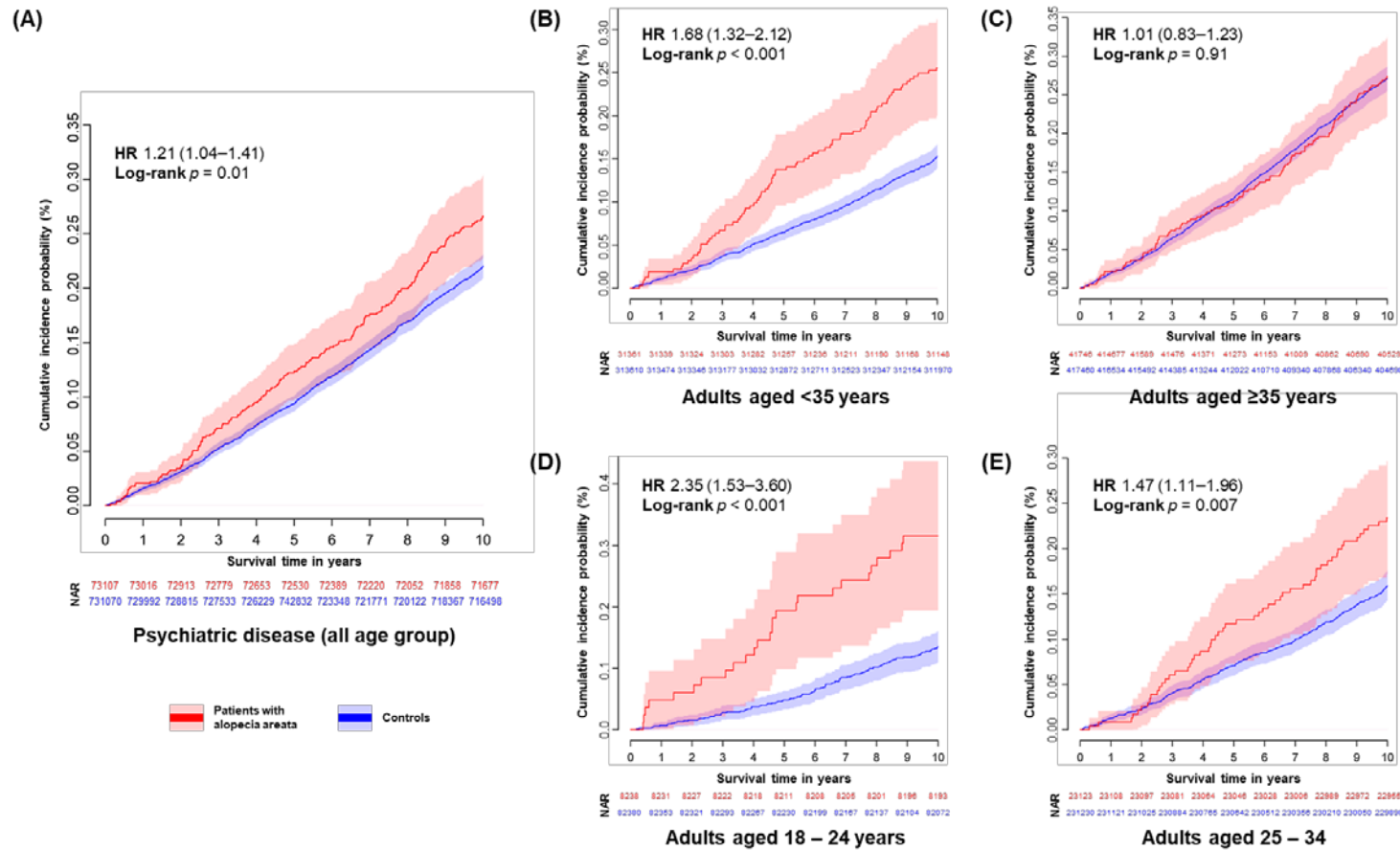
Abbreviations: HR, hazard ratio; NAR, numbers at risk



eFigure 2. Age group-stratified cumulative incidence functions for cause-specific deaths from intentional self-harm/psychiatric disease

In age group-stratified analysis, increased mortality risk from intentional self-harm/psychiatric disease was significantly associated with age <35 years. Patients aged <25 years were markedly affected, while the risk in those aged ≥35 years was not increased. In addition, no differences were found in subsequent analysis of subjects aged 35–44, those aged 45–54, those aged 55–64, and those aged ≥65 years (not shown). NAR in each age group for each year of follow-up is shown.

