Hospital variation in the risk of infections after hip fracture surgery: A population-based cohort study

Research year report

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Preface

This report is based on work conducted during my research year at Department of Clinical Epidemiology in 2019 – 2020. It has been a year filled with excitement and frustrations, which both has been necessary to make it a genuine educational year. I appreciate the opportunities I have been given through this year, which can be attributed to several people.

A particular thanks to my three supervisors (or as they describe themselves; the three old ladies). My main supervisor, Alma, who is largely credible to making this year amazing. Thank you for believing in me from the first day. You have guided me with both knowledge and motivation. Especially thank you for always helping me to stay proactive, your drive for always making something happen is truly inspiring. Also, a great thanks to my co-supervisor Pia, who has always answered all my questions with a smile. Thank you for challenging and keeping me reflective through the year. And a big thanks to Irene for always having a good and encouraging advice.

Furthermore, I express great gratitude for all my colleges at the Department of Clinical Epidemiology. You have always addressed both my academic and practical questions. Especially thanks to my fellow research year students. It has been remarkable to share office and everyday life with you.

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Abbreviations

AUC	Area Under receiver operating Curve
ATC	Anatomical Therapeutic chemical Classification system
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CI	Confidence Interval
DCRS	Danish Civil Registry Systems
DMHFR	Danish Multidisciplinary Hip Fracture Registry
DNHSPD	Danish National Service Health Prescription Database
DNPR	Danish National Patient Registry
ICC	Intra Class Coefficient
ICD	International Classification of Diseases
MRR	Median Risk Ratio
MAR	Missing at Random
MCAR	Missing Completely at Random
MNAR	Missing Not at Random
RCT	Randomized Control Trial
ROC	Receiver Operating Curve
UTI	Urinary Tract Infection

Table of content

Abstract

Background

Variation in postoperative infections between Danish hospitals after hip fracture surgery may direct quality-improvement initiatives if this variation accurately reflects hospital differences.

Objective

This study aimed to investigate the variation in the risk of infection after hip fracture surgery at Danish hospitals.

Method

This nationwide population-based cohort study used individual level data from Danish registers. All patients aged 65 years or older undergoing surgery for an incident hip fracture from 2012 to 2017 were included from the Danish Multidisciplinary Hip Fracture Registry. Patients were followed 30 days from surgery date. Postoperative infection was defined as any hospital-treated infection registered in the Danish National Patient Register. We also studied community-acquired infections based on antibiotic dispensings recorded in the prescription database. Multilevel Poisson regression analysis accounting for individual patient covariates nested within hospitals were performed. Hospital variation was evaluated by intra class coefficient (ICC), median risk ratio (MRR) and area under receiver operating curve (AUC).

Results

In 29,598 hip fracture patients, the risk of any hospital-treated infections was 15.3%. The risk of community-acquired infections was 23.5%. The adjusted risk varied between hospitals from 7.8% - 24.6% for any hospital-treated infection and 16.4% - 33.6% for community-acquired infection. The general hospital context effect, evaluated as ICC indicated that 18.8% (95% CI: 6.0 – 24.9) of the adjusted variance was due to hospital level for any hospital-treated infection, while the ICC for community-acquired infections were 13.3% (95% CI: 6.0 – 20.5). The hospital variance quantified as MRR showed an increased risk of 1.96 (95% CI: 1.57 - 2.33) for the average patient acquiring any hospital-treated infections at the highest risk hospital compared with the lowest risk hospital for any hospital-treated infection. For community-acquired infection, the MRR was 1.43 (95% CI: 1.25 - 1.56). For hospital-treated infection, the AUC changed 0.048, indicating a 4.8% better prediction for the outcome in a multilevel model compared with a single-level model. For community-acquired infections, the change in AUC were 0.029.

Conclusion

We observed a substantial variation between hospitals in the risk of infections following hip fracture surgery. Individual patient factors were responsible for the most of variation. However, nearly a fifth of the variation was at the hospital level suggesting that more standardized postoperative infection prevention programs are needed.

Dansk resumé

Baggrund
Variation i postoperative infektioner imellem danske hospitaler efter hoftenær fraktur, vil kunne dirigere kvalitetsforbedrende initiativer, hvis denne variation korrekt afspejler hospitals forskel.

Formål
Dette studie havde til formål at undersøge variationen i risiko for infektion efter hoftenær fraktur imellem danske hospitaler.

Metode
Dette nationale populations-baserede kohortestudie brugte individuelle data fra danske registre. Alle patienter på 65 år eller ældre, som blev opereret for en første gangs hoftenær fraktur fra 2012 til 2017 blev inkluderet fra Dansk Tværfaglig Register for Hoftenære Lårbensbrud. Patienterne blev fulgt 30 dage efter operationen. Postoperative infektioner blev defineret som hospitalsbehandlede infektioner registeret i landspatientregisteret. Vi identificerede også samfundsbehandlede infektioner fra data på udskrevet og afhentet antibiotika. Multilevel Poisson regression blev anvendt til at tage højde for individuelle patient variabler grupperet indenfor hospitaler. Hospital variation blev evalueret af intra-klasse-koefficient, median risiko ratio samt arealet under operationskarakterisktika kurven.

Resultater
I 29.598 hoftenær fraktur patienter, var risikoen for hospitalsbehandlet infektioner 15,3%. Risikoen for samfundsbehandlede infektioner var 23,5%. Den justerede risiko varierede fra 7,8% - 24,6% mellem hospitaler for hospitalsbehandlede infektioner. For samfundsbehandlede infektioner den justerede risiko varierede fra 16,4% - 33,5%. Hospitalernes kontekstuelle effekt for hospitalsbehandlede infektioner viste at 18,8% (95% CI: 6.0 - 24.9) af den justerede variation skyldes hospitalsniveau. Mens det for samfundsbehandlede var 13.3% (95% CI: 6.0 - 20.5). Hospitalsvariationen, kvantificeret som median risiko ratio viste en forøget risiko på 1.96 (95% CI: 1.57 - 2.33) for den gennemsnitlige patient for at pådrage sig en samfundsbehandlet infektion på hospitalet med den højeste risiko sammenlignet med hospitalet med den laveste risiko. For samfundsbehandlede infektioner var median risiko ratioen 1.43 (95% CI: 1.25 - 1.56). For hospitalsbehandlede infektioner ændrede arealet under operationskarakterisktika kurven 0.048, betydende en 4.8% bedre prædiktion for infektion i en multilevel model sammenlignet med singlelevel model. For samfundsbehandlede infektioner var dette 2.9%.

Konklusion
Vi fandt en betydelig variation mellem hospitaler i risikoen for infektion efter kirurgi for hoftenær fraktur. Individuelle patientfaktorer bidrog til den største del af variationen. Dog skyldes næsten en femtedel af variationen hospitalsniveau. Hvilket betyder en mangel på en mere standardiseret infektion forebyggelse.

Introduction

Hip fracture is a leading cause of hospital admission among older people[1]. The 30-day mortality following hip fracture surgery has been approximately 10% during the last few years in Denmark[2]. Higher mortality after hip fracture have seen associated with a range of hospital level factors[3–6] and patient level factors in observational studies[7–9]. Furthermore, variation in 30-day mortality after hip fracture surgery has been observed between Danish hospitals, but not fully explained[10,11].

Postoperative infection among hip fracture patients is associated with a three-fold increase in mortality compared with non-infected patients[12]. Additionally, postoperative infections are one of the most serious and challenging complications, adversely affecting quality of life and hospital costs[7,13–17] The increased risk of infections after hip fracture surgery is a consequence of multiple patients-, surgery- and hospital-related factors[18–20]. In the past decade, the 30-day cumulative incidence of postoperative infection after hip fracture has increased substantially in Denmark, reaching 14.3% (95% CI: 13.7–15.0) in 2015-2016[21], suggesting that there is room for quality improvement.

Postoperative infections could be a relevant quality performance measure for ranking hospitals since good treatment, rehabilitation and care of hip fracture patients should reduce postoperative infections. Although the postoperative infection is unmitigated disaster, no previous studies have investigated the hospital variation in postoperative infections among hip fracture patients. Furthermore, hospital variation in postoperative infections has been reported in other surgical areas[22–25], without being able to distinguish the contribution of hospital factors to variation from individual factors. There is a need for a scientifically valid, risk- and multilevel adjusted measure of postoperative infections that accurately reflects quality of care in all hospitals that perform hip fracture surgery. Thus, studying hospital variation in postoperative infection is an important step towards understanding the key drivers of high infection risk in general and implementation of targeted prevention strategy.

This comprehensive population-based nationwide cohort study aimed to investigate the variation between hospitals in the risk of infection within 30 days of hip fracture surgery.

Methods

Setting

The study was based on data from prospectively collected nationwide population-based medical registries in Denmark, which encompassed the entire Danish population (5.8 million inhabitants in 201926). The health care system is tax-supported with free access to care. Denmark is divided into five regions, responsible for hospitals, general practitioners, and private clinic specialists. Furthermore, there are 98 municipalities, which are responsible for home nursing and elder-care[27].

Data sources

We retrieved data from four sources:

The Danish Civil Registration System (DCRS) has assigned all residents in Denmark with a unique ten-digit personal identification number at birth or upon immigration since 1968. This number encodes age, gender, and date of birth. It is recorded at all contacts with the healthcare system. Therefore, an unambiguous record linkage between all medical registers in the population is possible[27]. The DCRS contains electronic records on date of death or immigration for the entire population[28]

The Danish Multidisciplinary Hip Fracture Registry (DMHFR) is a nationwide clinical quality registry on all patients aged ≥ 65 years operated at Danish hospitals with a medial (DS720), pertrochanteric (DS721), or subtrochanteric (DS722) femoral fracture since 2003. About 7,000 patients are registered in DMHFR each year[29,30].

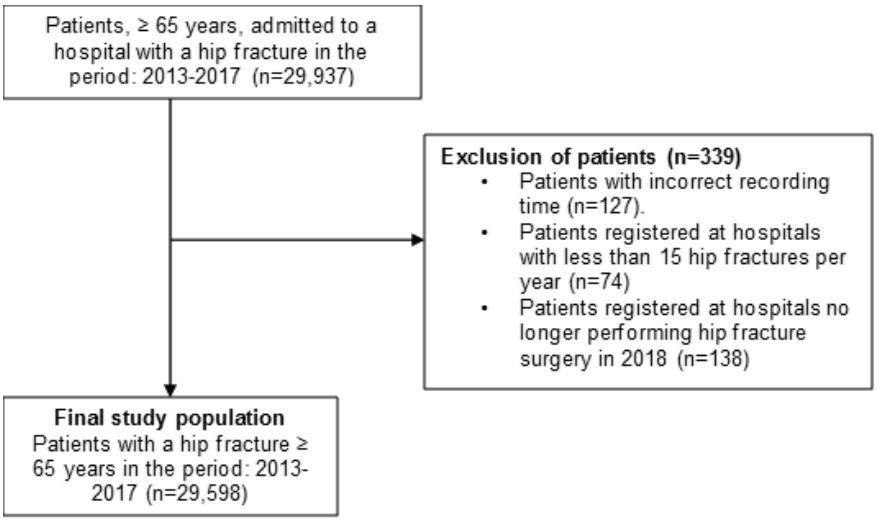
The Danish National Patient Registry (DNPR) has registered all non-psychiatric inpatient hospital admissions since 1977 and all hospital outpatient and emergency room visits since 1995. The DNPR contains records of dates of admission and discharge, discharge diagnoses, and up to 20 secondary discharge diagnosis codes according to the *International Classification of Diseases*, *Eighth revision* (ICD-8) until 1993 and the *Tenth revision* (ICD-10) [27,31]

The Danish National Health Service Prescription Database (DNHSPD) has registered all redeemed prescriptions from pharmacies in Denmark since 2004. The treatments are coded according to the Anatomical Therapeutic Chemical (ATC) classification[32].

Study population

All patients admitted to a hospital with a hip fracture from 1 January 2013 until 1 December 2017 were identified from DMHFR (n=29,937). Patients with surgery time before admission time (n=127) were excluded assuming incorrect recording of time. To avoid imprecise estimates, hospitals who performed less than 15 hip fracture surgeries per year (7 hospitals and 74 patients) or did no longer perform hip fracture surgery (1 hospital and 138 patients) were excluded. The final study cohort included 29,598 patients (Figure 1).

***Figure 1**: Flowchart describing selection of study population*



Infections

Outcomes were any hospital-treated infection and any community-acquired infection within 30 days of surgery. Any hospital-treated infections were identified from the DNPR (i.e. in-patients registered with primary or secondary diagnoses of infection) based on ICD-10 codes. We excluded urinary tract infections (UTI) because high risk of different registration praxis among hospitals due to no economic benefit in the coding for the hospitals. We found a variation in urinary tract infections (UTI) between 10.8% and 38.6% across hospitals. We concluded that this must be due to variation in coding of UTI. Firstly, there is no economic benefit in the coding for the department. Secondly, UTI is a vague diagnose for elderly, with often persistent symptomless bacteriuria, which may cause positive urinary culture without any symptoms[18,33]. Therefore, we expect an underestimation of UVI across hospitals and decided to exclude UTI as a postoperative infection. We further identified two of the most common subtypes of hospital-treated infection: pneumonia and sepsis.

Community-acquired infections were identified from the DNHSPD based on ATC-codes and defined as at least one dispensing of any antibiotic within 30 days of surgery.

A full list of ICD-10 codes and ATC codes used to identify infections and antibiotic is found in supplementary table 1a-1b.

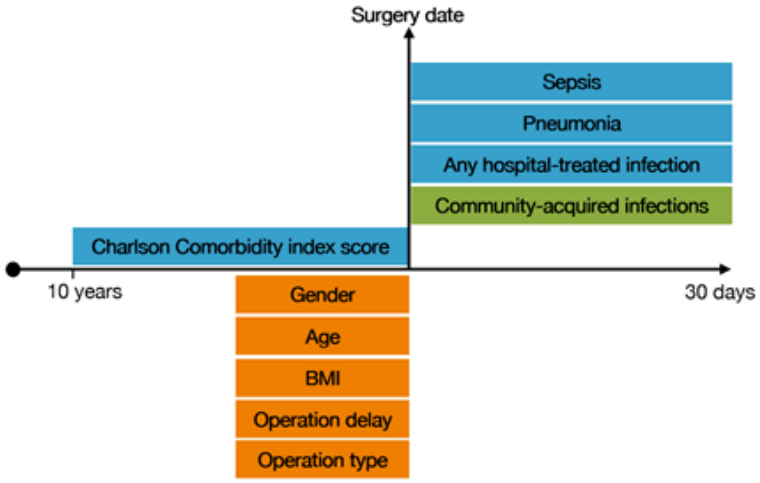
Covariates

To account for hospital case-mix, we collected a number of well-established prognostic factors known to increase infection risk[14,17,34]:

Comorbidity was summarized according to the Charlson Comorbidity Index (CCI)[35]. Diagnoses recorded in the DNPR were included in the CCI 10 years prior to hip fracture surgery[36]. The list of ICD-10 codes used to identify CCI is found in supplementary table 2. CCI was categorized in no comorbidity (CCI =0), low comorbidity (CCI=1-2) and high comorbidity (CCI ≥ 3). Data on gender, age, body mass index (BMI), surgery delay and surgery type were obtained from the DMHFR.

