52-year follow-up of a birth cohort reveals a high pneumonia incidence among young men

Pia Holma[1], Paula Pesonen[2], Olli Mustonen[1], Marjo-Riitta Järvelin[3,4,5], Heikki Kauma[1], Juha Auvinen[4] and Timo Hautala[1,6]

[1]Research Unit of Internal Medicine, Dept of Internal Medicine, Division of Infectious Diseases, University of Oulu and Oulu University Hospital, Oulu, Finland. [2]Northern Finland Birth Cohorts, Arctic Biobank, Infrastructure for Population Studies, Faculty of Medicine, University of Oulu, Oulu, Finland. [3]Dept of Epidemiology and Biostatistics, MRC-PHE Centre for Environment & Health, School of Public Health, Imperial College London, London, UK. [4]Center for Life Course Health Research, University of Oulu, Unit of Primary Care, Oulu University Hospital, Oulu, Finland. [5]Dept of Life Sciences, College of Health and Life Sciences, Brunel University London, London, UK. [6]Research Unit of Biomedicine, University of Oulu, Oulu, Finland.

Corresponding author: Timo Hautala (timo.hautala@oulu.fi)

Shareable abstract (@ERSpublications)
This prospective follow-up of Northern Finland Birth Cohorts up to 52 years shows a high peak in pneumonia incidence among young male adults, and reveals pneumonia risk factors among the young and working-age populations https://bit.ly/38S0tkZ

Cite this article as: Holma P, Pesonen P, Mustonen O, *et al*. 52-year follow-up of a birth cohort reveals a high pneumonia incidence among young men. *ERJ Open Res* 2022; 8: 00707-2021 [DOI: 10.1183/23120541.00707-2021].

Received: 18 Dec 2021
Accepted: 2 May 2022

Abstract

Background Knowledge of pneumonia incidence and risk factors in adults is mainly based on clinical studies of selected patient data and registers with ageing populations. Prospective population-based investigations, such as birth cohort studies, are needed to understand pneumonia incidence and risk factors among young and working-age populations.

Methods Northern Finland Birth Cohort (NFBC) 1966 data (n=6750) were analysed for pneumonia incidence and risk factors. Incidence analysis was replicated using data from an independent NFBC 1986 cohort (n=9207). Pneumonia in relation to chronic conditions and lifestyle factors was analysed.

Results A peak with a maximum of 227 pneumonia episodes per 10 000 among men between the ages of 19 and 21 years was found in two independent cohorts. Pneumonia was associated with male sex (relative risk 1.72, 95% CI 1.45–2.04; p<0.001), low educational level (relative risk 2.30, 95% CI 1.72–3.09; p<0.001), smoking (relative risk 1.55, 95% CI 1.31–1.84; p<0.001), asthma (relative risk 2.19, 95% CI 1.73–2.75; p<0.001), cardiovascular diseases (relative risk 2.50, 95% CI 2.04–3.07; p=0.001), kidney diseases (relative risk 4.14, 95% CI 2.81–6.10; p<0.001), rheumatoid arthritis (relative risk 2.69, 95% CI 1.80–4.01; p<0.001), psoriasis (relative risk 2.91, 95% CI 1.92–4.41; p<0.001) and type II diabetes (relative risk 1.80, 95% CI 1.34–2.42; p<0.001). Men with excessive alcohol consumption at age 31 years were at risk of future pneumonia (relative risk 2.40, 95% CI 1.58–3.64; p<0.001).

Conclusions Birth cohort data can reveal novel high-risk subpopulations, such as young males. Our study provides understanding of pneumonia incidence and risk factors among young and working age populations.

Introduction

Pneumonia is a major cause of hospitalisation, associated with a significant health burden and increased mortality [1]. The risk of pneumonia is particularly high among the young, the elderly and immunocompromised patients [1–4]. The highest pneumonia burden is suffered by the elderly, with male sex predominance [5–7]. Pneumonia risk factors include low socioeconomic status, smoking, excessive alcohol consumption, chronic respiratory disease, chronic heart, liver and kidney diseases, autoimmune conditions, diabetes or haematological conditions, which are especially described among the elderly [8–15]. However, risk profiles for pneumonia among the young and working-age adult populations are not equally assessed [13, 16–20].

Prospective and lifelong health information can be collected from birth cohorts. The Northern Finland Birth Cohorts (NFBC) programme offers invaluable longitudinal data to investigate a high number of variables from the entire population (www.oulu.fi/nfbc). We investigated the properties associated with pneumonia episodes among individuals born within the 1966 birth cohort (NFBC 1966) with a prospective follow-up for 52 years. An independent cohort, NFBC 1986, was explored until the age of 33 years to replicate selected findings of NFBC 1966. Health and lifestyle factors were analysed, in order to understand mechanisms associated with incidence of pneumonia.

Methods

NFBC 1966

The NFBC 1966 cohort includes all individuals born with the expected date set during the year 1966, comprising 12 231 children (96.3% of all births during 1966 in the area) in the northern provinces of Finland [21]. Lifelong health information and national register data have been collected until the age of 52 years (figure 1). At age 31 years, clinical examination data (n=6007), questionnaire data (n=8690) and/or information from the national register data (n=9392) were available. At 46 years, clinical examination data (n=5823), questionnaire data (n=7146) and consent to use their information in combination with the national register data (n=6750) were available. The study has been approved by the ethical committee of the Northern Ostrobothnia Hospital District (Finland). The health questionnaire completed at 46 years of age is provided (supplementary material).

NFBC 1986 and pneumonia among young males

The NFBC 1986 (www.oulu.fi/nfbc) data were collected to replicate the relationship between sex and age on pneumonia incidence in an independent birth cohort. The effect of self-reported data on tobacco consumption at age 16 years on pneumonia risk among the young males was investigated [22]. The NFBC 1986 cohort comprised subjects who were born with the expected date of birth set between 1 July 1985 and 30 June 1986, including 9479 children (99% of all the deliveries taking place in the target period of the cohort). For this analysis, we included those for whom the 16-year follow-up information and consent to use their data were available (n=9207).

