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Received 7 January 2015

Revised 22 April 2015

Accepted 26 April 2015

Published Online First

28 July 2015



CrossMark

**To cite:** Torres A, Blasi F, Dartois N, et al. *Thorax* 2015;**70**:984–989.

# Which individuals are at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease

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## ABSTRACT

Pneumococcal disease (including community-acquired pneumonia and invasive pneumococcal disease) poses a burden to the community all year round, especially in those with chronic underlying conditions. Individuals with COPD, asthma or who smoke, and those with chronic heart disease or diabetes mellitus have been shown to be at increased risk of pneumococcal disease compared with those without these risk factors. These conditions, and smoking, can also adversely affect patient outcomes, including short-term and long-term mortality rates, following pneumonia. Community-acquired pneumonia, and in particular pneumococcal pneumonia, is associated with a significant economic burden, especially in those who are hospitalised, and also has an impact on a patient's quality of life. Therefore, physicians should target individuals with COPD, asthma, heart disease or diabetes mellitus, and those who smoke, for pneumococcal vaccination at the earliest opportunity at any time of the year.

## INTRODUCTION

Pneumococcal disease in adults, including community-acquired pneumonia (CAP) and invasive pneumococcal disease (IPD), is a global problem,<sup>1–4</sup> especially in individuals with chronic diseases such as COPD, diabetes mellitus and chronic heart disease (CHD). Due to the chronic nature of these conditions, affected individuals are at risk of CAP and IPD all year round, not only during the winter, unlike seasonal influenza.<sup>5</sup>

This review addresses two key questions concerning the burden of pneumococcal disease to help physicians target vaccination to appropriate individuals: who is at increased risk of CAP and IPD; and what are the effects of risk factors on the severity and prognosis of pneumococcal disease? It also highlights the economic burden of pneumococcal disease, the impact of pneumococcal disease on underlying comorbidities, and the importance of timely vaccination. We have focused primarily on COPD, asthma, smoking, diabetes and/or CHD as these are common risk factors for pneumococcal disease in primary practice. There are, however, many other risk factors.<sup>6–8</sup> As *Streptococcus pneumoniae* is the most frequent cause of CAP irrespective of age and comorbidity,<sup>1,9</sup> information has been provided on all-cause pneumonia (ie, CAP) and pneumococcal pneumonia.

## SEARCH METHODOLOGY

A broad search strategy was used to find English language publications in human adults indexed on PubMed (2004–November 2014). Relevant publications were manually selected from the following searches: pneumonia AND risk factor, CHD AND pneumonia, diabetes AND pneumonia, lung disease AND pneumonia, asthma AND pneumonia, COPD AND pneumonia, tobacco OR smoking AND pneumonia, and economic data AND pneumonia. Data comparing the risk of pneumococcal disease in adults with the above risk factors versus those without risk factors were tabulated (excluding publications prior to 2008 or with data prior to 2000), and these data used to discuss the risk of pneumococcal disease in individuals with these risk factors.

## POPULATIONS AT RISK OF PNEUMOCOCCAL DISEASE

Individuals with COPD, asthma or who smoke, and those with CHD or diabetes mellitus, are at increased risk of pneumococcal disease (CAP and IPD) compared with those without these risk factors.<sup>7,10–15</sup> Similar rate ratios for all-cause pneumonia (CAP), pneumococcal pneumonia and IPD have been reported in individuals with comorbidities (versus those without comorbidities).<sup>7</sup>

## Chronic respiratory diseases

Patients with chronic respiratory disease (COPD, chronic bronchitis and/or asthma) are at a higher risk of CAP and IPD than individuals without these comorbidities with fold increases of between 1.3 and 13.5 for CAP and 1.3 and 16.8 for IPD (OR; [table 1](#); see online supplementary table S1).<sup>7,8,12,13,15–26</sup>

Risk of CAP varies with condition and age, with older individuals (≥65 years of age) with COPD being at especially high risk.<sup>19–21</sup> Among individuals with COPD, those aged 65–79 or ≥80 years have been shown to have an increasingly higher risk of CAP than those aged 45–65 years.<sup>21</sup> Having COPD, and greater age, lack of pneumococcal vaccination, and corticosteroid therapy have been identified as independent factors for recurrent CAP in adults.<sup>17</sup>

