

Data supplement

Table DS1 Summary of population-based cohort studies examining anxiety as a risk factor for mortality in elderly people									
Author	Study characteristics					Anxiety			
	Sample size	Age Years	Women %	Follow-up Years	Cohort	Anxiety criteria	Baseline prevalence, %	Mortality incidence, %	Statistical modelling
Holwerda <i>et al</i> , 2007 <sup>4</sup>	4051	65-84	62.4	10	AMSTEL cohort NL	GMS-AGECAT system Diagnostic	Anxiety: 3.2 Anxiety + depression: 1.9	51.7	Cox model adjusted for gender, age, education, MI, stroke, other diseases, MMSE, ADL, IADL, marital status, social support
Marckula <i>et al</i> , 2012 <sup>5</sup>	6372	30-70	50.1	8	Finnish representative sample	Diagnostic: CDI Symptoms: BDI and GHQ-12 Diagnostic	Anxiety: 3.5	4.9	Cox model adjusted for sociodemographic factors (education, marital status, income), health status, BMI, smoking and psychiatric comorbidity
Eaker <i>et al</i> , 2005 <sup>6</sup>	3682	18-77	51.9	10	Framingham Offspring Study USA	Study-specific scales for anxiety (continuous scale) Symptoms	-	Men: 9.9 Women: 4.8	Cox model stratified on gender adjusted for age, SBP, BMI, smoking, diabetes, cholesterol and cardiovascular diseases
Lavretsky <i>et al</i> , 2003 <sup>7</sup>	94	60+	0	2	US veterans, severely medically ill	MHI-38 Symptoms	-	21	Logistic regression (adjustments not mentioned)
Van Hout <i>et al</i> , 2004 <sup>8</sup>	659	55-85	57.6	7.5	LASA cohort NL (older strata oversampled)	Diagnostic interview DSM-III Anxiety: phobic, panic, GAD and OCD Diagnostic	17	30.2	Cox model adjusted for depression, activity, smoking, drinking, BMI, age, psychiatric treatment, functional limitations and chronic diseases. Interaction gender x anxiety P=0.04
Denollet <i>et al</i> , 2009 <sup>9</sup>	5073	46-54	100	10	Osteoporosis cohort NL	Three items of the Edinburgh Postnatal Depression Scale (range: 0-9) Anxiety: upper tertile Symptoms	32.8	2.2	Cox model adjusted for age, education, living alone, hormone intake, smoking, alcohol, physical activity, BMI, hypertension, diabetes and depression
Lann <i>et al</i> , 2011 <sup>10</sup>	129 781	15-90	69-61 (patients) 51 (controls)	5.7 (patients) 10.5 (controls)	4 groups based on psychiatric diagnostic and from national registers NL	Diagnostic for in- and out-patients of psychiatric services Diagnostic	n = 6919 anxiety diagnosis, n = 14 778 with depression, n = 4260 with both and 103 824 controls	Controls: n = 817 Anxiety: n = 922 Depression: 1493 Both: 1250 deaths/100 000 person-years	Cox model adjusted for gender, ethnicity, income and neighbourhood and with age as the timescale
Ostir & Goodwin, 2006 <sup>11</sup>	506	75+	50.8	5	HoP study USA Stratified by ethnicity	Generalised anxiety: Zung self-rating anxiety scale (continuous and 3-class variable) Symptoms	Non-Hispanic White: 21.6 Hispanics: 12.4 Non-Hispanic Black: 11.3	35.4	Cox model adjusted for age, gender, ethnicity, education, marital status, current smoking status, alcohol use, number of medical conditions, self-rated health and number of ADLs
Phillips <i>et al</i> , 2009 <sup>12</sup>	4256	31-49	0	15	US veterans	The Diagnostic Interview Schedule DSM-III Diagnostic of GAD Diagnostic	GAD: 9.7	5.5	Cox model adjusted for age, place of service, ethnicity, marital status, smoking habit, alcohol, IQ at enlistment, income in midlife, BMI, cholesterol, SBP, blood glucose and somatic illness

(continued)

**Table DS1** Summary of population-based cohort studies examining anxiety as a risk factor for mortality in elderly people (*continued*)

