

Published in final edited form as:

Epidemiol Infect. 2016 March ; 144(4): 803–809. doi:10.1017/S0950268815001971.

Long term mortality of hospitalised pneumonia in the EPIC-Norfolk cohort

Prof. Phyo Kyaw Myint^{*,1,2,4,7} [Professor of Medicine of Old Age], Dr Katie R Hawkins^{*,3} [General Practice Trainee], Dr Allan B Clark⁴ [Senior Lecturer in Medical Statistics], Mr Robert N Luben⁵ [Senior Research Associate], Prof. Nicholas J Wareham⁶ [MRC Epidemiology Unit Director], Prof. Kay-Tee Khaw⁷ [Professor of Clinical Gerontology], and Dr Andrew M Wilson^{3,4} [Clinical Senior Lecturer in Respiratory Health]

¹AGEING (Aberdeen Gerontological & Epidemiological Interdisciplinary Research Group), Epidemiology Group, Institute of Applied Health Sciences, School of Medicine & Dentistry, University of Aberdeen, AB25 2ZD, Aberdeen, Scotland, UK

²Academic Centre for Applied Clinical & Translational Research into Ageing (ACTRA), Department of Medicine for the Elderly, Aberdeen Royal Infirmary, NHS Grampian, AB25 2ZN, Aberdeen, Scotland, UK

³Department of Respiratory Medicine, Norfolk and Norwich University Hospital, NR4 7UY, Norwich, UK

⁴Norwich Medical School, University of East Anglia, Norwich Research Park, NR4 7TJ, Norwich, UK

⁵Strangeway Research Laboratory, Department of Public Health & Primary Care, CB1 8RN, Cambridge, UK

⁶MRC-Epidemiology Unit, Institute of Metabolic Science, Addenbrooke's Hospital, Hills Road, CB2 0QQ, Cambridge, UK

⁷Clinical Gerontology Unit, Department of Public Health & Primary Care, School of Clinical Medicine, University of Cambridge, CB2 0QQ, Cambridge, UK

Abstract

Little is known about the cause-specific long term mortality beyond 30 days in pneumonia. We aimed to compare the mortality of patients with hospitalised pneumonia compared to age-sex matched controls beyond 30-days. Participants were drawn from the European Prospective Investigation into Cancer (EPIC)-Norfolk prospective population study. Hospitalised pneumonia cases were identified from record linkage (ICD 10 J12-J18). For this study we excluded people

Correspondence to: Phyo Kyaw Myint, 4:013 Polwarth Building, School of Medicine & Dentistry, University of Aberdeen, Foresterhill, Aberdeen, AB25 2ZD, Tel: +44 (0)1224 437841, Fax: +44(0) 1224 437911, phyo.myint@abdn.ac.uk.

*Joint first authors

Conflict of interests: None for all authors

Contributors

KTK and NJW are PIs of EPIC-Norfolk study. RNL performed record linkage. PKM and AMW conceived the idea. KRH and ABC conducted statistical analyses and drafted the manuscript with critical input from AMW and PKM. All authors contributed in writing of the paper. PKM is the guarantor.

with hospitalised pneumonia who died within 30-days. Each case identified was matched for 4 controls and followed up till end June 2012 (total person year 15,074 years (mean 6.1 years, range 0.08–15.2 years). Cox-regression models were constructed to examine the all-cause, respiratory and cardiovascular mortality using date of pneumonia onset as baseline with binary pneumonia status as exposure. A total of 2,465 men and women (503 cases and 1962 controls) (mean age 64.5, SD 8.3 years) were included in the study. Between a 30-day to one year period, HRs of all-cause and cardiovascular mortality were 7.3 (5.4-9.9) and 5.9 (3.5-9.7) respectively (with very few respiratory deaths within the same period) in cases compared to controls after adjusting for age, sex, asthma, smoking status, pack years, systolic and diastolic blood pressure, diabetes, physical activity, waist-to-hip ratio, prevalent cardiovascular and respiratory diseases. All outcomes assessed also showed increased risk of death in cases compared to controls after one year; respiratory cause of death being the most significant during that period (16.4;8.9-30.1). Hospitalised pneumonia was associated with increased all-cause and specific-cause mortality beyond 30 days.