The severity of the underlying respiratory condition affects the risk of CAP.<sup>15,19,21</sup> Individuals aged ≥65 years who have mild lung disease (not requiring medication or oxygen) have been shown to be twice as likely to have CAP as those without lung



**Table 1** Overview of risk factors associated with community-acquired pneumonia and pneumococcal disease

Risk factor	Cohort studies		Case-control studies	
	Number of cohorts*	Risk range <sup>†</sup>	Number of cohorts*	Risk range <sup>†</sup>
<b>Community-acquired pneumonia</b>				
Chronic respiratory diseases	8 <sup>‡</sup>	OR: 1.5 HR: 2.9 Rate ratio: 3.8–8.6	15 <sup>§</sup>	OR: 1.3–13.5 RR: 1.6–2.8 HR: 1.2
Current smoking status	4	HR: 1.1 Rate ratio: 3.3–4.0	6	OR: 1.0–2.3 HR: 2.0 RR: 1.5
Diabetes mellitus	7	HR: 1.0–1.9 Rate ratio: 1.6–3.1	9	OR: 1.0–1.4 HR: 1.1 RR: 1.2–1.3
Chronic heart disease	6	HR: 1.5–3.1 Rate ratio: 3.8–4.9	17	OR: 1.0–3.3 HR: 1.3 RR: 1.3–2.6
<b>Pneumococcal pneumonia</b>				
Chronic respiratory diseases	6 <sup>¶</sup>	Rate ratio: 3.7–9.8	0	–
Current smoking status	3	Rate ratio: 3.0–4.4	0	–
Diabetes mellitus	6	RR: 2.3 Rate ratio: 1.5–3.1	0	–
Chronic heart disease	3	Rate ratio: 3.8–5.1	0	–
<b>Invasive pneumococcal disease</b>				
Chronic respiratory diseases	9 <sup>**</sup>	OR: 2.1–16.8 Rate ratio: 2.5–7.7	4 <sup>††</sup>	OR: 1.3–4.7
Current smoking status	5	OR: 2.2 RR: 2.7 Rate ratio: 3.6–4.3	1	OR: 1.1
Diabetes mellitus	10	OR: 1.4–4.6 Rate ratio: 1.5–3.9	2	OR: 1.5–1.7
Chronic heart disease	5	OR: 3.0–6.9 Rate ratio: 2.9–3.9	4	OR: 1.7–9.9

\*For studies that only reported data separately for each cohort, all cohorts were included; for studies that reported data for the overall study population, the summary data were used.

<sup>†</sup>Risk in individuals with factor versus risk in those without risk factor; ranges are based on the lowest and highest values from the publications evaluated using the risk terminology (eg, relative risk or risk ratio) as stated in the original publications.

<sup>‡</sup>Comprising the following diseases (number of cohorts): asthma (3), bronchitis (0), COPD (1), lung disease (not specified; 4).

<sup>§</sup>Comprising the following diseases (number of cohorts): asthma (3), bronchitis (1), COPD (5), lung disease (not specified; 6).

<sup>¶</sup>Comprising the following diseases (number of cohorts): asthma (3), lung disease (not specified; 3).

<sup>\*\*</sup>Comprising the following diseases (number of cohorts): asthma (4), lung disease (not specified; 5).

<sup>††</sup>Comprising the following diseases (number of cohorts): asthma (2), COPD (2).

HR, hazard ratio; OR, odds ratio; RR, relative risk.

disease, whereas those with severe lung disease (requiring oxygen) are eight times more likely to have CAP.<sup>19</sup> Similarly, moderate and severe lung disease (percentage predicted FEV<sub>1</sub>: 50–80% and <50%, respectively) have been identified as significant risk factors for CAP in individuals aged ≥65 years compared with normal or mild lung disease (HR: 1.78 and 2.90, respectively).<sup>15</sup> Moderate COPD exacerbation and hospitalisation due to severe COPD exacerbation have also been identified as independent risk factors for CAP in patients with COPD aged ≥45 years.<sup>21</sup>