See figure 2 for a chart of the study design.

***Figure 2**: Chart of study design. Orange indicates data obtained from the Danish Multidisciplinary Hip Fracture Database. Blue indicates data from the Danish National Patient Register. Green indicates data from the Danish Health Service Prescription Database*



Statistical analyses

Ranking of hospitals' performance on outcome data has been widely discussed[37,38]. An appropriate statistical methods to evaluate hospitals' performance is multilevel models[39,40]. We used such models to account that patients were nested within hospitals. Thereby, any unexplained variation in infection was divided into patient-specific variation and hospital-specific variation[41]. In the same analyses, differences among patients were taken into account by adjusting for patient-level characteristics.

For each outcome, two regression models were performed. Model 1 was a modified single-level Poisson regression analysis[42] adjusted for the patient-specific variables; age, gender, comorbidity, BMI, surgery delay and surgery type. The Poisson regression was chosen over a logistic regression to estimate relative risk (RR) with 95% confidence interval (CI), which were preferred over odds ratios as a measure of risk, because odds ratio is only a good approximation for relative risks when the outcome is rare[43]. Model 2 was a two-level Poisson regression analysis adjusted for the same patient-specific variables as in model 1; though in model 2, patients were nested within hospitals to isolate the contribution of the hospital from the individual risk of acquiring a postoperative infection[44].

The risk of postoperative infection for each hospital was calculated as a function, where all covariates were held fixed at their average value. Meanwhile, the hospital effect acts as random effect. Subsequent, the risk for each hospital, if all hospitals had the exact same patient case-mix where the case-mix is the average of the covariates from all hospitals, were computed. To illustrate this, league tables for each outcome were created. The league tables show the ranking of hospitals by risk of acquiring a postoperative infection. The crude tables are only adjusted for hospital level factors, while the adjusted tables have taken individual covariates into account. Hospitals with less than five outcomes were not shown in the league tables due to rules of the Danish data protection agency about personally identifiable data. However, all hospitals were included in the analyses.

The intra class coefficient (ICC) denotes the proportion of hospital variance compared to the total variance that is unexplained by the already defined covariates. An ICC value for hospital of 100% denotes all unexplained variation is due to hospital level, while an ICC of 0% denotes all that all unexplained variation is at the patient level. For a two-level Poission regression, the ICC is calculated as[45]:

$$ICC=\frac{exp(2\beta X+2\sigma^2)-exp(2\beta X+\sigma^2)}{exp(2\beta X+2\sigma^2)-exp(2\beta X+\sigma^2)+exp(\beta X+\frac{\sigma^2}{2})}$$

Where βX is the intercept of the model with fixed individual covariates. σ^2 is the hospital variance.

The median rate ratio (MRR) denotes the median relative change in the rate of the outcome between two patients with identical characteristics from different hospitals, comparing the highest risk hospital with the lowest risk hospital. An MRR of one is equal to no hospital variance.

MRR can be evaluated by the following equation[45]:

$$MRR = exp\left(\sqrt{2\sigma^2}\phi^{-1}(0.75)\right)$$

Where ϕ^{-1} is the inverse cumulative standard normal distribution function.

For both models, based on the relative risks we computed the receiving-operator curve (ROC) and the area under the curve (AUC). AUC measures the ability of the model to correctly distinguish between patients with and without the infection. An AUC = 1 will predict perfect, while an AUC = 0.5 will predict as well as random selection[46]. The change in AUC, calculated as $AUC_{model\ 2} - AUC_{model\ 1}$, gives information on whether nesting patients within hospitals (Model 2) gives a better outcome prediction than without (Model 1).

Confidence intervals for ICC and MRR were estimated with bootstrapping using 100 iterations.

For BMI, 13% of data were missing (see supplementary table 3 for characteristics of patients with and without missing BMI). We applied a multiple imputation strategy to impute BMI, assuming that data were missing at random[47], using a regression imputation model with the factors community-acquired infection, hospital-treated infection, reoperation, sepsis, pneumonia, gender, age, year of surgery, length of hospital stay, surgery delay, fracture type and surgery type. We computed 13 imputations after Robins rule[48].

Sensitivity analysis

A series of sensitivity analyses assessed the robustness of our estimates and account for variability in clinical practice:

First, we did not take loss to follow-up into account in the case of death. Therefore, we calculated the risk of infection and mortality as a combined outcome to investigate if the loss to follow-up would introduce bias. Second, hip fracture patients may have fallen and sustained a fracture due to an infection, thus already being infected at admission. Therefore, we repeated the analyses while excluding all patients who have redeemed any antibiotic prescription 14 days prior to hip fracture surgery date. Third, hospitals may have different strategies to identify infections before discharge. Therefore, we investigated whether patients were discharged with infection after the primary hospitalization for hip fracture or readmitted with an infection. Fourth, infections may go undetected at the hospital, but latter be detected by a general practitioner. Therefore, we combined hospital-treated infection and community-acquired infection to a single outcome and repeated the analysis. Fifth, patient have different length of hospital stay during which patients would not be able to redeem antibiotics and count in the community-acquired infections. To ensure identical follow-up time, we repeated the analyses for community-acquired infection starting follow-up at discharge date instead of surgery date.

All analyses were performed in STATA 15.1 or R version 3.6.1.

Results

In total, 29,598 patients were included; of which 20,554 (69.4%) were women. Four out of five were aged between 65 and 89 years. Overall, 4532 (15.3%) hip fracture patients were diagnosed with any infection, whereas 3005 (10.2%) were diagnosed with pneumonia, and 522 (1.8%) with sepsis. The number of patients having community-acquired infection within 30 days of surgery was 6942 (23.5%) (Table 1 and supplementary table 4).

Hospital-treated infections

Table 2 shows that increasing age and increasing comorbidity level were strongly associated with higher risk hospital-treated infection. Men had increased risk of acquiring a hospital-treated infection compared to women (RR=1.59, CI: 1.50-1.70). Underweight patients had 21% higher risk of hospital-treated infections compared to normal weight patients, whereas obese patients had 11% increased risk. Patients operated with total/hemi arthroplasty had 14% increased risk of infection compared with patient operated with osteosynthesis.

When looking into specific types of the hospital-treated infection such as pneumonia and sepsis, the results were similar to overall results, with few exceptions regarding obesity and surgery type.

Hospital variation in hospital-treated infections

The average risk of any hospital-treated infections varied between 8.2% and 26.6% among hospitals. After adjustment for patient differences, the risk varied from 7.8% to 24.6% (Figure 3). The adjusted variance attributed to hospital level was 18.8% (95% CI: 10.0 – 24.9). The risk of acquiring any hospital-treated infection at the highest risk hospital compared with the lowest risk hospital for a patient with identical characteristics were 1.96 (95% CI: 1.57 - 2.33). The change in AUC indicated a 4.9 % better prediction for the infection when taking hospital level into account (Table 2).

Analysing pneumonia and sepsis, the risk varied across hospitals and was reduced after adjustment (Supplementary figure 1 and 2). The hospital variance for pneumonia and sepsis were similar to any hospital-treated infections. The amount of variation attributed to hospital level were 12.1% (95% CI: 5.0 – 14.9) for pneumonia and 1.8 % (95% CI: 0.6 – 3.7) for sepsis (Table 2).

Community-acquired infections

Table 3 shows that increasing age and increasing burden of comorbidity were strongly associated with the risk for community-acquired infection. Obese patients had a 19% increased risk compared to normal weight patients. There were no differences in the risk of community-acquired infection by surgery delay, type of surgery or gender.

Hospital variation in community-acquired infections

The average risk for community-acquired infection varied between 16.7% and 33.7% among hospitals. After adjusting for gender, age, comorbidity, BMI, surgery delay and type of surgery, the variation in risk was reduced to 16.4% - 33.6% (Figure 4). The adjusted variance was 13.3% (95% CI: 10.0 – 24.9) attributed to hospital level. The risk of acquiring a community-acquired infection at the highest risk hospital compared with the lowest risk

hospital for a patient with identical characteristics were 1.42 (95% CI: 1.32 - 1.56). The change in AUC indicated a 2.9 % better prediction for the infection when taking hospital level into account (Table 3).

Sensitivity analysis

First, when combining mortality and hospital-treated infection as a single outcome, we found a variation between 15.4% - 28.8% for the multilevel model adjusted for patient characteristics (Supplementary table 5) with 8.4% (95% CI: 3.8 – 12.4) of the variation due to hospital level. The increased risk for a patient operated at the highest risk hospital were 1.46 (95% CI: 1.29 – 1.60) compared with the lowest risk hospital. Second, excluding all patient who had redeemed a prescription for antibiotics < 14 days prior to surgery did not changed the results considerably (Supplementary table 6). Third, three quarters of the hospital-treated infections were detected during the primary hospitalization for hip fracture with hospital variation between 50.0% and 83.3%. Hospitals with a high infection risk had more infections detected during primary hospitalisation (Supplementary table 7 and supplementary figure 3). Fourth, when combining hospital-treated infection and community-acquired infection, the risk of infection was 34.1 %, varying from 24.6% to 45.5% between hospitals after adjustment for gender, age, comorbidity, BMI, surgery delay and type of surgery (Supplementary figure 4). Hospital level explained 10.9% (95% CI: 4.1 – 16.2) of the variation (Supplementary table 8). Fifth, when starting follow-up at discharge, community-acquired infection varied between 15.1% and 28.9% (Supplementary figure 8). The MRR showed an increased risk of 1.28 (95% CI: 1.45 - 1.16) between the lowest risk hospital and the highest risk hospital. The ICC indicated 7.3% (95% CI: 3.3 - 12.1) of the adjusted variance was due to hospital level (Supplementary figure 9).

Discussion

Our study is the first to examine the variation between hospitals in the risk of hospital-treated and community-acquired infections following hip fracture surgery and to quantifying the hospital level contribution to the variation using a nationwide population-based cohort design. We found a more than threefold difference in any hospital-treated infections between hospitals in Denmark, where 18.8% of the variation was attributed to hospital level. The variation sustained when stratifying for pneumonia and sepsis. For community-acquired infection, we found a twofold difference between hospitals, with 13.3% of the variation attributed to hospital level. Additionally, we found the increased risk of infection if operated at the highest risk hospital compared with the lowest risk hospital for a patient with the same characteristics to be 1.96 (95% CI: 2.33 – 1.57).

Strength and limitations

This study was based on nationwide population-based cohort design, prospectively collected individual-level data, and complete follow-up of all patients. We included almost 30,000 patients with free-of-charge and equal access to healthcare services, thereby reducing the risk of selection bias. When investigating death and hospital-treated infection as combined

outcome, we found a minor decrease in variation. We therefore do not consider loss-to follow up from death to introduce any pertinent bias.

A limitation of this study regards the validity of data since these are collected by a numerous number of clinicians as part of daily routine clinical work. We cannot exclude the possibility that variation in reporting practice can between hospitals can overestimate or underestimate infections. We identified hospital-treated infections based on ICD-10 codes from DNPR, known to have a high positive predictive value (PPV), including pneumonia in other patient groups[49,50]. However, the PPV might vary between hospitals. Unfortunately, we did not have data on x-rays, changes in inflammatory markers etc. to confirm the diagnosis codes negative predictive value, and thereby asses the amount of misclassification of infections. However, since infections does not pass spontaneously, we combined hospital-treated infections with community-acquired infections, and found a slightly lower variation due to hospital level. Additionally, we only included infection diagnoses, which the hospitals have payment for based on their registration of diagnoses. We therefore assume that all patients treated for infection are registered. Furthermore, in the case of under reporting infections at specific hospitals, we would have observed some hospitals with negligible low infection risk, which were not the case. However, when analysing specific infections such as pneumonia and sepsis we observed a lower variation, as well as a lower amount of variation attributed to hospital level. This points towards that, the more severe the infection is, the easier the infection becomes to detect, leading to less misclassification by hospital variation.

Hip fracture patients in Denmark are usually admitted to the nearest hospital offering hip fracture surgery and are therefore not classified according to health status, fracture severity or other characteristics. This minimizes the risk of confounding by indication.

Finally, we adjusted for a range of well-established prognostic factors to reduce confounding. Including the CCI, that comprised complete in-hospital comorbidity history[36]. However, we did not have information about severity of diseases in the CCI or full information on all factors exposing for infection. Therefore, we cannot exclude the possibility of residual confounding.

Comparison with previous literature

Previous studies on hospital variation in postoperative infections have primarily focused on cardiac surgery[22,24,51] or combined multiple surgical procedures[23,25]. Though, one study on elective hip and knee arthroplasties has shown a fourfold difference in risk between hospitals in United States[52] for complications, including pneumonia. We presented a fivefold difference for pneumonia. However, our study population were acute operated, older, more frail, and had more comorbidities compared with patients undergoing elective hip arthroplasty. In addition, our absolute risk estimates were much higher suggesting that more standardized and complex care of patients could contribute to mortality reduction.

When looking at hospital variation attributed to hospital level in other outcomes, a Dutch study investigated the hospital variation in any-cause readmission within 30 days among patients operated with a femoral neck fracture. They reported the risk to vary among hospitals between 2.2% and 11.0%[53]. Moreover, the study found 2.3% of the variation explained by hospital level. We presented a higher risk of only postoperative infections,

probably due to our inclusion of infections detected during primary hospitalization. Furthermore, hospital level explained 18.8% of the variation in postoperative infections in our study. This suggest that variation due to hospital level for postoperative infections are more frequent than for any-cause readmission. Any-cause readmissions are thereby a less sensitive marker for hospital performance than postoperative infections. The same applies to mortality. This is supported by the fact that, the size of the general hospital effect measures, ICC, MRR and difference in AUC, in our study is higher compared to a previous Danish variation study on 30-day mortality after hip fracture. They found that less than one percent of the variation in mortality, was explained by hospital level[10].

