

Incidence of cognitive impairment and dementia after hospitalisation for pneumonia: a UK population-based matched cohort study

Christos V. Chalitsios, Vadsala Baskaran, Rowan H. Harwood, Wei Shen Lim, Tricia M. McKeever.

Table of Contents

DIAGNOSTIC CODES	2
METHODS	7
RESULTS.....	8

SUPPLEMENTS

Diagnostic codes

Table S1. ICD-10 codes for pneumonia.

ICD-10 code	Description
J12	Viral pneumonia, not elsewhere classified
J13	Pneumonia due to <i>Streptococcus pneumoniae</i>
J14	Pneumonia due to <i>Haemophilus influenzae</i>
J15	Bacterial pneumonia, not elsewhere classified
J16	Pneumonia due to other infectious organisms, not elsewhere classified
J17	Pneumonia in diseases classified elsewhere
J18	Pneumonia, unspecified organism

Table S2. Medcodes for cognitive impairment.

Medcode	Description
1993	memory loss - amnesia
3639	amnesia symptom
5777	memory loss symptom
2908	memory disturbance
27788	temporary loss of memory
103453	short-term memory loss
39507	poor visual sequential memory
40821	poor auditory sequential memory
67163	disturbance of memory for order of events
110307	memory impairment
7674	cognitive decline
107282	mild cognitive impairment
107482	moderate cognitive impairment
107402	severe cognitive impairment
108266	cognitive impairment
52947	memory: own age not known
53146	memory: present time not known
53014	memory: present place not known
52948	memory: present year not known
53125	memory: own dob not known
52825	memory: present month not known
52800	memory: important event not known
52801	memory: important person not known
52805	memory: count down unsuccessful
53016	memory: address recall unsuccessful
65856	gds level 2 - very mild cognitive decline
60263	gds level 3 - mild cognitive decline
60726	gds level 4 - moderate cognitive decline
70057	gds level 5 - moderately severe cognitive decline

94717	gds level 6 - severe cognitive decline
72520	gds level 7 - very severe cognitive decline
6387	mild memory disturbance
6061	organic memory impairment
11936	[x]mild cognitive disorder
110729	[x]cognitive communication disorder
31572	visual disorientation syndrome
7711	[d]memory deficit
20683	[d]disorientation, unspecified
112378	[x]symptoms/signs involving cognition, percept, emotion state & behaviour
52939	[x]other & unspecified symptom/signs involving cognitive function/awareness
52811	[x]disorientation, unspecified
10822	impaired cognition
61639	unable to recognise surroundings
47279	mistakes people's identity
67565	does not recognise self
61869	does not recognise photographs of self
92635	unable to recognise parts of own body
101458	unable to recognise objects
100788	unable to recognise faces
91516	unable to recognise familiar people
59539	unable to reason
52550	difficulty reasoning
46554	unable to use verbal reasoning
46320	difficulty using verbal reasoning
99474	difficulty using visuospatial reasoning
48506	unable to process information
50446	difficulty processing information
61308	unable to process information accurately
57609	difficulty processing information accurately
109311	unable to process information at normal speed
99588	difficulty processing information at normal speed
56044	unable to analyse information
57608	difficulty analysing information
50843	difficulty performing logical sequencing
66172	isolated memory skills
19719	orientation confused
64219	orientation poor
66012	disorientation for person
55460	spatial disorientation
51379	memory disturbance (& amnesia (& symptom))
67838	memory loss symptom
103375	memory loss - amnesia

105538	memory disturbance
102880	loss of memory
10123	memory loss
68230	memory gone
12805	memory loss - amnesia
19297	loss of memory
12277	lom - loss of memory
32367	impairment of working memory
65696	impairment of primary memory
37191	poor memory for remote events
9786	loss of memory for recent events
67802	no memory for recent events
67998	temporary loss of memory
47882	transient memory loss
10514	memory impairment
39915	memory dysfunction
50418	memory deficit
26434	bad memory
12057	memory problem
12583	poor memory
19073	memory lapses
51739	distortion of memory
64892	invents experiences to compensate for loss of memory
11410	poor short-term memory
10571	short-term memory loss
53978	poor long-term memory
47581	long-term memory loss
98798	delayed verbal memory
46860	difficulty making plans
46564	difficulty making decisions
53388	unable to use decision-making strategies
107021	difficulty using decision-making strategies
65319	unable to make considered choices
43204	difficulty making considered choices
59242	difficulty solving problems
40002	language-related cognitive disorder

Table S3. Medcodes for dementia diagnosis.