	Study characteristics					Anxiety			
	Sample size	Age Years	Women %	Follow-up Years	Cohort	Anxiety criteria	Baseline prevalence, %	Mortality incidence, %	Statistical modelling
Batterham <i>et al</i> , 2012 <sup>13</sup>	896	70–97	49	17	Canberra Longitudinal Study Australia	Golberg depression and anxiety scales Range 0–9 (continuous variable) Symptoms	Four anxiety symptoms or more: 19	76.7	Cox model in structural equation model including age, gender, grip strength, ADL score and heart attack and hypertension history
Mykletun <i>et al</i> , 2007 <sup>14</sup>	61 349	19–101	53	3–6	HUNT study Norway	HADS Cut-off of 8 for depression and anxiety Symptoms	Anxiety: 9.6 Anxiety and depression: 5.9	3.8	Cox model adjusted for age, gender, smoking, alcohol, physical activity, BMI, DBP, cholesterol, somatic symptoms and diagnoses, physical impairment, education, SES
Mykletun <i>et al</i> , 2009 <sup>29</sup>	61 349	19–101	53	3–6	HUNT study Norway	HADS Cut-off of 8 for depression and anxiety Symptoms	Anxiety: 9.6 Anxiety and depression: 5.9	3.8	Logistic regression adjusted for age, gender, somatic symptoms and diagnoses, physical impairment, physical activity, smoking, alcohol, education, SES, BMI, DPB, cholesterol. Interaction depression x anxiety $P = 0.02$

NL, Netherlands; GMS-AGECAT, Geriatric Mental State – Automated Geriatric Examination for Computer Assisted Taxonomy; MI, myocardial infarction; MMSE, Mini-Mental State Examination; ADL, activities of daily living; IADL, instrumental activities of daily living; CIDI, Composite International Diagnostic Interview; BDI, Beck Depression Inventory; GHQ, General Health Questionnaire; BMI, body mass index; SBP, systolic blood pressure; MHI, Mental Health Index; GAD, generalised anxiety disorder; OCD, obsessive-compulsive disorder; HADS, Hospital Anxiety and Depression Scale; DBP, diastolic blood pressure; SES, socioeconomic status.

**Table DS2 Risk factors for 10-year death stratified by gender (Cox model with age as timescale)**

	Men						Women							
	Censored			Deaths			Censored			Deaths				
	n	%		n	%	Hazard ratio (95% CI)	P	n	%		n	%	Hazard ratio (95% CI)	P
Education														
> 5 years	429	78.43		126	73.68	-	-	686	76.56		107	71.33	-	-
≥ 5 years	118	21.57		45	26.32	1.17 (0.83-1.65)	0.38	210	23.44		43	28.67	1.36 (0.95-1.94)	0.09
Income														
≥ 1500€	74	13.58		27	15.88	-	-	280	31.53		63	42.86	-	-
< 1500€	471	86.42		143	84.12	0.98 (0.64-1.49)	0.91	608	68.47		84	57.14	0.82 (0.59-1.14)	0.23
Alcohol														
0	30	5.57		12	7.06	-	-	192	21.92		45	31.47	-	-
1-36 g/day	388	71.99		130	76.47	0.93 (0.51-1.69)	0.81	670	76.48		95	66.43	0.82 (0.57-1.18)	0.28
> 36 g/day	121	22.45		28	16.47	0.79 (0.40-1.57)	0.50	14	1.60		3	2.10	1.33 (0.41-4.31)	0.63
Smoking														
Never	174	31.81		46	26.90	-	-	696	77.77		115	76.67	-	-
Former	323	59.05		108	63.16	1.14 (0.81-1.61)	0.46	164	18.32		29	19.33	1.10 (0.73-1.66)	0.63
Current	50	9.14		17	9.94	1.42 (0.81-2.49)	0.22	35	3.91		6	4.00	1.81 (0.78-4.15)	0.16
Body mass index														
Normal	244	44.61		75	43.86	-	-	561	62.61		93	62.00	-	-
Overweight	268	48.99		82	47.95	1.17 (0.85-1.61)	0.33	263	29.35		38	25.33	1.11 (0.76-1.63)	0.59
Obese	35	6.40		14	8.19	1.36 (0.77-2.42)	0.29	72	8.04		19	12.67	1.89 (1.15-3.11)	0.01
MMSE														
≥ 24	530	96.89		162	94.74	-	-	845	94.31		143	95.33	-	-
< 24	17	3.11		9	5.26	1.19 (0.60-2.34)	0.62	51	5.69		7	4.67	0.55 (0.26-1.19)	0.13
Recent hospital admission														
No	514	93.97		152	88.89	-	-	851	94.98		133	88.67	-	-
Yes	33	6.03		19	11.11	1.67 (1.03-2.70)	0.04	45	5.02		17	11.33	1.64 (0.98-2.73)	0.06
History of vascular diseases <sup>a</sup>														
No	421	76.97		96	56.14	-	-	725	80.92		95	63.33	-	-
Yes	126	23.03		75	43.86	1.95 (1.44-2.64)	0.0001	171	19.08		55	36.67	1.59 (1.13-2.23)	0.008
Diabetes <sup>b</sup>														
No	486	89.01		139	82.74	-	-	834	94.13		131	89.12	-	-
Yes	60	10.99		29	17.26	1.72 (1.15-2.58)	0.008	52	5.87		16	10.88	1.57 (0.93-2.64)	0.09
Respiratory disease <sup>c</sup>														
No	513	93.78		154	90.06	-	-	864	96.43		135	90.00	-	-
Yes	34	6.22		17	9.94	1.76 (1.06-2.90)	0.03	32	3.57		15	10.00	2.96 (1.72-5.06)	0.0001
Hypertension <sup>d</sup>														
No	293	53.56		62	36.26	-	-	530	59.15		71	47.33	-	-
Yes	254	46.44		109	63.74	1.50 (1.09-2.06)	0.01	366	40.85		79	52.67	1.11 (0.80-1.54)	0.55
Low HDL cholesterol <sup>e</sup>														
No	508	92.87		150	90.36	-	-	797	89.75		127	87.59	-	-
Yes	39	7.13		16	9.64	1.56 (0.93-2.62)	0.09	91	10.25		18	12.41	1.20 (0.73-1.98)	0.47

