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The effect of community-acquired bacteraemia on return to workforce, risk of sick leave, permanent disability pension and death: a Danish population-based cohort study

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ABSTRACT

Objectives: Little is known about the prognosis of community-acquired bacteraemia (CAB) in workforce adults. We assessed return to workforce, risk for sick leave, disability pension and mortality within 1 year after CAB in workforce adults compared with blood culture-negative controls and population controls.

Design: Population-based cohort study.

Setting: North Denmark, 1996–2011.

Participants: We used population-based healthcare registries to identify all patients aged 20–58 years who had first-time blood cultures obtained within 48 h of medical hospital admission, and who were part of the workforce (450 bacteraemia exposed patients and 6936 culture-negative control patients). For each bacteraemia patient, we included up to 10 matched population controls.

Primary and secondary outcome measures: Return to workforce, risk of sick leave, permanent disability pension and mortality within 1 year after bacteraemia. Regression analyses were used to compute adjusted relative risks (RRs) with 95% CIs.

Results: One year after admission, 78% of patients with CAB, 85.7% of culture-negative controls and 96.8% of population controls were alive and in the workforce, and free from sick leave or disability pension. Compared with culture-negative controls, bacteraemia was associated with an increased risk for long-term sick leave (4-week duration, 40.2% vs 23.9%, adjusted RR, 1.51; CI 1.34 to 1.70) and an increased risk for mortality (30-day mortality, 4% vs 1.4%, adjusted RR, 2.34, CI 1.22 to 4.50; 1-year mortality, 8% vs 3.9%, adjusted RR, 1.73; CI 1.18 to 2.55). Bacteraemia patients had a risk for disability pension similar to culture-negative controls (2.7% vs 2.6%, adjusted RR, 0.99, CI 0.48 to 2.02) but greater than population controls (adjusted RR, 5.20; 95% CI 2.16 to 12.50).

Conclusions: CAB is associated with long duration of sick leave and considerable mortality in working-age adults when compared with blood culture-negative controls, and an increased 1-year risk for disability pension when compared with population controls.

Strengths and limitations of this study

- To our knowledge, this is the first study to examine duration of sick leave and risk for permanent disability pension after community-acquired bacteraemia.
- Strengths include the population-based design and the use of highly valid prospectively collected data on bacteraemia, comorbidity and workforce affiliation.
- When comparing patients with community-acquired bacteraemia and controls, residual and unmeasured confounding may account for some of the increased risk for sick leave, disability pension and death.

INTRODUCTION

Hospitalisation for community-acquired bacteraemia (CAB) has increased markedly in recent decades, and more than 30% of hospitalisations for CAB are in working-age adults.[1]

Overall, CAB is associated with a 30-day mortality of 13–20% and a 1-year mortality of 25–45%,[2–6] with a lower mortality in working-age adults, for example, a 30-day mortality of 11–16% in 15–64-year-old patients.[4–7] Apart from mortality, information is sparse on outcomes of bacteraemia in working-age adults. Only a few small cohort studies in hospitalised patients with infection have secondarily detailed the proportion of patients who returned to work, with conflicting results: 68% of patients with pneumonia may return to work within 30 days,[8] 43% of survivors of septic shock within 1 year[9] and 93% of survivors of severe sepsis within 3.5 years.[10] None of these studies focused specifically on working-age patients, assessed risk for long-term sick leave or disability pension, accounted for retirement or

included a comparison group. To our knowledge, no study has examined the prognosis after CAB in working-age adults who are part of the workforce and no study has examined return to work after CAB. Because CAB is increasingly common in working-age adults, it is important for patients, families and the society to have detailed knowledge on the prognosis in this age group.

We conducted a 15-year population-based cohort study among 20–58-year-old Danes who were part of the workforce, to examine return to work and risk for sick leave, permanent disability pension and mortality after medical hospitalisation with CAB in comparison with blood culture-negative controls and matched population controls.

MATERIALS AND METHODS

Setting

The study was conducted in healthcare region of North Denmark from 1996 to 2011. This area had a stable urban/rural catchment population of approximately 500 000 inhabitants who received universal tax-financed primary and secondary care, free at the point of delivery. Throughout the study period, Aalborg University Hospital was the only referral hospital and all regional hospitals relied on its department of clinical microbiology for blood culture analyses.

For this study, we used prospectively collected data from seven Danish population-based registries. The Civil Registration System (CRS),[11] which is updated daily, was used for personal data, including date of birth and death, place of residence and marital status. Unique CRS numbers, which are recorded for all healthcare contacts, and in administrative databases, facilitated linkage between registries. We further used data from the North Denmark Bacteraemia Research Database,[12] the regional microbiology information system (ADBact; Autonik, Sköldinge, Sweden),[4] the DREAM register on social transfer payments,[13] the Aarhus University Prescription database[14] and the regional Hospital Discharge Registry (HDR).[15] Because data were acquired from registries which are generally available to Danish researchers, no informed consent was needed for this study.

Data on blood cultures

The bacteraemia database has registered all bacteraemia cases in the study area since 1981, prospectively since 1992.[12] The microbiology information system has been used since 1995 and contains basic information on all blood cultures examined in the region.[4] We used these databases for information on date of blood culture sampling, and also for information on infectious agent(s) and focus of infection in case of positive cultures. Throughout the study period, the blood culture system (BacT/Alert, bioMérieux, Marcy l'Etoil, France) was unchanged and is described in detail elsewhere.[4 12]

Data on social transfers

The DREAM database contains weekly information on social transfer benefits for all residents in Denmark who have received any such benefit, however, briefly, since 1991.[13 16] In Denmark, people who are part of the workforce (employed or unemployed) can receive sickness absence benefits (paid sick leave) during temporary illness. Paid sick leave is possible for a maximum of 52 weeks (with the possibility for extension) within an 18-month period. People whose illness causes a lasting reduced ability to work can receive permanent disability pension. During the study period, people who were in the workforce could go on early voluntary retirement when they turned 60 and optional retirement with public pension was possible from age 67 (1996–1999) or age 65 (2000–2011). For the present study, DREAM codes were categorised as work-ready codes (employed and unemployed), sick leave codes and permanent disability pension codes. DREAM codes are further detailed in online supplementary table S1. There is no universal definition of long-term sick leave; for this study and elsewhere, it is defined as a disease lasting at least four consecutive weeks.[17]

Data on hospital admissions and comorbidity

We used the HDR for data on hospital admissions and comorbidity. The HDR has recorded complete diagnosis codes from all inpatient hospitalisations in Denmark since 1977, and from outpatient clinic contacts since 1995. Diagnoses were coded by physicians according to the WHO's International Classification of Diseases (ICD)-8 until 1993 and ICD-10 thereafter).

We recorded the 19 disease categories in the Charlson Comorbidity Index (CCI) and alcohol-related disorders which we considered to be risk factors for death, sick leave and disability pension.[18 19] The comorbidity level was categorised as low (CCI=0), medium (CCI=1–2) or high (CCI>2).

The Aarhus University Prescription database was used for information on preadmission medication use including disulfiram, antidiabetics, drugs for cardiovascular and pulmonary disease and systemic antibiotics.[14] It contains Anatomical Therapeutic Chemical (ATC) classification code data on all reimbursed prescriptions since 1991. ICD and ATC codes used in this study are detailed in online supplementary table S2.

Study subjects

We included study participants who were 20–58 years of age and were part of the workforce in the 4 weeks prior to admission, that is, did not receive permanent disability benefits, were not retired or on long-term sick leave (ie, received sickness absence benefits for a maximum of 3 weeks within 4 weeks prior to admission). Further eligibility criteria were no record of recent hospitalisation (previous 30 days), no previous blood culture draw (since 1995) or bacteraemia (since 1981) and residence within the study area for ≥1 year.

