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Table S1. Age- and sex-specific incident rates of ARFIs, overall and by sex, related to Fig. 1.

Age group	Incident rates (cases / 1000 person-years)					
	Visual impairment	Hearing impairment	Cognitive impairment	Physical frailty ^a	Restless sleep	Depression
Both sexes						
51-55 years	46.8	29.8	23.0	NA	82.4	35.5
56-60 years	42.6	34.1	29.3	NA	77.1	34.1
61-65 years	50.3	43.5	39.4	NA	71.7	28.1
66-70 years	57.7	53.8	45.0	20.7	69.1	34.5
71-75 years	65.8	61.8	70.5	28.6	74.9	36.2
76-80 years	85.7	82.4	91.5	38.6	79.4	40.1
81-85 years	103.1	107.9	131.0	48.4	82.9	52.0
86-90 years	145.4	131.5	187.5	62.9	87.3	74.9
All ages	59.3	52.1	42.5	31.7	75.6	35.6
<i>P-trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.781
<i>P-nonlinear</i>	< 0.001	0.003	0.003	0.027	< 0.001	0.044
<i>P-exponential trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	0.173	< 0.001
Male						
51-55 years	42.6	42.8	24.9	NA	70.1	29.3
56-60 years	39.8	47.3	30.6	NA	66.4	27.8
61-65 years	48.9	62.0	42.5	NA	58.6	18.8
66-70 years	56.1	69.6	44.2	13.2	56.8	25.1
71-75 years	67.0	79.4	76.3	24.5	61.3	25.0
76-80 years	84.4	100.0	94.1	27.8	71.5	31.4
81-85 years	113.8	139.4	138.0	33.7	73.5	51.4
86-90 years	140.6	149.1	162.9	55.3	88.2	82.8
All ages	57.2	67.4	41.6	22.8	63.6	27.3
<i>P-trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.519
<i>P-nonlinear</i>	0.071	0.354	0.206	0.327	< 0.001	0.043
<i>P-exponential trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	0.040	< 0.001
Female						
51-55 years	49.2	23.4	22.0	NA	89.4	38.8
56-60 years	44.7	25.8	28.6	NA	84.8	38.4
61-65 years	51.5	31.1	37.2	NA	82.3	35.4
66-70 years	59.1	43.4	45.6	27.2	79.4	41.8
71-75 years	64.9	51.3	66.4	32.0	85.6	44.9
76-80 years	86.5	73.3	89.9	45.9	84.7	45.7
81-85 years	97.7	95.2	127.2	57.0	88.5	52.3
86-90 years	147.7	125.4	198.6	66.9	87.0	70.9
All ages	60.9	43.1	43.2	38.5	84.3	41.4
<i>P-trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.918

<i>P-nonlinear</i>	<0.001	0.102	0.008	0.073	0.196	0.497
<i>P-exponential trend</i>	< 0.001	< 0.001	< 0.001	< 0.001	0.730	< 0.001

ARFI: age-related functional impairment, NA: not applicable.

Person-time was calculated from the visit in a specific age group to the next visit for each individual.

^a Participants aged below 65 were not measured for physical frailty.

Table S2. Co-existence pairs of age-related functional impairments in 2000, overall and by cohorts, related to Fig. 2.

	VI	HI	CI	PF	RS	Depression
All participants (N = 15 852, n (%))						
VI	3191 (20.1)					
HI	1116 (7.0)	2925 (18.5)				
CI	921 (5.8)	720 (4.5)	2579 (16.3)			
PF	516 (3.3)	391 (2.5)	368 (2.3)	1130 (7.1)		
RS	1469 (9.3)	1179 (7.4)	1021 (6.4)	613 (3.9)	5241 (33.1)	
Depression	781 (4.9)	542 (3.4)	568 (3.6)	372 (2.3)	1307 (8.2)	1880 (11.9)
WB cohort (N = 1829, n (%))						
VI	290 (15.9)					
HI	64 (3.5)	198 (10.8)				
CI	56 (3.1)	23 (1.3)	150 (8.2)			
RS	155 (8.5)	80 (4.4)	67 (3.7)	NA	625 (34.2)	
Depression	68 (3.7)	30 (1.6)	45 (2.5)	NA	153 (8.4)	210 (11.5)
HRS original cohort (N = 8365, n (%))						
VI	1504 (18.0)					
HI	475 (5.7)	1326 (15.9)				
CI	348 (4.2)	261 (3.1)	960 (11.5)			
PF	151 (1.8)	98 (1.2)	78 (0.9)	328 (3.9)		
RS	710 (8.5)	556 (6.6)	400 (4.8)	190 (2.3)	2739 (32.7)	
Depression	377 (4.5)	244 (2.9)	223 (2.7)	114 (1.4)	663 (7.9)	929 (11.1)
CODA cohort (N = 1892, n (%))						
VI	360 (19.0)					
HI	127 (6.7)	370 (19.6)				
CI	135 (7.1)	100 (5.3)	386 (20.4)			
PF	82 (4.3)	63 (3.3)	62 (3.3)	204 (10.8)		
RS	173 (9.1)	158 (8.4)	151 (8.0)	115 (6.1)	611 (32.3)	
Depression	84 (4.4)	58 (3.1)	88 (4.7)	63 (3.3)	149 (7.9)	205 (10.8)
AHEAD cohort (N = 3766, n (%))						
VI	1037 (27.5)					
HI	450 (11.9)	1031 (27.4)				
CI	382 (10.1)	336 (8.9)	1083 (28.8)			
PF	283 (7.5)	230 (6.1)	228 (6.1)	598 (15.9)		
RS	431 (11.4)	385 (10.2)	403 (10.7)	308 (8.2)	1266 (33.6)	
Depression	252 (6.7)	210 (5.6)	212 (5.6)	195 (5.2)	342 (9.1)	536 (14.2)