(continued)

Table DS2 Risk factors for 10-year death stratified by gender (Cox model with age as timescale) (continued)

	Men						Women						
	Censored			Deaths			Censored			Deaths			
	n	%		n	%		n	%		n	%		
Cancer <sup>f</sup>													
No	540	98.72	166	97.08	–	–	886	98.88	148	98.67	–	–	–
Yes	7	1.28	5	2.92	3.31 (1.35–8.09)	0.009	10	1.12	2	1.33	0.94 (0.23–3.80)	0.93	–
Dyspnoea													
No	515	94.67	148	86.55	–	–	815	91.27	107	72.30	–	–	–
Yes	29	5.33	23	13.45	1.63 (1.04–2.55)	0.03	78	8.73	41	27.70	3.02 (2.10–4.35)	0.0001	–
Non-vascular chronic diseases <sup>g</sup>													
No	234	42.78	43	25.15	–	–	462	51.56	47	31.33	–	–	–
Yes	313	57.22	128	74.85	1.71 (1.21–2.42)	0.0024	434	48.44	103	68.67	1.64 (1.16–2.34)	0.0056	–
Depressive symptoms													
None	441	80.62	117	68.42	–	–	570	63.62	78	52.00	–	–	–
CES-D: 16–22	63	11.52	32	18.71	1.17 (0.79–1.74)	0.44	157	17.52	24	16.00	1.07 (0.67–1.69)	0.78	–
CES-D: ≥ 23 or major depressive disorder	43	7.86	22	12.87	1.76 (1.11–2.79)	0.02	169	18.86	48	32.00	1.70 (1.18–2.44)	0.004	–
Anxiolytic medication													
No	517	94.52	153	89.47	–	–	791	88.28	117	78.00	–	–	–
Yes	30	5.48	18	10.53	1.48 (0.90–2.44)	0.12	105	11.72	33	22.00	1.40 (0.94–2.07)	0.10	–
Mobility													
Not confined	537	98.17	157	91.81	–	–	851	94.98	123	82.00	–	–	–
Confined	10	1.83	14	8.19	1.46 (0.83–2.59)	0.19	45	5.02	27	18.00	1.68 (1.07–2.63)	0.02	–
IADL													
No	537	98.17	156	91.23	–	–	867	96.76	130	86.67	–	–	–
Yes	10	1.83	15	8.77	2.33 (1.34–4.06)	0.003	29	3.24	20	13.33	1.44 (0.84–2.47)	0.18	–
Physical activity													
Low	65	11.88	25	14.62	–	–	130	14.51	38	25.33	–	–	–
Moderate	260	47.53	71	41.52	0.88 (0.56–1.39)	0.58	452	50.45	78	52.00	0.77 (0.51–1.14)	0.19	–
High	222	40.59	75	43.86	1.07 (0.68–1.69)	0.77	314	35.04	34	22.67	0.66 (0.41–1.08)	0.10	–