Clinical implications

Our results extrapolated that quality of in-hospital care for hip fracture patients is not homogeneous regarding postoperative infections. Whether the variation we have detected is due to genuine variation in the incidence of postoperative infection or attributed to a disparity in emphasis on postoperative infection between hospitals is not completely clear. However, this may be irrelevant, since patients should not be at higher risk of acquiring a postoperative infection nor having a postoperative course with less attention on postoperative infections than on other hospitals. We exposed that patients predominantly had their infection detected during the primary hospitalization. We found nearly a fifth of the variation was explained by hospital level factors whereas the largest variation was due to individual level factors. Previous studies have evaluated interventions to decrease postoperative pneumonia with success. Since we showed the most common postoperative infection to be pneumonia, this should be the primary focus in such interventions. Kazaure et al.[54] proposes a standardised postoperative pneumonia program, including education of nursing staff, coughing and deep-breathing exercises, twice-daily oral hygiene, ambulation and elevated head of the bed during meals. This intervention showed a 44% decreased rate of postoperative pneumonia among 4,099 American, non-cardiac, surgical patients. Furthermore, a study from Taiwan included 240 hip fracture patients. They showed a pneumonia risk of 13.9% which we regard as comparable to ours at 10.2%[55]. Their study showed a decrease in postoperative pneumonia to 5.9% among an intervention group implemented with deep-breathing exercises, chest physiotherapy and cough-assisted manoeuvres. Since postoperative infections are associated with higher mortality, a decrease in postoperative infection would lead to a decreased mortality. Therefore, we advocate for improvement of national clinical guideline to detect and treat infections during primary hospitalization. This may be as a standardised infection screening of all hip fracture patient or implantation of a standardised infection prevention programme.

Supplementary

Danish registers contain an enormous research source, in the form of data on the entire population in a tax-funded and income-independent healthcare system. Furthermore, the Danish civil registry number gives a unique possibility to link data, which formed almost ideal conditions to investigate the association between our exposure (hospitals in Denmark) and the outcome (postoperative infections). However, every scientific study has several pitfalls, which may interrupt accuracy of the estimates. The following section aims to address possible errors in the present study. This includes consideration on study design, statistical approaches and the most common epidemiological errors. Furthermore, this section provides a more thorough argumentation and explanation for the decisions taken to conduct the present study. Lastly, future implication will be discussed.

Study design

We conducted a cohort study using prospectively collected data from population based Danish registries. Cohort studies measures the occurrence of an event during a given time period within a cohort[56,57]. In the present study, we measured the incidence of postoperative infections within 30 days of surgery for all Danish hip fracture patients.

The disadvantages of cohort studies are the time and costs of large cohorts, as well as loss to follow-up. In the section *"selection bias"* this will further be elaborated in relation to the present study.

On the other hand, a cohort study has several advantages. Firstly, ability to measure multiple outcomes in a single study. This gave us the possibility to measure six outcomes (any hospital-treated infection, pneumonia, sepsis, reoperation due to deep infection, any community-acquired infection and mortality). Secondly, the possibility to compute absolute risk estimates. Lastly, a cohort study with prospectively collected data eliminates the possibility of recall bias[56].

Several other observational studies are available. In the case-control study design, cases are identified based on their outcome. From the same source population as the cases, a control group without the outcome is sampled. The exposure is then evaluated within the groups of cases and controls. Case-control studies are usually regarded more efficient and less expensive than cohort studies. However, case-control studies only provide relative risk measures of the association between outcome and exposure[57]. In the present study, we had 23 different exposures (hospitals), whereas a relative risk measure between hospitals would be difficult to interpret. Another common study design is RCT. RCTs randomize individuals to the given exposures, thereby eliminating selection bias. Therefore, is the RCT study design traditionally regarded the golden standard[56]. However, in the present study it would be both difficult and unethical to randomize patients to specific a hospital after hip fracture. Additionally, would such a study be extremely expensive and inconvenient to conduct.

Therefore, based on the data available and the advantages versus disadvantages of the described studies, we are convinced a cohort study has been the best design to answer our research question.

Exposure and outcome

Hospitals

We identified all Danish hospitals performing hip fracture surgery in our study period. However, we excluded hospitals who performed less than 15 surgeries a year. This was done, to avoid hospitals with sporadic surgeries that would have given an unspecific estimate, which would be imprecise to compare with other hospitals. We also excluded hospitals no longer performing hip fracture surgery. This was done to of two reasons: Firstly, this hospital had fewer patients in the five-year period, thereby having a more imprecise estimate, as well as procedures and guidelines may have changed over time and thereby introducing bias. Secondly, we did not want to expose a hospital with no possibility to improve its treatment.

Postoperative infections

The primary outcome of interest was postoperative infection. To ensure that infections was due to surgery or postoperative course, we choose a follow-up period of 30 days. We included a comprehensive range of hospital-treated infection (Supplementary table 1a) from DNPR. We further stratified these in pneumonia and sepsis. Additionally, we aimed to include community-treated infections, meaning infections treated outside the hospital. This was done by including any type of redeemed antibiotics from DNHSPD. These antibiotics are prescribed from either the hospital or a general practitioner. Unfortunately, we do not have data on antibiotics given from the hospital which may validate our infections codes. However, if a hospital had prescribed antibiotics for the patients, we must expect the patient to be diagnosed with an infection and therefore being included in hospital-treated infection.

During our study, we found a variation in urinary tract infections (UTI) between 11% and 39% between hospitals. We concluded that this must be due to variation in coding of UTI. Firstly, there is no economic benefit in coding UTI for the departments. Secondly, UTI can be have different diagnostic criteries across departments. Since UTI is a vague diagnose for elderly, with often persistent symptomless bacteriuria, which may cause positive urinary culture without any symptoms[18], we expect an underestimation of UVI across hospitals[33] and decided threfore, to exclude UTI as a postoperative infection.

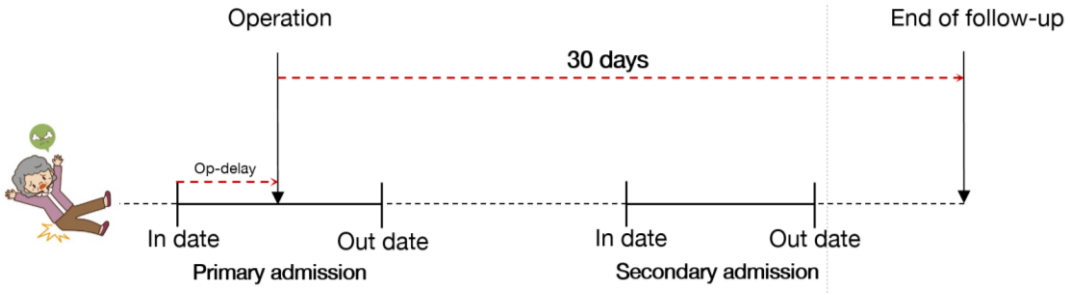
Only submission date and discharge date are available in DNPR. Unfortunately, the exact date of infection is unknown. To avoid missing infections from hospitalizations crossing the 30-day mark, submission date was chosen as date of infection (Illustrated as “In date” in Supplementary Figure 1). Therefore, patients submitted within 30 days acquiring an infection during the same submission after 30 days remained included. For patients either suffering a hip fracture during an already ongoing hospitalization or having an infection in the primary hospitalization following hip fracture surgery, their time from hip fracture to infection will become negative, since all patients were submitted before hip fracture surgery. To avoid counting infections incurred before surgery, no infections with a lower time from hip fracture

surgery to infection than two days where used. If the patient had a lower, information from the next hospitalization were included.

Mortality

We assessed mortality as outcome in a series of sensitivity analysis. Data on mortality were acquired from DCRS and counted as any death within 30 days of surgery.

Supplementary figure 1: Study design and DNPR registering.

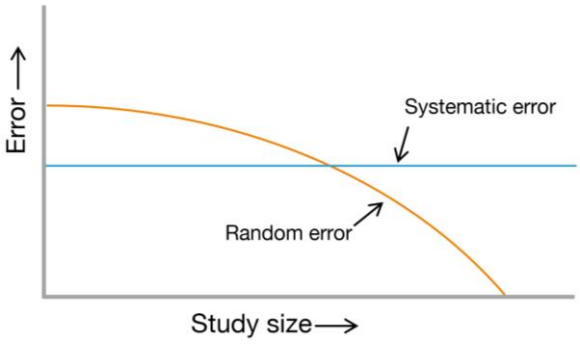


Potential errors in epidemiological studies

We aimed to describe the variation in postoperative infections between hospitals. However, the measures are only estimates of the true association. Since the true association is not possible to find, we do not know the exact magnitude of error. Nevertheless, we strived towards generating estimates as close to the true association as possible by having the following epidemiological pitfalls in mind[57].

Random error denotes the variability in the data. Random error cannot be readily explained. However, the larger a study is, the less random error influences the results. Since our study included almost 30,000 patients, random error does not have an impact on our results. Nevertheless, we added 95% confidence intervals to all our results, this was to quantify the random error in each result. Opposite to random error, systematic errors persists through the study despite the size (see Supplementary figure 2) Because of the size, virtually all errors in our study must be due to systematic errors. Three types of systemativ error exists; selectionbias, informationbias and confounding.

Supplementary figure 2: Relation between error types and



Selection bias

Selection bias stems from different association between exposure and outcome for those individuals included in the study compared with does who were not. We included all patients from DMHFR, which has a mandatory registration for all hip fracture surgery in Denmark. Since Denmark has a tax paid healthcare system with equal access for all, no hip fracture patients should go missed. Additionally, the DMHFR has shown a positive predictive value above 90% for both diagnoses and procedures in a validation study[30], where the DMHFR were compared with surgical procedure notes. Furthermore, the data used is prospectively collected, therefore were the outcome unknown at the start of follow-up and could not be related to the exposure[57]. The most worrying reason for selectionbias would be due to loss to follow-up. Loss to follow-up would be due to death or immigration. Unfortunately, we do not have the numbers on immigration, but we do not see it as a problem, since it seems highly unlikely for an elderly individual to immigrate within 30 days from a major trauma. More important is the high mortality after hip fracture. Therefore, death as a competing risk to infection is relevant to consider, which we did in a sensitivity analyses later described.

Information bias

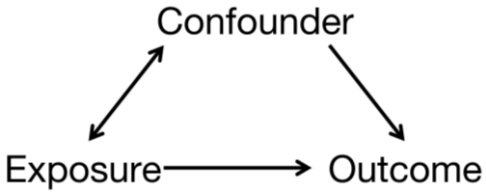
Information bias arise when the information collected about or from study subjects is erroneous. This may be referred to as misclassified information. Information bias is further divided in differential misclassification and non-differential misclassification. Differential misclassification occurs when the probability of being misclassified differ across outcome or exposure. This can amplify or underestimate an effect[57]. Differential misclassification might be observed for the outcome of postoperative infections in the case of under- or overestimating the true incidence, since some infections may go missed due to the difficulty of detecting infections in elderly, or if some hospitals detect false positive infections. However, as previously discussed, has the coding of infections within DNPR showed a high PPV in validations studies of other patient groups[49,50]. Thereby lowering the chance of an overestimation. To investigate the possibility of underestimating the incidence of infections, we included antibiotics prescribed outside hospitals, to account for infections not detected at hospitals. Therefore, we do not expect differential misclassification. Contrary differential misclassification, non-differential misclassification occurs when misclassification is independent of outcome. Non-differential misclassification of a dichotomous exposure tends to produce estimates closer to no effect than the actual effect[57]. In the present study, we do not expect non-differential misclassification to cause any bias. An example, we investigated whether patients were infected before admission. There seem to be no reasoning why some hospitals should have admitted more infected patients than others. When we tested this, by excluding patients having redeemed any antibiotics within 14 days of surgery, we did not see a change in results.

Confounding

The last group of systematic errors are confounding. It is the mixing of effect, where the effect of one variable is attributed to the effect of exposure. For a confounding variable, the following parameters must be present: 1) The confounder is associated with the outcome. 2) The confounder is associated with the exposure. 3) The confounder is not a part of the causal chain between exposure and outcome. This is illustrated in supplementary figure 3[56,57]. In our study,

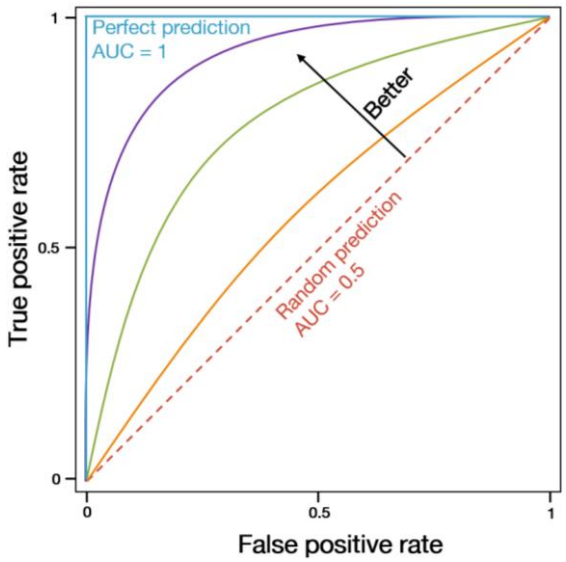
we included several well-established prognostic variables for infection after hip fracture surgery as they may be potential covariates in the associations. identified several confounding variables, such as gender, age, comorbidity, BMI, surgery delay and type of surgery. For example, comorbidity is associated with infection (associated with the outcome). It also varies between hospitals, whereas 34.8% have no comorbidity in the capital region, while 42.2% have no comorbidity in the northern region as seen supplementary table 11 (associated with the exposure). As well as comorbidity is not a part of the causal chain.

Supplementary figure 3: Relation between exposure, outcome and confounder.



Several strategies can be implied when adjusting for confounders, such as stratification, standardization, restriction, matching or multivariable adjustment [56]. Since we had several variables in our study as well as 23 different exposures (hospitals), we did multivariable adjustment through our regression model. Caution must be taken, when using multivariable adjustment. Firstly, the method is opaque, it can be hard to interpret how the results came to be. Secondly, caution must be taken to avoid over adjusting the models. Over adjustment happens when controlling for variables not affecting bias but leads to a more unprecise estimate. To clarify variables that may lead to over adjustment, causal diagrams can be drawn[56]. For example, we had the variable fracture type available. However, type of surgery is dependent on fracture type, since per/subtrochanteric fracture are most often operated with arthroplasty, while femoral neck fractures are operated with osteosynthesis. To evaluate which variable to use, we computed the area under the receiver operating curve (AUC). See supplementary figure 4 for an illustration of ROC curve. AUC measures the ability of the model to correctly distinguish between patients with and without the outcome. An AUC = 1 will predict perfect, while an AUC = 0.5 will predict as well as random selection[58]. As we build our model, we evaluated which variables increased the AUC. If a variable did not increase the AUC further, we did not include it in the final analysis.