Use of inhaled corticosteroids, a frequent medication in COPD, has been associated with an increased risk of CAP.<sup>16 18</sup> In a case-control study conducted in hospitalised patients aged ≥65 years, use of inhaled corticosteroids was found to be an independent risk factor for CAP (adjusted OR: 2.89).<sup>18</sup> Inhaled corticosteroids were also associated with CAP in another case-control study involving individuals over 14 years of age (OR: 3.09).<sup>16</sup> In both these studies, the risk of CAP was higher in those receiving inhaled corticosteroids than in those receiving  $\beta_2$ -adrenergic agonists.<sup>16 18</sup> Furthermore, the use of inhalers, especially with a chamber spacer, was identified as an independent risk factor for CAP (multivariate OR: 1.57),<sup>16</sup> which may be

due to contamination of the inhaler or deep inhalation of pressurised aerosols aiding penetration of microorganisms into the bronchial tree.

Another study found that inhaled corticosteroids increased the risk of CAP in patients with COPD, whereas inhaled anticholinergics increased the risk of CAP in patients with asthma.<sup>27</sup> Inhaled  $\beta_2$ -adrenergic agonists, however, did not appear to affect the risk of CAP.<sup>27</sup> The authors of this study concluded that these associations may not be causal but reflect the severity of the underlying conditions. A recent Cochrane review concluded that the inhaled corticosteroids budesonide and fluticasone, administered alone or in combination with a long-acting  $\beta_2$  agonist, increase the risk of pneumonia requiring hospitalisation in patients with COPD, although they do not significantly affect mortality compared with controls.<sup>28</sup>

Within a patient population with underlying lung diseases, patients with COPD have been found to have a higher risk of IPD than those with asthma, regardless of age (fourfold vs twofold increased risk of IPD).<sup>13</sup> The increased risk of IPD in individuals with COPD may be due to reduced innate defence mechanisms in the airways, smoking and/or use of corticosteroids.<sup>13</sup>

## Smoking status

Smoking has also been identified as a risk factor for CAP (ORs for current smoking: 1.0–2.3) with the risk varying according to smoking history (table 1; see online supplementary table S2).<sup>7 15 16 18 19 21 22 24 29</sup> The effect of smoking on the risk of CAP has been explored in a case-control study.<sup>16</sup> Compared with individuals who had never smoked, current smokers and ex-smokers were found to have a higher risk of CAP (OR: 1.34 and 1.37, respectively), with smoking confirmed as an independent risk factor in a multivariate analysis. This risk increased with the number of pack-years (OR vs 0 pack-years: 1.46 for >150 pack-years and 1.01 for ≤150 pack-years). Among the ex-smokers, those who had stopped smoking >4 years ago had a significantly reduced risk of CAP than those who had stopped smoking <1 year ago (OR: 0.39). Individuals aged >65 years who had never smoked but were exposed to passive smoking were also at significantly increased risk of CAP (OR adjusted for age and sex: 1.56).<sup>16</sup> Similarly, in a separate study, individuals aged ≥65 years who were exposed to passive smoke at home had an increased risk of CAP (relative risk (RR): 1.48 vs those not exposed to passive smoke).<sup>29</sup>

In another study in individuals aged ≥65 years, current smokers had a higher risk of CAP than ex-smokers irrespective of age (OR for all ages: 1.8 vs 1.3).<sup>19</sup> Based on the population attributable fraction, which is a measure of the proportion of cases attributed to a particular risk factor, Jackson *et al*<sup>19</sup> calculated that 2.4% of CAP cases are due to current smoking, increasing to 5.5% of cases in those with no cardiopulmonary disease. In contrast, in a study involving individuals with COPD, current smoking was not found to affect CAP incidence, which the authors attributed to inaccurate recording of current smoking status (20% of individuals were reported to have never smoked), other causes of COPD such as occupational exposures, or individuals with severe COPD ceasing to smoke.<sup>21</sup>

The effect of smoking status on IPD incidence is variable,<sup>7 25 26 30</sup> which may reflect the variable prevalence of smoking within different populations.<sup>26</sup> In US adults with chronic medical conditions, Shea *et al*<sup>7</sup> calculated rate ratios of 3.6 in smokers aged 18–49 years to 4.3 in those aged 50–64 years.