VI: visual impairment, HI: hearing impairment, CI: cognitive impairment, PF: physical frailty, RS: restless sleep, NA: not applicable, ARFI: age-related functional impairment, WB cohort: War Baby cohort born 1942 to

1947, HRS cohort: initial HRS cohort born 1931 to 1941, CODA cohort: Children of Depression cohort born 1924 to 1930, AHEAD cohort: Asset and Health Dynamics Among the Oldest Old cohort born before 1924. PF was only measured among participants aged over 64 years.

Table S3. Prevalence of co-existence of ARFIs from 2000 to 2020, overall and by cohorts, related to Fig. 2.

Status	Follow-up Year					
	2000	2004	2008	2012	2016	2020
All participants (N = 15 852, n (%))						
No ARFI	6433 (40.6)	4064 (25.6)	2645 (16.7)	1846 (11.6)	1196 (7.5)	493 (3.1)
One ARFI	4890 (30.8)	3699 (23.3)	2983 (18.8)	2230 (14.1)	1628 (10.3)	744 (4.7)
Two ARFIs	2564 (16.2)	2655 (16.7)	2454 (15.5)	2014 (12.7)	1501 (9.5)	785 (5.0)
Three ARFIs	1213 (7.7)	1585 (10.0)	1794 (11.3)	1627 (10.3)	1220 (7.7)	680 (4.3)
Four ARFIs	516 (3.3)	849 (5.4)	849 (5.4)	832 (5.2)	694 (4.4)	424 (2.7)
Five ARFIs	191 (1.2)	355 (2.2)	395 (2.5)	390 (2.5)	297 (1.9)	235 (1.5)
Six ARFIs	45 (0.3)	84 (0.5)	138 (0.9)	135 (0.9)	104 (0.7)	97 (0.6)
Not visited	0 (0.0)	1132 (7.1)	1317 (8.3)	1494 (9.4)	2085 (13.2)	4450 (28.1)
Death	0 (0.0)	1429 (9.0)	3277 (20.7)	5284 (33.3)	7127 (45.0)	7944 (50.1)
WB cohort (N = 1829, n (%))						
No ARFI	886 (48.4)	672 (36.7)	528 (28.9)	406 (22.2)	308 (16.8)	138 (7.5)
One ARFI	576 (31.5)	482 (26.4)	446 (24.4)	391 (21.4)	330 (18.0)	166 (9.1)
Two ARFIs	244 (13.3)	289 (15.8)	299 (16.3)	303 (16.6)	264 (14.4)	148 (8.1)
Three ARFIs	91 (5.0)	127 (6.9)	160 (8.7)	189 (10.3)	167 (9.1)	117 (6.4)
Four ARFIs	24 (1.3)	55 (3.0)	76 (4.2)	81 (4.4)	82 (4.5)	63 (3.4)
Five ARFIs	8 (0.4)	22 (1.2)	32 (1.7)	31 (1.7)	40 (2.2)	27 (1.5)
Six ARFIs	0 (0.0)	0 (0.0)	2 (0.1)	20 (1.1)	12 (0.7)	19 (1.0)
Not visited	0 (0.0)	142 (7.8)	184 (10.1)	231 (12.6)	346 (18.9)	817 (44.7)
Death	0 (0.0)	40 (2.2)	102 (5.6)	177 (9.7)	280 (15.3)	334 (18.3)
HRS original cohort (N = 8365, n (%))						
No ARFI	3784 (45.2)	2617 (31.3)	1769 (21.1)	1281 (15.3)	821 (9.8)	345 (4.1)
One ARFI	2572 (30.7)	2069 (24.7)	1841 (22.0)	1474 (17.6)	1137 (13.6)	533 (6.4)
Two ARFIs	1197 (14.3)	1344 (16.1)	1359 (16.2)	1232 (14.7)	987 (11.8)	556 (6.6)
Three ARFIs	518 (6.2)	787 (9.4)	980 (11.7)	948 (11.3)	801 (9.6)	465 (5.6)
Four ARFIs	217 (2.6)	368 (4.4)	428 (5.1)	462 (5.5)	428 (5.1)	294 (3.5)
Five ARFIs	64 (0.8)	159 (1.9)	190 (2.3)	232 (2.8)	189 (2.3)	172 (2.1)
Six ARFIs	13 (0.2)	37 (0.4)	76 (0.9)	77 (0.9)	72 (0.9)	58 (0.7)
Not visited	0 (0.0)	557 (6.7)	702 (8.4)	845 (10.1)	1246 (14.9)	2812 (33.6)
Death	0 (0.0)	427 (5.1)	1020 (12.2)	1814 (21.7)	2684 (32.1)	3130 (37.4)
CODA cohort (N = 1892, n (%))						
No ARFI	740 (39.1)	404 (21.4)	191 (10.1)	113 (6.0)	51 (2.7)	7 (0.4)
One ARFI	581 (30.7)	458 (24.2)	348 (18.4)	221 (11.7)	106 (5.6)	36 (1.9)
Two ARFIs	311 (16.4)	314 (16.6)	304 (16.1)	222 (11.7)	154 (8.1)	49 (2.6)
Three ARFIs	154 (8.1)	195 (10.3)	229 (12.1)	211 (11.2)	124 (6.6)	65 (3.4)
Four ARFIs	70 (3.7)	108 (5.7)	109 (5.8)	127 (6.7)	93 (4.9)	38 (2.0)
Five ARFIs	25 (1.3)	53 (2.8)	60 (3.2)	56 (3.0)	36 (1.9)	24 (1.3)
Six ARFIs	11 (0.6)	12 (0.6)	22 (1.2)	15 (0.8)	9 (0.5)	12 (0.6)