Medcode	Description
1916	Senile dementia
1350	Senile/presenile dementia
7323	Uncomplicated senile dementia
15165	Presenile dementia
42602	Uncomplicated presenile dementia
30032	Presenile dementia with paranoia
27677	Presenile dementia with depression
38438	Presenile dementia NOS
44674	Senile dementia with depressive or paranoid features
18386	Senile dementia with paranoia
21887	Senile dementia with depression
41089	Senile dementia with depressive or paranoid features NOS
37015	Senile dementia with delirium
19477	Arteriosclerotic dementia
43089	Uncomplicated arteriosclerotic dementia
55467	Arteriosclerotic dementia with paranoia
43292	Arteriosclerotic dementia with depression
42279	Arteriosclerotic dementia NOS
25386	Dementia in conditions EC
4951	Chronic confusional state
7664	[X]Dementia in Alzheimer's disease
49263	[X]Dementia in Alzheimer's disease with early onset
25704	[X]Presenile dementia,Alzheimer's type
60059	[X]Primary degen dementia, Alzheimer's type, presenile onset
61528	[X]Alzheimer's disease type 2
38678	[X]Dementia in Alzheimer's disease with late onset
46762	[X]Alzheimer's disease type 1
11379	[X]Senile dementia,Alzheimer's type
43346	[X]Primary degen dementia of Alzheimer's type, senile onset
30706	[X]Dementia in Alzheimer's dis, atypical or mixed type
29386	[X]Dementia in Alzheimer's disease, unspecified
8195	[X]Alzheimer's dementia unspec
6578	[X]Vascular dementia
9565	[X]Arteriosclerotic dementia
46488	[X]Vascular dementia of acute onset
55838	[X]Predominantly cortical dementia
8934	[X]Subcortical vascular dementia
31016	[X]Mixed cortical and subcortical vascular dementia
55313	[X]Other vascular dementia
19393	[X]Vascular dementia, unspecified
12621	[X]Dementia in other diseases classified elsewhere

28402	[X]Dementia in Pick's disease
26270	[X]LEWY BODY DEMENTIA
64267	[X]Dementia in other specified diseases classif elsewhere
4693	[X] Unspecified dementia
48501	[X] Presenile dementia NOS
34944	[X] Primary degenerative dementia NOS
4357	[X] Senile dementia NOS
27759	[X] Senile dementia, depressed or paranoid type
1917	ALZHEIMER'S DISEASE
16797	ALZHEIMER'S DISEASE WITH EARLY ONSET
32057	ALZHEIMER'S DISEASE WITH LATE ONSET
11136	pick's disease
29512	senile degeneration of brain
7572	lewy body disease
59122	[x]other alzheimer's disease
8634	Multi infarct dementia
11175	[X]Multi-infarct dementia
9509	[X]Dementia in Parkinson's disease
68125	[x]delirium not superimposed on dementia, so described
112783	[x]delirium of mixed origin
25066	[x]delirium, not induced by alcohol+other psychoactive subs
53924	[x]delirium, unspecified
52394	[x]other delirium
22466	delirium - acute organic
24077	delirium - subacute organic
5367	o/e - delirious
49513	presenile dementia with delirium
53446	[x]delirium superimposed on dementia
56912	arteriosclerotic dementia with delirium