We identified all inpatients who had a first-time blood culture taken within 48 h of admission during 1996–2010. We defined CAB as the presence of viable bacteria or fungi in the bloodstream, determined by blood cultures performed within 48 h of admission, among patients who were not admitted to the hospital within the previous 30 days. Study participants were categorised as patients with CAB or as blood culture-negative controls. Furthermore, for each patient with CAB, we sampled 10 eligible population controls, who were alive on the date of hospital admission of the patient with CAB and with no recent hospitalisation, matched on sex and year of birth.

Statistics

We followed all study participants from the date of blood culture draw until death, emigration from Denmark or completion of 1 year of follow-up, whichever occurred first. We first computed the median number and IQR of weeks that patients were on paid sick leave during the year before and after blood culture draw. We then computed the risk of being on sick leave (receiving sickness absence benefits) for at least 4 and for 52 consecutive weeks, respectively, beginning in the week of blood culture draw. Log-binomial regression[20 21] was used to compute the risk difference (RD) and relative risk (RR) with 95% CI of 4-week and 52-week sick leave for patients with CAB versus culture-negative controls. In time-to-event analyses, we first constructed cumulative incidence curves for permanent disability pension and Kaplan-Meier curves for mortality. We used regression analyses based on pseudo-observations[22] to compute RDs and RRs of permanent disability pension and mortality with 95% CIs for patients with CAB versus culture-negative controls and population controls. We considered death as a competing risk for permanent disability pension in all time-to-event analyses. In regression analyses, we adjusted for potential risk factors for sick leave, disability pension and death: age, gender, CCI score, alcoholism-related disease (including disulfiram use), medication use (antidiabetics, drugs for cardiovascular disease and pulmonary disease), civil status and immigrant status.[3 18 19 23–25] Because of few events among population controls, analyses concerning patients with CAB versus population controls were only adjusted for age and gender. In subgroup analyses, we examined the risk for long-term sick leave, disability pension and mortality according to etiological infectious agent and focus of infection. We also stratified analyses by gender, age group and employment status in the 4 weeks prior to admission. Because the management of CAB may have changed throughout the study period, we conducted up-to-date supplementary analyses pertaining to the latter half of the study period (2003–2011). Because previous antibiotic use could bias the risk estimates in our study when comparing patients with CAB and culture-negative controls, we conducted supplementary analyses in which we restricted to patients who had blood culture draw performed on admission and no recent out-of-hospital antibiotic use.

Stata V.11.2 for Windows (Stata Corp, College Station, Texas, USA) was used for all data analyses.

RESULTS

Baseline characteristics

We included 7386 acutely hospitalised patients who were part of the workforce immediately before hospitalisation and had a first-time blood culture drawn within 48 h of admission, 450 patients with CAB and 6936 controls with negative blood cultures. Patients with CAB were matched to 4500 population controls, of whom 3765 were included in the study (see flow diagram in the online supplement). Baseline characteristics for study participants can be found in table 1. Patients with CAB were older than culture-negative controls (median age in years 47.7 vs 41.4, p<0.001) but the burden of pre-existing disease was similar and relatively low in both groups. Still, the disease burden was even lower among population controls. In the year before blood culture draw, study participants were on sick leave for a median of 0 weeks (IQR 0–1 week for patients with CAB and culture-negative controls, and 0–0 for population controls).

Return to work, duration of sickness leave and disability pension

Exactly 1 year after blood culture draw 350 patients with CAB (78.0%), 5944 culture-negative controls (85.7%) and 3644 population controls (96.8%) were alive and part of the workforce, and thus free from sick leave and disability pension (figure 1). In the year after blood culture draw, 50% of patients with CAB were on sick leave for at least 4 weeks (median 4, IQR 0–14 weeks) and 50% of culture-negative controls were on sick leave for 0 weeks (median 0, IQR 0–7 weeks). When compared with blood culture-negative controls, CAB was associated with an increased risk of sick leave for ≥4 consecutive weeks (40.2% vs 23.9%, adjusted RR, 1.51; 95% CI 1.34 to 1.70) and ≥52 weeks (5.8% vs 2.6%, adjusted RR, 1.96; 95% CI 1.31 to 2.93; table 2). However, the 1-year risk for disability pension was similar in the two groups, 2.7% for patients with CAB and 2.6% for culture-negative controls (adjusted RR, 0.99; 95% CI 0.48 to 2.02), see table 2 and figure 2. When compared with population controls, CAB was associated with an increased risk for 1-year disability pension (2.7% vs 0.6%, adjusted RR, 5.20; 95% CI 2.16 to 12.50).

Mortality

Mortality rose sharply to 4% for patients with CAB within the first 30 days (see online supplementary figure S2), 1.4% for culture-negative controls (adjusted RR, 1.87; 95% CI 1.03 to 3.40; table 2) and 0 for population controls. Within 1 year the mortality was 8.0% for patients with CAB, 3.9% for culture-negative controls (adjusted

Table 1 Descriptive characteristics of workforce community-acquired bacteraemia patients and blood culture-negative controls, North Denmark, 1996–2010

	Patients with CAB (n=450)	Blood culture-negative patients (n=6936)	Population controls (n=3765)
Age, years			
20–34	85 (18.9)	2338 (33.7)	767 (20.4)
35–49	178 (39.6)	2676 (38.6)	1554 (41.3)
50–58	187 (41.6)	2693 (27.7)	1444 (38.3)
Gender			
Female	224 (49.8)	3100 (44.7)	1851 (49.2)
Male	226 (50.2)	3836 (55.3)	1914 (50.8)
Marital status			
Married	261 (58.0)	3592 (51.8)	2311 (61.4)
Never married or unknown*	129 (28.7)	2521 (36.3)	982 (26.1)
Divorced or widowed	60 (13.3)	823 (11.9)	472 (12.5)
Immigrant status			
Native Dane†	429 (95.3)	6520 (94.0)	3536 (93.9)
Immigrant	21 (4.7)	416 (6.0)	229 (6.1)
Comorbidity, any previous‡			
Myocardial infarction	4 (0.9)	76 (1.1)	19 (0.5)
Congestive heart failure	1 (0.2)	22 (0.3)	3 (0.1)
Peripheral vascular disease	5 (1.1)	55 (0.8)	18 (0.5)
Cerebrovascular disease	8 (1.8)	85 (1.2)	29 (0.8)
Hemiplegia	0 (0)	6 (0.1)	2 (0.1)
Chronic pulmonary disease	24 (5.3)	523 (7.5)	102 (2.7)
Diabetes mellitus	26 (5.8)	276 (4.0)	36 (1.0)
Diabetes with end-organ damage	10 (2.2)	133 (1.9)	7 (0.2)
Connective tissue disease	9 (2.0)	118 (1.7)	29 (0.8)
Moderate to severe renal disease	3 (0.7)	93 (1.3)	15 (0.4)
Peptic ulcer disease	8 (1.8)	122 (1.8)	48 (1.3)
Mild liver disease	6 (1.3)	80 (1.2)	10 (0.3)
Moderate to severe liver disease	4 (0.9)	17 (0.3)	3 (0.1)
Any tumour	15 (3.3)	193 (2.8)	65 (1.7)
Leukaemia	1 (0.2)	25 (0.4)	3 (0.1)
Lymphoma	0 (0)	24 (0.4)	1 (0.0)
Metastatic solid tumour	2 (0.4)	19 (0.3)	6 (0.2)
Dementia	0 (0)	1 (0.0)	0 (0)
HIV/AIDS	3 (0.7)	11 (0.2)	1 (0.0)
Alcoholism-related disease	33 (7.3)	428 (6.2)	95 (2.5)
Medication use, any previous			
Drugs for cardiovascular disease	120 (26.7)	1741 (25.1)	579 (15.4)
Inhalers for pulmonary disease	119 (26.4)	2104 (30.3)	1159 (30.8)
Antidiabetics	35 (7.8)	375 (5.4)	51 (1.4)
Disulfiram	19 (4.2)	202 (2.9)	25 (0.7)
Antibiotics (past 4 weeks)	74 (16.4)	2031 (29.3)	83 (2.2)
Charlson Comorbidity Index‡			
0	357 (79.3)	5468 (78.8)	3414 (90.7)
1–2	87 (19.3)	1403 (20.2)	347 (9.2)
>2	6 (1.3)	65 (0.9)	4 (0.1)
Employment status			
Employed, past 4 weeks§	281 (62.4)	4624 (66.7)	3166 (84.1)
Unemployed, past 4 weeks¶	107 (23.8)	1384 (20.0)	538 (13.8)
Sick leave, past 4 weeks**	62 (13.8)	928 (13.4)	61 (1.6)
1 week	43 (9.6)	605 (8.7)	35 (0.9)
2 weeks	11 (2.4)	231 (3.3)	17 (0.5)
3 weeks	8 (1.8)	92 (1.3)	9 (0.2)