Keywords

Pneumonia; Longer term mortality; All cause mortality; Cardiovascular mortality; Respiratory mortality

Introduction

Pneumonia is common and combined with influenza is the fifth leading cause of death in the UK (1). It is the third leading cause of death globally accounting for 7.1% of all deaths along with other lower respiratory tract infections (2). Pneumonia is also one of the main causes of hospital admissions (3) and according to US figures up to 10-20% of all hospitalisations with pneumonia require treatment in the intensive care unit (4). The short term mortality from pneumonia is well documented and is consistently between 10-11% (5,6). Mortality from pneumonia is typically assessed at 30 days or at discharge from hospital (7,8) and patients who have clinical resolution of their symptoms at this time are classified as having survived the episode (9).

It is also suggested that pneumonia produces a chronic inflammatory response which may accelerate the process of cardiovascular disease in the intermediate term (10). Indeed, it has been shown in a study of 1,799 patients hospitalised with pneumonia, those with raised pro-inflammatory cytokines at discharge had an increased risk of cardiovascular death at one year, which was independent of the severity of the pneumonia (10). More recent studies suggest that pneumonia may influence the patient's longer term survival (12–14). Mortality was 10% higher at 1 year for elderly patients with pneumonia compared to other hospitalised survivors (15) and though few studies have analysed specific cause of death post pneumonia diagnosis, cardiovascular disease caused a third of all deaths from 300 patients at one year follow up in a hospital-based study (10).

It is not known whether pneumonia has impact on longer term mortality in an unselected general population and whether it is linked to cardiovascular cause of death post one year follow up. While there appears to be a greater incidence of cardiovascular disease at 1 year

following pneumonia, the risk of cardiovascular disease at different time points post pneumonia diagnosis has not been assessed. The goals of this study were to examine the association of hospitalised pneumonia on both short (beyond 30 days up to a year) and long term all cause and cause-specific mortality focusing on respiratory and cardiovascular causes of death in a general population of middle and older age participants after taking into account potential confounders.

Material and Methods

Study Population

All study participants were selected from the participants of European Prospective Investigation into Cancer (EPIC)-Norfolk prospective population based cohort study. This cohort forms part of a Europe-wide multicentre prospective population study, primarily designed to investigate the relationship between diet and cancer. The study was approved by the Norwich Research Ethics Committee (R&D Reference No. 98CN01).

The methods of the EPIC-Norfolk study have been described in depth elsewhere (16). The Norfolk population is a mix of urban and rural populations and has high coverage of primary care physicians (General Practitioners). It is for the most part representative of the UK population, however, there is lower ethnic diversity in this area than the general UK population and the EPIC-Norfolk cohort is 99.6% white. Briefly, participants were men and women aged 40 -79 years recruited between 1993 and 1998. Participants underwent a detailed baseline health examination in which demographic, physiological and behavioural factors were ascertained. This included prevalent illness, smoking status, body mass index (BMI) measured using standard protocols (16). They were followed up for health events using record linkage.

Hospitalised cases of pneumonia were identified through linkage with hospital records using ICD 10 J12-J18. 1064 cases and 4120 controls (1:4) matched for age, sex and year of recruitment in the EPIC-Norfolk. All participants who reported cancer, myocardial infarction and stroke at the EPIC-Norfolk study baseline were excluded. To reduce the bias of excess mortality within 30-days from respiratory cause of death of cases which are identified through death certification from the Office of National Statistics, we excluded any cases who died within 30-days of hospitalisation and their matched controls leaving 503 cases and 1962 controls for the analyses. The start date for analysis for the current study was the date of diagnosis of pneumonia for cases and the same date for case matched controls. The study follow up period was from the start date to date of death or end of follow up (end June 2012). Prevalent cardiovascular disease (CVD) for the current report was defined as new diagnosis of CVD after EPIC-Norfolk enrolment but made before the pneumonia date for cases and respective corresponding date for controls.