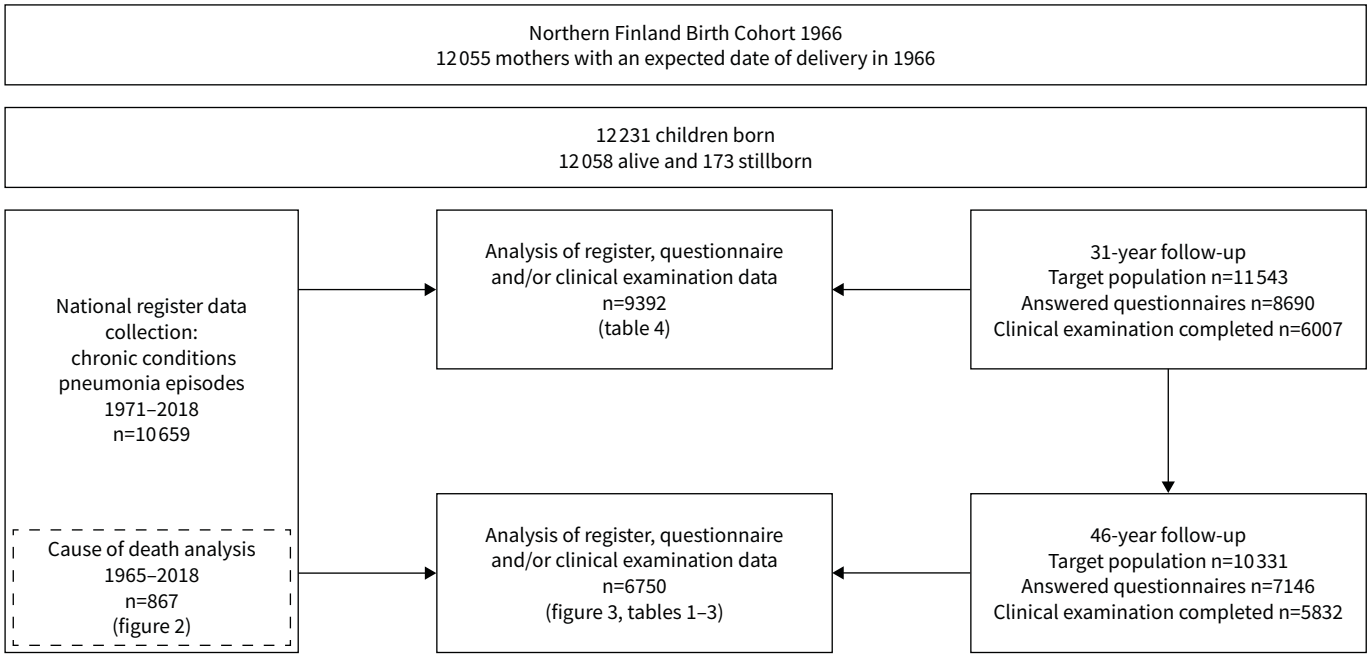

FIGURE 1 The flow of the Northern Finland Birth Cohort (NFBC) 1966 data collection. The study includes all individuals born with an expected date of birth in the year 1966. All study participants were subjects to careful analysis of their lifestyle and health properties at the ages of 31 and 46 years. Health data from 1971 to 2018 were obtained from national registers. Information on numbers of study participants and deceased individuals are shown.

Statistical analysis

Two approaches to NFBC 1966 cohort data analysis were used (figure 1). First, those with clinical and/or questionnaire data in the 46-year follow-up and consent to use their data in combination with the national register data (n=6750) were included. Second, we analysed register data of those from whom permission at age 31 years (n=9392) and/or clinical and/or questionnaire data in the 31-year follow-up were available.

For the first approach, table 1 shows the proportion of each risk factor by sex. Pearson's Chi-squared tests were used to evaluate association of risk factors between the males and females as well as between at least one pneumonia episode *versus* no pneumonia episodes (table 2). Risk factors with an incidence of <10 were not evaluated. Pneumonia incidence categorised by sex at ages 19–21 years in both cohorts were compared using Pearson's Chi-squared test. The lifelong pneumonia incidences per 10 000 were calculated by sex using the formula ((10 000×n)/N), where N is number of subjects in the data and n is number of subjects with a first pneumonia episode in one age group. Most of the pneumonia episodes were detected before the age of 46 years; therefore, time correlation was not evaluated, only association in general. We used the number of pneumonia episodes by 2018 as a dependent variable and the risk factors (table 1) as independent variables to evaluate relative risk and its 95% confidence interval for pneumonia with unadjusted Poisson regression models in whole data and separated by sex (table 3).

TABLE 1 Distribution of education, obesity, lifestyle factors and chronic diseases by sex in the Northern Finland Birth Cohort 1966 (n=6750) at age 46 years

	Males	Females	p-value
Subjects	3079 (45.6)	3671 (54.4)	<0.001
Education			<0.001
Basic	305 (9.9)	223 (6.1)	
Secondary	2069 (67.4)	2330 (63.6)	
Tertiary	694 (22.6)	1113 (30.4)	
Obesity			
BMI >30 kg·m^{-2}	502 (21.0)	644 (20.7)	0.767
Waist[#]	1410 (59.7)	2079 (67.7)	<0.001
Smoking, current or former[¶]	1586 (59.8)	1580 (47.7)	<0.001
Excessive alcohol consumption[+]	513 (16.7)	287 (7.8)	<0.001
Asthma	202 (6.6)	312 (8.5)	0.003
Cardiovascular disease	339 (11.0)	316 (8.6)	0.001
Cardiac arrhythmias	171 (5.6)	188 (5.1)	0.430
Ischaemic heart disease	105 (3.4)	46 (1.3)	<0.001
Valve disease	37 (1.2)	34 (0.9)	0.269
Hypertensive disease	8 (0.3)	4 (0.1)	0.143
Cardiomyopathy and heart failure	29 (0.9)	25 (0.7)	0.231
Other	60 (1.9)	82 (2.2)	0.416
Liver disease	43 (1.4)	41 (1.1)	0.302
Kidney disease	37 (1.2)	45 (1.2)	0.928
Sarcoidosis	33(1.1)	23(0.6)	0.035
Autoimmune disease			
Rheumatoid arthritis	28 (0.9)	85 (2.3)	<0.001
Psoriasis	48 (1.6)	48 (1.3)	0.317
Coeliac disease	17 (0.6)	42 (1.2)	0.012
Vasculitis	10 (0.3)	28 (0.8)	0.021
Purpura	15 (0.5)	24 (0.7)	0.413
Multiple sclerosis	2 (0.1)	24 (0.7)	<0.001
Diabetes mellitus	216 (7.0)	164 (4.4)	<0.001
Type 1 diabetes	27 (0.9)	16 (0.4)	
Type 2 diabetes	189 (6.1)	148 (4.0)	
Cancer			
Solid	21 (0.7)	18 (0.5)	0.263
Haematology	16 (0.5)	14 (0.4)	0.355

Data are presented as n (%), unless otherwise stated. BMI: body mass index. [#]: International Diabetes Association cut-off points for obesity are indicated with a waist circumference of ⩾94 cm for males and ⩾80 cm for females; [¶]: compares "never-" *versus* "current or former" smokers; [+]: excessive alcohol consumption is defined as self-reported daily consumption of ⩾30 g for males and ⩾20 g for females. Pearson's Chi-squared test was used.