*Unknown for 0.7%.
†Includes 0.18% children of first-generation immigrants.
‡Based on ICD-codes that are detailed in the online supplement.
§Participants who were registered as employed and actively working during all 4 weeks before admission.
¶Participants who spent all 4 weeks as unemployed and participants who were employed/unemployed.
**Participants who were on sick leave for a maximum of 3 weeks in the previous 4 weeks, and otherwise employed or unemployed.
CAB, community-acquired bacteraemia; ICD, International Classification of Diseases.

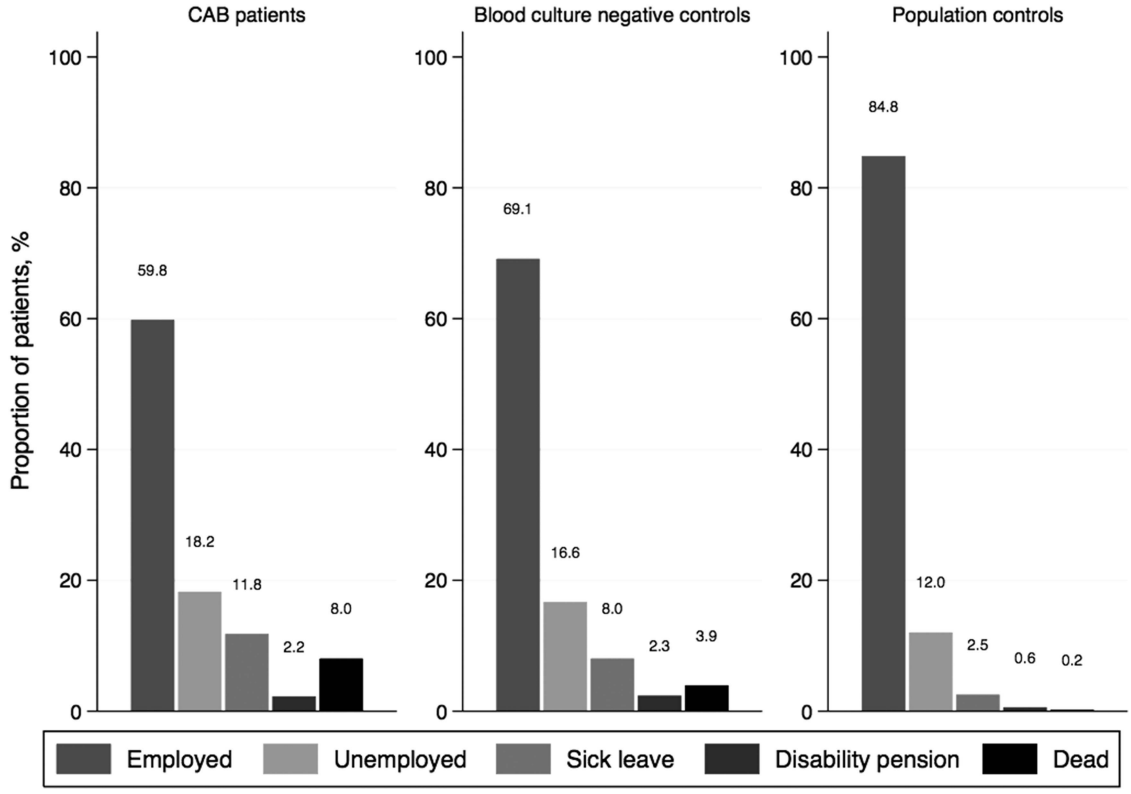

Figure 1 Employment status and mortality at 1 year after blood culture draw. Note, the cumulative incidence of sick leave and disability pension within 1 year is higher than the proportion of patients that received either benefit at 1 year after blood culture draw (eg, some patients went on sick leave or became disability pensioners and later died during 1 year of follow-up).

RR, 1.52; 95% CI 1.10 to 2.10; table 2) and 0.2% for population controls (adjusted RR, 37.83; 95% CI 15.67 to 91.29).

Subgroup and stratified analyses

Subgroups of patients with pneumococcal or other Gram-positive infection had a higher risk for 4-week sick leave, 52-week sick leave and 1-year disability pension after CAB than patients with *Escherichia coli* infection or other Gram-negative infection (table 3). Of note, pneumococcal infection was associated with the lowest level of comorbidity (85% with CCI score of 0), the lowest 30-day (1.7%) and 1-year mortality (4.5%) and the highest 1-year risk for permanent disability pension

Table 2 Sick leave, disability pension and mortality among patients with CAB (N=450) and blood culture-negative controls (N=6936)

		Risk number of events (% of N)		Risk difference, % (95% CI)		Relative risk (95% CI)	
		patients with CAB	Controls	Crude	Adjusted	Crude	Adjusted
Sick leave*	≥4 weeks	181 (40.2)	1658 (23.9)	16.3 (11.7 to 21.0)	14.1 (9.5 to 18.7)	1.68 (1.49 to 1.90)	1.51 (1.34 to 1.70)
	≥52 weeks	26 (5.8)	181 (2.6)	3.2 (1.0 to 5.4)	3.0 (0.8 to 5.2)	2.21 (1.48 to 3.30)	1.96 (1.31 to 2.93)
Disability pension	1 year	12 (2.7)	183 (2.6)	0.0 (−1.5 to 1.6)	−0.5 (−2.1 to 1.0)	1.01 (0.57 to 1.80)	0.99 (0.48 to 2.02)
Mortality	30 days	18 (4.0)	99 (1.4)	2.6 (0.7 to 4.4)	2.2 (0.4 to 4.0)	2.80 (1.71 to 4.59)	2.34 (1.22 to 4.50)
	1 year	36 (8.0)	271 (3.9)	4.1 (1.5 to 6.6)	3.1 (0.6 to 5.6)	2.05 (1.47 to 2.86)	1.73 (1.18 to 2.55)

*Sick leave for ≥4 and ≥52 consecutive weeks after blood culture draw.
Relative risk and risk difference computed by log-binomial regression (sick leave analyses) and regression analyses based on pseudo-observations (disability pension and mortality analyses). Estimates are adjusted for age, gender, Charlson comorbidity score, alcoholism-related disease, medication use, marital and immigrant status. Because of few events, 30-day mortality estimates were not adjusted for medication use, marital and immigrant status. Because of failure to converge, risk difference estimates for sick leave were not adjusted for immigrant status.
CAB, community-acquired bacteraemia.