Outcome Measurements

The primary outcome of interest was all-cause mortality. Secondary outcomes were respiratory mortality and cardiovascular mortality. Mortality data were obtained from linkage with Office of National Statistics in UK. Mortality was assessed between 30 days

and 1 year for short term and greater than 1 year for long term (11,14,17). Specific causes of death were coded by a nosologist with ICD 10 codes J00-J99 (ICD 9 460-496) for respiratory and ICD 10 codes L10-179 (ICD 9 401-448) for cardiovascular causes, respectively.

Statistical analysis

Statistical analyses were conducted using Stata 11.2/SE (StatCorp, USA). The baseline characteristics were given as means and standard deviations for normally distributed continuous data and by number and percentages for categorical data. Comparisons between groups at baseline were based on univariable conditional logistic regression models in order to take into account the non-independence due to the matching of cases and controls. Respiratory and cardiovascular mortality in pneumonia cases compared to controls were analysed at different time frames. The cut off between short term and long term mortality were 1 year and until the end of the follow up, respectively.

The difference in mortality in pneumonia cases compared to controls was examined using Cox regression (18) with a frailty term to account for the non-independence due to the matching of cases and controls. Covariates in the multiple variable models were chosen for the characteristics that differ significantly between group means for at least one cause of mortality using Cox regression on all of the available risk factors (Table 1) at univariate analysis. Multivariate analysis was thus adjusted for history of asthma, smoking status, pack years, forced expiratory volume 1 (FEV1), forced vital capacity (FVC), and physical activity levels (as outlined previously(16)), waist-to-hip ratio, diabetes mellitus, pre-existing cardiovascular disease and pre-existing respiratory disease. A final model was constructed after additionally adjusting for aspirin use (statin use was not included as there were too few participants who were on statin to provide any meaningful results). No adjustment for age and sex was required due to the matching criteria.

Results

A total of 503 participants were identified as hospitalised pneumonia cases and these cases were matched by age, gender and year of entry into the EPIC-Norfolk study with 1962 controls (1:3.9) after exclusion of cases who died within 30 days of pneumonia and their respective controls. Participants were followed from the date of diagnosis of pneumonia in cases or the same date for matched controls for a total of 15,074 person-years (mean 6.1 years, range 0.08–15.2 years). The mean time from entry into EPIC-Norfolk (which began in 1993) and the diagnosis of pneumonia was 9.0 years.

As controls were age and sex matched, these baseline characteristics were comparable between cases and controls (Table 1). However, the cases had a significantly higher proportion of current smokers and a higher mean number of pack years than the control group. The prevalence of diabetes mellitus, cardiovascular and respiratory diseases including asthma were significantly higher within the case population. Mean FEV1 and FVC were lower within the case group compared to the controls. Although the difference in body mass index between the two groups was non-significant, the case group had a significantly higher waist to hip ratio than controls.

There was a higher incidence of mortality in the case group which was maintained throughout both time frames and this difference was greatest in terms of respiratory mortality (Table 2). There was an increased risk of mortality for the case group compared to the control group after adjusting for significant risk factors identified (Table 3). There was an increased risk of all-cause mortality and specific-cause mortality between 30 days and 1 year, and greater than longer than 1 year. The all-cause mortality rate was highest initially following pneumonia then reduced over time whereas the initial higher respiratory and cardiovascular mortality rates for cases compared to controls was maintained throughout the study period.

The risk of cardiovascular mortality was increased in the case groups for both time periods, and the highest risk period was between 30 days and 1 year. Interestingly risk of death due to respiratory cause was excessively high one year post pneumonia and the overall risk was driven mainly by this.

Additionally adjusting for aspirin use did not alter the results (data not shown).

Discussion

Our findings indicate that hospitalised pneumonia is associated with increased risk of mortality not only in the short term beyond 30 days up to one year, but also in longer term (beyond 1 year) compared to age, sex matched controls within the general population of middle and older age. This increase in mortality persisted throughout the entire length of follow up for all-cause respiratory, and cardiovascular mortality. Risk of death due to cardiovascular cause appeared to be particularly high within 1 yr of pneumonia and increased risk of mortality from respiratory causes appeared to be very high after one year in cases (who did not die within one month) compared to the control normal population who did not have hospitalised pneumonia during the study period.