Supplementary figure 4: Receiver operating curve



Statistical considerations

Media rate ratio (MRR) denotes the median relative change in the rate of the outcome between two patients with identical characteristics from different hospitals, comparing the patients at highest risk with the patient at lowest risk.

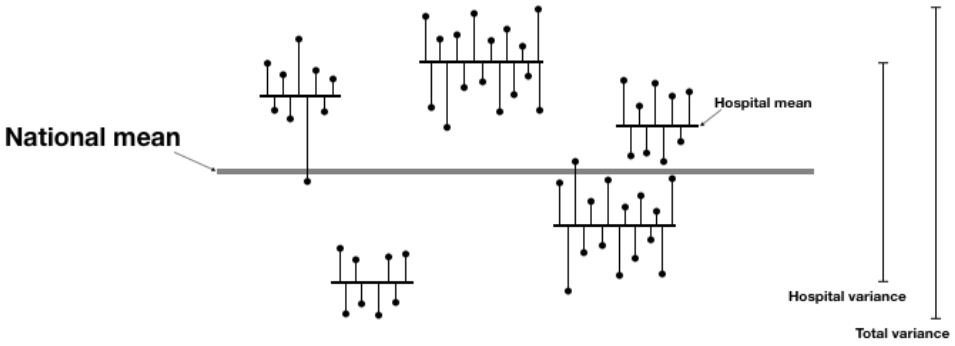
The intra class coefficient (ICC) denotes the proportion of variance that is unexplained by the already defined covariates. An ICC value of 100 % denotes all unexplained variation is due to hospital level factors, while an ICC of 0 % denotes all that all unexplained variation is due to patient level factors.

The change in AUC of the ROC curve is found by performing both a single level and multilevel analysis adjusting for the same variables, the change in the AUC between models, quantifies whether the multilevel model predicts better than single level.

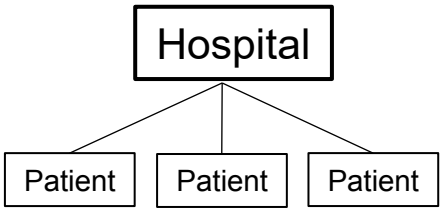
Different analyses can be performed on cohort studies. We choose to perform a regression model for a measure of risk. We did consider time to-event-analysis. This would have given us the possibility to only account for the time patients had in the cohort before either acquiring an infection or death. However, based on our data gathering, we did not have the exact time of infection. Most medical studies on dichotomous variable that performs multivariable adjustment is performed as a logistic regression. However, logistic regression generates an odds ratio, which is only a good measure for rare outcomes[43]. Since our outcomes on any hospital-treated infection and community-treated infection were of 15.3% and 23.5%, we would not acquire precise estimates with logistic regression. Therefore, we choose to perform a modified Poisson regression analysis, as described by G. Zou. et. Al.[42]Patients operated at the same hospitals may have more in common than patients operated at different hospitals. Firstly, patients will most often be admitted to the nearest hospital. Therefore, we expect patient to have a common geographic sphere. It is intuitive that people from the same geographical area is more alike than people from other geographical areas. This may be expressed in differing political, economic or health contexts. Secondly, people operated at the

same hospital, have a more alike hospital admission, including the same quality of care. These contextual phenomenons of patients operated at the same hospital being more alike than patients operated at different hospitals can also be defined as clustering within hospitals. Summarizing, the clustering within hospitals, is a portion of differences among patients, attributable to the hospitals they were operated at[59]. This is illustrated by supplementary figure 5[59]. To account for clustering by considering dependence of postoperative infection between patients operated at the same hospital, multilevel analysis is the most appropriate method. Multilevel analyses consider, that patients are nested within hospitals, as illustrated by figure supplementary figure 6.

Supplementary figure 5: Clustering effect.



Supplementary figure 6: Multilevel model.



By performing multilevel analysis, we gain the following measures as previously described: The median rate ratio (MRR), the intra class coefficient (ICC), AUC of the ROC curve[44]. Including these measurements in the evaluation of variation, creates a clearer and elaborated picture of the origin of variation. If we only had implied a single level analyses of each hospital's incidence of postoperative infection, we would have shown a variation as seen in supplementary table 4. From this, we might still conclude a need for intervention at the high-risk hospitals. However, we would not have the insight whether to intervene at individual level or hospital level.

Therefore, by performing multilevel models contrary to single level models, we gain a more comprehensive insight into the variation. Additionally, by accounting for hospital level independent of individual characteristics, we avoid the ecological fallacy and atomistic

fallacy. Ecological fallacy is to make an incorrect interpretation at an individual level based on information from a higher level. The opposite called the atomistic fallacy is making an incorrect interpretation at a higher level on the basis of information at an individual level[60]

Missing data

Our data had complete information on all variables, except for the BMI values, where 13% was missing. Missing data is categorised in missing at completely random (MCAR), missing not at random (MNAR) and missing at random (MAR)[47,48]. Data are MCAR if the missing values are not dependent of observed or unobserved values. Example if a laboratory sample are broken by accident on the way to analyses and therefore missing, since this could have happened to any laboratory sample without influence from any other variables. Data are MNAR if the missing values are dependent of unobserved values. Example if self-reported income is missing for groups of lower or higher income, since the missing data is dependent on the income group, but the income group is unknown. Data are MAR if the missing values are dependent on other known values and patient characteristics. Example if data on a specific disease is missing, but the disease is dependent on other variables like age, comorbidity, gender and other diseases which known. If the missing BMI values in our study is MCAR, this could be due to a random break down of the measurement tools. However, this is very unlikely since this would be the case with 13% of the patients. Therefore, the missing BMI values are probably MNAR or MAR. We can presume that more frail and old individuals are less likely to have their BMI measured, and thereby will BMI be dependent on age and comorbidity, therefore our missing BMI values would be MAR. Different methods can be used for handling missing values. First, all missing values can be categorised as "unknown" and be included in the analysis. This method is called missing indicator method. However, this method would lead to biased estimates due to residual confounding, since the "unknown" category is a combination of the other values. Second, only patients with complete data would be included. This method is called complete-case analysis. However, this method assumes that the missing BMI values are MCAR. Furthermore, 13% of the patients would be excluded, leading to a weakened statistical power with less precision. Lastly, missing data can be handled using multiple imputation. Multiple imputations assumes MAR, since the method uses known variables to predict the missing values. However, multiple imputation can also handle MCAR. We did perform all analyses with complete-case analysis as well as multiple imputed data. For the imputation, we used data on community-treated infection, hospital-treated infection, reoperation, sepsis, pneumonia, gender, age, year of surgery, length of hospital stay, surgery delay, fracture type and type of surgery. We imputed 13 times after Robins rule. The results did not differ, apart from broader confidence interval when only using complete-case analysis. Therefore, we choose to perform the final analysis using multiple imputed data, to ensure a more precise estimate.

Sensitivity analysis

We performed a series of sensitivity analyses. In this section, the rationale for the chosen sensitivity analysis is elaborated and discussed.

Mortality and infection as combined outcome
Since we did not take loss to follow-up into account in the case of death, we calculated the risk of infection and mortality as a combined outcome to investigate if the loss to follow-up would introduce bias.

Hospital-treated infection and community-treated infection as combined outcome
To avoid differential misclassification in the case of underreporting infections at hospital, we combined hospital-treated infection with community-treated infection. We thereby identified all patients with an infection. This did show a slightly lower variation (Supplementary table 5 and supplementary figure 4).

Infection before fracture
It is well known that elderly affected differently at infections than younger individuals. Therefore, an infection may be the reason for falling and sustaining a hip fracture[18]. In the present study, this may be seen as non-differential misclassification, since there is no justification for some hospitals to receive higher volume of already infected patients than others. However, to prove this, we first identified all patients redeeming a prescription for antibiotics <14 days prior to surgery. We excluded this patient group and repeated the analyses again. This showed no difference from the main results (Supplementary table 6).

Infection during primary hospitalization
Hospitals have different strategies for the postoperative course. Therefore, hospitals may differ in the attention to postoperative infections during primary hospitalization. To account for this, we investigated if infections were detected during primary hospitalization or a latter hospitalization. This showed that hospitals with high incidence of infection detected more infections during primary hospitalization (Supplementary table 7 and Supplementary figure 3).

Identical follow-up for community-treated infections
In our main analyses, our follow-up time were 30 days from surgery. However, patient did have different length of hospital stay. Therefore, the follow-up would differ for community-treated infections. Since, patients would not redeem antibiotics during hospitalization. To ensure identical follow-up, we repeated our analysis for community-treated infections, starting follow-up at discharge. This showed a slightly lowered variation and clustering effect (Supplementary table 9 and Supplementary figure 5).

Mortality among infected
Early detected infections are usually less harmfull and could lower mortality. To disentangle whether infections detected at hospitals with numerous infections were due to discernment of less severe infections, we collated mortality with infections at different hospitals. The best approach would be to compare the mortality among infected patients with the mortality

among uninfected. However, this was not possible without introducing immortal time bias. Immortal time bias is introduced, when a time period in the follow-up period where the study outcome cannot occur is introduced. In the present study, this would be expressed if patients acquiring an infection would have to be a live at a certain time point later than the surgery. Consequently, would infected patient have gained an advantage by being alive at the time of infection. Unfortunately, we cannot account for this advantage. Therefore, to avoid immortal time bias, we calculated mortality among infected patients. We included all patients in the cohort who acquired a postoperative infection and followed them for 30 days after infection. The outcome was mortality, calculated using a multilevel Poisson regression model, adjusted for the same variables as the previous models. The crude mortality after hip fracture surgery varied between 8.2% - 12.9%. This was reduced to 5.9% - 9.6% after adjusting for gender, age, comorbidity, BMI, surgery delay and type of surgery. The 30-day mortality risk after infection varied between 15.9% and 34.4%. Some, but not all hospitals with high infection risk had the low mortality among infected patients and vice versa (Supplementary table 12 and Supplementary figure 6).

Detailed discussion and future implications

We extrapolated that quality of care for hip fracture patients are neither homogeneous nor ideal regarding postoperative infections. Our results suggest a room for improvement in the treatment and focus on postoperative infections at hospital level.

Infections in geriatric patients

Geriatric patients have an increased risk of infection. This is due to an impaired immune system with ageing. A process called "immonosence". Ageing is associated with increased blood levels of anti inflammatory cytokines such as TNF-alpha and IL-6[18]. As well as increased apoptosis of lymphocytes. Vester et. al.[61] showed a different immune response after fracture trauma in elderly compared with younger individuals. Furthermore, did IL-6 levels increase more after surgery in the elder population than the younger. These results may suggest a further investigation in the immune system in elderly. Potentially with the aim of modulating the immune response at elderly after fracture.

Clinically, is infection in elderly also presented differently from younger patients. Whereas, a typical constellation of several symptoms are present in the younger population, elderly tend to have fewer symptoms during infection. Infection in elderly is often presented as non-specific manifestations, for example, generalised weakness, delirium, falls or anorexia. All sign of which also commonly is presented in a non-infectious geriatric context. Therefore, can infections in elderly individuals easily go missed[3].

Prevention interventions for postoperative infections

We suggested a standardized infection screening or prevention programme. However, our results on any-infections covers a broad range of infections. Regarding infections following orthopaedic surgery, the literature is often most specific on pneumonia. We also found pneumonia to be the most frequent hospital-treated infection. In the following, we therefore summarize the literature for prevention intervention for postoperative pneumonia. Several

studies have investigated different prevention programs for postoperative pneumonia. However, to our knowledge, only one study has investigated pneumonia prevention programs among hip fracture patients. The interventions suggested are deep breathing exercises with incentive spirometry, chest physiotherapy, cough-assisted manoeuvres, head-of-bed elevation to at least 30 degrees during all meals, oral hygiene with chlorhexidine, early mobilisation and education of ward staff.

A small review of interventions for postoperative pneumonia on non-thoracic patients is summarized in supplementary table 13. However, some of these results must be interpreted with caution. Wren et. al used a preintervention time period as baseline. While Kazaure et. used data from American College of Surgeons National Surgical Quality Improvement Program as baseline. Both studies investigated the same intervention. However, both studies reported a remarkable low incidence of pneumonia on 0.18% and 0.44%. This has been suggested as inadequate detection techniques used at their ward.

We suggest a RCT investigating a postoperative pneumonia programme in a larger setting among hip fracture patients. Furthermore, a successful intervention programme could be the solution to streamline the treatment and perioperative care of hip fracture patients. Potentially, decreasing variation in the incidence of postoperative pneumonia and improving quality of care.

References

1.Abrahamsen, B., Van Staa, T., Ariely, R., Olson, M. & Cooper, C. Excess mortality following hip fracture: A systematic epidemiological review. *Osteoporos. Int.* **20**, 1633–1650 (2009).

2.Pedersen, A. B. *et al.* Thirty-five-year trends in first-time hospitalization for hip fracture, 1-year mortality, and the prognostic impact of comorbidity: A Danish nationwide cohort study, 1980-2014. *Epidemiology* **28**, 898–905 (2017).

3.Kristensen, P. K., Thillemann, T. M. & Johnsen, S. P. Is Bigger Always Better? A Nationwide Study of Hip Fracture Unit Volume, 30-Day Mortality, Quality of In-Hospital Care, and Length of Hospital Stay. *Med. Care* **52**, 1 (2014).

4.Nielsen, K. A. *et al.* Quality of care and 30 day mortality among patients with hip fractures: a nationwide cohort study. *BMC Health Serv. Res.* **9**, 186 (2009).

5.Kristensen, P. K., Thillemann, T. M., Søballe, K. & Johnsen, S. P. Are process performance measures associated with clinical outcomes among patients with hip fractures ? A population-based cohort study. *Int. J. Qual. Heal. Care* **28**, 698–708 (2016).

6.Sheehan, K. J. *et al.* In-hospital mortality after hip fracture by treatment setting. *Cmaj* **188**, 1219–1225 (2016).

7.Roche, J. J. W., Wenn, R. T., Sahota, O. & Moran, C. G. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: Prospective observational cohort study. *Br. Med. J.* **331**, 1374–1376 (2005).