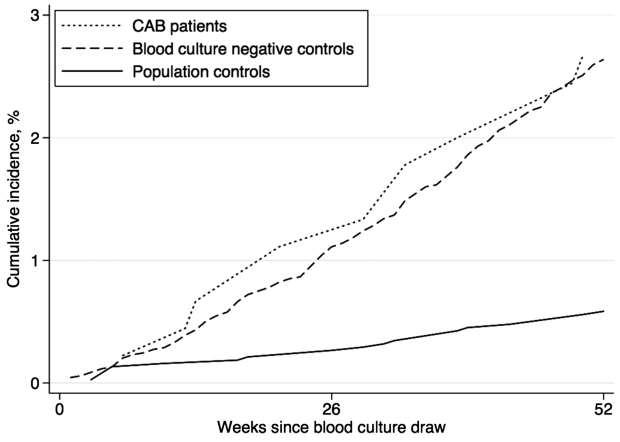

Figure 2 Cumulative incidence of permanent disability pension in workforce patients with community-acquired bacteraemia (CAB), blood culture-negative controls, and population controls in North Denmark, 1996–2011.

(3.4%; table 3). Patients with *Staphylococcus aureus* bacteraemia and polymicrobial bacteraemia had the highest levels of comorbidity (71% with CCI score of 0 in both groups) and also had the highest 30-day mortality (*S aureus*, 3/31, 9.7% and polymicrobial CAB, 3/14, 21.4%) and 1-year mortality (*S aureus*, 5/31, 16.1% and polymicrobial CAB, 4/14, 28.6%). In these small subgroups with high mortality, a high proportion of patients were on sick leave for a long time after infection (eg, 6/31, 19.4% of patients with *S aureus* infection were on sick leave for 52 consecutive weeks) but the 1-year risk for disability pension was 0. Irrespective of type of focus, CAB was associated with an increased risk for long-term sick leave when compared with culture-negative controls (eg, 40.2% of patients with CAB with respiratory tract infection were on sick leave for at least 4 weeks, adjusted RR, 1.51; 95% CI 1.26 to 1.83). Mortality was particularly high among patients with an unknown focus or more than one focus of infection (30-day mortality of 14.3%), see online supplementary table S3.

When stratifying analyses according to age group and employment status, older age and unemployment were associated with the highest absolute risks for disability pension and mortality (see online supplementary table S4). When comparing patients with CAB to blood culture-negative controls in stratified analyses, CAB was consistently associated with an increased risk for 4-week sick leave, 52-week sick leave and for 30-day and 1-year mortality, table 4 in supplementary S4.

During 2003 to 2011, the association between CAB and study outcomes remained essentially unchanged when compared with culture-negative controls (4-week sick leave 37.7% vs 23.6%, adjusted RR, 1.40; 95% CI 1.18 to 1.66; 1-year disability pension 3.4% vs 2.4%, adjusted RR, 1.58; 95% CI 0.54 to 4.59; 30-day mortality 3.0% vs 1.1%, adjusted RR, 2.09; 95% CI 0.76 to 5.70 and 1-year mortality 7.6% vs 3.3%, adjusted RR, 2.14; 95% CI 1.29 to 3.52).

Analyses restricted to 352 patients with CAB and 4078 culture-negative controls who had no previous antibiotic therapy (blood culture draw performed on admission and no recent out-of-hospital antibiotic use) did not materially influence the association between CAB and 4-week sick leave (adjusted RR, 1.71; 95% CI 1.48 to 1.97), 1-year disability pension (adjusted RR, 1.00; 95% CI 0.06 to 16.82), 30-day mortality (adjusted RR, 1.73; 95% CI 0.68 to 4.41) or 1-year mortality (adjusted RR, 1.70; 95% CI 1.02 to 2.84).

DISCUSSION

In this large population-based cohort study of adults in the Danish workforce, we found that CAB was associated with a 40% risk for sick leave of at least 4 weeks duration and a nearly 6% risk for 52 weeks of sick leave. Compared with blood culture-negative controls, CAB increased the risk for long-term sick leave by 50–100% but the risk for permanent disability pension within 1 year was similar (~2.7%). Compared with population controls, CAB was associated with a fivefold increased risk for disability pension. While CAB more than doubled the 30-day risk for death and remained associated with a 70% increased risk for death within 1 year when compared with culture-negative controls, the absolute mortality was low after CAB in this study (4% within 30 days and 8% within 1 year). One year after the blood culture draw, nearly 80% of patients with CAB were back in the workforce.

We are not aware of any study that has examined duration of sick leave and risk for permanent disability pension after CAB. Very few previous studies have examined return to work after severe bacterial infection, and in most of these studies this outcome has been a secondary focus and examined in small subgroups of included patients. Poulsen *et al*[9] conducted a study of 172 Danish intensive care unit (ICU) patients with septic shock, and examined physical outcomes in a subgroup of 70 of 80 1-year survivors. At 1-year follow-up, 43% (10/23) of previously employed patients had returned to work, which is considerably fewer than the approximately 80% of patients with CAB who were in the workforce after 1 year in our study. The discrepancy may relate to ICU patients with septic shock being more critically ill than average patients with CAB and it may be related to older study participants in the ICU-based study who may have had the possibility of public retirement pension during the follow-up. In a study from Scotland, Cuthbertson *et al*[10] followed 439 ICU patients with sepsis and asked employment-related questions to survivors at 3.5 and 5 years. At 3.5 years, 93% (53/62 respondents) of previously employed patients had returned to work, and at 5 years the proportion was 75% (46/58 respondents) with some reduction in employment due to retirement.

Return to work after community-acquired pneumonia has been described by Fine *et al*[8] who followed 2287 patients for 30 days, including 539 previously employed

Table 3 Risk for sick leave, permanent disability pension and mortality in CAB by aetiological agent compared with blood culture-negative controls