In another US study, the risk of bacteraemic pneumococcal pneumonia in adults was significantly higher in current smokers than in those who have never smoked or are not currently smoking (multivariate adjusted OR: 2.2).<sup>25</sup> Smokers were also shown to be 3.7 times more likely to develop pneumococcal bacteraemic pneumonia than non-smokers in an Australian study.<sup>30</sup> In contrast, former or current smoking was not associated with IPD in Navajo adults in whom the prevalence of smoking was low.<sup>26</sup>

## Diabetes mellitus

Patients with diabetes have an increased risk of up to 1.4 for CAP and ranging from 1.4 to 4.6 for IPD (ORs; table 1; see online supplementary table S3).<sup>7 8 12–16 19 21 23–26 30–34</sup> Analysis of long-term UK data suggests that the risk of lobar pneumonia, pneumococcal pneumonia, septicaemia and meningitis in patients hospitalised with diabetes declined little between 1963 and 2011. However, a decreased risk of pneumococcal disease was observed in individuals aged <60 years in recent years (2007–11), which coincided with the introduction of pneumococcal conjugate vaccines (PCVs) in childhood vaccination programmes in 2006.<sup>14</sup>

Diabetes has the greatest impact on the risk of IPD and CAP in individuals aged <64 years and especially in those aged

≤40 years or without other comorbidities.<sup>12 32</sup> In a Danish case-control study, individuals <40 years of age with diabetes were found to have a threefold higher risk of hospitalisation due to pneumonia than individuals without diabetes of a similar age, with the RR decreasing in older age groups. The risk of pneumonia-related hospitalisation associated with diabetes was also greater in those with no other comorbidities, and in those with a longer duration of diabetes and/or poor glycaemic control (based on A1C levels).<sup>32</sup> Similarly, in a US study, increasing levels of A1C were associated with an increasing risk of CAP in patients with diabetes.<sup>31</sup> It has been suggested that the increased risk of pneumococcal infection in patients with diabetes results from the harmful effects of hyperglycaemia on immune and/or pulmonary function.<sup>35 36</sup>

## Chronic heart disease

Patients with CHD (including congestive heart failure (CHF) and cardiovascular and valve diseases) have up to a 3.3-fold increased risk (OR) of CAP and up to a 9.9-fold increased risk (OR) of IPD compared with those without CHD, with risk varying according to the condition and age of the individual (table 1; see online supplementary table S4).<sup>7 8 10–13 15 16 18 19 21 22 24 26</sup> In individuals living in the US and aged ≥65 years, heart disease was identified as an independent risk factor for CAP with 16% of cases attributed to heart disease. The risk of CAP was greater in those with heart disease of a greater severity: individuals with non-CHF heart disease had only a modest increase in the risk of CAP (OR: 1.2 vs those with no heart disease), whereas those with mild or severe CHF had a twofold and threefold increased risk, respectively.<sup>19</sup>

These findings are supported by data from a large population-based study of 67 000 patients with pneumonia, in which patients with CHF had an almost twofold increased risk of hospitalisation as a result of pneumonia relative to those without CHF.<sup>10</sup> The risk of pneumonia was affected by the underlying condition associated with the heart failure and the medical treatment administered. Patients with cardiomyopathy, as well as those treated with loop diuretics, were found to be especially at risk of hospitalised CAP. Similarly, in a separate study, treatment of heart failure with amiodarone was found to be an independent risk factor for CAP.<sup>16</sup>

The incidence of CAP and IPD in US individuals has also been found to increase with increasing age, although the rate ratios between patients with CHD and healthy individuals was higher in the 18–49-year age group than in the older age groups due to the low background incidence in the younger age group.<sup>7</sup> This reflects the fact that increasing age is itself a risk factor for pneumococcal disease and as such has a diluting effect on the increased risk associated with comorbidities in the older age groups.