TABLE 2 Male and female Northern Finland Birth Cohort 1966 study participants by no pneumonia episodes and those with at least one pneumonia episode (age 5–52 years, n=6750) in relation to pneumonia risk factors

	Male			Female		
	No pneumonia	⩾1 pneumonia	p-value	No pneumonia	⩾1 pneumonia	p-value
Subjects	3079			3671		
Sex	2812 (91.3)	267 (8.7)		3489 (95.0)	182 (5.0)	
Education						
Basic	263 (86.2)	42 (13.8)	0.006	211 (94.6)	12 (5.4)	0.162
Secondary	1895 (91.6)	174 (8.4)		2193 (94.1)	137 (5.8)	
Tertiary	638 (91.9)	56 (8.1)		1065 (95.7)	48 (4.3)	
BMI						
<30 kg·m^{-2}	1728 (91.6)	158 (8.4)	0.675	2343 (94.9)	125 (5.1)	0.144
⩾30 kg·m^{-2}	457 (91.0)	45 (9.0)		602 (93.5)	42 (6.5)	
Waist circumference[#]						
Low	865 (91.1)	85 (8.9)	0.498	945 (95.3)	47 (4.7)	0.258
High	1295 (91.8)	115 (8.2)		1960 (94.3)	119 (5.7)	
Smoking[¶]						
Never	1257 (92.6)	101 (7.4)	0.020	1969 (95.4)	94 (4.6)	0.014
Current or former	1504 (90.2)	164 (9.8)		1459 (93.6)	100 (6.4)	
Alcohol consumption[+]						
No	2331 (91.1)	228 (8.9)	0.920	3194 (94.6)	181 (5.4)	0.921
Yes	468 (91.2)	45 (8.8)		272 (94.8)	15 (5.2)	
Asthma						
No	2636 (91.6)	241 (8.4)	<0.001	3194 (95.1)	165 (4.9)	<0.001
Yes	169 (83.7)	33 (16.3)		280 (89.7)	32 (10.3)	
Cardiovascular disease						
No	2519 (91.9)	221 (8.1)	<0.001	3188 (95.0)	167 (5.0)	0.001
Yes	286 (84.4)	53 (15.6)		286 (90.5)	30 (9.5)	
Cardiac arrhythmias						
No	2657 (91.4)	251 (8.6)	0.031	3303 (94.8)	180 (5.2)	0.022
Yes	148 (86.5)	23 (13.5)		171 (91.0)	17 (9.0)	
Ischaemic heart disease						
No	2722 (91.5)	252 (8.5)	<0.001	3432 (94.7)	193 (5.3)	0.313
Yes	83 (79.0)	22 (21.0)		42 (91.3)	4 (8.7)	
Valve disease						
No	2775 (91.2)	267 (8.8)	0.031	3443 (94.7)	194 (5.3)	0.369
Yes	30 (81.1)	7 (18.9)		31 (91.2)	3 (8.8)	
Cardiomyopathy/heart failure						
No	2784 (91.3)	266 (8.7)	<0.001	3451 (94.7)	195 (5.3)	0.558
Yes	21 (72.4)	8 (27.6)		23 (92.0)	2 (8.0)	
Other cardiovascular disease						
No	2755 (91.3)	264 (8.7)	0.033	3401 (94.8)	188 (5.2)	0.023
Yes	50 (83.3)	10 (16.7)		73 (89.0)	9 (11.0)	
Liver disease						
No	2767 (91.1)	269 (8.9)	0.527	3439 (94.7)	191 (5.3)	0.008
Yes	38 (88.4)	5 (11.6)		35 (85.4)	6 (14.6)	
Kidney disease						
No	2776 (91.3)	266 (8.7)	0.006	3437 (94.8)	189 (5.2)	<0.001
Yes	29 (78.4)	8 (21.6)		37 (82.2)	8 (17.8)	
Sarcoidosis						
No	2652 (90.7)	271 (9.3)	0.972	3400 (94.5)	196 (5.5)	0.816
Yes	30 (90.9)	3 (9.1)		22 (95.7)	1 (4.3)	
Rheumatoid arthritis						
No	2659 (90.8)	269 (9.2)	0.115	3347 (94.7)	187 (5.3)	0.009
Yes	23 (82.1)	5 (17.9)		75 (88.2)	10 (11.8)	
Psoriasis						
No	2639 (90.7)	269 (9.3)	0.782	3381 (94.7)	190 (5.3)	0.005
Yes	43 (89.6)	5 (10.4)		41 (85.4)	7 (14.6)	

Continued

TABLE 2 Continued

	Male			Female		
	No pneumonia	⩾1 pneumonia	p-value	No pneumonia	⩾1 pneumonia	p-value
Coeliac disease						
No	2668 (90.8)	271 (9.2)	0.232	3381 (94.5)	196 (5.5)	0.379
Yes	14 (82.4)	3 (17.6)		41 (97.6)	1 (2.4)	
Vasculitis						
No	2674 (90.8)	272 (9.2)	0.241	3396 (94.6)	195 (5.4)	0.691
Yes	8 (80)	2 (20)		26 (92.9)	2 (7.1)	
Purpura						
No	2669 (90.8)	272 (9.2)	0.586	3400 (94.6)	195 (5.4)	0.531
Yes	13 (86.7)	2 (13.3)		22 (91.7)	2 (8.3)	
Multiple sclerosis						
No	2680 (90.7)	274 (9.3)	0.651	3401 (94.6)	194 (5.4)	0.126
Yes	2 (100)	0 (0)		21 (87.5)	3 (12.5)	
Diabetes						
No diabetes	2610 (91.3)	249 (8.7)	0.112	3323 (94.8)	183 (5.2)	0.002
Type 1 diabetes	26 (96.3)	1 (3.7)		12 (75.0)	4 (25.0)	
Type 2 diabetes	165 (87.3)	24 (12.7)		138 (93.2)	10 (6.8)	
Cancer, solid						
No	2662 (90.7)	273 (9.3)	0.457	3406 (94.6)	195 (5.4)	0.288
Yes	20 (95.2)	1 (4.8)		16 (88.9)	2 (11.1)	
Haematological						
No	2666 (90.7)	274 (9.3)	0.200	3412 (94.6)	193 (5.4)	<0.001
Yes	16 (100)	0 (0)		10 (71.4)	4 (28.6)	

[#]: waist circumference indicates ⩾94 cm for males and ⩾80 cm for females; [¶]: self-reported data at the age of 46 years on smoking (no smoking history *versus* former or current smokers); [+]: self-reported data at the age of 46 years on excessive alcohol consumption (males ⩾30 g·day^{-1}, females ⩾20 g·day^{-1}). Pearson's Chi-squared test was used.

For the second approach, with risk factors at age 31 years (table 4), we evaluated the relative risk (95% CI) of future pneumonias with unadjusted Poisson regression models in whole data and separated by sex. The number of pneumonia episodes after the 31-year follow-up was a dependent variable.

To evaluate the adjusted relative risk (95% CI) of pneumonia and future pneumonias, we used the multivariate Poisson regression models. The criterion to select the independent variables (at 46 years: sex, education, smoking and cardiovascular diseases; at 31 years: sex, smoking, alcohol) to the models were the significance level of unadjusted results and the sufficiency of the number of samples per category. In addition, the adjusted relative risks of pneumonia were analysed separately by smoking categories. $p<0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 26; IBM, Armonk, NY, USA).

Pneumonia definition

Data on pneumonia episodes were obtained (until the age of 52 years for NFBC 1966 and until the age of 33 years for NFBC 1986) from the Care Register for Health Care (CRHC), previously named the Finnish Hospital Discharge Register, maintained by the Finnish Institute for Health and Welfare. The CRHC has nationwide hospital discharge information on inpatient episodes of community-acquired and hospital-acquired pneumonias (supplementary table S1) from all hospitals, starting from 1972 [23]. From 1998 onwards, the register also includes outpatient care episodes diagnosed by secondary or tertiary healthcare. In case of multiple diagnoses of pneumonia, episodes of ⩾90 days apart were counted as separate events. Microbiological data were not available.