Our findings support previous studies. Recently, it was reported that hospitalization for pneumonia was associated with increased short-term and long-term risk of CVD, suggesting that pneumonia may be a risk factor for CVD (19). Furthermore, Kaplan found that mortality in elderly patients hospitalised with community acquired pneumonia was 10% higher at one year than those hospitalised for other reasons (15). Boden et al, based on their study on hospitalised population, also found an increased 7 year all-cause mortality amongst patients hospitalised with CAP compared to hospitalised controls (20).

A cohort study, also using the general population as controls, found that the patients with pneumonia were almost 46 times as likely to die in the first 30 days as the participants without pneumonia (17). They found that for pneumonia cases the adjusted risk of all-cause mortality over total follow up period was 4.6, which is in line with our findings.

This study further supports the evidence that the increase in cardiovascular risk persists past one year. In light of this finding, patients admitted to hospital with pneumonia should have a cardiac risk assessment including medication review, to consider interventions for cardiovascular disease prevention if appropriate. The reason why people with pneumonia had increased CV mortality risk is unclear. However, there are plausible mechanisms which

could lead to this observed link between pneumonia and subsequent CV mortality. Pneumonia increases the levels of inflammatory cytokines promoting thrombogenesis (21) and reduces ventricular function (22,23), both of which could lead to an increase in cardiac events in the short term. It is also thought that pneumonia produces a chronic inflammatory response which would accelerate the process of cardiovascular disease in the intermediate term(10). It was shown that patients hospitalised with pneumonia who experience persistently raised pro-inflammatory cytokines at discharge had an increased risk of cardiovascular death at one year, independent of the severity of illness(10).

This study has limitations. Firstly, neither the clinical severity of pneumonia nor the virulence of the disease causing organisms was accounted for. Neither were the different levels of inflammatory markers which indicate an extent of host immune response, both of which have had a demonstrated effect on mortality (10,14). A possible weakness is the misclassification of pneumonia diagnosis due to variable coding practices and lack of confirmatory radiological evidence as a requirement for inclusion. Evidence is unclear as to how accurate the pneumonia diagnosis is in hospital (24). However, the main misclassified diagnosis is likely to be other causes of lower respiratory tract infection and this inclusion bias would result in a lower mortality within the case group as lobar pneumonia is the LRTI with the highest mortality rate (25) thus the observed associations if any would be attenuation of the actual impact of pneumonia. We identified only individuals with hospitalised pneumonia so those with episodes of pneumonia treated only the community were not included. Hospitalised pneumonia cases are likely to be more severe so the generalizability of findings to all pneumonias occurring in the community is limited. To reduce such bias associated with high mortality due to pneumonia related death (i.e. respiratory cause) we deliberately excluded cases within EPIC-Norfolk who died within 30 days of pneumonia diagnosis. We were also unable to examine the specific cause of CVD mortality.

People who are admitted to hospital for pneumonia are also more likely to have co-morbidities which may predispose to increased mortality risk. Although we adjusted for many covariates including lung function as well as history of asthma and chronic respiratory illnesses, there may be unknown confounders or there may be residual confounding effect of known confounders. Whilst any hospitalisation may increase the risk of mortality, more relevant issue perhaps is whether people who had pneumonia were associated with increased CV risk in longer term. We acknowledge that we were not able to examine this issue in people with pneumonia who were not hospitalised. Indeed, it is possible that a proportion of controls might have had pneumonia which did not result in hospitalisation during follow up of the study. This misclassification as well as any hospitalisation with increased risk of death however would only attenuate the results. Finally in clinical practice especially in older people where conditions such as pneumonia and heart failure co-exist and there may be possibility of mis-diagnosis. Nevertheless, such error is likely to contribute mostly to within 30 day mortality and unlikely to influence the beyond 30-day relationships between pneumonia and mortality outcome.

The EPIC-Norfolk cohort comprised community dwelling middle and older aged participants who agreed to participate at baseline recruitment therefore there may be healthy

responder bias. However, truncation of sample distribution would be likely to attenuate the findings.