	Streptococcus pneumoniae (N=177)	Other Gram-positive (N=78)	*Escherichia coli* (N=103)	Other Gram-negative (N=78)	Polymicrobial (N=14)
Sick leave, ≥4 weeks					
Risk, n (% of N)	75 (42.4)	44 (56.4)	30 (29.1)	30 (38.5)	2 (14.3)
Adj. RD % (95% CI)*	15.3 (8.0 to 22.6)	30.1 (19.2 to 41.1)	3.5 (−5.2 to 12.2)	12.8 (2.1 to 23.5)	−6.4 (−24.3 to 11.5)
Adj. RR (95% CI)*	1.57 (1.32 to 1.87)	2.03 (1.66 to 2.49)	1.14 (0.84 to 1.54)	1.46 (1.10 to 1.93)	0.55 (0.15 to 2.03)
Sick leave, ≥52 weeks					
Risk, n (% of N)	9 (5.1)	11 (14.1)	2 (1.9)	3 (3.8)	1 (7.1)
Adj. RD % (95% CI)*	1.9 (−1.3 to 5.0)	11.5 (3.7 to 19.3)	−1.2 (−1.8 to −0.1)	1.3 (−3.0 to 5.6)	5.9 (−8.7 to 20.4)
Adj. RR (95% CI)*	1.73 (0.90 to 3.33)	4.65 (2.62 to 8.24)	0.64 (0.16 to 2.56)	1.33 (0.44 to 4.07)	2.49 (0.36 to 17.29)
Disability pension, 1 year					
Risk, n (% of N)	6 (3.4)	2 (2.6)	2 (1.9)	2 (2.6)	0 (0)
Adj. RD % (95% CI)*	0.5 (−2.2 to 3.1)	−0.8 (−4.3 to 2.6)	−1.7 (4.5 to 1.0)	−0.5 (−3.9 to 2.9)	−3.1 (−4.7 to −1.5)
Adj. RR (95% CI)*	1.63 (0.66 to 4.05)	0.79 (0.18 to 3.54)	0.35 (0.07 to 4.75)	1.19 (0.30 to 4.75)	–
Mortality, 30 days					
Risk, n (% of N)	3 (1.7)	5 (6.4)	5 (4.9)	2 (2.6)	3 (21.4)
Adj. RD % (95% CI)*	−0.1 (−2.1 to 1.8)	4.6 (−0.8 to 10.0)	3.0 (−1.2 to 7.2)	0.8 (−2.6 to 4.3)	20.0 (−1.5 to 41.5)
Adj. RR (95% CI)*	1.05 (0.30 to 3.67)	3.82 (1.49 to 9.81)	1.90 (0.55 to 6.61)	1.81 (0.45 to 7.34)	13.97 (3.26 to 59.86)
Mortality, 1 year					
Risk, n (% of N)	8 (4.5)	12 (15.4)	9 (8.7)	3 (3.8)	4 (28.6)
Adj. RD % (95% CI)*	−0.1 (−3.2 to 3.0)	10.1 (2.4 to 17.8)	3.6 (−1.6 to 8.7)	−0.8 (−5.0 to 3.5)	23.8 (−0.4 to 48.0)
Adj. RR (95% CI)*	0.81 (0.36 to 1.81)	3.46 (2.22 to 5.38)	1.97 (1.04 to 3.73)	0.67 (0.19 to 2.35)	3.55 (0.78 to 16.10)

*Risk difference and relative risk pertaining to patients with CAB versus blood culture-negative controls (absolute risk estimates for controls can be found in table 2). Risk difference and relative risk computed by log-binomial regression (sick leave analyses) and regression analyses based on pseudo-observations (disability pension and mortality analyses). Estimates are Adj for age, gender, Charlson comorbidity score and alcoholism-related disease (due to few events, 30-day mortality estimates are Adj for age and gender only).
Adj, adjusted; CAB, community-acquired bacteraemia.

outpatients and 218 previously employed inpatients. Among less sick outpatients, nearly all (95.3%) of the previously employed had returned to work at day 30. In contrast, 68.1% of previously employed inpatients had returned to work at day 30 and the median time to return to work was 22 days, which is comparable with our findings of a median of 4 weeks on sick leave after CAB.

This is also the first study to examine the mortality after CAB in relatively healthy adults who belong to the workforce immediately before onset of CAB. Some previous cohort studies have examined mortality after CAB according to age group. Søgaard *et al*[3] found a 30-day mortality of 11% in 15–64-year-old patients with CAB, and Leibovici *et al*[5] found a 1-year mortality of 29% after bacteraemia in patients with 18–60 years of age. In a Danish population-based cohort study of 8653 bacteraemia patients aged 30–65 years, Koch *et al*[7] examined mortality according to socioeconomic status and found the highest 30-day mortality (19.7%) in the subgroup with most disability pensioners (the lowest income group). As we excluded nearly 30% of 20–58-year-old patients with CAB because of disability pension or sick leave, the higher short-term and long-term mortality described in previous studies is likely due to the inclusion of multimorbid patients outside the workforce. Our study supports previous studies that have examined the economic costs of sepsis and bacteraemia and found that the indirect costs (productivity loss due to mortality, temporary and permanent morbidity) may outweigh the direct costs (eg, medical expenses associated with hospitalisation) by as much as twofold, and that these severe infections place a high economic burden on individuals, families and the society.[26 27]

Physical and psychological stress is put on hospitalised patients with CAB, and may endure beyond the duration of hospitalisation. In surviving working-age patients, this may lead to prolonged sick leave or permanent disability. During hospitalisation, patients with severe infections are at risk for complications, including some that may be long-lasting/permanent (eg, renal impairment and cardiovascular disease).[28 29] Patients with severe infections may occasionally have abnormal vital signs and ongoing inflammatory activity at discharge.[30] After discharge, they remain at high risk for mortality and for other diseases such as cardiovascular events, and may experience worsened cognitive status and quality of life.[29 31–33]

This study has several strengths. It is large, including more than 10 000 study participants, and it has complete and long follow-up of all study participants. Moreover, data were obtained from high-quality databases, in which they were prospectively recorded, which limits recall bias.

However, this study also has limitations. Sick leave of short duration is under-reported to the social services in

Denmark and we may, therefore, underestimate the true duration of sick leave in hospitalised participants, especially the lower quartile values of sick leave (0 weeks in both groups). However, data on sick leave of at least 15 days duration have been found to be highly valid.[34] Another limitation is that Danes in their late 50s who have declining health may wait for voluntary early retirement instead of applying for disability pension.[35] Since patients with CAB were older than controls, this could lead to falsely increased risk estimates for long-term sick leave and falsely decreased risk estimates for disability pension. In analyses of mortality by focus of infection, immortal-time bias may have prompted falsely low risks of death in patients with an identified focus of infection (and a high risk of death in patients with an unknown focus). Moreover, although we adjusted for many potential confounders, residual and unmeasured confounding is a possibility. Finally, findings from the present study may not directly apply to other countries with dissimilar laws and regulations regarding the job market and social benefits.

In conclusion, our study highlights that CAB is a debilitating condition in adults who are part of the workforce. CAB is associated with long duration of sick leave, but in this relatively healthy population, a low risk for permanent disability and death.

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Contributors MD-P, KK, RWT, HCS and HN made substantial contributions to study conception and design, interpreted the data and critically revised the manuscript. MDP, RWT and HCS were responsible for acquisition of data. MDP analysed the data and drafted the manuscript. All authors approved the final version of the manuscript.