Methods

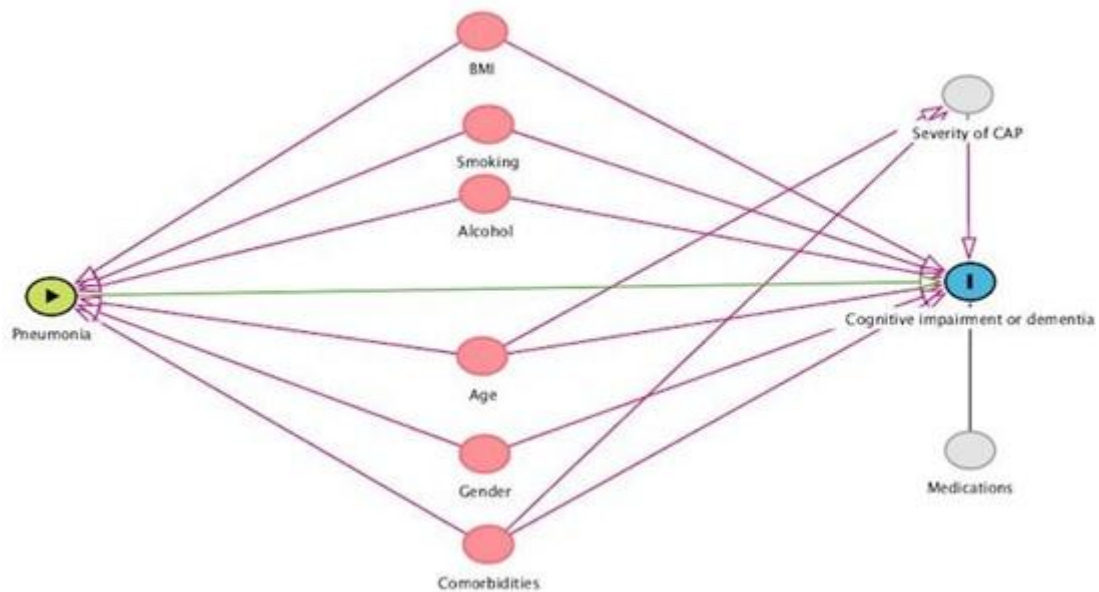


Figure S1. Directed acyclic graph illustrating the association between admission for pneumonia (exposure) and developing cognitive impairment and dementia (outcome).

Defining smoking status

Smoking status was divided into three categories: never smokers, ex-smokers, and current smokers. If patients had more than one record for smoking status, the most recent record of smoking status was used. Never smokers were reclassified to ex-smokers if they had any record of smoking recorded in their entire clinical record entered on CPRD prior to study entry. Read code lists for smoking status were developed using validated medical Read codes.

Defining alcohol status

Self-reported alcohol consumption was collected prospectively and coded by general practitioners or practice nurses on the consultation date in CPRD. The most recent alcohol consumption record prior the index date was used to classify participants drinking behaviour. Four categories were defined including: (1) non-drinkers (Read codes such as "Non-drinker alcohol"), (2) former drinkers (Read codes such as "stopped drinking alcohol"), (3) occasional drinkers (Read codes such as "drinks rarely"), and (4) current drinkers (Read codes such as "drinks wine", and "alcohol misuse"). Data based on the alcohol status and the alcohol units per week from the additional file of CPRD were also extracted to define patients in the above categories, where available. The information about the alcohol status helped to include more patients as "non-drinkers" or "former-drinkers", and if a patient had more than 0 alcohol units per week classified as "current drinker". Non-drinkers were reclassified as former drinkers if they had any record of drinking

recorded in their entire clinical record entered on CPRD prior to study entry, otherwise their category remained the same.

Power study calculation

Outcome: Dementia/Cognitive impairment	Ratio of unexposed to exposed	Hazard ratio (unexposed v. Exposed)	Exposed patients	Unexposed patients
Exposure: Hospitalisation for pneumonia	4	1.10	2,617	10,468

Standard assumptions:

Powered at 90% with a type 1 error probability of 0.05

Median survival time in unexposed cases is assumed to be 6 years (based on previous work in this topic area) with the ratio of unexposed to exposed subjects 4:1; accrual time of 5 years and follow-up of 1 year

Hazard ratios based on previous point estimates obtained from scientific literature and consultation with study collaborators considering the clinical significance