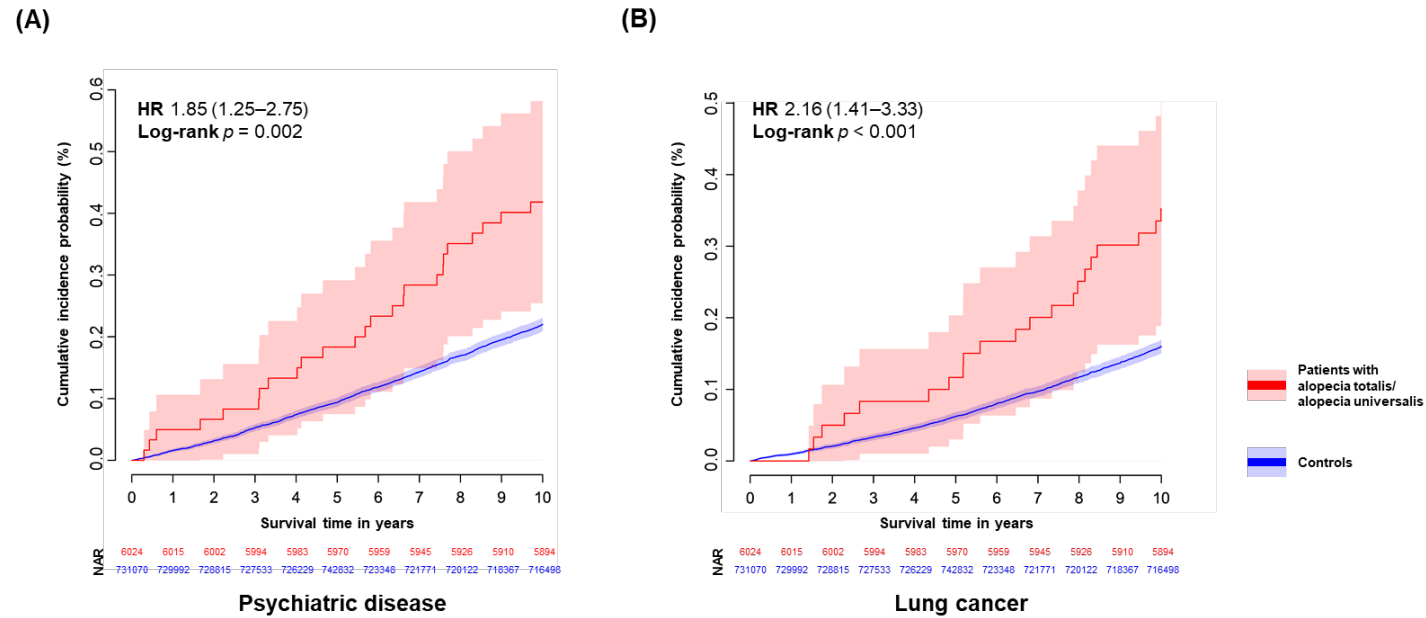
Abbreviations: HR, hazard ratio; NAR, number at risk



eFigure 3. Cumulative incidence functions for cause-specific death from lung cancer and intentional self-harm/psychiatric disease in patients with alopecia totalis/universalis

Cumulative incidence function for each cause of death in patients with alopecia totalis/universalis (red color) and controls (blue color), and NAR in each year of follow-up.