Not visited	0 (0.0)	145 (7.7)	160 (8.5)	167 (8.8)	235 (12.4)	426 (22.5)
Death	0 (0.0)	203 (10.7)	469 (24.8)	760 (40.2)	1084 (57.3)	1235 (65.3)
AHEAD cohort (N = 3766, n (%))						
No ARFI	1023 (27.2)	371 (9.9)	157 (4.2)	46 (1.2)	16 (0.4)	3 (0.1)
One ARFI	1161 (30.8)	690 (18.3)	348 (9.2)	144 (3.8)	55 (1.5)	9 (0.2)
Two ARFIs	812 (21.6)	708 (18.8)	492 (13.1)	257 (6.8)	96 (2.5)	32 (0.8)
Three ARFIs	450 (11.9)	476 (12.6)	425 (11.3)	279 (7.4)	128 (3.4)	33 (0.9)
Four ARFIs	205 (5.4)	318 (8.4)	236 (6.3)	162 (4.3)	91 (2.4)	29 (0.8)
Five ARFIs	94 (2.5)	121 (3.2)	113 (3.0)	71 (1.9)	32 (0.8)	12 (0.3)
Six ARFIs	21 (0.6)	35 (0.9)	38 (1.0)	23 (0.6)	11 (0.3)	8 (0.2)
Not visited	0 (0.0)	288 (7.6)	271 (7.2)	251 (6.7)	258 (6.9)	395 (10.5)
Death	0 (0.0)	759 (20.2)	1686 (44.8)	2533 (67.3)	3079 (81.8)	3245 (86.2)

ARFI: age-related functional impairment, WB cohort: War Baby cohort born 1942 to 1947, HRS cohort: initial HRS cohort born 1931 to 1941, CODA cohort: Children of Depression cohort born 1924 to 1930, AHEAD cohort: Asset and Health Dynamics Among the Oldest Old cohort born before 1924.

Table S4. Prevalence of co-existence of ARFIs (without loss to follow-up and death) from 2000 to 2020, overall and by cohorts, related to Fig. 2.