The participant's baseline characteristics (e.g. FEV1/FEV) were taken from entry into the EPIC-Norfolk cohort which predated the current study entry date by a mean of 9.0 years. There could be significant differences between characteristics at entry into EPIC-Norfolk study and at the point of pneumonia diagnosis, resulting in measurement error in the co-variables. However we were able to control for wide ranging demographic, lifestyle and medical factors including prevalent cardiovascular and chronic lower respiratory tract illnesses.

In summary, hospitalised pneumonia is associated with subsequent increased risk of mortality and this persists beyond 1 year after diagnosis in middle and older ages. Clinicians should be aware of the increased mortality from not only respiratory causes but also cardiovascular causes.

Acknowledgements

We gratefully acknowledge the participants of the study and participating General Practitioners. We also like to thank our funders.

Funding

The EPIC-Norfolk study is supported by programme grants from the Medical Research Council G1000143 and the Cancer Research UK 8257. Funders have no roles in study design, analysis, and interpretation of the findings.

References

- Office for National Statistics. [cited 2013 Feb 22] Deaths registered in England and Wales in 2010, by cause. 2011. [Internet]. Available from: <http://www.ons.gov.uk/ons/rel/vsob1/mortality-statistics--deaths-registered-in-england-and-wales--series-dr-/2010/stb-deaths-by-cause-2010.html#tab-Leading-causes-of-mortality-in-2010>
- Mathers CD, Fat DM, Boerma JT. Organization WH. The Global Burden of Disease: 2004 Update. World Health Organization; 2008.
- Guest JF, Morris A. Community-acquired pneumonia: the annual cost to the National Health Service in the UK. *European Respiratory Journal*. 1997 Jul; 10(7):1530–4. [PubMed: 9230242]
- File TM Jr, Marrie TJ. Burden of community-acquired pneumonia in North American adults. *Postgraduate Medicine*. 2010 Mar; 122(2):130–41. [PubMed: 20203464]
- Lave JR, Fine MJ, Sankey SS, Hanusa BH, Weissfeld LA, Kapoor WN. Hospitalized pneumonia. Outcomes, treatment patterns, and costs in urban and rural areas. *Journal of General Internal Medicine*. 1996 Jul; 11(7):415–21. [PubMed: 8842934]
- Marrie TJ, Carriere KC, Jin Y, Johnson DH. Mortality during hospitalisation for pneumonia in Alberta, Canada, is associated with physician volume. *European Respiratory Journal*. 2003 Jul 1; 22(1):148–55. [PubMed: 12882465]
- Eurich DT, Majumdar SR, Marrie TJ. Population-based cohort study of outpatients with pneumonia: rationale, design and baseline characteristics. *BMC Infectious Diseases*. 2012; 12:135. [PubMed: 22709357]
- Hoo Lee J, Hyung Kim Y. Comparison of clinical characteristics between healthcare-associated pneumonia and community-acquired pneumonia in patients admitted to secondary hospitals. *Brazilian Journal of Infectious Diseases*. 2012 Aug; 16(4):321–8. [PubMed: 22846118]
- Ramirez JA, Anzueto AR. Changing needs of community-acquired pneumonia. *J Antimicrobial Chemotherapy*. 2011 Apr; 66(Suppl 3):iii3–9.