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REFERENCES

1. Søgaard M, Nørgaard M, Dethlefsen C, *et al*. Temporal changes in the incidence and 30-day mortality associated with bacteremia in hospitalized patients from 1992 through 2006: a population-based cohort study. *Clin Infect Dis* 2011;52:61–9.
2. Bearman GML, Wenzel RP. Bacteremias: a leading cause of death. *Arch Med Res* 2005;36:646–59.
3. Søgaard M, Schønheyder HC, Riis A, *et al*. Short-term mortality in relation to age and comorbidity in older adults with community-acquired bacteremia: a population-based cohort study. *J Am Geriatr Soc* 2008;56:1593–600.
4. Søgaard M, Nørgaard M, Pedersen L, *et al*. Blood culture status and mortality among patients with suspected community-acquired bacteremia: a population-based cohort study. *BMC Infect Dis* 2011;11:139.
5. Leibovici L, Samra Z, Konigsberger H, *et al*. Long-term survival following bacteremia or fungemia. *JAMA* 1995;274:807–12.
6. Laupland KB, Svenson LW, Gregson DB, *et al*. Long-term mortality associated with community-onset bloodstream infection. *Infection* 2011;39:405–10.
7. Koch K, Nørgaard M, Schønheyder HC, *et al*. Effect of socioeconomic status on mortality after bacteremia in working-age patients. A Danish population-based cohort study. *PLoS ONE* 2013;8:e70082.
8. Fine MJ, Stone RA, Singer DE, *et al*. Processes and outcomes of care for patients with community-acquired pneumonia: results from the Pneumonia Patient Outcomes Research Team (PORT) cohort study. *Arch Intern Med* 1999;159:970–80.
9. Poulsen JB, Møller K, Kehlet H, *et al*. Long-term physical outcome in patients with septic shock. *Acta Anaesthesiol Scand* 2009; 53:724–30.
10. Cuthbertson BH, Elders A, Hall S, *et al*. Mortality and quality of life in the five years after severe sepsis. *Crit Care* 2013;17:R70.
11. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22–5.
12. Schønheyder HC, Søgaard M. Existing data sources for clinical epidemiology: the North Denmark Bacteremia Research Database. *Clin Epidemiol* 2010;2:171–8.
13. Lund T, Labriola M, Christensen KB, *et al*. Physical work environment risk factors for long term sickness absence: prospective findings among a cohort of 5357 employees in Denmark. *BMJ* 2006;332:449–52.
14. Ehrenstein V, Antonsen S, Pedersen L. Existing data sources for clinical epidemiology: Aarhus University Prescription Database. *Clin Epidemiol* 2010;2:273–9.
15. Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health* 2011;39:30–3.
16. Hjollund NH, Larsen FB, Andersen JH. Register-based follow-up of social benefits and other transfer payments: accuracy and degree of completeness in a Danish interdepartmental administrative database compared with a population-based survey. *Scand J Public Health* 2007;35:497–502.
17. National Institute for Health and Clinical Excellence. *Long-term sickness absence and incapacity for work*. 2009. http://www.nice.org.uk/ph19 (accessed 8 Oct 2013).
18. Sidorchuk A, Hemmingsson T, Romelsjö A, *et al*. Alcohol use in adolescence and risk of disability pension: a 39 year follow-up of a population-based conscription survey. *PLoS ONE* 2012;7:e42083.
19. Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
20. Cummings P. Methods for estimating adjusted risk ratios. *Stata J* 2009;9:175–96. http://www.stata-journal.com/article.html?article=st0162 (accessed 19 Aug 2013).
21. Cummings P. Estimating adjusted risk ratios for matched and unmatched data: an update. *Stata J* 2011;11:290–8. http://www.stata-journal.com/article.html?article=st0162_1 (accessed 8 Oct 2013).
22. Parner E, Andersen P. Regression analysis of censored data using pseudo-observations. *Stata J* 2010;10:408–22. http://www.stata-journal.com/article.html?article=st0202 (accessed 11 May 2013).
23. Johansson B, Helgesson M, Lundberg I, *et al*. Work and health among immigrants and native Swedes 1990-2008: a register-based study on hospitalization for common potentially work-related disorders, disability pension and mortality. *BMC Public Health* 2012;12:845.
24. Seymour CW, Iwashyna TJ, Cooke CR, *et al*. Marital status and the epidemiology and outcomes of sepsis. *Chest* 2010;137:1289–96.
25. Beskæftigelsesministeriet [Ministry of Employment]. *Analyse af sygefraværet [Analysis of sickness absence]*. 2008. http://bm.dk/

~/media/BEM/Files/Dokumenter/Publikationer/2008/Sygefravaer.ashx (accessed 8 Oct 2013).
26. Chalupka AN, Talmor D. The economics of sepsis. *Crit Care Clin* 2012;28:57–76, vi.
27. Schmid A, Burchardi H, Clouth J, *et al*. Burden of illness imposed by severe sepsis in Germany. *Eur J Health Econ* 2002;3:77–82.
28. Mackenzie I, Lever A. Management of sepsis. *BMJ* 2007;335:929–32.
29. Corrales-Medina VF, Madjid M, Musher DM. Role of acute infection in triggering acute coronary syndromes. *Lancet Infect Dis* 2010;10:83–92.
30. Yende S, D'Angelo G, Kellum JA, *et al*. Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. *Am J Respir Crit Care Med* 2008;177:1242–7.
31. Leibovici L. Long-term consequences of severe infections. *Clin Microbiol Infect* 2013;19:510–12.
32. Winters BD, Eberlein M, Leung J, *et al*. Long-term mortality and quality of life in sepsis: a systematic review. *Crit Care Med* 2010;38:1276–83.
33. Semmler A, Widmann CN, Okulla T, *et al*. Persistent cognitive impairment, hippocampal atrophy and EEG changes in sepsis survivors. *J Neurol Neurosurg Psychiatry* 2013;84:62–9.
34. Stapelfeldt CM, Jensen C, Andersen NT, *et al*. Validation of sick leave measures: self-reported sick leave and sickness benefit data from a Danish national register compared to multiple workplace-registered sick leave spells in a Danish municipality. *BMC Public Health* 2012;12:661.
35. Dansk Økonomi [Danish Economic Council]. *Efterløn [Early retirement]*. 2005. http://www.dors.dk/sw1147.asp (accessed 8 Oct 2013).

Supplement to:

The effect of community-acquired bacteraemia on return to workforce, risk of sick leave, permanent disability pension and death: A Danish population-based cohort study

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Supplement, Table 1. DREAM codes (version 28) used in the study.

Supplement, Table 2. ICD and ATC codes used in the study.

Supplement, Table 3. Bacteremia patients' risk for sick leave, permanent disability pension, and mortality by focus of infection compared to blood culture negative controls.

Supplement, Table 4. Risk for sick leave, disability pension, and mortality by age, gender, and employment status.

Supplement, Figure 1. Flow chart of hospitalised medical study subjects with first-time blood cultures, North Denmark, 1996-2010.

Supplement, Figure 2. Cumulative mortality in workforce CAB patients, blood culture negative controls, and population controls, North Denmark, 1996-2011.

Supplement, Table 1. DREAM codes (version 28) used in the study.

DREAM category	Subcategory	Transfer payment, examples	DREAM codes
Work-ready	Employed	No transfer payment, leave, apprentice (adult), student support, maternity leave payment	No code if no transfer payment, 121-126, 412-413, 511-522, 611, 651-661, 881
	Unemployed	Unemployment benefit, vocational pre-rehabilitation and rehabilitation benefit	111-113, 130-138, 211-299, 730-738, 750,752-758, 760, 762-768
Sick leave		Sickness absence benefit	890, 892-899
Permanent disability pension		”Flex-job” payment	740-748, 771-774
		Disability pension	781-783

During the study period, Danes who were ≥60 years of age could go on voluntary early retirement pension (“efterløn”), and those who were ≥65 years of age could go on public retirement pension. Since we studied subjects 20-58 years of age, retirement codes are not detailed here. All DREAM codes are detailed elsewhere (http://www.dst.dk/da/TilSalg/Forskningsservice/Data/Andre_Styrelser.aspx)