Status	Follow-up Year					
	2000	2004	2008	2012	2016	2020
All participants (N = 15 852, n (%))						
No ARFI	6433 (40.6)	4064 (30.6)	2645 (23.5)	1846 (20.3)	1196 (18.0)	493 (14.3)
One ARFI	4890 (30.8)	3699 (27.8)	2983 (26.5)	2230 (24.6)	1628 (24.5)	744 (21.5)
Two ARFIs	2564 (16.2)	2655 (20.0)	2454 (21.8)	2014 (22.2)	1501 (22.6)	785 (22.7)
Three ARFIs	1213 (7.7)	1585 (11.9)	1794 (15.9)	1627 (17.9)	1220 (18.4)	680 (19.7)
Four ARFIs	516 (3.3)	849 (6.4)	849 (7.5)	832 (9.2)	694 (10.5)	424 (12.3)
Five ARFIs	191 (1.2)	355 (2.7)	395 (3.5)	390 (4.3)	297 (4.5)	235 (6.8)
Six ARFIs	45 (0.3)	84 (0.6)	138 (1.2)	135 (1.5)	104 (1.6)	97 (2.8)
WB cohort (N = 1829, n (%))						
No ARFI	886 (48.4)	672 (40.8)	528 (34.2)	406 (28.6)	308 (25.6)	138 (20.4)
One ARFI	576 (31.5)	482 (29.3)	446 (28.9)	391 (27.5)	330 (27.4)	166 (24.5)
Two ARFIs	244 (13.3)	289 (17.5)	299 (19.4)	303 (21.3)	264 (21.9)	148 (21.8)
Three ARFIs	91 (5.0)	127 (7.7)	160 (10.4)	189 (13.3)	167 (13.9)	117 (17.3)
Four ARFIs	24 (1.3)	55 (3.3)	76 (4.9)	81 (5.7)	82 (6.8)	63 (9.3)
Five ARFIs	8 (0.4)	22 (1.3)	32 (2.1)	31 (2.2)	40 (3.3)	27 (4.0)
Six ARFIs	0 (0.0)	0 (0.0)	2 (0.1)	20 (1.4)	12 (1.0)	19 (2.8)
HRS original cohort (N = 8365, n (%))						
No ARFI	3784 (45.2)	2617 (35.5)	1769 (26.6)	1281 (22.5)	821 (18.5)	345 (14.2)
One ARFI	2572 (30.7)	2069 (28.0)	1841 (27.7)	1474 (25.8)	1137 (25.6)	533 (22.0)
Two ARFIs	1197 (14.3)	1344 (18.2)	1359 (20.5)	1232 (21.6)	987 (22.3)	556 (22.9)
Three ARFIs	518 (6.2)	787 (10.7)	980 (14.8)	948 (16.6)	801 (18.1)	465 (19.2)
Four ARFIs	217 (2.6)	368 (5.0)	428 (6.4)	462 (8.1)	428 (9.7)	294 (12.1)
Five ARFIs	64 (0.8)	159 (2.2)	190 (2.9)	232 (4.1)	189 (4.3)	172 (7.1)
Six ARFIs	13 (0.2)	37 (0.5)	76 (1.1)	77 (1.3)	72 (1.6)	58 (2.4)
CODA cohort (N = 1892, n (%))						
No ARFI	740 (39.1)	404 (26.2)	191 (15.1)	113 (11.7)	51 (8.9)	7 (3.0)
One ARFI	581 (30.7)	458 (29.7)	348 (27.6)	221 (22.9)	106 (18.5)	36 (15.6)
Two ARFIs	311 (16.4)	314 (20.3)	304 (24.1)	222 (23.0)	154 (26.9)	49 (21.2)
Three ARFIs	154 (8.1)	195 (12.6)	229 (18.1)	211 (21.9)	124 (21.6)	65 (28.1)
Four ARFIs	70 (3.7)	108 (7.0)	109 (8.6)	127 (13.2)	93 (16.2)	38 (16.5)
Five ARFIs	25 (1.3)	53 (3.4)	60 (4.8)	56 (5.8)	36 (6.3)	24 (10.4)
Six ARFIs	11 (0.6)	12 (0.8)	22 (1.7)	15 (1.6)	9 (1.6)	12 (5.2)
AHEAD cohort (N = 3766, n (%))						
No ARFI	1023 (27.2)	371 (13.6)	157 (8.7)	46 (4.7)	16 (3.7)	3 (2.4)
One ARFI	1161 (30.8)	690 (25.4)	348 (19.2)	144 (14.7)	55 (12.8)	9 (7.1)
Two ARFIs	812 (21.6)	708 (26.0)	492 (27.2)	257 (26.2)	96 (22.4)	32 (25.4)
Three ARFIs	450 (11.9)	476 (17.5)	425 (23.5)	279 (28.4)	128 (29.8)	33 (26.2)

Four ARFIs	205 (5.4)	318 (11.7)	236 (13.0)	162 (16.5)	91 (21.2)	29 (23.0)
Five ARFIs	94 (2.5)	121 (4.5)	113 (6.2)	71 (7.2)	32 (7.5)	12 (9.5)
Six ARFIs	21 (0.6)	35 (1.3)	38 (2.1)	23 (2.3)	11 (2.6)	8 (6.3)

ARFI: age-related functional impairment, WB cohort: War Baby cohort born 1942 to 1947, HRS cohort: initial HRS cohort born 1931 to 1941, CODA cohort: Children of Depression cohort born 1924 to 1930, AHEAD cohort: Asset and Health Dynamics Among the Oldest Old cohort born before 1924.

Table S5. Hazard ratios for the associations between the ARFIs and mortality, related to Fig. 3.