Deceased NFBC 1966 participants

The data were obtained from the Causes of Death Register (Statistics Finland; www.stat.fi/meta/til/ksyyt_en.html). The number of deaths is shown in figure 1 and the causes of deaths are summarised in figure 2. Details of unnatural causes of deaths in the NFBC 1966 have been reported elsewhere [24].

TABLE 3 Risk of pneumonia by known susceptibility factors in male and female Northern Finland Birth Cohort 1966 participants

	All		Male		Female	
	Relative risk (95% CI)	p-value	Relative risk (95% CI)	p-value	Relative risk (95% CI)	p-value
Subjects n	6750		3079		3671	
Sex (n=6750)						
Male *versus* female	1.72 (1.45–2.04)	<0.001				
Education (n=6734)						
Basic *versus* tertiary	2.30 (1.72–3.09)	<0.001	2.16 (1.50–3.11)	<0.001	1.70 (0.98–2.94)	0.060
Secondary *versus* tertiary	1.39 (1.12–1.71)	0.003	1.17 (0.88–1.56)	0.273	1.54 (1.12–2.11)	0.008
Obesity (n=5500)						
BMI ⩾30 kg·m^{-2} *versus* BMI <30 kg·m^{-2}	1.09 (0.87–1.37)	0.473	1.03 (0.76–1.41)	0.833	1.15 (0.82–1.62)	0.415
Waist circumference (n=5431)						
High *versus* low	0.96 (0.79–1.17)	0.698	0.93 (0.71–1.20)	0.558	1.13 (0.82–1.55)	0.455
Smoking (n=5964)						
Current or former *versus* never	1.55 (1.31–1.84)	<0.001	1.50 (1.19–1.89)	0.001	1.43 (1.10–1.86)	0.007
Excessive alcohol intake (n=6734)	1.27 (1.00–1.60)	0.049	1.19 (0.90–1.56)	0.224	1.01 (0.63–1.64)	0.960
Asthma (n=6750)	2.19 (1.73–2.75)	<0.001	1.81 (1.28–2.54)	0.001	2.87 (2.09–3.95)	<0.001
Cardiovascular disease (n=6750)	2.50 (2.04–3.07)	0.001	2.43 (1.88–3.14)	<0.001	2.40 (1.72–3.35)	<0.001
Cardiac arrhythmias	1.64 (1.22–2.21)	0.001	1.64 (1.12–2.41)	0.011	1.59 (0.98–2.57)	0.060
Ischaemic heart disease	3.66 (2.68–4.99)	<0.001	3.70 (2.64–5.19)	<0.001	1.77 (0.73–4.29)	0.208
Valve disease	2.43 (1.43–4.12)	0.001	2.84 (1.56–5.19)	0.001	1.43 (0.46–4.46)	0.541
Cardiomyopathy and heart failure	7.06 (4.89–10.20)	<0.001	6.45 (4.06–10.24)	<0.001	7.39 (4.03–13.55)	<0.001
Other	2.10 (1.39–3.15)	<0.001	2.24 (1.31–3.82)	0.003	2.01 (1.07–3.78)	0.031
Liver disease (n=6750)	1.60 (0.88–2.90)	0.123	1.09 (0.45–2.64)	0.849	2.39 (1.06–5.38)	0.035
Kidney disease (n=6750)	4.14 (2.81–6.10)	<0.001	5.04 (3.17–8.01)	<0.001	2.93 (1.45–5.93)	0.003
Sarcoidosis (n=6575)	0.84 (0.32–2.25)	0.732	0.81 (0.26–2.54)	0.724	0.69 (0.10–4.91)	0.710
Autoimmune disease (n=6575)						
Rheumatoid arthritis	2.69 (1.80–4.01)	<0.001	1.94 (0.87–4.36)	0.107	3.78 (2.36–6.05)	<0.001
Psoriasis	2.91 (1.92–4.41)	<0.001	1.13 (0.50–2.52)	0.774	6.00 (3.66–9.83)	<0.001
Coeliac disease	1.20 (0.54–2.69)	0.653	1.59 (0.51–4.96)	0.423	1.14 (0.36–3.55)	0.827
Vasculitis	1.87 (0.84–4.19)	0.126	3.63 (1.35–9.72)	0.010	1.14 (0.28–4.57)	0.859
Purpura	1.21 (0.45–3.24)	0.701	1.20 (0.30–4.82)	0.798	1.33 (0.33–5.33)	0.691
Multiple sclerosis	1.36 (0.44–4.24)	0.592			2.00 (0.64–6.24)	0.234
Diabetes mellitus (n=6745)						
Type 1 diabetes	1.77 (0.79–3.95)	0.166	0.73 (0.18–2.94)	0.661	4.10 (1.52–11.01)	0.005
Type 2 diabetes	1.80 (1.34–2.42)	<0.001	1.99 (1.42–2.79)	<0.001	1.11 (0.59–2.09)	0.753
Cancer (n=6575)						
Solid	0.91 (0.29–2.82)	0.867	0.43 (0.06–3.03)	0.394	1.77 (0.44–7.12)	0.421
Haematology	1.58 (0.59–4.22)	0.363			4.60 (1.71–12.36)	0.002

The relative risk (95% CI) for pneumonia was analysed using unadjusted Poisson regression models, where the number of pneumonia episodes by 2018 was a dependent variable and the risk factors were independent variables. BMI: body mass index.

Definitions of chronic diseases

Lifetime information of chronic conditions based on the International Classification of Diseases (ICD)-8, -9 and -10 diagnostic codes listed in supplementary table S1 was collected from national registers until the age of 52 years (n=9392). Those suffering from asthma were identified based on reimbursement of medical expenses from the Social Insurance Institution of Finland. The diabetes variable was created by combining the data of hospital registers from CRHC, medicine purchases and reimbursement documentation from the Social Insurance Institution. Gestational diabetes and polycystic ovary syndrome were excluded. Diagnoses for diabetes type 1 (DMI) and 2 (DMII) were obtained from the care register. Metformin medication obtained from medicine purchases was used to indicate DMII in cases where the differentiation between DMI and DMII was not well defined.

Education

Information on formal education was obtained at the age of 46 years from self-reported data classified into basic (⩾9 years of primary school), secondary (1–4 years of vocational or secondary school after basic education) and tertiary (applied sciences or university degree) categories.