8.Belmont, P. J. *et al.* Risk factors for complications and in-hospital mortality following hip fractures: A study using the National Trauma Data Bank. *Arch. Orthop. Trauma Surg.* **134**, 597–604 (2014).

9.Smith, T., Pelpola, K., Ball, M., Ong, A. & Myint, P. K. Pre-operative indicators for mortality following hip fracture surgery: A systematic review and meta-analysis. *Age Ageing* **43**, 464–471 (2014).

10.Kristensen, P. K., Merlo, J., Ghith, N. & Johnsen, S. P. Hospital differences in mortality rates after hip fracture surgery in Denmark. *Clin. Epidemiol.* **2019**, 605–614 (2019).

11.*Dansk Tvaerfagligt Register for Hoftenaere Lårbensbrud*. (2018). Available at https://www.sundhed.dk/sundhedsfaglig/kvalitet/kliniske-kvalitetsdatabaser/akutte-sygdomme/hoftebrud-nip/. Access date: 02-26-2020.

12.Kjørholt, K. E., Kristensen, N. R., Prieto-Alhambra, D., Johnsen, S. P. & Pedersen, A. B. Increased risk of mortality after postoperative infection in hip fracture patients. *Bone* **127**, 563–570 (2019).

13.Cameron, I. D. *et al.* Hip Fracture Causes Excess Mortality Due to Cardiovascular and Infectious Disease in Institutionalized Older People: A Prospective Five-Year Study. *J. Bone Miner. Res.* **25**, 866–872 (2010).

14.Poh, K. S. & Lingaraj, K. Complications and their risk factors following hip fracture surgery. **21**, 154–157 (2013).

15.Shander, A. *et al.* Clinical and economic burden of postoperative pulmonary complications: Patient safety summit on definition, risk-reducing interventions, and preventive strategies. *Crit. Care Med.* **39**, 2163–2172 (2011).

16.Lawrence, V. A., Hilsenbeck, S. G., Noveck, H., Poses, R. M. & Carson, J. L. Medical complications and outcomes after hip fracture repair. *Arch. Intern. Med.* **162**, 2053–2057 (2002).

17.Glassou, E. N., Hansen, T. B. & Pedersen, A. B. Risk of pneumonia and urinary tract infection within the first week after total hip arthroplasty and the impact on survival. *Clin. Epidemiol.* **9**, 31–39 (2017).

18.Gavazzi, G. & Krause, K. Ageing and infection. *Lancet* **2**, 659–666 (2002).

19.Taylor, M. E. & Oppenheim, B. A. Hospital-acquired infection in elderly patients. *J. Hosp. Infect.* **38**, 245–260 (1998).

20.Miskovic, A. & Lumb, A. B. Postoperative pulmonary complications. *Br. J. Anaesth.* **118**, 317–334 (2017).

21.Kjørholt, K. E., Johnsen, S. P., Kristensen, N. R., Prieto-Alhambra, D. & Pedersen, A. B. Increasing Risk of Hospital-Treated Infections and Community-Based Antibiotic Use After Hip Fracture Surgery: A Nationwide Study 2005–2016. *J. Bone Miner. Res.* **34**, 437–446 (2019).

22.Brescia, A. A. *et al.* Determinants of Variation in Pneumonia Rates After Coronary Artery Bypass Grafting. *Ann. Thorac. Surg.* **105**, 513–520 (2018).

23.Dimick, J. B. *et al.* Variation in postoperative complication rates after high-risk surgery in the United States. *Surgery* **134**, 534–540 (2003).

24.Pasquali, S. K. *et al.* Hospital variation in postoperative infection and outcome after congenital heart surgery. *Ann. Thorac. Surg.* **96**, 657–663 (2013).

25.Wakeam, E. *et al.* Hospital-level variation in secondary complications after surgery. *Ann. Surg.* **263**, 493–501 (2016).

26.*Denmark in figures*. (2019). Statistic Denmark. Available at: https://www.dst.dk/Site/Dst/Udgivelser/GetPubFile.aspx?id=28924&sid=dkinfigures2019. Access date: 26-02-2020.

27.Schmidt, M. *et al.* The Danish health care system and epidemiological research : from health care contacts to database records. *Clin. Epidemiol.* **2019**, 563–591 (2019).

28.Schmidt, M., Pedersen, L. & Sørensen, H. T. The Danish Civil Registration System as a tool in epidemiology. *Eur. J. Epidemiol.* **29**, 541–549 (2014).

29.Kristensen, P. K. & Röck, N. D. The Danish Multidisciplinary Hip Fracture Registry 13-Year Results from a Population-Based Cohort of Hip Fracture Patients. *Clin. Epidemiol.* **12**, 9—21 (2020).

30.Hjelholt, T. J., Edwards, N. M., Vesterager, J. D., Kristensen, P. K. & Pedersen, A. B. The Positive Predictive Value of Hip Fracture Diagnoses and Surgical Procedure Codes in the Danish Multidisciplinary Hip Fracture Registry and the Danish National Patient Registry. *Clin. Epidemiol.* **12**, 123–131 (2020).

31.Sandegaard, J. L., Ehrenstein, V. & Pedersen, L. The Danish National Patient Registry : a review of content , data quality , and research potential. 449–490 (2015).

32.Ehrenstein, V. Existing data sources for clinical epidemiology : The Danish National Database of Reimbursed Prescriptions. 303–313 (2012).

33.Bliemel, C. *et al.* Urinary tract infection in patients with hip fracture: An underestimated event? *Geriatr. Gerontol. Int.* **17**, 2369–2375 (2017).

34.Smektala, R. *et al.* The effect of time-to-surgery on outcome in elderly patients with proximal femoral fractures. *BMC Musculoskelet. Disord.* **9**, 1–9 (2008).

35.Charlson, M., Szatrowski, T. P., Peterson, J. & Gold, J. Validation of a combined comorbidity index. *J. Clin. Epidemiol.* **47**, 1245–1251 (1994).

36.Thygesen, S. K., Christiansen, C. F., Christensen, S., Lash, T. L. & Sørensen, H. T. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med. Res. Methodol.* **11**, 83 (2011).

37.Adab, P., Rouse, A. M., Mohammed, M. A. & Marshall, T. Information in practice Performance league tables : the NHS deserves better. **324**, 95–98 (2002).

38.Goldstein, H. & Spiegelhalter, D. J. League Tables and Their Limitations : Statistical Issues in Comparisons of Institutional Performance. *J. R. Stat. Soc.* **159**, 385–443 (1996).

39.Abel, G. & Elliott, M. N. Identifying and quantifying variation between healthcare organisations and geographical regions: using mixed-effects models. *BMJ Qual. Saf.* 1–7 (2019).

40.A. Yucel, E.A. Ferries, M. Sharma, M. Johnson, R. A. Do different modeling techniques change rankings of hospital performanCe? : Multilevel Modeling vs. Standard Logistic RegRession. *Value Heal.* **18**, A13 (2015).

41.Errigo, P. D., Tosti, M. E., Fusco, D. & Perucci, C. A. Use of hierarchical models to evaluate performance of cardiac surgery centres in the Italian CABG outcome study. **9**, 1–9 (2007).

42.Zou, G. A modified poisson regression approach to prospective studies with binary data. *Am. J. Epidemiol.* **159**, 702–6 (2004).

43. Nurminen, M. To use or not to use the odds ratio in epidemiologic analyses?. *Eur J Epidemiol* 11, 365–371 (1995).

44.Merlo, J., Chaix, B., Yang, M., Lynch, J. & Råstam, L. A brief conceptual tutorial of multilevel analysis in social epidemiology: Linking the statistical concept of clustering to the idea of contextual phenomenon. *J. Epidemiol. Community Health* **59**, 443–449 (2005).

45.Austin, P. C. Measures of clustering and heterogeneity in multilevel Poisson regression analyses of rates / count data. 572–589 (2018).

46.Hanley, J. A. & McNeil, B. J. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* (1982).

47.Pedersen, A. B. *et al.* Missing data and multiple imputation in clinical epidemiological research. *Clin. Epidemiol.* **9**, 157–166 (2017).

48.Donders, A. R. T., van der Heijden, G. J. M. G., Stijnen, T. & Moons, K. G. M. Review: A gentle introduction to imputation of missing values. *J. Clin. Epidemiol.* **59**, 1087–1091 (2006).

49.Holland-bill, L. *et al.* Positive predictive value of primary inpatient discharge diagnoses of infection among cancer patients in the Danish National Registry of Patients. *Ann. Epidemiol.* **24**, 593-597.e18 (2014).

50.Thomsen, R. W. *et al.* Rising incidence and persistently high mortality of hospitalized pneumonia: a 10-year population-based study in Denmark. *J. Intern. Med.* **259**, 410–417 (2006).

51.Hirahara, N. *et al.* Procedure- and hospital-level variation of deep sternal wound infection from all-Japan registry. *Ann. Thorac. Surg.* (2019).

52.Bozic, K. J. *et al.* Variation in Hospital-Level Risk-Standardized Complication Rates Following Elective Primary Total Hip and Knee Arthroplasty. *J. Bone Jt. Surg.* 640–647 (2014).

53.Hekkert, K. *et al.* To what degree can variations in readmission rates be explained on the level of the hospital? a multilevel study using a large Dutch database. *BMC Health Serv. Res.* **18**, 13–15 (2018).

54.Kazaure, H. S., Martin, M., Yoon, J. K. & Wren, S. M. Long-term results of a postoperative pneumonia prevention program for the inpatient surgical ward. *JAMA Surg.* **149**, 914–918 (2014).

55.Chang, S. C. *et al.* Reduction in the incidence of pneumonia in elderly patients after hip fracture surgery: An inpatient pulmonary rehabilitation program. *Med. (United States)* **97**, 1–5 (2018).

56.Fletcher, R. H., Fletcher, S. W. & Fletcher, G. S. *Clinical epidemiology: The essentials: Fifth edition. Clinical Epidemiology: The Essentials: Fifth Edition* (2013).

57.Rothman, K. *Epidemiology. An introduction. Oxford University Press* (2012).

58.Carter, J. V., Pan, J., Rai, S. N. & Galandiuk, S. ROC-ing along: Evaluation and interpretation of receiver operating characteristic curves. *Surg. (United States)* **159**, 1638–1645 (2016).

59.Merlo, J., Yang, M., Chaix, B., Lynch, J. & Råstam, L. A brief conceptual tutorial on multilevel analysis in social epidemiology: Investigating contextual phenomena in different groups of people. *J. Epidemiol. Community Health* **59**, 729–736 (2005).

60.Diez Roux, A. V. A glossary for multilevel analysis. *J. Epidemiol. Community Health* **56**, 588–594 (2002).

61.Vester, H. *et al.* The immune response after fracture trauma is different in old compared to young patients. *Immun. Ageing* **11**, 1–8 (2014).

62.Lawrence, V. A., Cornell, J. E. & Smetana, G. W. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: Systematic review for the American College of Physicians. *Ann. Intern. Med.* **144**, 596–608 (2006).

63.Wren, S. M., Martin, M., Yoon, J. K. & Bech, F. Postoperative Pneumonia-Prevention Program for the Inpatient Surgical Ward. *J. Am. Coll. Surg.* **210**, 491–495 (2010).

64.Cassidy, M. R., Rosenkranz, P., McCabe, K., Rosen, J. E. & McAneny, D. I COUGH: Reducing postoperative pulmonary complications with a multidisciplinary patient care program. *JAMA Surg.* **148**, 740–745 (2013).

Tables

***Table 1**: Patient characteristics*

Number of patients in the population	29598	
Number of hospitals	23	
Median number of patients at the hospitals (min-max)	1314	(244-2823)
Overall 30-day infection, N (%)		
Any infection	4532	15.3 %
Pneumonia	3005	10.2 %
Sepsis	522	1.8 %
Community-acquired infection	6942	23.5 %
Gender, N (%)		
Female	20554	69.4 %
Male	9044	30.6 %
Age, N (%)		
65-79	11046	37.3 %
80-89	12548	42.4 %
>89	6004	20.3 %
Comorbidity (CCI), N (%)		
No comorbidity (0 point)	11112	37.5 %
Low comorbidity (1-2 points)	11778	39.8 %
High comorbidity (>3points)	6708	22.7 %
Body Mass index, N (%)		
Underweight (<18.5)	3917	13.2 %
Normal (18.5-24.9)	12052	40.7 %
Overweight (25-29.9)	6623	22.4 %
Obese (≥30)	2004	6.8 %
Missing	5002	16.9 %
Surgery delay in hours, N (%)		
<24	20406	68.9 %
24-48	7310	24.7 %
>48 hours	1882	6.4 %
Surgery type, N (%)		
Osteosynthesis	19073	64.4 %
Total/hemi arthroplasty	10525	35.6 %

***Table 2**: Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for any hospital-treated infection, and stratified for pneumonia and sepsis (95% CI).*