10. Yende S, D'Angelo G, Kellum JA, Weissfeld L, Fine J, Welch RD, et al. Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. *American Journal of Respiratory and Critical Care Medicine*. 2008 Jun 1; 177(11):1242–7. [PubMed: 18369199]
11. Yende S, Angus DC, Ali IS, Somes G, Newman AB, Bauer D, et al. Influence of comorbid conditions on long-term mortality after pneumonia in older people. *Journal of the American Geriatrics Society*. 2007 Apr; 55(4):518–25. [PubMed: 17397429]
12. Mortensen EM, Kapoor WN, Chang C-CH, Fine MJ. Assessment of mortality after long-term follow-up of patients with community-acquired pneumonia. *Clinical Infectious Diseases*. 2003 Dec 15; 37(12):1617–24. [PubMed: 14689342]
13. Waterer GW, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneumonia. *American Journal of Respiratory and Critical Care Medicine*. 2004 Apr 15; 169(8):910–4. [PubMed: 14693672]
14. Johnstone J, Eurich DT, Majumdar SR, Jin Y, Marrie TJ. Long-term morbidity and mortality after hospitalization with community-acquired pneumonia: a population-based cohort study. *Medicine (Baltimore)*. 2008 Nov; 87(6):329–34. [PubMed: 19011504]
15. Kaplan V, Clermont G, Griffin MF, Kasal J, Watson RS, Linde-Zwirble WT, et al. Pneumonia: still the old man's friend? *Archives of Internal Medicine*. 2003 Feb 10; 163(3):317–23. [PubMed: 12578512]
16. Day N, Oakes S, Luben R, Khaw KT, Bingham S, Welch A, Wareham N. EPIC-Norfolk: study design and characteristics of the cohort. *European Prospective Investigation of Cancer. British Journal of Cancer*. 1999 Jul; 80(Suppl 1):95–103. [PubMed: 10466767]
17. Myles PR, Hubbard RB, Gibson JE, Pogson Z, Smith CJP, McKeever TM. Pneumonia mortality in a UK general practice population cohort. *European Journal of Public Health*. 2009 Oct 1; 19(5): 521–6. [PubMed: 19549803]
18. Cox D. Regression models and life tables. *J R Stat Soc B*. 1972; 34:187–220. *Journal of Royal Statistical Society*. 1972;34(2):187–220.
19. Corrales-Medina VF, Alvarez KN, Weissfeld LA, Angus DC, Chirinos JA, Chang CC, Newman A, Loehr L, Folsom AR, Elkind MS, Lyles MF, et al. Association between hospitalization for pneumonia and subsequent risk of cardiovascular disease. *Journal of the American Medical Association*. 2015; 313(3):264–74. [PubMed: 25602997]
20. Bordon J, Wiemken T, Peyrani P, Paz ML, Gnoni M, Cabral P, et al. Decrease in Long-term Survival for Hospitalized Patients With Community-Acquired Pneumonia. *CHEST*. 2010 Aug 1; 138(2):279–83. [PubMed: 20382718]
21. Mendall MA, Patel P, Asante M, Ballam L, Morris J, Strachan DP, et al. Relation of serum cytokine concentrations to cardiovascular risk factors and coronary heart disease. *Heart*. 1997 Sep 1; 78(3):273–7. [PubMed: 9391290]
22. Kumar A, Thota V, Dee L, Olson J, Uretz E, Parrillo JE. Tumor necrosis factor alpha and interleukin 1beta are responsible for in vitro myocardial cell depression induced by human septic shock serum. *Journal of Experimental Medicine*. 1996 Mar 1; 183(3):949–58. [PubMed: 8642298]
23. Mann DL. Inflammatory Mediators and the Failing Heart Past, Present, and the Foreseeable Future. *Circulation Research*. 2002 Nov 29; 91(11):988–98. [PubMed: 12456484]
24. Pink KL, Mitchell I, Davies HE. P17 The Accuracy of a Diagnosis of Pneumonia in a UK Teaching Hospital. *Thorax*. 2012 Dec 1; 67(Suppl 2):A71–A71.
25. Moellering RC. The Continuing Challenge of Lower Respiratory Tract Infections. *Clinical Infectious Diseases*. 2002 Mar 1; 34(Supplement 1):S1–S3. [PubMed: 11810605]

Table 1
Comparison of characteristics of pneumonia cases and controls without pneumonia