TABLE 4 Prediction of relative risk and its 95% confidence interval of future pneumonia episodes analysed by unadjusted Poisson regression models in the Northern Finland Birth Cohort 1966 cohort based on risk factors determined at the age of 31 years

	All		Male			Female		
	Relative risk (95% CI)	p-value	Subjects n (%)	Relative risk (95% CI)	p-value	Subjects n (%)	Relative risk (95% CI)	p-value
Subjects n	9392			4556			4836	
Sex (n=9392)	1.44 (1.21–1.71)	<0.001	4556 (48.5)			4836 (51.5)		
Obesity (n=6012)[#]								
BMI ⩾30 kg·m^{-2} *versus* BMI <30 kg·m^{-2}	1.07 (0.69–1.66)	0.755	208 (7.7)	1.08 (0.58–2.01)	0.801	273 (8.2)	1.07 (0.58–2.00)	0.830
Waist (n=4289)								
High *versus* low[¶]	0.08 (0.73–1.33)	0.904	514 (25.9)	1.02 (0.65–1.59)	0.940	838 (36.3)	0.99 (0.65–1.50)	0.961
Smoking[+] **(n=8514)**								
Current or former *versus* never	1.71 (1.40–2.08)	<0.001	2537 (62.2)	1.91(1.44–2.54)	<0.001	2210 (49.8)	1.40 (1.05–1.86)	0.020
Excessive alcohol consumption[§] **(n=5854)**	2.25 (1.60–3.17)	<0.001	297 (11.4)	2.40 (1.58–3.64)	<0.001	155 (4.8)	1.77 (0.93–3.37)	0.085
Asthma[f] **(n=9392)**	1.91 (1.31–2.78)	0.001	124 (2.7)	2.85 (1.85–4.40)	<0.001	159 (3.3)	0.97 (0.46–2.05)	0.930

The number of pneumonia episodes after 31-year follow-up was a dependent variable and gender, obesity, waist, smoking, excessive alcohol consumption and asthma were independent variables in the models. BMI: body mass index. [#]: BMI cut-off point 30 kg·m^{-2}; [¶]: cut-off point ⩾94 cm for males and ⩾80 cm for females; [+]: any history of smoking *versus* never smoked; [§]: self-reported alcohol consumption (males ⩾30 g·day^{-1}, females ⩾20 g·day^{-1}); [f]: doctor-diagnosed.

Body weight definitions

Body mass index (BMI) and waist circumference of the NFBC 1966 participants were measured at 31 years and 46 years. Obesity is defined by a waist circumference of ⩾94 cm for males and ⩾80 cm for females (International Diabetes Association) and/or BMI of ⩾30 kg·m^{-2}.

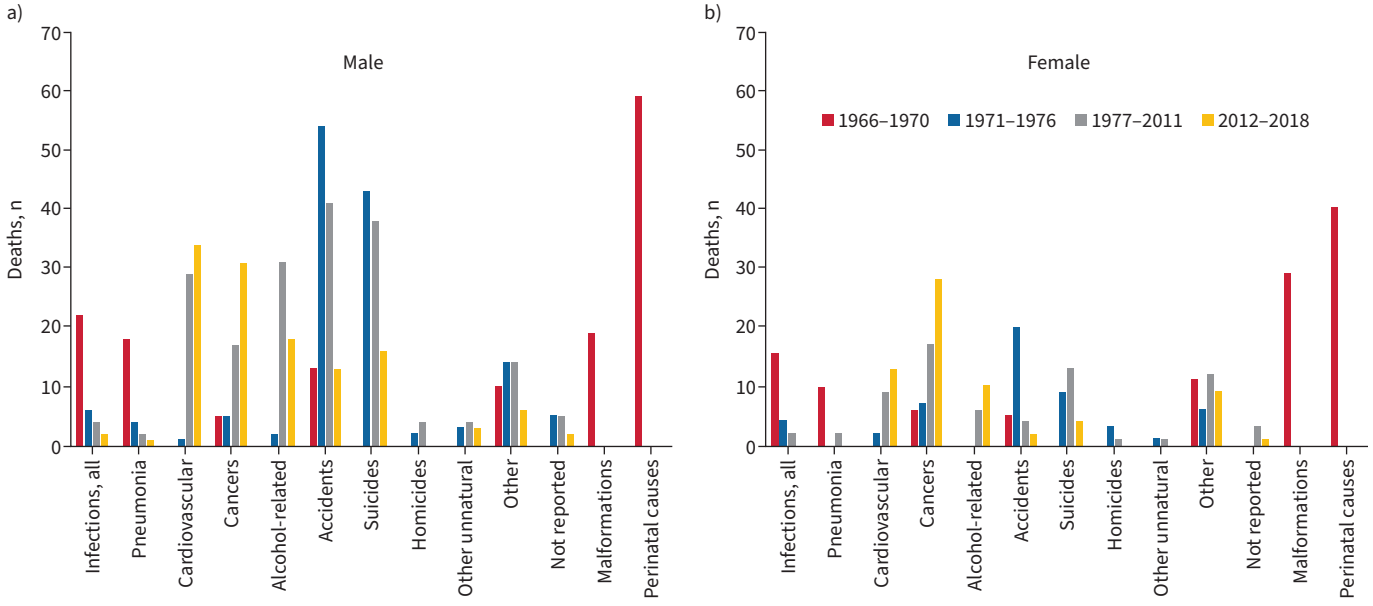

FIGURE 2 The figure shows the number of deaths among the a) male and b) female Northern Finland Birth Cohort (NFBC) 1966 participants divided into four time periods (1966–1970, 1971–1976, 1977–2011, 2012–2018). The number of deaths in major cause of death categories are shown.

Smoking and alcohol consumption

NFBC 1966 self-reported health information including alcohol and tobacco consumption was collected at the ages of 31 years and 46 years. Daily alcohol doses exceeding 20 g in women or 30 g in men were considered excessive [25].

Results

Characteristics of the NFBC 1966 cohort participants by sex at 46 years

Table 1 summarises the demographic data of the NFBC 1966 (n=6750) at age 46 years. While women had a higher level of education ($p<0.001$), smoking ($p<0.001$) and excessive alcohol consumption ($p<0.001$) were more common among men compared to women [21]. Women had more commonly an asthma diagnosis ($p=0.003$) while men were affected by cardiovascular diseases ($p=0.001$). Autoimmune diseases (rheumatoid arthritis ($p<0.001$), coeliac disease ($p=0.012$), vasculitis ($p=0.021$) and multiple sclerosis ($p<0.001$)) were more common among women compared to men. Men had a higher diabetes mellitus incidence compared to women ($p<0.001$).

Pneumonia incidence is high among young males in two independent birth cohorts

Pneumonia incidence among 6750 participants of NFBC 1966 (episodes per 10 000) at ages ranging from 5 to 52 years is summarised in figure 3a. Pneumonia hospitalisation was high, with a maximum of 227 episodes per 10 000 among young males between the ages of 19 and 21 years. Despite this high peak among young males, the average number of pneumonias over the life course was within the range of <20 episodes per 10 000 with an increase of up to 50 episodes per 10 000 in the oldest age categories of the NFBC 1966 cohort. In the NFBC 1966 cohort, 25.2% of pneumonia episodes in males occurred between the ages of 19 and 21 years. In turn, female cohort participants had 1.8% of their pneumonia episodes within the same age category ($p<0.001$).

Data obtained from the NFBC 1986 cohort (n=9207), an independent birth cohort, confirmed the high pneumonia incidence among young adult males with a maximum of 80 episodes per 10 000 (figure 3b). 21.1% of pneumonia episodes in males and 6.7% of pneumonia episodes in females occurred between the ages of 19 and 21 years ($p<0.001$).