	Any Hospital-treated infection – Model 1		Any Hospital-treated – Model 2		Pneumonia – Model 1		Pneumonia – Model 2		Sepsis – Model 1		Sepsis – Model 2	
Individual Variables	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Sex												
Female	Ref.				Ref.		Ref.		Ref.		Ref.	
Male	1.56	(1.47 - 1.65)	1.59	(1.50 – 1.70)	1.76	(1.65 – 1.89)	1.81	(1.68 – 1.95)	2.21	(1.85 – 2.64)	2.23	(1.87 – 2.67)
Age												
65-79	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
80-89	1.37	(1.29 - 1.46)	1.40	(1.31 – 1.50)	1.55	(1.43 – 1.68)	1.59	(1.46 – 1.73)	1.70	(1.39 – 2.09)	1.72	(1.40 – 2.12)
>89	1.55	(1.44 – 1.66)	1.55	(1.43 – 1.68)	1.83	(1.66 – 2.01)	1.84	(1.66 – 2.03)	1.83	(1.44 – 2.34)	1.83	(1.43 – 2.39)
Comorbidity (CCI)												
No comorbidity (0 point)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Low comorbidity (1-2 points)	1.40	(1.31 – 1.50)	1.36	(1.27 – 1.46)	1.52	(1.40 – 1.68)	1.48	(1.35 – 1.61)	1.33	(1.07 – 1.64)	1.31	(1.06 – 1.62)
High comorbidity (>3points)	1.69	(1.57 – 1.81)	1.60	(1.48 – 1.73)	1.78	(1.66 – 2.01)	1.68	(1.53 – 1.86)	1.74	(1.39 – 2.18)	1.69	(1.34 – 2.12)
Body Mass index (BMI)												
Underweight (<18.5)	1.21	(1.12 – 1.30)	1.21	(1.11 – 1.31)	1.28	(1.17 – 1.40)	1.28	(1.16 – 1.41)	1.20	(0.95 – 1.52)	1.20	(0.95 – 1.52)
Normal (18.5-24.9)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Overweight (25-29.9)	0.99	(0.93 – 1.05)	1.00	(0.93 – 1.07)	0.99	(0.91 – 1.08)	1.00	(0.91 – 1.09)	0.85	(0.69 – 1.05)	0.86	(0.69 – 1.06)
Obese (≥30)	1.08	(0.98 – 1.19)	1.11	(0.99 – 1.24)	1.01	(0.88 – 1.15)	1.04	(0.90 – 1.19)	0.88	(0.54 – 1.11)	0.78	(0.55 – 1.12)
Surgery delay (hours)												
<24	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
24-48	1.10	(1.04 – 1.17)	1.09	(1.02 – 1.17)	1.16	(1.08 – 1.25)	1.15	(1.06 – 1.24)	1.09	(0.89 – 1.32)	1.09	(0.89 – 1.33)
>48 hours	1.01	(0.90 – 1.12)	1.06	(0.94 – 1.19)	0.96	(0.83 – 1.10)	1.01	(0.86 – 1.17)	1.31	(0.96 – 1.79)	1.38	(1.00 – 1.89)
Operation type												
Osteosynthesis	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Total/hemi arthroplasty	1.15	(1.08 – 1.21)	1.14	(1.08 – 1.22)	1.15	(1.07 – 1.23)	1.14	(1.06 – 1.23)	0.94	(0.78 – 1.12)	0.93	(0.78 – 1.12)
Hospital contextual effects												
ICC hospital (%)			18.8%	(10.0%– 24.9%)			12.1%	(5.7 – 18.8)			1.8%	(0.6 – 3.7)
MRR			1.96	(2.33 – 1.57)			2.08	(0.40 – 0.97)			1.82	(2.33 – 1.41)
AUC	0.618	(0.610 – 0.627)	0.667	(0.659 – 0.675)	0.639	(0.629 – 0.649)	0.683	(0.674 – 0.693)	0.65	(0.628 – 0.675)	0.678	(0.656 – 0.701)
Change in AUC			0.049				0.044				0.027	

CCI=Charlson Comorbidity Index, ICC= Intra Class Coefficient, AUC= Area Under the receiver operating characteristic Curve, MRR=Median Risk Ratio, RR=Relative Risk, CI=Confidence Interval.

***Table 3**: Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for community-acquired infection (95% CI).*

	Community-acquired infection – Model 1		Community-acquired infection – Model 2	
Individual Variables	RR	(95% CI)	RR	(95% CI)
Sex				
Female	Ref.		Ref.	
Male	0.94	(0.90 – 0.98)	0.94	(0.89 – 0.99)
Age				
65-79	Ref.		Ref.	
80-89	1.29	(1.23 – 1.36)	1.29	(1.22 – 1.36)
>89	1.44	(1.36 – 1.53)	1.44	(1.35 – 1.53)
Comorbidity (CCI)				
No comorbidity (0 point)	Ref.		Ref.	
Low comorbidity (1-2 points)	1.16	(1.11 – 1.22)	1.17	(1.10 – 1.23)
High comorbidity (>3points)	1.24	(1.18 – 1.31)	1.24	(1.16 – 1.32)
Body Mass index (BMI)				
Underweight (<18.5)	1.02	(0.96 – 1.08)	1.02	(0.94 – 1.09)
Normal (18.5-24.9)	Ref.		Ref.	
Overweight (25-29.9)	1.04	(0.99 – 1.09)	1.05	(0.99 – 1.11)
Obese (≥30)	1.20	(1.11 – 1.29)	1.19	(1.10 – 1.30)
Surgery delay (hours)				
<24	Ref.		Ref.	
24-48	0.99	(0.94 – 1.04)	1.01	(0.96 – 1.07)
>48 hours	1.00	(0.92 – 1.09)	1.04	(0.95– 1.15)
Operation type				
Osteosynthesis	Ref.		Ref.	
Total/hemi arthroplasty	0.98	(0.94 – 1.02)	0.97	(0.93 – 1.02)
Hospital contextual effects				
ICC hospital (%)			13.3 %	(6.0 – 20.5)
MRR			1.43	(1.56 – 1.25)
AUC	0.564	(0.557 – 0.572)	0.593	(0.585 – 0.600)
Change in AUC			0.029	

CCI=Charlson Comorbidity Index, ICC= Intra Class Coefficient, AUC= Area under the receiver operating characteristic curve, MRR=Median Risk Ratio, RR=Relative Risk, CI=Confidence Interval.

Figures

Figure 3: *League tables ranking hospitals for any-hospital treated infections.*
** Sex, age, comorbidity, BMI, surgery delay and operation type*

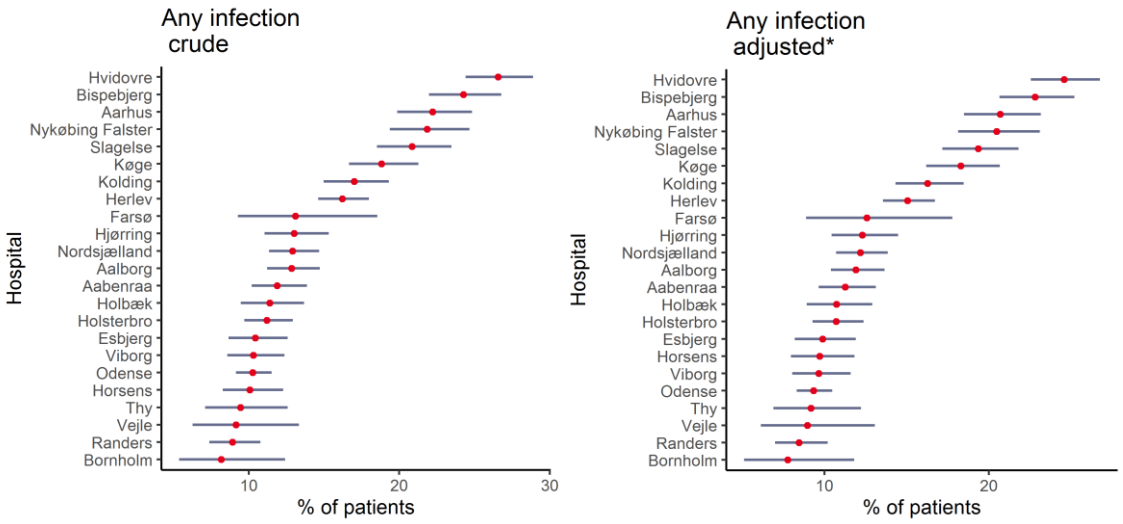
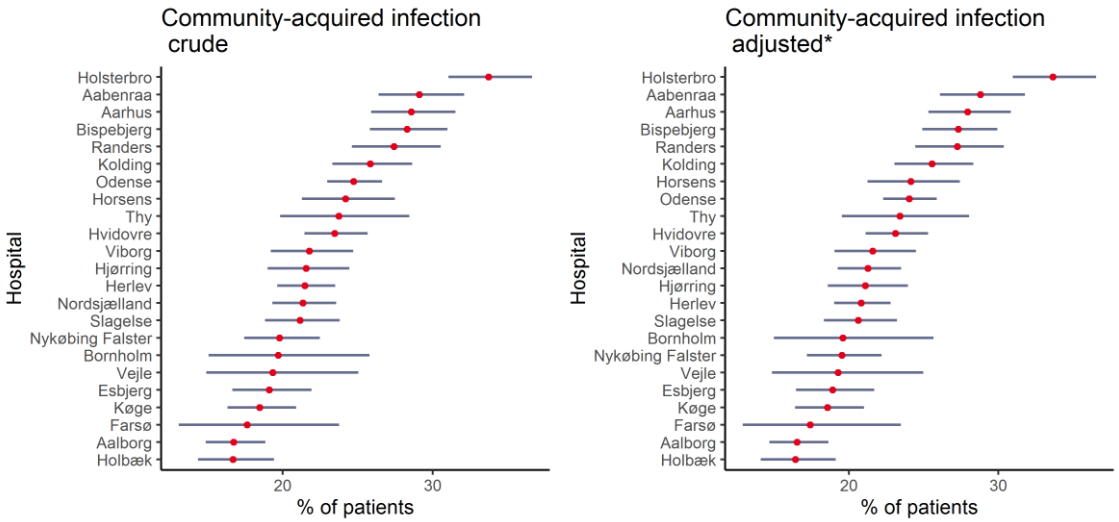


Figure 4: League tables ranking hospitals for community-acquired infection.
** Sex, age, comorbidity, BMI, surgery delay and operation type*



Supplementary tables

Supplementary table 1a: *International classification of diseases, tenth revision (ICD-10) codes used to identify hospital-treated infection.*

Hospital-diagnosed infectious diseases	ICD-10 codes
Miscellaneous bacterial infections	A20-A38, A42-A44, A48-A49, A65A79
Miscellaneous viral infections	A90-A99, B03-B09, B25-B34
Candidiasis and other fungal infections	B35-B49
Parasitic infections	B50-B89
Herpes simplex or zoster	B00-B02, G05.1I, G05.1M, H03.1F, H13.1M, H19.0D, H19.2D, H19.2J, H22.0C, H62.1B, G53.0, G63.0F)
HIV	B20-B24
Tuberculosis	A15-A19
Atypical mycobacteria	A31
Bacteremia	A49.9, A39.4
Sepsis	A40-A41, B37.7, A32.7, A54.8G, A02.1, A22.7, A26.7, A42.7, A28.2B
Abscess	A06.5, A54.1, B43, D73.3, E06.0A, E23.6A, E32.1, G06, G07, H00.0A, H05.0A, H44.0A, H60.0, J34.0A, J36, J38.3D, J38.7G, J39.0, J39.1, J39.8A, J85.1, J85.2, J85.3, K04.6, K04.7, K11.3, K12.2, K13.0A, K14.0A, K20.9A, K35.3A, K35.3B, K57.0, K57.2, K57.4, K57.8, K61, K63.0, K65.0, K75.0, K81.0A, K85.8A, L02, L05.0, L05.9, M60.8A, M86.8A, M86.9A, N15.1, N34.0, N41.2, N45.0, N48.2, N49.2A, N61.9A, N61.9B, N70.0A, N70.0B, N71.0A, N73.0A, N73.0B, N73.2A, N73.2B, N73.3A, N73.5A, N73.8A, N73.8C, N75.1, N76.4, N76.8A *(Except: A54.1B, B43.0, B43.8, B43.9, K57.0B, K57.0C, K57.2B, K57.2C, K57.4A, K65.0M, K65.0N, K65.0O, K65.0P)*
Skin infections	A46, H01.0, H03, H60.0, H60.1, H60.2, H60.3, H62, K12.2, K13.0, K61, M72.6, L01, L08
Cellulitis	L03
Other skin infections (including carbuncle, furuncle, lymphadenitis, cutaneous abscess, cyst, and dermatitis)	J34.0, L00, L02, L04, L05, L06, L07, L30.3, L73.8
Eye infections	H00, H01.0, H03.0, H03.1, H04.3, H05.0, H06.1, H10, H13.0, H13.1, H15.0, H19.1, H19.2, H22.0, H32.0, H44.0, H44.1
Ear infections	H60, H61.0, H62.0, H62.1, H62.2, H62.3, H65, H66, H67.0, H67.1, H68, H70, H73.0, H75.0, H83.0, H94.0 *(Except: H60.4, H60.4A, H605, H60.5B, H60.8, H608.A, H65.2, H65.3, H65.4, H65.4C, H66.1, H66.2, H66.3, H68.1, H70.1, H70.8)*
Central Nervous System infections (except meningococcal disease	G00-G07, A80-A89
Meningitis	G00, G01, G02, G03, A32.1, A39.0, A17.0, A20.3, A87, A54.8D, A02.2C, B37.5, B00.3, B01.0, B02.1, B05.1, B26.1, B38.4
Gastrointestinal infections	A00-A09
Intra-abdominal infection	K35, K37, K57.0, K57.2, K57.4, K57.8, K61, K63.0, K65.0, K65.9, K67, K75.0, K75.1, K80.0, K80.3, K80.4, K81.0, K81.9, K83.0, K85.9
Viral hepatitis	B15-B19
Heart infections(acute rheumatic fever, infectious pericarditis or myocarditis, endocarditis)	I30.1, I32.0, I33, I38, I40.0, I39.8, B37.6
Upper respiratory tract infection	J00-J06, J36, J39.0, J39.1
Influenza	J10-J11
Pneumonia	J12-J18
Other lower-respiratory tract infections	J20-J22, J44.0, J85.1, J86, J20-J22, J34.0, J35.0, J38.3C, J38.3D, J38.7B, J38.7F, J38.7G *(Except: J34.0E, J34.0F, J34.0G, J34.0H)*
Sexually transmitted diseases	A50-A64
Male genital infections (prostatitis, orchitis, epididymitis)	N41, N45, N48.1, N48.2, N49, N51.1, N51.2
Female pelvic infections (salpingo-oophritis, uterine infections, vulvovaginitis)	N70-N77
Septic arthritis, osteomyelitis, myositis	M00, M01, M86, M63.0, M63.2
Infectious complications of procedures, catheters etc.	T80.2, T81.4, T82.6, T82.7, T83.5, T83.6, T84.5, T84.6, T84.7, T85.7, T88.0, T89.9
Other infections or sequelae	B90-B99, K04.0, K05.2

***Supplementary table 2**: International classification of diseases, tenth revision (ICD-10)codes used to Charlson comorbidity index*

Disease	ICD-10	Score
Myocardial infarction	I21;I22;I23	1
Congestive heart failure	I50; I11.0; I13.0; I13.2	1
Peripheral vascular disease	I70; I71; I72; I73; I74; I77	1
Cerebrovascular disease	I60-I69; G45; G46	1
Dementia	F00-F03; F05.1; G30	1
Chronic pulmonary disease	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3	1
Connective tissue disease	M05; M06; M08; M09;M30;M31; M32; M33; M34; M35; M36; D86	1
Ulcer disease	K22.1; K25-K28	1
Mild liver disease	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0	1
Diabetes type1 Diabetes type2	E10.0, E10.1; E10.9 E11.0; E11.1; E11.9	1
Hemiplegia	G81; G82	2
Moderate to severe renal disease	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
Diabetes with end organ damage type1 type2	 E10.2-E10.8 E11.2-E11.8	2
Any tumor	C00-C75	2
Leukemia	C91-C95	2
Lymphoma	C81-C85; C88; C90; C96	2
Moderate to severe liver disease	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
Metastatic solid tumor	C76-C80	6
AIDS	B21-B24	6