Characteristics	Cases	Controls	P Value*
Total	503	1962	
Males	269 (53.5%)	1030 (52.5%)	N/A
Age Mean (sd)	64.7 (8.4)	64.4 (8.3)	N/A
(Range)	41-77	41-77	
<50yrs	35 (7.0%)	132 (6.7%)	
50-65yrs	189 (37.6%)	752 (38.3%)	
>65yrs	279 (55.5%)	1078 (54.9%)	
Smoking status			<0.001
Current	93 (18.7%)	162 (8.4%)	
Previous	225 (45.3%)	944 (48.7%)	
Never	179 (36.0%)	834 (43.0)	
Pack Years Mean (sd)	14.8 (17.9)	10.4 (15.2)	<0.001
BMI Mean (sd)	26.7 (3.7)	26.64 (3.7)	0.58
(Range)	16.9 - 46.4	16.0-43.5	
<18.5	5 (1.0)	9(0.5)	0.12
18.5 - 25	174 (34.6)	681 (34.7)	
25 - 30	226 (44.9)	949 (48.4)	
30	98 (19.5)	321 (16.4)	
Asthma	73 (14.5)	151 (7.7)	<0.001
Diabetes Mellitus	26 (5.2)	52 (2.7)	0.005
FEV1 Mean (sd)			<0.001
N=5037	210.51 (75.0)	235.66 (70.93)	
FVC Mean (sd)			<0.001
N=5037	268.4 (93.93)	291.2 (90.6)	
Systolic Mean(sd)			0.60
N = 5170	141.1 (19.5)	140.5 (18.9)	
Alcohol Intake Mean(sd)			0.30
N = 5017	8.5 (13.0)	7.9 (11.7)	
Inactive	351 (69.8)	1243 (63.4)	0.004
Active	152 (30.2)	719 (36.7)	
Social class			0.162
I	26 (5.3)	132 (7.0)	
II-IV	440 (90.2)	1703 (89.9)	

Characteristics	Cases	Controls	P Value*
V	22 (4.5)	59 (3.1)	
Cholesterol Mean (sd)	6.2 (1.2)	6.3 (1.2)	0.19
Waist:hip Ratio Mean (sd)	0.88 (0.09)	0.87 (0.09)	0.001
Statin use	6 (1.2)	15 (0.8)	0.076
Aspirin use	43 (8.6)	124 (6.3)	0.319
Respiratory Disease prior to censored pneumonia	73 (14.5)	300 (15.3)	
Respiratory disease within 1 year prior to pneumonia date	46 (9.2)	36 (1.8)	
Cardiovascular Disease prior to pneumonia date[#]	168 (33.4)	449 (22.9)	
Cardiovascular disease within 1 year prior to censored pneumonia date	57 (11.3)	72 (3.7)	

Data presented are mean (sd) for continuous data and number (%) for categorical data.

* indicates that overall P values are provided for categorical comparisons where there are more than 2 categories

[#] prevalent MI and stroke at the time of baseline of the EPIC-Norfolk study were excluded from the outset and these numbers indicate the number (%) of participants with incident cardiovascular disease diagnosed between EPIC-Norfolk study enrolment and pneumonia date (baseline of the current report).

Table 2
Short, intermediate and long term crude mortality rates for both pneumonia cases and controls by causes of death

Time and cause of mortality	Cases			Controls			P Value
	N at risk	Deaths		N at risk	Deaths		
		N	(%)		N	(%)	
All-Cause Mortality							
Total	503	304	60.4	1962	488	24.9	<0.001
30 days <1 year	503	122	24.3	1962	72	3.7	<0.001
1year	381	182	47.8	1890	416	22.0	<0.001
Respiratory Mortality							
Total	503	63	12.5	1962	21	1.1	<0.001
30 days <1 year	503	19	3.8	1962	4	0.2	<0.001
1year	381	44	11.5	1890	17	0.9	<0.001
CVS Mortality							
Total	503	83	16.5	1962	177	9.0	<0.001
30 days <1 year	503	39	7.8	1962	28	1.4	<0.001
1year	381	44	11.5	1890	149	7.9	0.013

Table 3
Hazard Ratios (HR) and corresponding 95% Confidence Intervals (95%CI) of incident mortality for cases using the control group as a reference category

Time	All-Cause Mortality			Respiratory Mortality			Cardiovascular Mortality		
	HR	95% CI	P Value	HR	95% CI	P Value	HR	95% CI	P Value
Total	4.0	3.4-4.7	<0.001	20.4	11.7-35.8	<0.001	2.6	2.0-3.5	<0.001
30 days <1 year	7.3	5.4-9.9	<0.001				5.9	3.5-9.7	<0.001
1year	2.8	2.3-3.4	<0.001	16.4			1.6	1.1-2.3	0.02
					8.9-30.1	<0.001			

Covariates adjusted are smoking status, pack years, physical activity levels, waist to hip ratio, diabetes mellitus, prevalent cardiovascular disease and prevalent respiratory disease for all modes of mortality and all time frames. Matching is account for by a shared frailty term of each matched-set.