Results

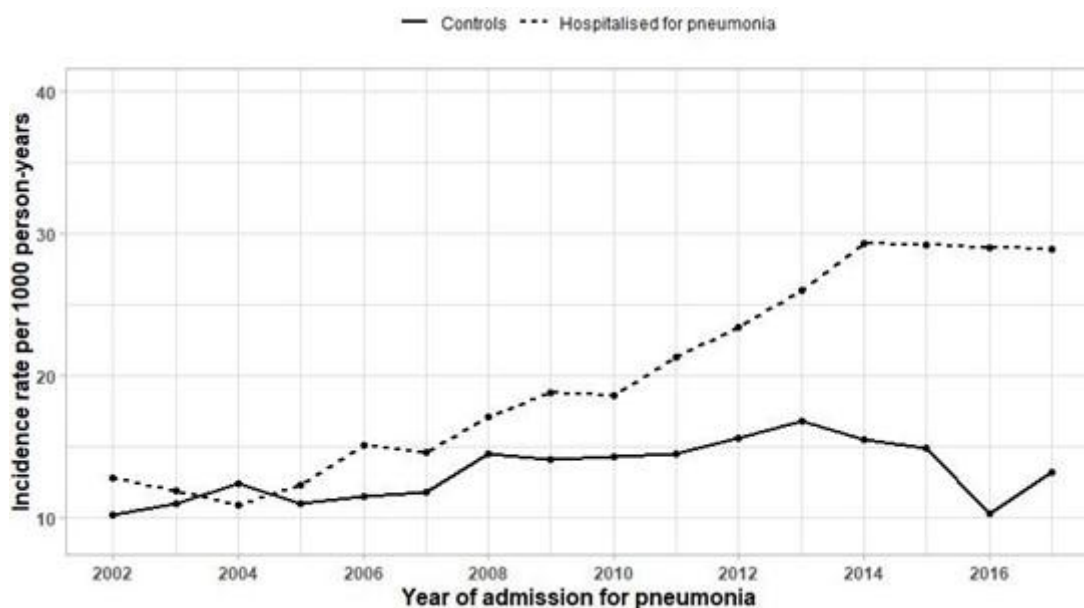


Figure S2. Incidence rate for cognitive impairment and dementia events by year of admission for pneumonia.