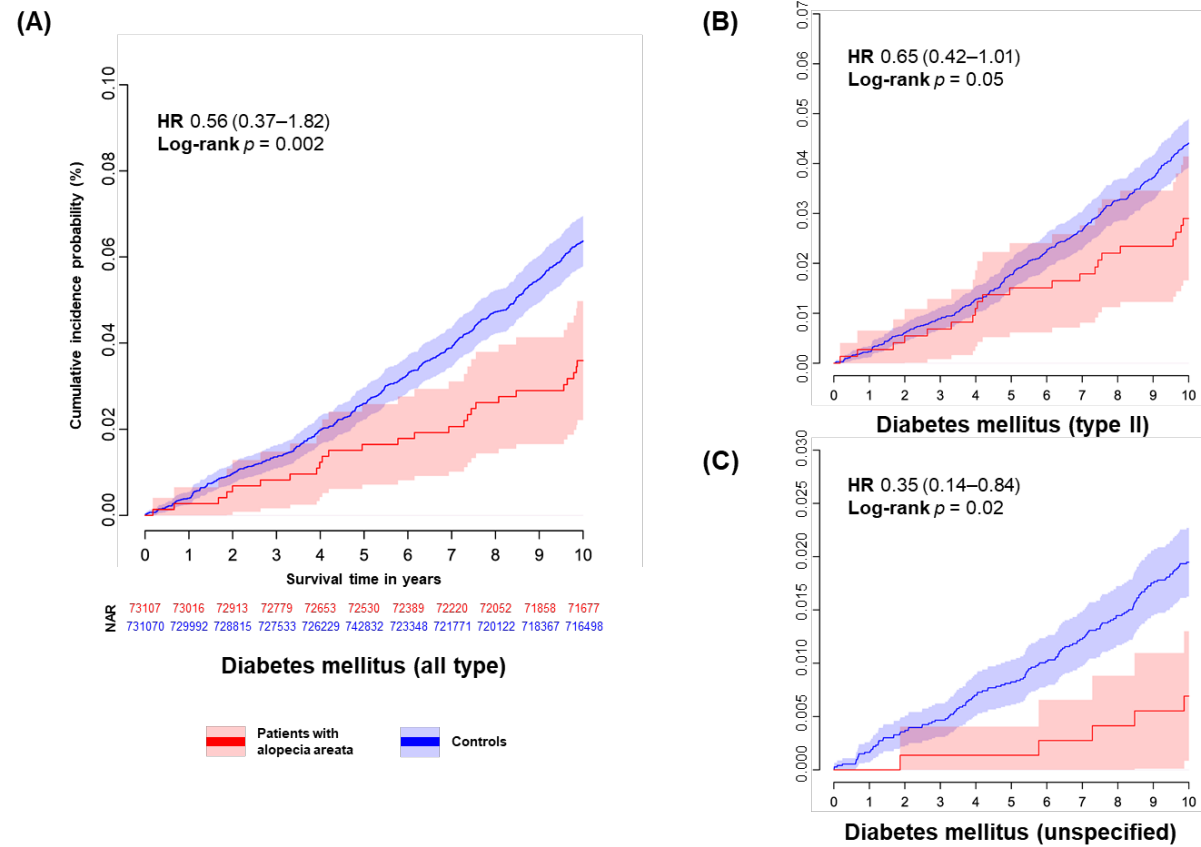
Abbreviations: HR, hazard ratio; NAR, number at risk



eFigure 4. Cumulative incidence functions for diabetes mellitus according to subtype

Among 26 deaths from diabetes mellitus in patients with alopecia areata and 461 in controls, only 1 death in controls was documented as type I diabetes. The number of deaths from type II diabetes was 21 in patients and 319 in controls, and the number from unspecified-type diabetes was 5 in patients and 184 in controls..

Abbreviation: HR, hazard ratio; NAR, number at risk



eFigure 5. Comparison of the original analysis and sensitivity analysis

Sensitivity analysis was performed, in which subjects who died during the first 2 years of follow-up (2007–2008) were excluded from the study population.

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval.