General properties associated with pneumonia

In general, males had a higher risk of pneumonia across the life course than females (relative risk 1.72, 95% CI 1.45–2.04; $p<0.001$). Although men with low education had a high number of pneumonia episodes ($p=0.006$; table 2), the education did not explain the peak in pneumonias between the ages of 19 and 21 years. The episodes among the young males in the 1966 cohort appeared mostly during the cold season (figure 3c). However, in the 1986 cohort, this seasonal association was not seen. Pneumonia at a young age was not associated with a higher risk of developing recurrent pneumonia.

Smoking and pneumonia

NFBC 1966 participants who reported at the age of 46 years that they were “current or former smokers” (table 2) had a higher lifetime number of pneumonia episodes (relative risk 1.55, 95% CI 1.31–1.84; $p<0.001$; table 3) compared to those who had “never” smoked. In addition, we confirmed that smoking at 31 years is a significant risk factor for future pneumonia (relative risk 1.71, 95% CI 1.40–2.08; $p<0.001$; table 4). However, smoking at 31 years in the NFBC 1966 cohort did not explain the high number of pneumonia episodes among the young males between the ages of 19 and 21 years. Unfortunately, our data on smoking in the NFBC 1966 at a young age was incomplete. In the NFBC 1986 cohort, we did not find a difference in the number of pneumonia episodes between those who smoked occasionally or regularly (68 pneumonia episodes), compared to those who had “never” smoked at the age of 16 years (81 pneumonia episodes; $p=0.965$).

Excessive alcohol consumption and pneumonia

In the NFBC 1966 cohort, excessive alcohol consumption was more common among men than in women (table 1). Excessive alcohol consumption (men $\geqslant 30\ g \cdot day^{-1}$, women $\geqslant 20\ g \cdot day^{-1}$) at 31 years was associated with future pneumonia, especially among men (relative risk 2.40, 95% CI 1.58–3.64; $p<0.001$) in the NFBC 1966 cohort compared to those with low or moderate alcohol consumption (table 4). However, excessive alcohol consumption at 46 years was not associated with a total lifetime pneumonia burden (table 2), possibly because 36.3% of individuals with high alcohol consumption at 31 years did not participate in the study at the age of 46 years.

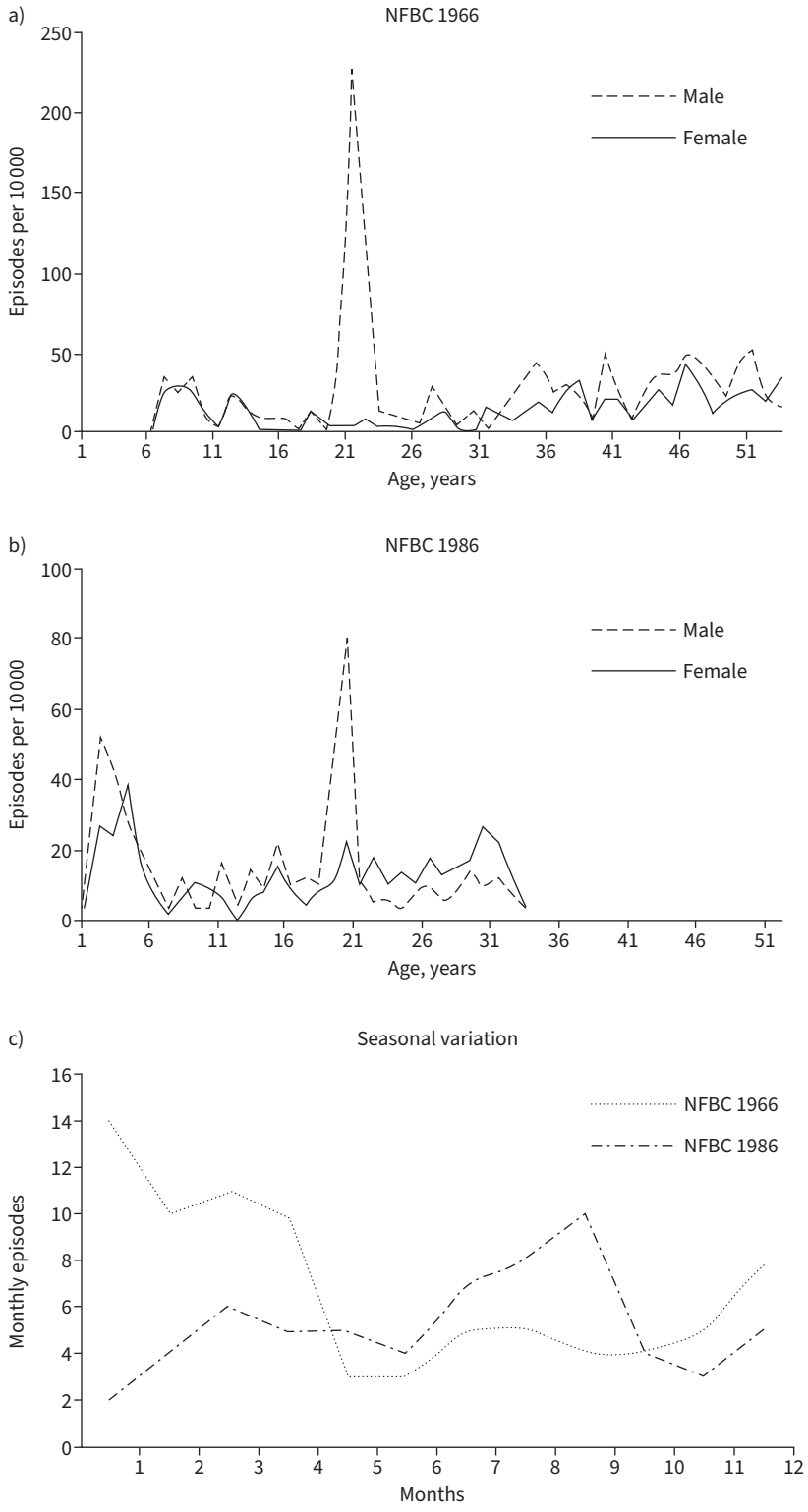

FIGURE 3 a) Lifelong pneumonia incidence (per 10 000) among the male and female Northern Finland Birth Cohort (NFBC) 1966 participants between the ages of 5 and 52 years (1971 to 2018). b) Pneumonia incidence (per 10 000) in the NFBC 1986 study cohort between the ages of 0 and 33 years (1986–2019) among male and female participants. c) Seasonal distribution of pneumonia episodes in the NFBC 1966 and 1986 cohorts among males between 19 and 21 years of age with high pneumonia incidence. The vertical axis indicates the numbers of monthly pneumonia episodes from January to December (months 1–12) in the NFBC 1966 and 1986 cohorts.

Asthma and pneumonia

In the NFBC 1966 cohort, asthma was more common in women compared to men (8.5% *versus* 6.6%; p=0.003; table 1). We found an association between asthma and a lifetime number of pneumonia episodes both among men (p<0.001) and women (p<0.001) (table 2). For the most part, men who had received asthma diagnosis before the age of 31 years were at risk of developing pneumonia in the future (relative risk 2.85, 95% CI 1.85–4.40; p<0.001; table 4).