***Supplementary table 1b:** Anatomical Therapeutical Chemical Classification system (ATC) codes to identify community-acquired infections.*

Type of antibiotic	ATC codes
Beta-lactamase sensitive penicillins	J01CE
Beta-lactamase resistant penicillins	J01CF
Cephalosporins (First generation)	J01DB
Cephalosporins (Second generation)	J01DC
Cephalosporins (Third generation)	J01DD
Cephalosporins (Fourth generation)	J01DE
Carbapenems	J01DH
Other cephalosporins and penems	J01DI
Combinations of penicillins, incl. Beta-lactamase inhibitors	J01CR
Penicillins with extended spectrum	J01CA
Macrolides, lincosamides and streptogramins.	J01F
Trimethoprim and derivatives	J01E
Fluroquinolones	J01MA
Tetracyclines	J01A

Supplementary table 3: *Patient characteristics for observations with and without missing BMI*

	Overall % (n)		No missing BMI % (n)		Missing BMI % (n)	
Number of patients	100	29598	83.1	(24596)	16.9	5002
Overall 30-day infection						
Any infection	15.3	4532	14.9	(3659)	17.5	(873)
Pneumonia	10.2	3005	9.8	(2412)	11.9	(693)
Sepsis	1.8	522	1.8	(431)	1.8	(91)
Gender						
Female	69.4	20554	69.6	(17116)	68.7	(3438)
Male	30.6	9044	30.4	(7480)	31.3	(1564)
Age						
65-79	37.3	11046	37.5	(9218)	36.6	(1828)
80-89	42.4	12548	42.7	(10515)	40.6	(2033)
>89	20.3	6004	19.8	(4863)	22.8	(1141)
Comorbidity (CCI)						
No comorbidity (0 point)	37.5	11112	38.1	(9375)	34.7	(1737)
Low comorbidity (1-2 points)	39.8	11778	39.4	(9699)	41.6	(2079)
High comorbidity (>3points)	22.7	6708	22.5	(5522)	23.7	(1186)
Surgery delay in hours						
<24	68.9	20406	69.6	(17116)	65.8	(3290)
24-48	24.7	7310	24.5	(6016)	25.9	(1294)
>48 hours	6.4	1882	5.9	(1464)	8.3	(418)
Surgery type						
Osteosynthesis	64.4	19073	64.3	(15809)	65.2	(3264)
Total/hemi arthroplasty	35.6	10525	35.7	(8787)	34.8	(1738)

Supplementary table 4: *Crude risk of any hospital-treated infection, pneumonia, sepsis and community-acquired infection*

	No. Of patients	% any-infection (n)		% Pneumonia (n)		% Sepsis (n)		% Community-aquired infection (n)	
Total	29598	15.3	(4549)	10.1	(3016)	1.8	(525)	23.5	(6942)
Hospitals									
Aabenraa	1371	11.9	(163)	7.8	(107)	1.0	(14)	29.1	(1371)
Aalborg	1626	12.9	(209)	8.9	(144)	1.7	(28)	16.7	(1626)
Aarhus	1386	22.2	(308)	13.8	(191)	2.0	(28)	28.6	(1386)
Bispebjerg	1623	24.3	(394)	16.4	(266)	2.5	(41)	28.3	(1623)
Bornholm	269	8.2	(22)	4.1	(11)	.	(<5)	19.7	(269)
Esbjerg	1053	10.5	(110)	7.4	(78)	0.6	(6)	19.1	(1053)
Farsø	244	13.1	(32)	9.0	(22)	.	(<5)	17.6	(244)
Herlev	2207	16.2	(358)	9.4	(208)	1.9	(41)	21.5	(2207)
Hjørring	1114	13.0	(145)	9.3	(103)	1.1	(12)	21.5	(1114)
Holbæk	1001	11.4	(114)	6.8	(68)	1.6	(16)	16.7	(1001)
Holstebro	1669	11.2	(187)	7.6	(127)	1.6	(26)	33.7	(1669)
Horsens	972	10.1	(98)	7.1	(69)	1.4	(14)	24.2	(972)
Hvidovre	2029	26.6	(539)	19.6	(397)	2.5	(51)	23.5	(2029)
Kolding	1405	18.0	(239)	12.6	(177)	1.4	(19)	25.8	(1405)
Køge	1365	18.8	(257)	11.6	(158)	2.3	(31)	18.5	(1365)
Nordsjælland	1805	12.9	(233)	8.8	(158)	1.3	(24)	21.3	(1805)
Nykøbing Falster	1203	21.9	(263)	15.8	(190)	2.4	(29)	19.8	(1203)
Odense	2823	10.3	(290)	6.3	(177)	1.7	(48)	24.7	(2823)
Randers	1211	8.92	(108)	5.7	(69)	1.2	(15)	27.4	(1211)
Slagelse	1314	20.9	(274)	13.0	(171)	2.7	(35)	21.2	(1314)
Thy	497	9.5	(47)	6.2	(31)	.	(<5)	23.7	(497)
Vejle	295	9.2	(27)	5.1	(15)	.	(<5)	19.3	(295)
Viborg	1116	10.3	(115)	6.1	(68)	3.0	(33)	21.8	(1116)

Supplementary table 6: *Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for any hospital-treated infection (95% CI). Patients who redeemed a prescription for antibiotics 14 days prior surgery are excluded*

	Hospital-treated infection – Model 1		Hospital –treated infection – Model 2	
Individual Variables	RR	(95% CI)	RR	(95% CI)
Sex				
Female	Ref.		Ref.	
Male	1.59	(1.50 – 1.68)	1.63	(1.53 – 1.74)
Age				
65-79	Ref.		Ref.	
80-89	1.37	(1.28 – 1.46)	1.40	(1.30 – 1.50)
>89	1.58	(1.47 – 1.71)	1.58	(1.46 – 1.72)
Comorbidity (CCI)				
No comorbidity (0 point)	Ref.		Ref.	
Low comorbidity (1-2 points)	1.40	(1.31 - 1.50)	1.36	(1.26 – 1.46)
High comorbidity (>3points)	1.64	(1.52 – 1.77)	1.55	(1.43 – 1.68)
Body Mass index (BMI)				
Underweight (<18.5)	1.19	(1.10 – 1.29)	1.19	(1.10 – 1.30)
Normal (18.5-24.9)	Ref.		Ref.	
Overweight (25-29.9)	1.01	(0.95 – 1.08)	1.02	(0.95 – 1.10)
Obese (≥30)	1.10	(1.00 – 1.23)	1.13	(1.01 – 1.27)
Surgery delay (hours)				
<24	Ref.		Ref.	
24-48	1.10	(1.03 – 1.17)	1.08	(1.01 – 1.16)
>48 hours	0.98	0.88- 1.17)	1.03	(0.91 – 1.17)
Operation type				
Osteosynthesis	Ref.		Ref.	
Total/hemi arthroplasty	1.16	(1.09 – 1.22)	1.16	(1.09 – 1.23)
General contextual effects				
ICC hospital (%)			18.4%	(10.0 – 22.7)
MRR			1.96	(2.38 – 1.64)
AUC	0.619	(0.610 – 0.627)	0.667	(0.659 – 0.675)
Change in AUC			0.048	

CCI=Charlson Comorbidity Index, ICC= Intra Class Coefficient, AUC= Area under the receiver operating characteristic curve, MRR=Median Risk Ratio, RR=Relative Risk, CI=Confidence Interval.

Supplementary table 5: *Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for combined outcome of death and hospital-treated infection within 30 days*

	Death or infection – Model 1		Death or infection – Model 2	
Individual Variables	**RR**		**RR**	
Sex				
Female	Ref.		Ref.	
Male	1.58	(1.52 – 1.65)	1.60	(1.53 – 1.69)
Age				
65-79	Ref.		Ref.	
80-89	1.55	(1.48 – 1.64)	1.57	(1.48 – 1.67)
>89	2.18	(2.06 – 2.30)	2.18	(2.04 – 2.33)
Comorbidity (CCI)				
No comorbidity (0 point)	Ref.		Ref.	
Low comorbidity (1-2 points)	1.47	(1.39 – 1.54)	1.44	(1.36 – 1.53)
High comorbidity (>3points)	1.83	(1.73 – 1.94)	1.78	(1.67 – 1.90)
Body Mass index (BMI)				
Underweight (<18.5)	1.27	(1.20 – 1.34)	1.27	(1.19 – 1.35)
Normal (18.5-24.9)	Ref.		Ref.	
Overweight (25-29.9)	0.89	(0.85 – 0.94)	0.89	(0.84 – 0.95)
Obese (≥30)	0.99	(0.91 – 1.07)	1.00	(0.91 – 1.10)
Surgery delay (hours)				
<24	Ref.		Ref.	
24-48	1.08	(1.03 – 1.13)	1.07	(1.01 – 1.13)
>48 hours	1.05	(0.97 – 1.14)	1.07	(0.97 – 1.18)
Operation type				
Osteosynthesis	Ref.		Ref.	
Total/hemi arthroplasty	1.09	(1.05 – 1.14)	1.09	(1.04 – 1.15)
Hospital contextual effects				
ICC hospital (%)			8.4%	(3.8 – 12.4)
MRR			1.46	(1.29 - 1.60)
AUC	0.613	(0.605 – 0.622)	0.648	(0.640 – 0.657)
Change in AUC			0.045	

CCI=Charlson Comorbidity Index, ICC= Intra Class Correlation Coefficient, AUC= Area under the receiver operating characteristic curve, MRR=Median Risk Ratio

Supplementary table 7: *Risk of hospital-treated infection during primary hospitalisation and in of all 30-day infection detected during primary hospitalisation*

	No. Of patients	% 30-day infection (95% - CI)		% hospital infection during primary hospitalization (95% - CI)		% 30-day infection during primary hospitalization
Total	29598	15.3	(14.9-15.7)	11.1	(11.1-11.9)	74.8
Hospitals						
Aabenraa	1371	11.9	(10.3-13.7)	8.1	(6.8-9.7)	68.1
Aalborg	1626	12.9	(11.3-14.6)	10.6	(9.2-12.2)	82.3
Aarhus	1386	22.2	(20.1-24.5)	18.3	(16.4-20.5)	82.1
Bispebjerg	1623	24.3	(22.3-26.4)	19.3	(17.5-21.3)	79.7
Bornholm	269	8.2	(5.4-12.1)	4.1	(2.3-7.3)	50.0
Esbjerg	1053	10.5	(8.7-12.4)	7.1	(5.7-8.8)	67.3
Farsø	244	13.1	(9.4-18.0)	9.8	(6.7-14.3)	75.0
Herlev	2207	16.2	(14.7-17.8)	12.8	(11.4-14.2)	78.2
Hjørring	1114	13.0	(11.2-15.1)	10.0	(8.3-11.9)	76.6
Holbæk	1001	11.4	(9.6-13.5)	7.0	(5.6-8.8)	61.4
Holstebro	1669	11.2	(9.8-12.8)	8.5	(7.2-9.9)	75.9
Horsens	972	10.1	(8.3-12.1)	6.3	(5.0-8.1)	63.3
Hvidovre	2029	26.6	(24.7-28.5)	22.3	(20.5-24.1)	83.3
Kolding	1405	18.0	(15.1-19.1)	13.6	(11.9-15.5)	79.5
Køge	1365	18.8	(16.8-21.0)	14.6	(12.8-16.6)	77.0
Nordsjælland	1805	12.9	(11.4-14.5)	8.9	(7.6-10.3)	68.2
Nykøbing Falster	1203	21.9	(19.6-24.3)	17.5	(15.4-19.7)	79.9
Odense	2823	10.3	(9.2-11.4)	6.5	(5.6-7.5)	62.4
Randers	1211	8.9	(7.4-10.7)	4.7	(3.6-6.1)	52.8
Slagelse	1314	20.9	(18.7-23.1)	16.7	(14.8-18.9)	80.3
Thy	497	9.5	(7.1-12.4)	5.6	(3.9-8.0)	59.6
Vejle	295	9.2	(6.3-13.0)	5.4	(3.3-8.7)	59.3
Viborg	1116	10.3	(8.7-12.2)	5.9	(4.7-7.5)	56.5

Supplementary table 9: *Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for community-acquired infection with 30 day follow up from discharge (95% CI). Patients died during hospitalisation are excluded.*

	Community-acquired infection – Model 1		Community-acquired infection – Model 2	
Individual Variables	RR	(95% CI)	RR	(95% CI)
Sex				
Female	Ref.		Ref.	
Male	1.02	(0.97 – 1.07)	1.02	(0.97 – 1.09)
Age				
65-79	Ref.		Ref.	
80-89	1.31	(1.24 – 1.38)	1.31	(1.24 – 1.39)
>89	1.55	(1.46 – 1.64)	1.55	(1.45 – 1.67)
Comorbidity (CCI)				
No comorbidity (0 point)	Ref.		Ref.	
Low comorbidity (1-2 points)	1.21	(1.15 – 1.28)	1.21	(1.14 – 1.28)
High comorbidity (>3points)	1.36	(1.28 – 1.44)	1.35	(1.26 – 1.44)
Body Mass index (BMI)				
Underweight (<18.5)	1.03	(0.96 – 1.09)	1.03	(0.95 – 1.11)
Normal (18.5-24.9)	Ref.		Ref.	
Overweight (25-29.9)	1.03	(0.98 – 1.08)	1.03	(0.97 – 1.10)
Obese (≥30)	1.21	(1.12 – 1.31)	1.21	(1.11 – 1.33)
Surgery delay (hours)				
<24	Ref.		Ref.	
24-48	1.00	(0.95 – 1.05)	1.02	(0.96 – 1.08)
>48 hours	1.03	(0.94 – 1.13)	1.06	(0.95 – 1.19)
Operation type				
Osteosynthesis	Ref.		Ref.	
Total/hemi arthroplasty	0.96	(0.92 – 1.00)	0.96	(0.91 – 1.01)
Hospital contextual effects				
ICC hospital (%)			7.3%	(3.3 - 12.1)
MRR			1.28	(1.45 – 1.16)
AUC	0.575	(0.567 – 0.583)	0.592	(0.584 – 0.600)
Change in AUC			0.017	

CCI=Charlson Comorbidity Index, ICC= Intra Class Coefficient, AUC= Area under the receiver operating characteristic curve, MRR=Median Risk Ratio, RR=Relative Risk, CI=Confidence Interval.