Exposure	Outcome	Cases/N	HR (95% CI)	P-value
Visual impairment	Hearing impairment	2043/4781	2.48 [2.29, 2.69]	< 0.001
	Cognitive impairment	3117/5704	1.63 [1.53, 1.74]	< 0.001
	Depression	1696/5458	2.18 [2.00, 2.39]	< 0.001
	Physical frailty	2518/6080	2.08 [1.92, 2.24]	< 0.001
	Restless sleep	1717/3559	1.72 [1.59, 1.86]	< 0.001
	Mortality	5287/9463	1.19 [1.13, 1.26]	< 0.001
Hearing impairment	Visual impairment	1980/4044	2.10 [1.95, 2.27]	< 0.001
	Cognitive impairment	2858/5323	1.37 [1.29, 1.46]	< 0.001
	Depression	1429/5202	1.56 [1.42, 1.70]	< 0.001
	Physical frailty	2252/5773	1.67 [1.55, 1.81]	< 0.001
	Restless sleep	1583/3455	1.43 [1.32, 1.55]	< 0.001
	Mortality	4818/8610	0.95 [0.90, 1.00]	0.073
Cognitive impairment	Visual impairment	1894/4006	1.72 [1.57, 1.88]	< 0.001
	Hearing impairment	1705/4427	1.43 [1.30, 1.57]	< 0.001
	Depression	1262/4790	1.50 [1.35, 1.68]	< 0.001
	Physical frailty	2139/5485	1.56 [1.42, 1.71]	< 0.001
	Restless sleep	1268/3202	1.25 [1.13, 1.38]	< 0.001
	Mortality	5019/8678	1.13 [1.06, 1.21]	< 0.001
Depression	Visual impairment	1290/2445	2.04 [1.89, 2.21]	< 0.001
	Hearing impairment	1159/2952	1.71 [1.57, 1.86]	< 0.001
	Cognitive impairment	1860/3500	1.51 [1.41, 1.61]	< 0.001
	Physical frailty	1569/3205	2.31 [2.14, 2.49]	< 0.001
	Restless sleep	622/1097	2.41 [2.17, 2.67]	< 0.001
	Mortality	2844/5341	1.38 [1.30, 1.46]	< 0.001
Physical frailty	Visual impairment	1277/2651	2.08 [1.90, 2.29]	< 0.001
	Hearing impairment	1153/3170	1.87 [1.70, 2.06]	< 0.001
	Cognitive impairment	1949/3756	1.62 [1.50, 1.75]	< 0.001
	Depression	1008/3040	2.95 [2.65, 3.28]	< 0.001
	Restless sleep	784/1625	2.14 [1.92, 2.38]	< 0.001
	Mortality	4078/6780	1.59 [1.49, 1.69]	< 0.001
Restless sleep	Visual impairment	2874/6365	1.43 [1.34, 1.53]	< 0.001
	Hearing impairment	2619/3838	1.43 [1.33, 1.54]	< 0.001
	Cognitive impairment	3866/7963	1.12 [1.06, 1.19]	< 0.001
	Depression	2318/7024	3.67 [3.32, 4.05]	< 0.001
	Physical frailty	3228/7787	1.74 [1.61, 1.87]	< 0.001
	Mortality	5038/10 444	1.05 [1.00, 1.11]	0.052

ARFI: age-related functional impairment, HR: hazard ratio, CI: confidence interval.

All analyses were adjusted for age, gender, BMI, race, education, family income, smoking status, drinking status and vigorous exercise at baseline and other baseline and incident ARFIs.

Table S6. Subgroup analysis of hazard trajectory network of ARFIs by gender, related to Fig. 3.