Supplement, Table 2. ICD and ATC codes used in the study

Comorbidities (previous)	**ICD codes**
Myocardial infarction	ICD-8: 410; ICD-10: I21-I23
Cerebrovascular disease	ICD-8: 430-438; ICD-10: I60-I69, G45, G46
Congestive heart failure	ICD-8: 427.09, 427.10, 427.11, 427.19, 428.99, 782.49, ICD-10: I11.0, I13.0, I13.2, I50
Peripheral vascular disease	ICD-8: 440, 441, 442, 443, 444, 445; ICD-10: I70, I71, I72, I73, I74, I77
Hemiplegia	ICD-8: 344; ICD-10: G81, G82
Diabetes	ICD-8: 249.00, 249.06, 249.07, 249.09, 250.00, 250.06, 250.07, 250.09; ICD-10: E10.0, E10.1, E10.9, E11.0, E11.1, E11.9; ATC: A10A, A10B
Diabetes with end-organ damage	ICD-8: 249.01-249.05, 249.08, 250.01-250.05, 250.08; ICD-10: E10.2-E10.8, E11.2-E11.8
Chronic pulmonary disease	ICD-8: 490-493, 515-518; ICD-10: J40-J47, J60-J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3; ATC: R03
Any tumor	ICD-8: 140-194; ICD-10: C00-C75
Leukemia	ICD-8: 204-207; ICD-10: C91-C95
Lymphoma	ICD-8: 200-203, 275.59; ICD-10: C81-C85, C88, C90, C96
Metastatic solid tumor	ICD-8: 195-199; ICD-10: C76-C80
Connective tissue disease	ICD-8: 712, 716, 734, 446, 135.99; ICD-10: M05, M06, M08, M09, M30-M36, D86
Ulcer disease	ICD-8: 530.91, 530.98, 531-534; ICD-10: K22.1, K25-K28
Moderate to severe renal disease	ICD-8: 403, 404, 580-583, 584, 590.09, 593.19, 753.10-753.19, 792; ICD-10: I12, I13, N00-N05, N07, N11, N14, N17-N19, Q61
Mild liver disease	ICD-8: 571, 573.01, 573.04; ICD-10: B18, K70.0-K70.3, K70.9, K71, K73, K74, K76.0
Moderate to severe liver disease	ICD-8: 070.00, 070.02, 070.04, 070.06, 070.08, 573.00, 456.00-456.09; ICD-10: B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85

Alcoholism-related disease	ICD-8: 291, 303, 979, 980, 577.10; ICD-10: F.10, K29.2, K.86.0, Z72.1, R78.0, T51; ATC: N07BB01
Dementia	ICD-8: 290.09-290.19, 293.09; ICD-10: F00-F03, F05.1, G30
AIDS	ICD-8: 079.83; ICD-10: B21-B24
Medication use	**ATC codes (any previous use unless specified)**
Drugs for cardiovascular disease	
Nitrates	C01DA (if ≥2 prescriptions are registered).
Diuretics	C03
Beta-blockers	C07
Calcium-channel antagonists	C08
ACE inhibitors	C09 (C02 before 1 January 1996)
Aspirin	B01AC06, N02BA01 (previous 125 days)
Antidiabetics	A10A, A10B
Inhaled drugs for pulmonary disease	R03
Disulfiram	N07BB01
Systemic antibiotics	J01 (past 4 weeks)

Supplement, Table 3. Bacteremia patients' risk for sick leave, permanent disability pension, and mortality by focus of infection compared to blood culture negative controls.

	Respiratory tract infection (N=164)	Urinary tract infection (N=93)	Miscellaneous (N=144)	Unknown or multiple (N=49)
Sick leave, ≥4 weeks				
Risk, n (% of N)	66 (40.2)	26 (28.0)	72 (50.0)	17 (34.7)
Adj. RD % (95% CI)[a]	13.6 (6.2-21.2)	2.1 (-7.0-11.2)	24.1 (15.9-32.2)	7.9 (-5.3-21.0)
Adj. RR (95% CI)[a]	1.51 (1.26-1.83)	1.05 (0.76-1.46)	1.87 (1.58-2.21)	1.32 (0.90-1.92)
Sick leave, ≥52 weeks				
Risk, n (% of N)	7 (4.3)	1 (1.1)	16 (11.1)	2 (7.1)
Adj. RD % (95% CI)[a]	1.1 (-1.8-4.1)	-2.0 (-2.4--1.6)	8.3 (3.1-13.4)	1.2 (-4.4-6.7)
Adj. RR (95% CI)[a]	1.73 (0.90-3.33)	4.65 (2.62-8.24)	1.33 (0.44-4.07)	2.49 (0.36-17.29)
Disability pension, 1-year				
Risk, n (% of N)	6 (3.7)	2 (2.2)	2 (1.4)	2 (4.1)
Adj. RD % (95% CI)[a]	0.7 (-2.2-3.5)	-1.2 (-4.2-1.8)	-1.6 (-3.5-3.4)	-0.2 (-5.6-5.2)
Adj. RR (95% CI)[a]	1.40 (0.52-3.77)	0.52 (0.11-2.52)	0.63 (0.15-2.70)	1.18 (0.29-4.85)
Mortality, 30-day				
Risk, n (% of N)	3 (1.8)	0 (0)	8 (5.6)	7 (14.3)
Adj. RD % (95% CI)[a]	0.1 (-2.0-2.2)	-1.9 (-2.3--1.4)	3.8 (0.1-7.5)	12.4 (2.6-22.2)
Adj. RR (95% CI)[a]	0.47 (0.09-2.35)	-	3.39 (1.55-7.42)	10.14 (3.82-26.89)
Mortality, 1-year				
Risk, n (% of N)	8 (4.9)	2 (2.2)	15 (10.4)	11 (22.5)
Adj. RD % (95% CI)[a]	-0.1 (-3.2-3.0)	-2.6 (-5.4-3.2)	5.8 (0.9-10.7)	16.0 (4.6-27.5)
Adj. RR (95% CI)[a]	1.26 (0.65-2.44)	0.68 (0.17-2.83)	2.46 (1.53-3.97)	3.66 (1.76-7.64)

Abbreviations: CAB, community-acquired bacteraemia. Adj., adjusted. [a]Risk difference and relative risk pertains to CAB patients versus blood culture negative controls (absolute risk estimates for controls can be found in main manuscript, Table 2). Risk difference and relative risk computed by log-binomial regression (sick leave analyses) and regression analyses based on pseudo-observations (disability pension and mortality analyses). Estimates are adjusted for age, gender, Charlson comorbidity score, and alcoholism-related disease (due to few events, 30 day mortality estimates are adjusted for age and gender only).

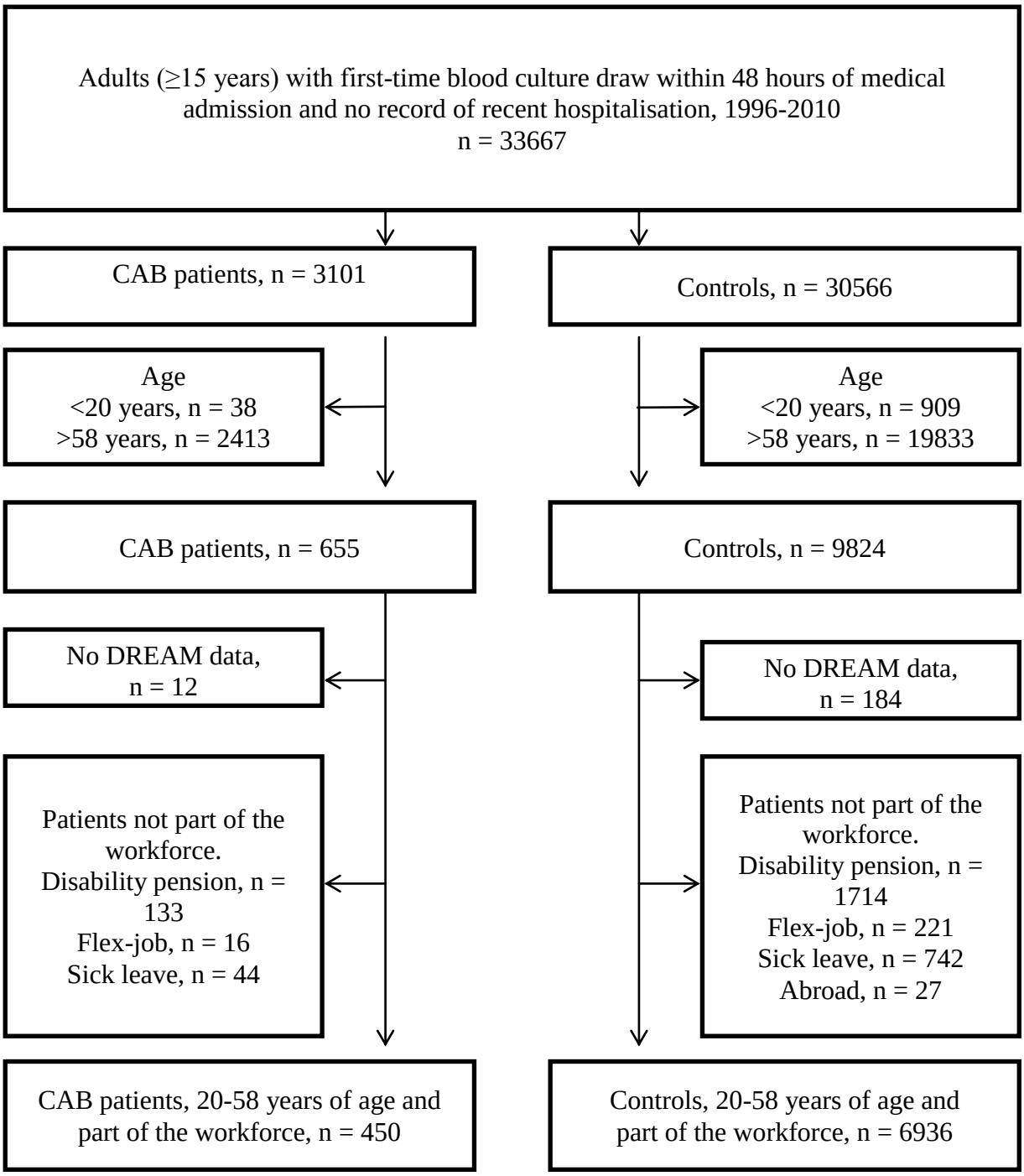
Supplement, Table 4. Risk for sick leave, disability pension, and mortality by age, gender, and employment status for community-acquired bacteraemia patients and blood culture negative controls.