Diabetes

In the NFBC 1966 cohort, an increased risk of pneumonia was associated with type II diabetes (relative risk 1.80, 95% CI 1.34–2.42; p<0.001). This risk was predominantly seen in males (relative risk 1.99, 95% CI 1.42–2.79; p<0.001). Women with type I diabetes were at risk of developing pneumonia (relative risk 4.10, 95% CI 1.52–11.01; p=0.005) (table 3). However, the low number of cases may have impact on the association, which is reflected in wide confidence intervals.

Autoimmune diseases

Women of the NFBC 1966 cohort were affected by autoimmunity (table 1). Rheumatoid arthritis (relative risk 3.78, 95% CI 2.36–6.05; p<0.001) and psoriasis (relative risk 6.00, 95% CI 3.66–9.83; p<0.001) were associated with pneumonia among women (table 3).

Cardiovascular diseases are associated with pneumonia in NFBC 1966

Cardiovascular conditions such as arrhythmias, ischaemic heart disease, valve disease, cardiomyopathy and heart failure were associated with a lifelong burden of pneumonia episodes in the NFBC 1966 cohort (relative risk 2.50, 95% CI 2.04–3.07; p=0.001) (table 3). Pneumonia was common both in males (15.6% *versus* 8.1%; p<0.001) and females (9.5% *versus* 5.0%; p=0.001) suffering from cardiovascular diseases (table 2).

Multivariable analysis of NFBC 1966 pneumonia risk factors

Low educational level (male, relative risk 1.80, 95% CI 1.23–2.63; p=0.003; female relative risk 3.00, 95% CI 1.47–6.10; p=0.002) and cardiovascular diseases were associated with pneumonia (male, relative risk 1.83, 95% CI 1.06–3.16; p=0.030) when considering education, smoking and cardiovascular diseases. Among those who had never smoked, being a male (relative risk 1.48, 95% CI 1.13–1.93; p=0.004), having low educational level (relative risk 2.07, 95% CI 1.25–3.42; p=0.005) or cardiovascular diseases (relative risk 1.50, 95% CI 1.01–2.22; p=0.042) associated significantly with pneumonia risk. Similarly, among current or former smokers, male sex (relative risk 1.99, 95% CI 1.06–3.72; p=0.032), low educational level (relative risk 2.05, 95% CI 1.25–3.336; p=0.005) and cardiovascular diseases (relative risk 2.78, 95% CI 2.15–3.59; p<0.001) were associated with pneumonia. At age 31 years, excessive alcohol consumption was a risk factor (relative risk 2.99, 95% CI 1.59–5.60; p=0.001) for future pneumonia, regardless of an individual's smoking status.

Discussion

Most epidemiological studies on pneumonia have focused on populations aged >65 years [10, 26]. Previously, birth cohorts have been investigated for at least Norovirus [27], influenza [28] and childhood respiratory infections [29]. To our knowledge, for the first time, this study provides lifelong information on risk factors and incidence of pneumonia from birth up to the age of 52 years in a birth cohort. Data obtained from our longitudinal birth cohorts are exceptionally well suited for providing insights on risk factors and possibilities for pneumonia prevention. We believe that extended investigation of these birth cohorts' participants to the age of their retirement will provide valuable information on pneumonia among the elderly.

Pneumonia incidence is well understood among the elderly [10, 26]. In our study, a high pneumonia incidence among young males between the ages of 19 and 21 years was found independently in two birth cohorts (figure 3a and b). In both cohorts, a need for hospitalisation due to pneumonia among the young males was comparable or even higher than that observed among the elderly [1, 30]. The results cannot be explained, for example, by influenza activity [31], seasonal factors such as cold exposure (figure 3c) or smoking at the ages of 16 or 31 years. We can only speculate that the high number of pneumonia episodes among the young males is associated with compulsory military service in Finland. Previous studies among military recruits are in agreement with this hypothesis [32–34].

Male sex is associated with pneumonia incidence and severity, especially among the elderly [35]. Our study of the young and working age cohorts shows that males suffer from several unfavourable health properties such as smoking and alcohol consumption (table 1), and they are at an elevated pneumonia risk

compared to women (table 3). For example, smoking and excessive alcohol consumption at 31 years predict a future risk of pneumonia (table 4). In addition, those who reported to be current or former smokers at the age of 46 years had a larger lifetime burden of pneumonia (table 3). However, at 46 years, excessive alcohol consumption was not associated with a lifetime pneumonia burden. We believe that selection of the study population caused by alcohol-related conditions or deaths, especially among men (figure 2), may have affected the results.

Chronic conditions associated with pneumonia risk are well documented in advanced age categories [8, 26, 36]. We confirmed that asthma, diabetes, cardiovascular diseases and selected autoimmune conditions were also associated with pneumonia incidence in our young and working-age cohorts. However, selected pneumonia risk factors such as malignancies, dementia, COPD, chronic liver conditions and kidney diseases are rare within the age categories of our cohorts. Those conditions commonly seen among the elderly do not explain the major pneumonia burden among our younger study participants at a maximum of 52 years of age. Conditions involving immunity, such as rheumatoid arthritis and psoriasis, were associated with a risk of pneumonia, especially among women. We believe that immunological properties, including possibility of primary or secondary immunodeficiency, may explain the pneumonia incidence among those suffering from autoimmunity and infection susceptibility.

Although the cohort participants were highly adhered to the study, selection of patients may have affected our results. It is possible that patients with a severe burden of infections, for example, were incompletely documented due to their poor health. It is also possible that patients with a high disease burden and infection susceptibility may have died, thus creating a study population selection bias. We also acknowledge that only pneumonia episodes that required hospitalisation at specialised units were included, and true pneumonia numbers are higher than those recorded in our study.

In conclusion, our study demonstrates that novel populations, such as young males, with a high pneumonia risk can be identified by exploring properties of birth cohorts. Our study also demonstrates that a burden of unhealthy habits especially among males at least in part explains the overall burden of pneumonia. Our study highlights a need for further studies of immunological properties especially among females with autoimmune diseases. The high peak among young males, which cannot be explained by the known conventional pneumonia risk factors, should also be subject to future studies. Most importantly, preventive measures for pneumonia among these novel high-risk populations should be considered.

Provenance: Submitted article, peer reviewed.

Support statement: The study was supported by Oulu University Hospital VTR K74809. T. Hautala has received support from CSL-Behring. NFBC1966 and NFBC1986 have received core support from multiple funders. The NFBC 1966 31-year follow-up received financial support from University of Oulu Grant number 65354; Oulu University Hospital grant numbers 2/97 and 8/97; Ministry of Health and Social Affairs grant numbers 23/251/97, 160/97 and 190/97; National Institute for Health and Welfare, Helsinki grant number 54121; and Regional Institute of Occupational Health, Oulu, Finland grant numbers 50621 and 54231. The NFBC 1966 46-year follow-up received financial support from University of Oulu grant number 24000692, Oulu University Hospital grant number 24301140 and ERDF European Regional Development Fund grant number 539/2010 A31592. The data generation, curation and manpower were also supported by the following EU H2020 grants: DynaHEALTH (grant number 633595), LifeCycle (733206), LongITools (873749), EarlyCause, EDCMET (825762) and the Medical Research Council, UK (MRC/BBSRC MR/S03658X/1) (JPI HDHL H2020). M-R. Järvelin is partly supported by the MRC Centre for Environment and Health at ICL, which is currently funded by the Medical Research Council (MR/S019669/1). Funding information for this article has been deposited with the Crossref Funder Registry.