Exposure	Outcome	Male		Female	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Visual impairment	Hearing impairment	2.43 [2.15, 2.74]	< 0.001	2.73 [2.45, 3.04]	<0.001
	Cognitive impairment	1.56 [1.41, 1.72]	< 0.001	1.76 [1.62, 1.92]	<0.001
	Depression	2.29 [1.97, 2.65]	< 0.001	2.30 [2.06, 2.57]	<0.001
	Physical frailty	2.16 [1.89, 2.46]	< 0.001	2.04 [1.85, 2.24]	<0.001
	Restless sleep	1.61 [1.42, 1.82]	< 0.001	1.86 [1.67, 2.06]	<0.001
	Mortality	1.19 [1.10, 1.30]	< 0.001	1.19 [1.11, 1.29]	<0.001
Hearing impairment	Visual impairment	2.00 [1.80, 2.23]	< 0.001	2.23 [2.01, 2.47]	<0.001
	Cognitive impairment	1.35 [1.23, 1.48]	< 0.001	1.43 [1.31, 1.56]	<0.001
	Depression	1.39 [1.21, 1.60]	< 0.001	1.74 [1.55, 1.95]	<0.001
	Physical frailty	1.51 [1.34, 1.71]	< 0.001	1.76 [1.60, 1.94]	<0.001
	Restless sleep	1.32 [1.18, 1.48]	< 0.001	1.57 [1.41, 1.75]	<0.001
	Mortality	0.92 [0.85, 0.99]	0.031	0.99 [0.92, 1.07]	0.765
Cognitive impairment	Visual impairment	1.55 [1.35, 1.79]	<0.001	1.91 [1.70, 2.15]	<0.001
	Hearing impairment	1.25 [1.08, 1.45]	0.003	1.59 [1.40, 1.81]	<0.001
	Depression	1.43 [1.19, 1.71]	<0.001	1.59 [1.39, 1.83]	<0.001
	Physical frailty	1.54 [1.32, 1.80]	<0.001	1.58 [1.41, 1.78]	<0.001
	Restless sleep	1.32 [1.14, 1.54]	<0.001	1.20 [1.05, 1.37]	0.008
	Mortality	1.07 [0.98, 1.18]	0.151	1.19 [1.09, 1.30]	<0.001
Depression	Visual impairment	1.92 [1.66, 2.22]	<0.001	2.18 [1.98, 2.40]	<0.001
	Hearing impairment	1.65 [1.41, 1.92]	<0.001	1.73 [1.56, 1.92]	<0.001
	Cognitive impairment	1.13 [1.00, 1.27]	0.059	1.73 [1.59, 1.88]	<0.001
	Physical frailty	2.28 [1.99, 2.63]	<0.001	2.35 [2.14, 2.58]	<0.001
	Restless sleep	2.67 [2.22, 3.20]	<0.001	2.45 [2.16, 2.79]	<0.001
	Mortality	1.35 [1.23, 1.48]	<0.001	1.42 [1.31, 1.53]	<0.001
Physical frailty	Visual impairment	2.16 [1.82, 2.56]	<0.001	2.10 [1.88, 2.36]	<0.001
	Hearing impairment	1.84 [1.53, 2.20]	<0.001	1.91 [1.70, 2.15]	<0.001
	Cognitive impairment	1.52 [1.32, 1.74]	<0.001	1.69 [1.54, 1.86]	<0.001
	Depression	3.01 [2.49, 3.64]	<0.001	3.09 [2.71, 3.52]	<0.001
	Restless sleep	2.09 [1.74, 2.52]	<0.001	2.16 [1.90, 2.47]	<0.001
	Mortality	1.59 [1.44, 1.76]	<0.001	1.56 [1.44, 1.69]	<0.001
Restless sleep	Visual impairment	1.46 [1.31, 1.62]	<0.001	1.50 [1.38, 1.64]	<0.001
	Hearing impairment	1.42 [1.27, 1.59]	<0.001	1.52 [1.38, 1.67]	<0.001
	Cognitive impairment	1.07 [0.98, 1.17]	0.137	1.20 [1.11, 1.29]	<0.001
	Depression	4.26 [3.61, 5.04]	<0.001	3.65 [3.22, 4.13]	<0.001
	Physical frailty	1.65 [1.46, 1.86]	<0.001	1.79 [1.63, 1.96]	<0.001