	Age group, years			Gender		Employment status, 4 weeks before blood culture draw		
	20-34	35-49	50-58	Female	Male	Employed[a]	Unemployed[b]	Sick leave[c]
Sick leave ≥4 weeks								
Risk, CAB pts.	28/85 (32.9)	67/178 (37.6)	86/187 (46.0)	79/224 (35.3)	102/226 (45.1)	98/281 (34.9)	28/107 (26.2)	55/62 (88.7)
Risk, Controls	335/2338 (14.3)	721/2676 (26.9)	602/1922 (31.3)	707/3100 (22.8)	951/3836 (24.8)	843/4624 (18.2)	200/1384 (14.5)	615/928 (66.3)
Adj. RR (CI)[d]	2.29 (1.68-3.13)	1.39 (1.14-1.70)	1.47 (1.24-1.74)	1.33 (1.11-1.61)	1.66 (1.42-1.93)	1.71 (1.44-2.03)	1.81 (1.37-2.40)	1.23 (1.12-1.36)
Sick leave ≥52 weeks								
Risk, CAB pts.	6/85 (7.1)	5/178 (2.8)	15/187 (8.0)	11/224 (4.9)	15/226 (6.6)	11/281 (3.9)	6/107 (5.6)	9/62 (14.5)
Risk, Controls	29/2338 (1.2)	80/2676 (3.0)	72/1922 (3.8)	77/3100 (2.5)	104/3836 (2.7)	78/4624 (1.7)	29/1384 (2.1)	74/928 (8.0)
Adj. RR (CI)[d]	5.69 (2.43-3.34)	0.94 (0.38-2.28)	2.16 (1.27-3.70)	1.76 (0.95-3.27)	2.17 (1.28-2.67)	1.97 (1.06-3.68)	2.33 (0.99-5.49)	1.74 (0.91-3.32)
1-year disability pension								
Risk, CAB pts.	0/85 (0)	5/178 (2.8)	7/187 (3.7)	4/224 (1.8)	8/226 (3.5)	6/281 (2.1)	5/107 (4.7)	1/62 (1.6)
Risk, Controls	20/2338 (0.9)	69/2676 (2.6)	94/1922 (4.9)	81/3100 (2.6)	102/3836 (2.7)	69/4624 (1.5)	102/1384 (7.4)	12/928 (1.3)
Adj. RR (CI)[d]	-	0.85 (0.22-3.34)	0.97 (0.42-2.23)	0.44 (0.13-1.51)	1.45 (0.65-3.21)	1.52 (0.52-4.35)	0.54 (0.17-1.74)	1.25[e] (0.16-9.45)
30-day mortality								
Risk, CAB pts.	1/85 (1.2)	7/178 (3.9)	10/187 (5.4)	8/224 (3.6)	10/226 (4.4)	10/281 (3.6)	7/107 (6.5)	1/62 (1.6)
Risk, Controls	9/2338	36/2676	54/1922	44/3100	55/3836	55/4624	30/1384	14/928

	(0.4)	(1.4)	(2.8)	(1.4)	(1.4)	(1.2)	(2.2)	(1.5)
Adj. RR (CI)[d]	3.01[e] (0.39-23.9)	2.36 (0.82-6.81)	1.87 (0.88-4.03)	1.82 (0.61-5.40)	2.53 (1.00-6.43)	1.95 (0.89-4.28)	2.63 (1.09-6.36)	1.07[e] (0.14-8.00)
1-year mortality								
Risk, CAB pts.	2/85 (2.4)	11/178 (6.2)	23/187 (12.3)	16/224 (7.1)	20/226 (8.8)	19/281 (6.8)	12/107 (11.2)	5/62 (8.1)
Risk, Controls	25/2338 (1.1)	100/2676 (3.7)	146/1922 (7.6)	99/3100 (3.2)	172/3836 (4.5)	139/4624 (3.0)	76/1384 (5.5)	56/928 (6.0)
Adj. RR (CI)[d]	2.19[e] (0.53-9.1)	1.66 (0.86-3.20)	1.59 (1.03-2.46)	1.52 (0.93-2.49)	1.73 (0.99-3.02)	1.81 (1.06-3.08)	1.59 (0.86-2.93)	1.12 (0.42-3.00)

Abbreviations: Adj., adjusted. RR, relative risk. CI, confidence interval. [a]Subjects who were registered as employed and actively working during all 4 weeks before admission. [b]Subjects who spent all 4 weeks as unemployed (84.7%) and subjects who were employed/unemployed (15.3%). [c]Subjects who were on sick leave for a maximum of 3 weeks in the previous 4 weeks, and otherwise employed or unemployed. Absolute risk estimates "Risk" are n/N (%). [d]Relative risk estimates with 95% confidence intervals pertain to CAB patients versus blood culture negative controls, and are adjusted for age, gender, and Charlson comorbidity score. [e]Unadjusted estimates presented due to few events.

Supplement, Figure 1. Flow chart of hospitalised medical study subjects with first-time blood cultures, North Denmark, 1996-2010.



Abbreviations: CAB, community-acquired bacteraemia. Each CAB patient was matched to 10 population controls who had no recent hospital admission (previous 30 days) on year of birth, gender, and calendar-time (population controls had to be alive on the date of blood culture draw). Of these 4500 population controls some were excluded because of previous blood culture draw (n=132), age of 59 years (n=35), no DREAM data (n=99), or for not being part of the workforce in the previous four weeks (disability pension [n=336], long-term sick leave [88], abroad [55]) which left 3765 population controls for analysis.

Supplement, Figure 2. Cumulative mortality in workforce CAB patients, blood culture negative controls, and population controls, North Denmark, 1996-2011.