## Multiple risk factors

Multiple risk factors for pneumococcal disease are frequently observed in individuals >65 years of age, with more than 60% having two or more underlying medical conditions.<sup>37–39</sup> Multiple conditions have been shown to have a cumulative effect on the risk of CAP/IPD, as well as on the mortality associated with these diseases.<sup>7 9 40</sup> The risk of pneumococcal disease (all-cause pneumonia, pneumococcal pneumonia and IPD) increases as the number of risk factors increases in different age groups (18–49, 50–64 and ≥65 years).<sup>7</sup> Rates are particularly high in those with three or more conditions (eg, RR for pneumococcal pneumonia relative to healthy individuals: 16.5, 12.8 and 9.2, respectively).

## CONSEQUENCES OF CHRONIC DISEASES ON PNEUMOCOCCAL DISEASE OUTCOMES

The presence of chronic diseases not only increases the risk of an individual acquiring a pneumococcal disease, but can also adversely affect the severity and outcome of that disease. Both COPD and diabetes have been shown to be significant predictors of hospitalisation in patients with CAP.<sup>41</sup> Furthermore, the risk of respiratory and cardiac complications—both of which are associated with increased mortality—is greater in individuals with chronic lung and/or heart diseases than in other individuals.<sup>42 43</sup>

In adults hospitalised due to IPD, the following independent risk factors for respiratory failure were identified: age >50 years (OR 1.63), chronic lung disease (OR 1.54), CHD (OR 1.49), and infection caused by serotype 3 (OR 1.97), serotype 19A (OR 2.34) and serotype 19F (OR 3.55).<sup>42</sup>

Cardiac complications have also been found to affect more than one-quarter of individuals hospitalised as a result of CAP and were associated with a 60% increased risk of 30-day mortality.<sup>43</sup> An increased risk of cardiac complications was observed in individuals with increased cardiovascular risk, such as those with preexisting heart failure (OR: 4.3), cardiac arrhythmias (OR: 1.8), coronary artery disease (OR: 1.5) or arterial hypertension (OR: 1.5).

Patients with chronic comorbidities are at increased risk of death from CAP or IPD over both the short term (eg, 30 days) and long term (1 year).<sup>44–48</sup> Adamuz *et al* investigated the incidence, causes and risk factors associated with 1-year mortality in patients with CAP after hospital discharge. They reported a 7% 1-year mortality rate following discharge from hospital, with most patients dying as a result of infectious diseases (mostly pneumonia) or acute cardiovascular events.<sup>45</sup> Independent risk factors for 1-year mortality in these patients were comorbidity (including COPD and diabetes mellitus), rehospitalisation within 30 days of hospital discharge, and nursing home residence.<sup>45</sup>

The risk of mortality from CAP or IPD in patients with COPD varies according to the study.<sup>49</sup> COPD (defined using spirometry) was found to be an independent risk factor for 30-day mortality in Spanish patients with CAP,<sup>48</sup> whereas other studies in patients with CAP or pneumococcal bacteraemic pneumonia have not demonstrated increased 30-day mortality in patients with COPD compared with those without COPD.<sup>44 46 50</sup>

This variability may reflect differences in the definitions used for COPD, as not all of these studies used spirometric measurements to diagnose COPD.<sup>44 46</sup> However, Liapikou *et al*<sup>50</sup> observed a similar mortality rate in patients with spirometry-confirmed COPD to that in patients without COPD. Although patients with COPD presented with more severe respiratory failure (arterial oxygen tension/inspiratory oxygen fraction) and more severe pneumonia (pneumonia severity index), they had less multilobar infiltration and fewer pulmonary complications compared with those without COPD.<sup>50</sup> This reduction in pulmonary complications has been attributed to the use of inhaled corticosteroids, possibly reducing the inflammatory response in the lung in these patients. This is supported by findings that prior treatment with inhaled corticosteroids in patients with chronic respiratory disorders who develop pneumonia is associated with a lower incidence of parapneumonic effusion.<sup>51</sup>

Mortality risk appears to increase in those with COPD and prior cardiovascular disease; older patients with COPD and prior cardiovascular disease have been reported to have a significantly increased 12-month mortality risk (adjusted OR: 1.34) compared with those without cardiovascular disease.<sup>52</sup>