Mortality	1.11 [1.03, 1.19]	0.005	1.00 [0.94, 1.08]	0.901
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ARFI: age-related functional impairment, HR: hazard ratio, CI: confidence interval.

All analyses were adjusted for age, BMI, race, education, family income, smoking status, drinking status and vigorous exercise at baseline and other baseline and incident ARFIs.

Table S7. Sensitivity analysis of hazard trajectory network of ARFIs, related to Fig. 3.

Exposure	Outcome	Sensitivity analysis 1 ^a		Sensitivity analysis 2 ^b		Sensitivity analysis 3 ^c	
		HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Visual impairment	Hearing impairment	2.49 [2.27, 2.72]	< 0.001	2.06 [1.70, 2.50]	< 0.001	2.23 [2.06, 2.41]	< 0.001
	Cognitive impairment	1.61 [1.50, 1.74]	< 0.001	1.58 [1.35, 1.84]	< 0.001	1.43 [1.34, 1.52]	< 0.001
	Depression	2.18 [1.96, 2.42]	< 0.001	2.40 [1.91, 3.02]	< 0.001	1.97 [1.81, 2.15]	< 0.001
	Physical frailty	1.99 [1.82, 2.18]	< 0.001	1.83 [1.53, 2.19]	< 0.001	1.94 [1.80, 2.09]	< 0.001
	Restless sleep	1.61 [1.47, 1.77]	< 0.001	1.71 [1.42, 2.07]	< 0.001	1.59 [1.47, 1.71]	< 0.001
	Mortality	1.14 [1.06, 1.22]	< 0.001	1.04 [0.90, 1.21]	0.590		< 0.001
Hearing impairment	Visual impairment	2.12 [1.94, 2.31]	< 0.001	1.81 [1.50, 2.19]	< 0.001	2.02 [1.87, 2.17]	< 0.001
	Cognitive impairment	1.40 [1.30, 1.50]	< 0.001	1.40 [1.20, 1.63]	< 0.001	1.32 [1.24, 1.40]	< 0.001
	Depression	1.58 [1.42, 1.75]	< 0.001	1.56 [1.23, 1.97]	< 0.001	1.44 [1.32, 1.57]	< 0.001
	Physical frailty	1.74 [1.59, 1.90]	< 0.001	1.51 [1.25, 1.81]	< 0.001	1.69 [1.57, 1.82]	< 0.001
	Restless sleep	1.43 [1.31, 1.57]	< 0.001	1.46 [1.21, 1.76]	< 0.001	1.40 [1.30, 1.50]	< 0.001
Cognitive impairment	Visual impairment	1.78 [1.60, 1.97]	< 0.001	1.53 [1.26, 1.86]	< 0.001	1.56 [1.43, 1.70]	< 0.001
	Hearing impairment	1.45 [1.30, 1.62]	< 0.001	1.53 [1.24, 1.89]	< 0.001	1.27 [1.16, 1.40]	< 0.001
	Depression	1.53 [1.34, 1.74]	< 0.001	1.29 [0.97, 1.70]	0.076	1.37 [1.23, 1.52]	< 0.001
	Physical frailty	1.61 [1.45, 1.80]	< 0.001	1.47 [1.20, 1.81]	< 0.001	1.46 [1.34, 1.60]	< 0.001
	Restless sleep	1.23 [1.10, 1.38]	< 0.001	1.21 [0.97, 1.50]	0.086	1.18 [1.07, 1.29]	< 0.001
	Mortality	1.17 [1.08, 1.27]	< 0.001	1.07 [0.92, 1.25]	0.354		< 0.001
Depression	Visual impairment	1.89 [1.72, 2.08]	< 0.001	1.90 [1.52, 2.39]	< 0.001	1.76 [1.63, 1.9]	< 0.001
	Hearing impairment	1.60 [1.44, 1.78]	< 0.001	1.47 [1.15, 1.89]	0.002	1.45 [1.33, 1.58]	< 0.001
	Cognitive impairment	1.46 [1.34, 1.59]	< 0.001	1.80 [1.49, 2.17]	< 0.001	1.20 [1.12, 1.29]	< 0.001
	Physical frailty	2.13 [1.94, 2.35]	< 0.001	2.07 [1.67, 2.57]	< 0.001	2.03 [1.87, 2.19]	< 0.001
	Restless sleep	2.08 [1.83, 2.37]	< 0.001	1.93 [1.42, 2.63]	< 0.001	2.06 [1.86, 2.28]	< 0.001
	Mortality	1.31 [1.22, 1.42]	< 0.001	1.40 [1.15, 1.69]	< 0.001		< 0.001
Physical frailty	Visual impairment	1.98 [1.76, 2.22]	< 0.001	1.91 [1.47, 2.49]	< 0.001	1.77 [1.61, 1.94]	< 0.001
	Hearing impairment	1.83 [1.62, 2.06]	< 0.001	2.45 [1.85, 3.23]	< 0.001	1.54 [1.40, 1.70]	< 0.001
	Cognitive impairment	1.50 [1.36, 1.65]	< 0.001	1.61 [1.30, 2.00]	< 0.001	1.28 [1.18, 1.38]	< 0.001
	Depression	2.83 [2.48, 3.24]	< 0.001	2.94 [2.10, 4.10]	< 0.001	2.36 [2.12, 2.63]	< 0.001
	Restless sleep	2.00 [1.75, 2.29]	< 0.001	1.61 [1.17, 2.22]	0.004	1.81 [1.63, 2.01]	< 0.001
	Mortality	1.59 [1.47, 1.73]	< 0.001	1.70 [1.40, 2.05]	< 0.001		< 0.001
Restless sleep	Visual impairment	1.40 [1.30, 1.52]	< 0.001	1.31 [1.12, 1.54]	0.001	1.40 [1.31, 1.49]	< 0.001
	Hearing impairment	1.42 [1.30, 1.54]	< 0.001	1.16 [0.98, 1.38]	0.086	1.39 [1.30, 1.49]	< 0.001
	Cognitive impairment	1.12 [1.05, 1.20]	< 0.001	1.20 [1.04, 1.37]	0.010	1.08 [1.02, 1.14]	0.011
	Depression	3.58 [3.19, 4.02]	< 0.001	2.95 [2.40, 3.62]	< 0.001	3.56 [3.23, 3.93]	< 0.001
	Physical frailty	1.73 [1.59, 1.88]	< 0.001	1.75 [1.50, 2.05]	< 0.001	1.75 [1.63, 1.88]	< 0.001