Conflict of interest: None declared.

References

1 Jain S, Self WH, Wunderink RG, *et al.* Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med* 2015; 373: 415–427.
2 Sterrantino C, Trifirò G, Lapi F, *et al.* Burden of community-acquired pneumonia in Italian general practice. *Eur Respir J* 2013; 42: 1739–1742.
3 Millett ERC, Quint JK, Smeeth L, *et al.* Incidence of community-acquired lower respiratory tract infections and pneumonia among older adults in the United Kingdom: a population-based study. *PLoS One* 2013; 8: e75131.
4 Bjarnason A, Westin J, Lindh M, *et al.* Incidence, etiology, and outcomes of community-acquired pneumonia: a population-based study. *Open Forum Infect Dis* 2018; 5: ofy010.

5 Rivero-Calle I, Pardo-Seco J, Aldaz P, *et al.* Incidence and risk factor prevalence of community-acquired pneumonia in adults in primary care in Spain (NEUMO-ES-RISK project). *BMC Infect Dis* 2016; 16: 645.
6 Ewig S, Birkner N, Strauss R, *et al.* New perspectives on community-acquired pneumonia in 388 406 patients. Results from a nationwide mandatory performance measurement programme in healthcare quality. *Thorax* 2009; 64: 1062–1069.
7 Gonzalez Quero B, Serrano Fernandez L, Garcia Moyano M, *et al.* Differences in community acquired pneumonia according to gender. *Eur Respir J* 2017; 50: Suppl. 61, PA4101.
8 Torres A, Peetermans WE, Viegi G, *et al.* Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax* 2013; 68: 1057–1065.
9 Weiser JN, Ferreira DM, Paton JC. *Streptococcus pneumoniae*: transmission, colonization and invasion. *Nat Rev Microbiol* 2018; 16: 355–367.
10 McLaughlin JM, Khan FL, Thoburn EA, *et al.* Rates of hospitalization for community-acquired pneumonia among US adults: a systematic review. *Vaccine* 2020; 38: 741–751.
11 Curcio D, Cané A, Isturiz R. Redefining risk categories for pneumococcal disease in adults: critical analysis of the evidence. *Int J Infect Dis* 2015; 37: 30–35.
12 Campling J, Jones D, Chalmers JD, *et al.* The impact of certain underlying comorbidities on the risk of developing hospitalised pneumonia in England. *Pneumonia* 2019; 11: 4.
13 Klemets P, Lyytikäinen O, Ruutu P, *et al.* Risk of invasive pneumococcal infections among working age adults with asthma. *Thorax* 2010; 65: 698–702.
14 Shea KM, Edelsberg J, Weycker D, *et al.* Rates of pneumococcal disease in adults with chronic medical conditions. *Open Forum Infect Dis* 2014; 1: ofu024.
15 Alvis-Zakzuk NJ, Arroyave I, Castañeda-Orjuela C, *et al.* Education and pneumonia mortality: a trend analysis of its inequalities in Colombian adults. *BMJ Open Respir Res* 2020; 7: e000695.
16 Säynäjäkangas P, Keistinen T, Honkanen PO, *et al.* Hospitalization for pneumonia in the Finnish working-age population. *Cent Eur J Public Health* 1997; 5: 27–29.
17 Labarere J, Stone RA, Obrosky DS, *et al.* Factors associated with the hospitalization of low-risk patients with community-acquired pneumonia in a cluster-randomized trial. *J Gen Intern Med* 2006; 21: 745–752.
18 Pelton SI, Shea KM, Farkouh RA, *et al.* Rates of pneumonia among children and adults with chronic medical conditions in Germany. *BMC Infect Dis* 2015; 15: 470.
19 Juvonen R, Bloigu A, Peitso A, *et al.* Risk factors for acute respiratory tract illness in military conscripts. *Respirology* 2008; 13: 575–580.
20 Theilacker C, Sprenger R, Leverkus F, *et al.* Population-based incidence and mortality of community-acquired pneumonia in Germany. *PLoS One* 2021; 16: e0253118.
21 Nordström T, Miettunen J, Auvinen J, *et al.* Cohort profile: 46 years of follow-up of the Northern Finland Birth Cohort 1966 (NFBC1966). *Int J Epidemiol* 2022; 50: 1786–1787j.
22 Miettunen J, Murray GK, Jones PB, *et al.* Longitudinal associations between childhood and adulthood externalizing and internalizing psychopathology and adolescent substance use. *Psychol Med* 2014; 44: 1727–1738.
23 Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. *Scand J Public Health* 2012; 40: 505–515.
24 Junno J-A, Pakanen L, Oura P. Unnatural-cause mortality patterns of Northern Finnish men and women diverge in adolescence – a 52-year follow-up. *Prev Med Rep* 2021; 22: 101337.
25 Vladimirov D, Niemelä S, Auvinen J, *et al.* Changes in alcohol use in relation to sociodemographic factors in early midlife. *Scand J Public Health* 2016; 44: 249–257.
26 Torres A, Cilloniz C, Niederman MS, *et al.* Pneumonia. *Nat Rev Dis Primers* 2021; 7: 25.
27 Cannon JL, Lopman BA, Payne DC, *et al.* Birth cohort studies assessing norovirus infection and immunity in young children: a review. *Clin Infect Dis* 2019; 69: 357–365.
28 Budd AP, Beacham L, Smith CB, *et al.* Birth cohort effects in influenza surveillance data: evidence that first influenza infection affects later influenza-associated illness. *J Infect Dis* 2019; 220: 820–829.
29 Lambert SB, Ware RS, Cook AL, *et al.* Observational Research in Childhood Infectious Diseases (ORChID): a dynamic birth cohort study. *BMJ Open* 2012; 2: 002134.
30 Ferreira-Coimbra J, Sarda C, Rello J. Burden of community-acquired pneumonia and unmet clinical needs. *Adv Ther* 2020; 37: 1302–1318.
31 Centers for Disease Control and Prevention (CDC). Estimates of deaths associated with seasonal influenza – United States, 1976–2007. *MMWR Morb Mortal Wkly Rep* 2010; 59: 1057–1062.
32 Amundson DE, Weiss PJ. Pneumonia in military recruits. *Mil Med* 1994; 159: 629–631.
33 Banerjee A, Kalghatgi AT, Saiprasad GS, *et al.* Outbreak of pneumococcal pneumonia among military recruits. *Med J Armed Forces India* 2005; 61: 16–21.
34 Radin J, Hansen C, Hawksworth A, *et al.* Etiology of pneumonia in United States military recruits. *Open Forum Infect Dis* 2015; 5: 1590.

35 Barbagelata E, Cillóniz C, Dominedò C, *et al.* Gender differences in community-acquired pneumonia. *Minerva Med* 2020; 111: 153–165.
36 Almirall J, Serra-Prat M, Bolíbar I. Risk factors for community-acquired pneumonia in adults: a review. *Clin Pulm Med* 2016; 23: 99–104.