Smoking has been identified as an independent risk factor for mortality associated with pneumococcal bacteraemic pneumonia

and CAP. In patients with pneumococcal bacteraemic pneumonia, smoking was attributed to 14.9% of the 30-day mortality, based on the population attributable proportion.<sup>44</sup> In a separate study of patients hospitalised with CAP, current smokers had a fivefold increased risk of 30-day mortality from pneumococcal CAP compared with non-smokers and ex-smokers, and current smoking status remained an independent risk factor for pneumococcal CAP compared with non-smoking status alone and ex-smoking status alone (OR: 4.0 and 3.9, respectively).<sup>53</sup>

Diabetes is an independent risk factor (OR: 1.67) for the development of bacteraemia in patients with pneumococcal pneumonia, which in turn is associated with significantly increased mortality versus non-bacteraemic pneumonia (OR: 2.57).<sup>54</sup>

Patients with CHF are at increased risk of a complicated episode of CAP (based on a combined endpoint of 30-day home-treated complications, hospitalisation or all-cause mortality; OR: 3.13),<sup>55</sup> and at increased risk of 30-day mortality.<sup>46 47</sup>

Analysis of data from the German Competence Network for Community-Acquired Pneumonia (CAPNETZ) study found that CHF and CHD were risk factors for 30-day mortality in patients with CAP in a univariate analysis (ORs: 4.91 and 2.76, respectively) but not in a multivariate analysis.<sup>46</sup> In a separate study involving Danish patients hospitalised for pneumonia, those with CHF had an increased 30-day mortality rate versus other patients (adjusted mortality rate ratio (MRR): 1.40).<sup>47</sup> Mortality increased with increasing severity of CHF before admission, based on medication regimen. Patients receiving loop-diuretics and spironolactone (drugs used for CHF New York Heart Association Functional Classification III–IV) were at a particularly high risk for death due to pneumonia (MRR: 1.72), whereas those using a thiazide as the sole diuretic had a mortality rate similar to that of other patients with pneumonia (MRR: 1.09).<sup>47</sup>

A hospital-based epidemiological study of IPD in adults in Belgium also demonstrated a significantly higher case fatality rate during hospitalisation in those with heart failure compared with those without heart failure (OR: 1.70).<sup>56</sup>

CAP may also worsen a patient's underlying condition, as reported in a US survey of adults aged ≥50 years with CAP, in which ≥20% of individuals experienced a worsening of COPD, asthma or hypertension.<sup>57</sup> This deterioration in the patient's underlying condition may in turn adversely affect the patient's prognosis. For example, previously diagnosed pneumonia in patients hospitalised for COPD exacerbation has been shown to increase inpatient mortality.<sup>58</sup> In another study, patients with COPD exacerbations and pneumonia had poorer outcomes, including inpatient and 90-day mortality, compared with those with non-pneumonic COPD exacerbations.<sup>59</sup>

Patients have been reported to have ongoing subclinical inflammation following recovery from pneumonia, and this has been associated with an increased risk of death due to cardiovascular disease in these individuals.<sup>60</sup> Worsening prior cardiovascular disease in patients with COPD has also been attributed as a cause of increased long-term mortality following pneumonia.<sup>52</sup> Similarly, deterioration of underlying cardiovascular disease has been associated with increased 1-year mortality following pneumonia in patients with diabetes mellitus versus those without diabetes.<sup>61</sup>

The mechanisms linking pneumonia to cardiac events such as myocardial infarction, arrhythmias and CHD are multifactorial. They include thrombogenesis/rupture of vulnerable plaques, and myocardial stress and suppression resulting from increased myocardial oxygen demand, lowered blood oxygen levels, depressed ventricular function and elevated levels of cytokines.<sup>60 62 63</sup>



## ECONOMIC BURDEN OF PNEUMOCOCCAL DISEASE

Pneumococcal pneumonia results in a more severe disease course requiring more medical resources than non-pneumococcal pneumonia.<sup>64</sup> Data from the CAPNETZ study suggest that patients with pneumococcal pneumonia are more likely to be hospitalised, to have higher pneumonia severity (Confusion, Urea, Respiratory Rate and Blood Pressure (CURB)) score values on admission and pleural effusion, and to require oxygen insufflation than those with non-pneumococcal pneumonia.<sup>64</sup> CAP, and specifically pneumococcal pneumonia, therefore imposes a significant economic burden.<sup>65</sup>