ARFI: age-related functional impairment, HR: hazard ratio, CI: confidence interval.

All analyses were adjusted for age, gender, BMI, race, education, family income, smoking status, drinking status and vigorous exercise at baseline and other baseline and incident ARFIs.

^a In sensitivity analysis 1, we excluded participants with prevalent stroke, cancer, memory-related diseases or other psychological diseases

^b In sensitivity analysis 2, we restricted analyses in participants with no ARFI at baseline.

^c In sensitivity analysis 3, we used Fine and Grey's competing risk models in place of Cox models, treating death as the competing risk.

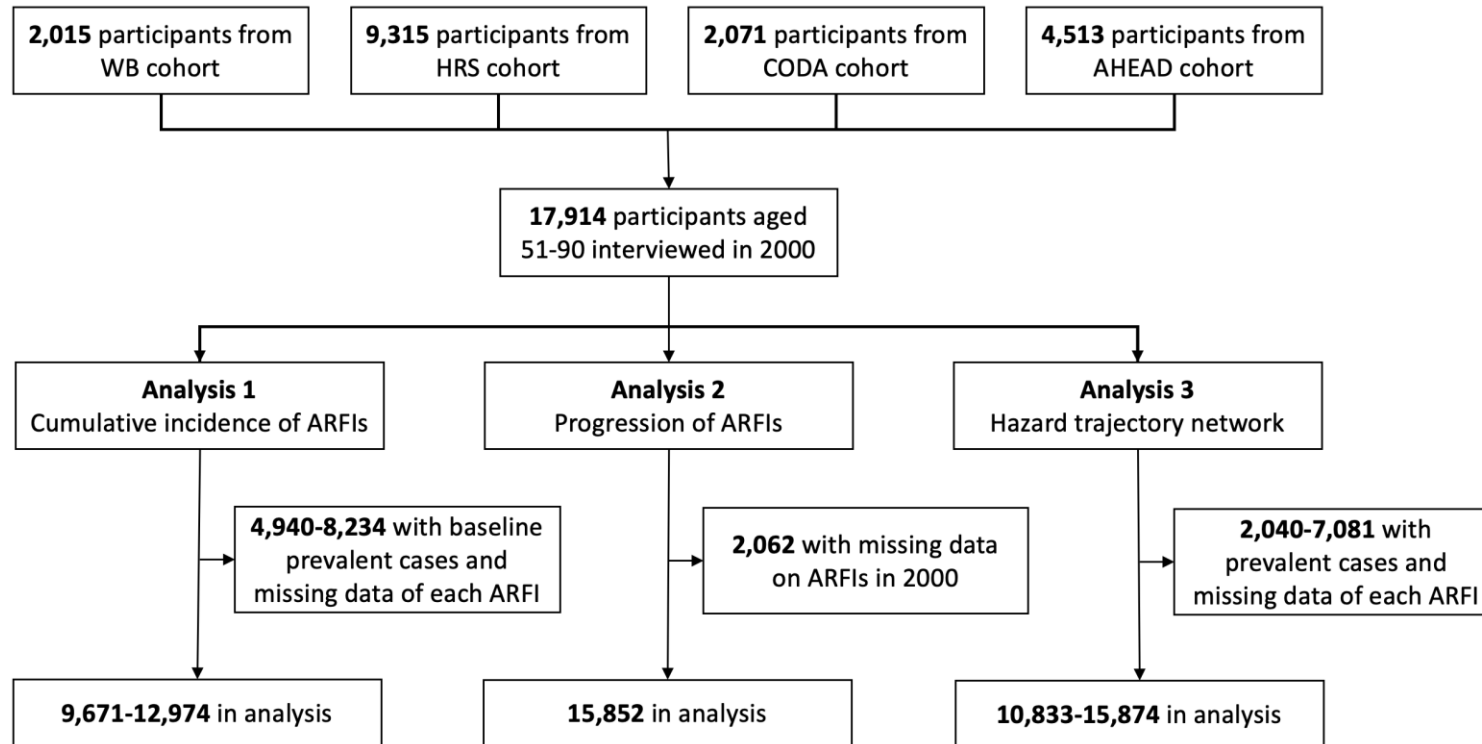
Table S8. Differences in relative risks between women and men in the associations of the exposure diseases with outcome diseases in the Danish National Patient Registry, related to Fig. 3.

EXPOSURE	OUTCOME	SEX DIFFERENCE IN RR (95%CI)
F32 (MAJOR DEPRESSIVE DISORDER)	G47/F51 (Sleep disorders)	0.12 (-1.22, 1.04)
	F00/02/01 (Dementia)	-0.16 (-0.36, 0.04)
	H53/H54 (Blindness and low vision)	NP
	H90/91 (Hearing loss)	NP
	R54 (Senility)	0.27 (-0.18, 0.80)
G47/F51 (SLEEP DISORDERS)	F32 (Major depressive disorder)	0.02 (1.02, 1.15)
	F00/02/01 (Dementia)	NP
	H53/H54 (Blindness and low vision)	NP
	H90/91 (Hearing loss)	NP
	R54 (Senility)	NP
F00/02/01 (DEMENTIA)	F32 (Major depressive disorder)	0.04 (-0.08, 0.17)
	G47/F51 (Sleep disorders)	NP
	H53/H54 (Blindness and low vision)	0.01 (-0.15, 0.17)
	H90/91 (Hearing loss)	NP
	R54 (Senility)	0.19 (-0.58, 1.18)
H53/H54 (BLINDNESS AND LOW VISION)	F32 (Major depressive disorder)	NP
	G47/F51 (Sleep disorders)	NP
	F00/02/01 (Dementia)	0.14 (-0.33, 0.60)
	H90/91 (Hearing loss)	-0.01 (-0.09, 0.08)
	R54 (Senility)	NP
H90/91 (HEARING LOSS)	F32 (Major depressive disorder)	NP
	G47/F51 (Sleep disorders)	NP
	F00/02/01 (Dementia)	NP
	H53/H54 (Blindness and low vision)	NP
	R54 (Senility)	NP
R54 (SENILITY)	F32 (Major depressive disorder)	0.08 (-0.15, 0.34)
	G47/F51 (Sleep disorders)	NP
	F00/02/01 (Dementia)	0.48 (-0.26, 1.40)
	H53/H54 (Blindness and low vision)	NP
	H90/91 (Hearing loss)	NP

Source: Westergaard, D., Moseley, P., Sørup, F.K.H. *et al.* Population-wide analysis of differences in disease progression patterns in men and women. *Nat Commun* **10**, 666 (2019). <https://doi.org/10.1038/s41467-019-08475-9>

RR: Relative risk; NP: Not presented.

Fig. S1 Flow chart of the study population, related to Table 1.



ARFI: age-related functional impairment, VI: visual impairment, HI: hearing impairment, CI: cognitive impairment, PF: physical frailty, RS: restless sleep, WB: War Baby cohort born in 1942 to 1947, HRS: initial HRS cohort born in 1931 to 1941, CODA: Children of Depression cohort born in 1924 to 1930, AHEAD: Asset and Health Dynamics Among the Oldest Old cohort born before 1924.

The numbers of participants in Analysis 1 were 12,756, 12,974, 11,028, 14,346, 9,671, and 12,786 for incident VI, HI, CI, PF, RS, and depression, respectively, and the numbers in Analysis 3 were 13,913, 14,270, 13,609, 15,874, 10,833, and 14,247 for incident VI, HI, CI, PF, RS, and depression, respectively.