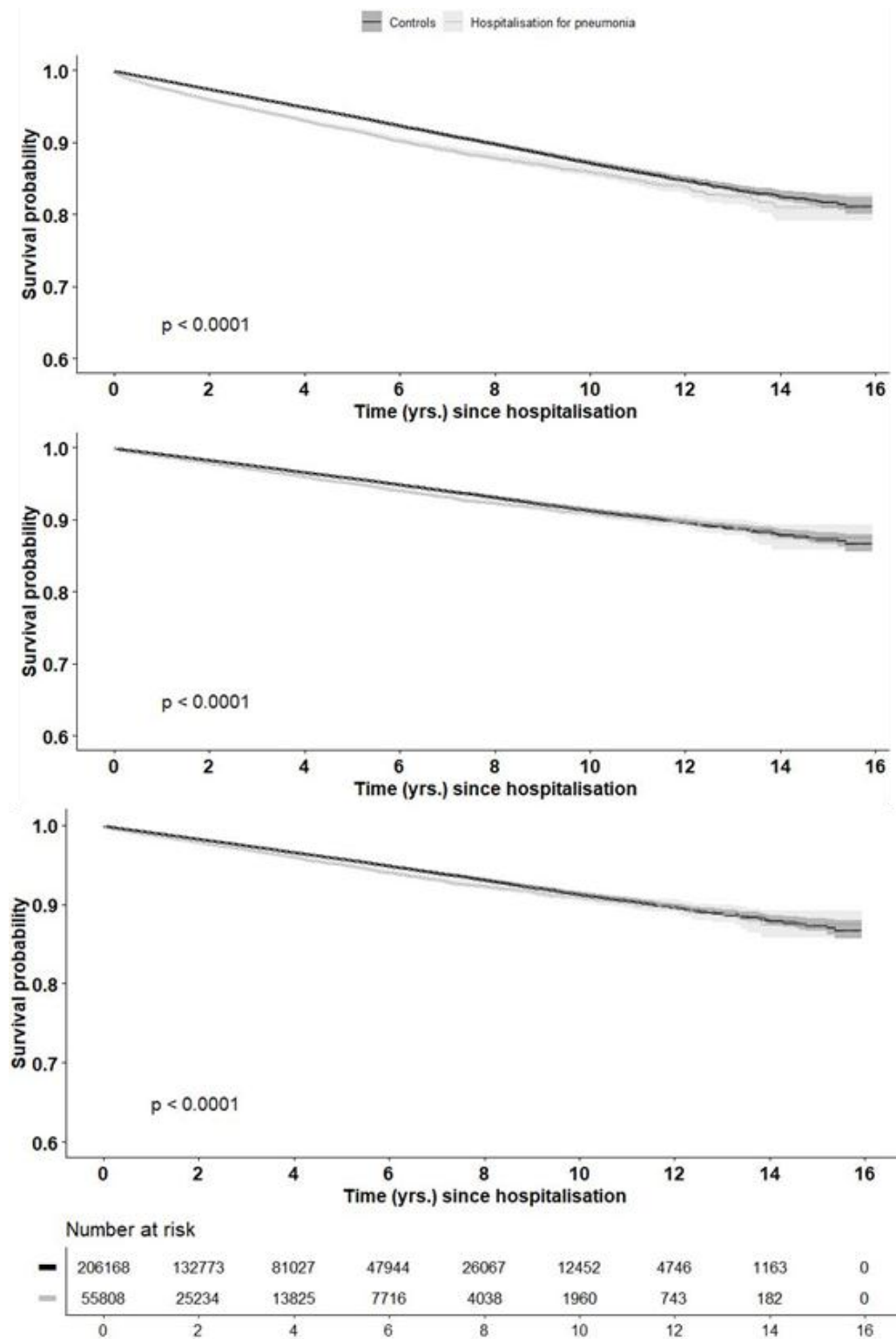


Figure S3. Kaplan-Meier plot with 95%CI and the log-rank test of incidence of time post hospitalisation to first either cognitive impairment or dementia episode (top), first cognitive impairment episode (middle), first dementia episode (bottom) in people previously hospitalised for pneumonia and controls.

Table S4. Adjusted hazard ratios (aHR) for the association of cognitive impairment and/or dementia comparing people previously hospitalised for pneumonia and controls after a complete case and multiple imputation analysis.

Variables	Either cognitive impairment or dementia		Cognitive impairment	
	Adjusted HR ¹ (95%CI)	P value	Adjusted HR ¹ (95%CI)	P value
Either cognitive impairment or dementia Males				
Controls	1.00		1.00	
People hospitalised for pneumonia	1.49 (1.41-1.58)	<.0001	1.55 (1.48-1.63)	<.0001
Cognitive impairment				
Controls	1.00		1.00	
People hospitalised for pneumonia	1.29 (1.20-1.38)	<.0001	1.32 (1.24-1.40)	<.0001
Dementia				
Controls	1.00		1.00	
People hospitalised for pneumonia	2.01 (1.81-2.22)	<.0001	2.07 (1.91-2.25)	<.0001

² *Cox model accounting for matched set (age, sex, and practice) and adjusting for smoking, body mass index, alcohol consumption, depression, cerebrovascular diseases, type II diabetes, traumatic brain injury, and hypertension*

Table S5. Hazard ratios (HR) for association of cognitive impairment and dementia with exposure to hospitalisation for pneumonia stratified by gender and age groups.

Variables	Either cognitive impairment or dementia		Cognitive impairment		Dementia	
	Adjusted HR (95%CI)	P value	Adjusted HR (95%CI)	P value	Adjusted HR (95%CI)	P value
Males						
Age¹						
18-44	0.98 (0.25-3.88)	.98	0.89 (0.22-3.55)	.867	NA	
45-60	2.42 (1.61-3.63)		2.18 (1.41-3.38)	<.001	2.03 (0.51-8.32)	.323
61-74	1.65 (1.41-1.92)	<.0001	1.46 (1.22-1.75)	<.0001	2.60 (1.86-3.66)	<.0001
75-83	1.52 (1.33-1.72)	<.0001	1.27 (1.09-1.50)	.002	2.15 (1.73-2.68)	<.0001
>83	1.35 (1.17-1.55)	<.0001	0.89 (0.72-1.09)	.254	1.98 (1.64-2.41)	<.0001
Age¹						
18-44	2.84 (1.24-6.47)	.014	2.65 (1.15-6.10)	.022	NA	
45-60	1.97 (1.32-2.94)	<.001	1.97 (1.30-2.98)	.001	1.29 (0.90-1.86)	.851
61-74	1.74 (1.47-2.05)	<.0001	1.53 (1.27-1.85)	<.0001	2.60 (1.82-3.70)	<.0001
75-83	1.54 (1.33-1.70)	<.0001	1.26 (1.10-1.47)	.002	2.11 (1.75-2.57)	<.0001
>83	1.38 (1.25-1.54)	<.0001	1.08 (0.92-1.26)	.347	1.74 (1.50-2.01)	<.0001

¹ *Age at the index date.*

² *Cox model accounting for matched set (age, sex, and practice) and adjusting for smoking, body mass index, alcohol consumption, depression, cerebrovascular diseases, type II diabetes, traumatic brain injury, and hypertension*