MMSE, Mini-Mental State Examination; HDL, high-density lipoprotein; CES-D, Center for Epidemiologic Studies – Depression scale; IADL, instrumental activities of daily living.

a. History of stroke, myocardial infarction, angina pectoris, arteritis, cardiac insufficiency, arrhythmia and cardiovascular surgery.

b. Diabetes defined as glucose  $\geq 7.2$  mmol/l or treated.

c. Chronic bronchitis or asthma attacks (over the past 12 months).

d. Systolic blood pressure  $\geq 160$  or diastolic blood pressure  $\geq 95$  mmHg or intake of antihypertensive drugs.e. High-density lipoprotein cholesterol  $< 1.0$  mmol/l in men and  $< 1.3$  mmol/l in women.

f. Cancer over the past 2 years.

g. Respiratory disease, cancer, diabetes, dyspnoea or hypertension.

**Table DS3** Description of baseline sample (*n* = 1764)

	%		$\chi^2$ , <i>P</i>
	Men ( <i>n</i> = 718) <sup>a</sup>	Women ( <i>n</i> = 1046) <sup>a</sup>	
<i>Potential confounders</i>			
Age, years			0.41
65–69	32.6	35.8	
70–74	35.8	33.7	
75–80	21.9	19.9	
80+	9.7	10.6	
Education, ≤5 years	22.7	24.2	0.47
Income, <1500€ ( <i>n</i> = 1750)	14.1	33.1	<0.0001
Alcohol ( <i>n</i> = 1728)			<0.0001
0	5.9	23.3	
1–36 g/day	73.1	75.1	
>36 g/day	21.0	1.7	
Smoking			<0.0001
Never	30.6	77.6	
Former	60.0	18.5	
Current	9.3	3.9	
Body mass index			<0.0001
Normal	44.4	62.5	
Overweight	48.8	28.8	
Obese	6.8	8.7	
Mini-Mental State Examination <24	3.6	5.5	0.06
Hospital admission over past 2 years	7.2	5.9	0.27
History of vascular disease <sup>b</sup>	28.0	21.6	0.002
Diabetes <sup>c</sup>	12.5	6.6	<0.0001
Respiratory disease <sup>d</sup>	7.1	4.5	0.02
Hypertension <sup>e</sup>	50.6	42.5	0.0009
Low HDL cholesterol <sup>f</sup> ( <i>n</i> = 1746)	7.7	10.6	0.05
Cancer over past 2 years	1.7	1.2	0.35
Dyspnoea ( <i>n</i> = 1756)	7.3	11.4	0.004
Non-vascular chronic pathologies <sup>g</sup>	61.4	51.3	<0.0001
Depressive symptomatology			<0.0001
CES-D: 16–22	13.2	17.3	
CES-D ≥23 or major depressive episode	9.1	20.8	
Mobility, confined (home or neighbourhood)	3.3	6.9	0.001
IADL (at least one activity limitation)	3.5	4.7	0.22
Physical activity			0.002
Low	12.5	16.0	
Moderate	46.1	50.7	
High	41.4	33.3	
<b>Anxiety criteria</b>			
Current anxiety disorder <sup>h</sup> ( <i>n</i> = 1708)	9.3	19.9	<0.0001
History of anxiety disorder ( <i>n</i> = 1715)	18.0	32.2	<0.0001
Generalised anxiety disorder only ( <i>n</i> = 1717)	1.7	4.1	0.006
Phobia only ( <i>n</i> = 1710)	5.8	12.9	<0.0001
Spielberger Trait (top tertile)	21.7	39.7	<0.0001
Spielberger State (top tertile)	24.5	35.8	<0.0001
Anxiolytic medication	6.7	13.2	<0.0001

HDL, high-density lipoprotein; IADL, instrumental activities of daily living; CES-D, Center for Epidemiologic Studies – Depression scale.

a. Unless otherwise specified in first column.

b. History of stroke, myocardial infarction, angina pectoris, arteritis, cardiac insufficiency, arrhythmia or cardiovascular surgery.

c. Diabetes defined as glucose ≥7.2 mmol/l or treated.

d. Chronic bronchitis or asthma attacks (over the past 12 months).

e. Systolic blood pressure ≥160 or diastolic blood pressure ≥95 mmHg or intake of antihypertensive drugs.

f. High-density lipoprotein cholesterol <1.0 mmol/l in men and <1.3 mmol/l in women.

g. Respiratory disease, cancer, diabetes, dyspnoea or hypertension.

h. Current anxiety disorder: current generalised anxiety disorder, social phobia, agoraphobia, obsessive–compulsive disorder, panic disorder and post-traumatic stress disorder.