Economic studies conducted in the US and in Eastern Europe suggest that healthcare costs for CAP requiring hospitalisation are high and increase with increasing risk level of CAP.<sup>66–68</sup> Major determinants of total healthcare costs are admission to an intensive care unit,<sup>69 70</sup> and length of hospital stay,<sup>69 71</sup> which is in turn dependent on the presence of specific comorbidities, the development of complications and the severity of the pneumonia.

Bacteraemia and CHF have been found to be positive predictors of length of hospital stay in adults with pneumococcal pneumonia.<sup>70</sup> Independent predictors of longer length of hospital stay in patients with CAP also include chronic respiratory disease, diabetes, multilobar CAP, as well as older age ( $\geq 70$  years), pneumonia severity index class on admission, and development of CAP-associated complications.<sup>72</sup>

In addition to inpatient care, long duration of antibiotic therapy and a large number of visits at different healthcare levels (primary care, hospital outpatient and emergency departments) have been shown to contribute to the high cost of treating CAP.<sup>73</sup>

It has been suggested that the higher costs of treating those with comorbidities and CAP than those without comorbidities are due to exacerbation of the underlying conditions, leading to additional costs.<sup>74</sup> In line with this, the proportion of CAP-related costs has been found to decrease with increasing risk for CAP, suggesting that a greater proportion of healthcare costs are associated with treating underlying conditions in high-risk versus low-risk patients.<sup>66</sup> Furthermore, a 20% increase in hospitalisation for pneumonia observed among US individuals aged  $\geq 65$  years from 1988–1990 to 2000–2002 has, in part, been attributed to an increase in comorbidities in these individuals.<sup>75</sup> Complications (especially infectious diseases), hypoalbuminaemia and previous hospital admission have also been linked with the high costs associated with hospitalised patients with CAP.<sup>71</sup>

Pneumococcal disease (CAP/IPD) significantly affects patients' quality of life, causing extra days off work, more frequent visits to primary care providers, and requiring additional medication and assistance from caregivers.<sup>1 57 74</sup> Patients with a serious chronic condition who are hospitalised for CAP are also more likely to leave their job.<sup>74</sup> The US survey (mentioned above) suggested that cough and weakness associated with CAP adversely affects an individual's capacity to carry out daily activities, such as housework and visiting places/other individuals.<sup>57</sup>

## CONCLUSIONS

Adults with chronic conditions and other risk factors such as COPD, asthma, smoking, diabetes mellitus and CHD are not only at increased risk of pneumococcal infections, but also at increased risk of complications/mortality if they have pneumococcal disease. This highlights the need for timely pneumococcal vaccination in these patients.

**Acknowledgements** The authors take full responsibility for the content of this article and thank Neostar Communications Ltd, Oxford, UK (supported by Pfizer, France), for their assistance in preparing the manuscript, including preparing the first draft in close collaboration with the authors, and the collation of author comments.

**Contributors** All authors were involved in the content development of the manuscript, reviewed all drafts and approved the final version. Neostar Communications Ltd (Oxford, UK) prepared the first draft in close collaboration with the authors.

**Funding** Editorial assistance with the preparation of this review article was supported by Pfizer, France.

**Competing interests** AT has received consulting fees/honorarium from AstraZeneca, Bayer, Curetis, GlaxoSmithKline, Pfizer and Polyphor. FB has received financial support for travel to meetings from Pfizer; consultancy fees from AstraZeneca, Pfizer and Zambon; fees for board membership from AstraZeneca, Chiesi, GlaxoSmithKline, Novartis and Pfizer; lecture fees/speaker bureau fees from AstraZeneca, Chiesi, Novartis, Pfizer and Zambon; and his institution has received grants from Chiesi, Novartis, Pfizer and Zambon. ND is an employee of Pfizer, France. MA has received lecture fees and an honorarium for consultation from Pfizer, MSD, Gilead, Novartis and Astellas.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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