**Table DS4** Risks of death as a function of anxiety, stratified by gender and with adjustments entered separately ( $n = 1764$ )<sup>a</sup>

	Men			Women		
	Events/total, $n$	Hazard ratio (95%CI)	$P$	Events/total, $n$	Hazard ratio (95%CI)	$P$
Univariate model						
Anxiety disorder	162/702	1.02 (0.58–1.78)	0.96	136/1006	1.76 (1.21–2.57)	0.003
Trait anxiety	168/710	1.04 (0.72–1.50)	0.85	147/1031	1.38 (1.00–1.92)	0.05
State anxiety	161/687	1.30 (0.93–1.83)	0.13	137/973	1.33 (0.95–1.87)	0.10
Adjusted for number of cardiovascular diseases						
Anxiety disorder		1.03 (0.59–1.80)	0.91		1.67 (1.14–2.45)	0.008
Trait anxiety		1.00 (0.69–1.45)	0.98		1.38 (1.00–1.92)	0.05
State anxiety		1.28 (0.88–1.74)	0.23		1.32 (0.94–1.86)	0.11
Adjusted for number of non-vascular chronic diseases <sup>b</sup>						
Anxiety disorder		0.91 (0.52–1.60)	0.75		1.68 (1.15–2.45)	0.007
Trait anxiety		1.00 (0.69–1.44)	0.98		1.34 (0.96–1.85)	0.08
State anxiety		1.22 (0.87–1.71)	0.25		1.25 (0.89–1.76)	0.20
Adjusted for cognition (MMSE <24)						
Anxiety disorder		1.02 (0.58–1.79)	0.95		1.84 (1.26–2.68)	0.002
Trait anxiety		1.04 (0.72–1.50)	0.84		1.43 (1.03–1.99)	0.03
State anxiety		1.30 (0.93–1.83)	0.13		1.38 (0.98–1.94)	0.07
Adjusted for mobility and IADL						
Anxiety disorder		1.05 (0.59–1.84)	0.88		1.67 (1.14–2.45)	0.009
Trait anxiety		1.01 (0.70–1.47)	0.95		1.36 (0.98–1.89)	0.06
State anxiety		1.35 (0.96–1.89)	0.09		1.29 (0.91–1.82)	0.15
Adjusted for obesity and physical activity						
Anxiety disorder		1.04 (0.59–1.83)	0.89		1.69 (1.15–2.47)	0.007
Trait anxiety		1.07 (0.73–1.55)	0.74		1.35 (0.97–1.87)	0.08
State anxiety		1.35 (0.96–1.91)	0.08		1.29 (0.91–1.81)	0.15
Adjusted for hospital admission in the past 2 years						
Anxiety disorder		1.05 (0.60–1.84)	0.86		1.79 (1.23–2.61)	0.002
Trait anxiety		1.04 (0.72–1.50)	0.84		1.39 (1.00–1.93)	0.05
State anxiety		1.30 (0.92–1.82)	0.13		1.36 (0.97–1.91)	0.08
Adjusted for depressive symptomatology						
Anxiety disorder		0.99 (0.57–1.75)	0.98		1.62 (1.09–2.39)	0.02
Trait anxiety		0.89 (0.59–1.36)	0.59		1.14 (0.76–1.71)	0.53
State anxiety		1.21 (0.83–1.75)	0.32		1.13 (0.78–1.64)	0.52
Multivariate (adjusted for all factors above and education)						
Anxiety disorder		1.00 (0.57–1.78)	0.99		1.53 (1.02–2.27)	0.04
Trait anxiety		0.91 (0.62–1.35)	0.65		1.22 (0.83–1.78)	0.32
State anxiety		1.18 (0.82–1.70)	0.39		1.08 (0.74–1.58)	0.68

MMSE, Mini-Mental State Examination; IADL, instrumental activities of daily living.

a. Anxiety disorder: current generalised anxiety disorder, social phobia, agoraphobia, obsessive-compulsive disorder and panic and post-traumatic stress disorder. Spellberger trait: top tertile, Spellberger state: top tertile.

b. Respiratory diseases, cancer, diabetes, dyspnoea, hypertension.