Supplementary table 8: *Single level Poisson regression (model 1) and multilevel Poisson regression (model 2), for any hospital-treated infection and community-acquired infections as a combined outcome (95% CI).*

	Infection – Model 1		Infection – Model 2	
Individual Variables	RR	(95% CI)	RR	(95% CI)
Sex				
Female	Ref.		Ref.	
Male	1.13	(1.09 – 1.17)	1.14	(1.09 – 1.20)
Age				
65-79	Ref.		Ref.	
80-89	1.30	(1.25 – 1.35)	1.31	(1.25 – 1.37)
>89	1.47	(1.41 – 1.53)	1.47	(1.39 – 1.55)
Comorbidity (CCI)				
No comorbidity (0 point)	Ref.		Ref.	
Low comorbidity (1-2 points)	1.22	(1.18 – 1.27)	1.21	(1.15 – 1.26)
High comorbidity (>3points)	1.39	(1.33 – 1.44)	1.35	(1.29 – 1.43)
Body Mass index (BMI)				
Underweight (<18.5)	1.04	(0.99 – 1.09)	1.04	(0.98 – 1.10)
Normal (18.5-24.9)	Ref.		Ref.	
Overweight (25-29.9)	1.01	(0.98 – 1.05)	1.02	(0.97 – 1.07)
Obese (≥30)	1.11	(1.05 – 1.18)	1.13	(1.05 – 1.21)
Surgery delay (hours)				
<24	Ref.		Ref.	
24-48	1.03	(1.00 – 1.07)	1.04	(0.99 – 1.09)
>48 hours	1.04	(0.97 – 1.11)	1.07	(0.99 – 1.16)
Operation type				
Osteosynthesis	Ref.		Ref.	
Total/hemi arthroplasty	1.02	(0.99 – 1.05)	1.02	(0.98 – 1.06)
General contextual effects				
ICC hospital (%)			10.9%	(4.1 – 16.2)
MRR			1.32	(1.41 – 1.19)
AUC	0.606	(0.597 – 0.614)	0.643	(0.635 – 0.652)
Change in AUC			0.037	

CCI=Charlson Comorbidity Index, ICC= Intra Class Coefficient, AUC= Area under the receiver operating characteristic curve, MRR=Median Risk Ratio, RR=Relative Risk, CI=Confidence Interval.

***Supplementary table 10**: Risk of community-acquired infection with 30 day follow up from discharge. Patients died during hospitalisation are excluded.*

	No. Of patients	% Community-acquired infection (95% - CI)	
Total	27982	25.4	(24.9 – 25.9)
Hospitals			
Aabenraa	1315	29.9	(27.5 – 32.4)
Aalborg	1519	18.6	(16.7 – 20.6)
Aarhus	1333	26.3	(24.0 – 28.8)
Bispebjerg	1519	31.4	(29.1 – 33.8)
Bornholm	251	25.5	(20.5 – 31.3)
Esbjerg	998	21.2	(18.8 – 23.9)
Farsø	232	16.4	(12.1 – 21.7)
Herlev	2060	26.5	(24.6 – 28.4)
Hjørring	1059	23.8	(21.3 – 26.5)
Holbæk	949	20.2	(17.8 – 22.9)
Holstebro	1610	29.6	(27.4 – 31.8)
Horsens	930	22.8	(20.2 – 25.6)
Hvidovre	1868	30.5	(28.4 – 32.6)
Kolding	1327	25.1	(22.8 – 27.5)
Køge	1272	23.7	(21.5 – 26.2)
Nordsjælland	1711	25.5	(23.5 – 27.7)
Nykøbing Falster	1128	22.2	(19.8 – 24.7)
Odense	2666	25.6	(24.0 – 27.3)
Randers	1160	27.3	(24.8 – 30.0)
Slagelse	1244	23.3	(21.0 – 25.7)
Thy	478	24.7	(21.0 – 28.8)
Vejle	283	23.3	(18.7 – 28.6)
Viborg	1070	23.7	(21.3 – 26.4)

***Supplementary table 11:** Patient characteristics stratified in Danish regions*

	Denmark		Capital		Zealand		Southern		Central		Northern	
Gender	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**
Female	69.4	(20554)	71.6	(5677)	69.3	(3384)	68.4	(4752)	68.6	(4357)	68.5	(2384)
Male	30.6	(9044)	28.4	(2256)	30.7	(1499)	31.6	(2195)	31.4	(1997)	31.5	(1097)
Age (years)												
65-79	37.3	(11046)	37.3	(2961)	40.2	(1964)	36.8	(2557)	37.0	(2348)	34.9	(1216)
80-89	42.4	(12548)	41.5	(3288)	40.6	(1980)	43.8	(3044)	42.4	(2699)	44.2	(1537)
>89	20.3	(6004)	21.2	(1684)	19.2	(939)	19.4	(1346)	20.6	(1307)	20.9	(728)
Comorbidity (CCI)												
No comorbidity (0 point)	37.5	(11112)	34.8	(2758)	36.2	(1768)	37.1	(2578)	40.0	(2539)	42.2	(1469)
Low comorbidity (1-2 points)	39.8	(11778)	41	(3256)	40.3	(1967)	40.0	(2781)	38.0	(2417)	39.0	(1357)
High comorbidity (>3points)	22.7	(6708)	24.2	(1919)	23.5	(1148)	22.9	(1588)	22.0	(1398)	18.8	(655)
Body Mass index (BMI)												
Underweight (<18.5)	13.2	(3917)	12.4	(983)	11.8	(574)	13.2	(918)	16.5	(1049)	11.3	(393)
Normal (18.5-24.9)	40.7	(12052)	36.9	(2929)	40.1	(1959)	40.6	(2821)	46.4	(2951)	40.0	(1392)
Overweight (25-29.9)	22.4	(6623)	18.1	(1432)	23.1	(1128)	25.6	(1780)	22.6	(1435)	24.4	(848)
Obese (≥30)	6.8	(2004)	4.7	(376)	7.3	(357)	7.9	(544)	7.7	(487)	6.9	(240)
Missing	16.9	(5002)	27.9	(2219)	17.7	(865)	12.7	(884)	6.8	(430)	17.5	(608)
Surgery delay (hours)												
<24	68.9	(20406)	66.7	(5293)	67.9	(3318)	71.2	(4949)	76.0	(4831)	57.9	(2015)
24-48	24.7	(7310)	27.5	(2178)	24.4	(1190)	21.6	(1502)	20.5	(1303)	32.7	(1137)
>48 hours	6.4	(1882)	5.8	(462)	7.7	(375)	7.2	(496)	3.5	(220)	9.4	(329)
Surgery type												
Osteosynthesis	64.4	(19073)	63.9	(5068)	64.8	(3165)	64.0	(4449)	65.6	(4169)	63.8	(2222)
Total/hemi arthroplasty	35.6	(10525)	36.1	(2865)	35.2	(1718)	36.0	(2498)	34.4	(2185)	36.2	(1259)

Supplementary table 12: *30-day mortality among infected patients. Follow up from day of infection diagnose*

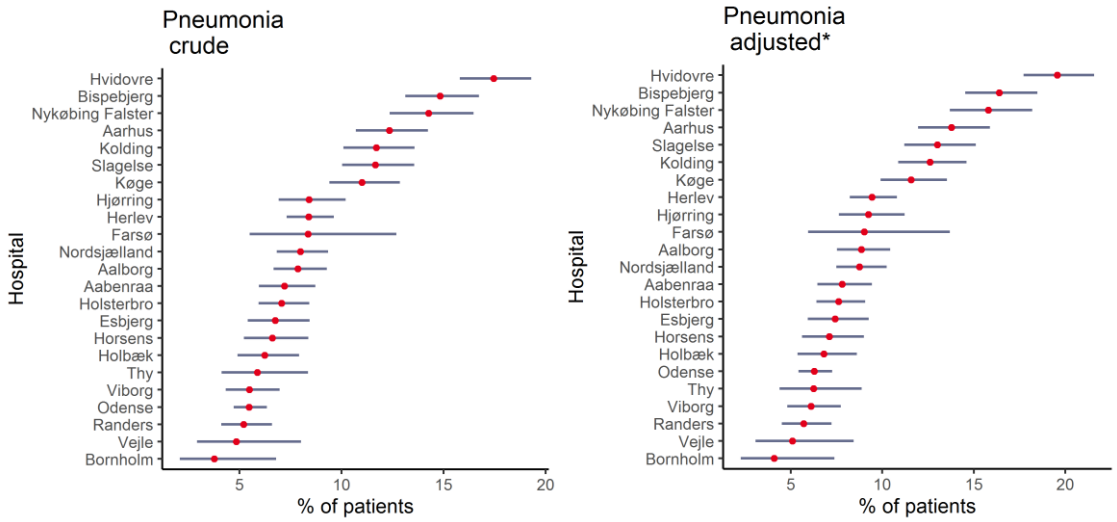
	No. Of patients	% any-infection (n)		% mortality among all patients (n)		% mortality among infected patients (n)	
Total	29598	15.3	(4532)	10.3	(3041)	20.3	(918)
Hospitals							
Aabenraa	1371	11.9	(163)	10.0	(107)	20.2	(33)
Aalborg	1626	12.9	(209)	12.9	(144)	23.0	(48)
Aarhus	1386	22.2	(308)	8.2	(191)	15.9	(49)
Bispebjerg	1623	24.3	(394)	10.0	(266)	19.0	(75)
Bornholm	269	8.2	(22)	11.5	(11)	22.7	(5)
Esbjerg	1053	10.5	(110)	9.0	(78)	20.9	(23)
Farsø	244	13.1	(32)	7.8	(22)	34.4	(11)
Herlev	2207	16.2	(358)	10.6	(208)	17.3	(62)
Hjørring	1114	13.0	(145)	10.5	(103)	23.5	(34)
Holbæk	1001	11.4	(114)	9.5	(68)	16.7	(19)
Holstebro	1669	11.2	(187)	10.2	(127)	19.3	(36)
Horsens	972	10.1	(98)	8.4	(69)	17.3	(17)
Hvidovre	2029	26.6	(539)	10.7	(397)	18.9	(102)
Kolding	1405	18.0	(239)	10.8	(177)	18.4	(44)
Køge	1365	18.8	(257)	10.1	(158)	18.7	(48)
Nordsjælland	1805	12.9	(233)	9.8	(158)	25.3	(59)
Nykøbing Falster	1203	21.9	(263)	12.1	(190)	22.1	(58)
Odense	2823	10.3	(290)	10.3	(177)	23.1	(67)
Randers	1211	8.92	(108)	10.7	(69)	29.6	(32)
Slagelse	1314	20.9	(274)	9.9	(171)	20.8	(57)
Thy	497	9.5	(47)	10.7	(31)	19.2	(9)
Vejle	295	9.2	(27)	8.5	(15)	.	(<5)
Viborg	1116	10.3	(115)	10.7	(68)	23.5	(27)

Supplementary table 13: *30-day mortality among infected patients. Follow up from day of infection diagnose*

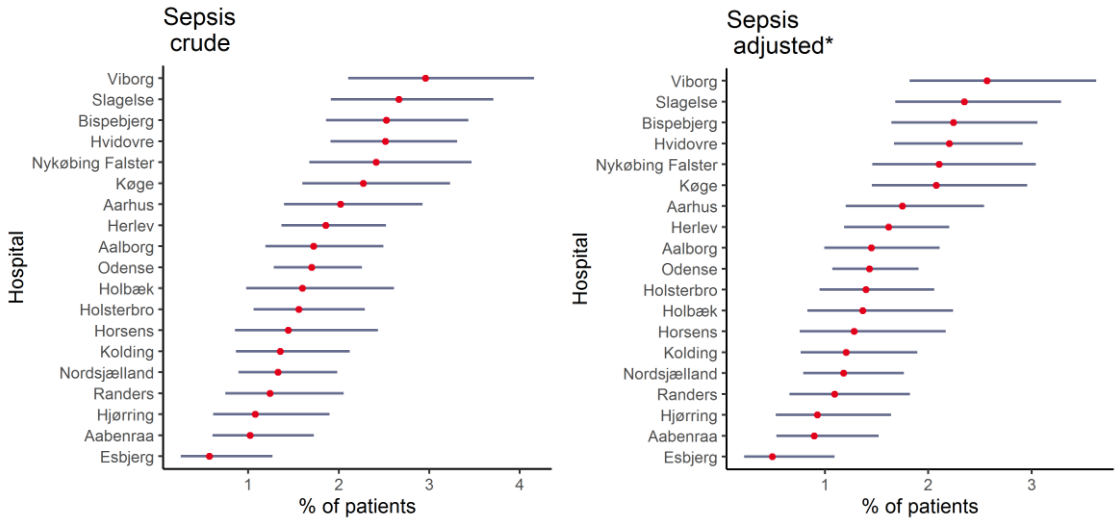
Study	Study design	Intervention	Results
Chang et. al.[55]	Quasi-experimental study with 240 hip fracture patients.	Pulmonary rehabilitation program, including deep breathing exercises/incentive spirometry, chest physiotherapy and cough-assisted maneuvers such as oscillaroty techniques	Intervention group: 5.9% pneumonia. Control group: 13.9% pneumonia.
Lawrence et. Al.[62]	Systematic review of non-cardiothoracic surgery.	*Review*	Postoperative lung expansion therapy, for example incentive spirometry, deep breathing exercises and continuous positive airway pressure reduces postoperative pneumonia.
Wren et. Al.[63]	Retrospective cohort study of noncardiac surgical patients.	Education of physicians and ward staff and a standardized postoperative electronic order set consisting of incentive spirometer, chlorhexidine oral hygiene, ambulation, and head-of-bed elevation. Quarterly staff meetings discussed the results of and compliance with the program.	The pneumonia risk decreased from 0.78 in preintervention time period to 0.18% in postintervention time period.
Kazaure et. Al.[54]	Retrospective cohort study of noncardiac surgical patients.	Same as above	The pneumonia risk decreased from 0.78 in preintervention time period to 0.44% in postintervention time period.
Cassidy et. al.[64]	A before-after trial with vascular and general surgical patients.	Incentive spirometry, coughing and deep breathing, oral care, patient and family education, ambulation and head-of bed elevation.	The incidence of postoperative pneumonia reduced to 1.6% from 2.6% after intervention.

Supplementary figures

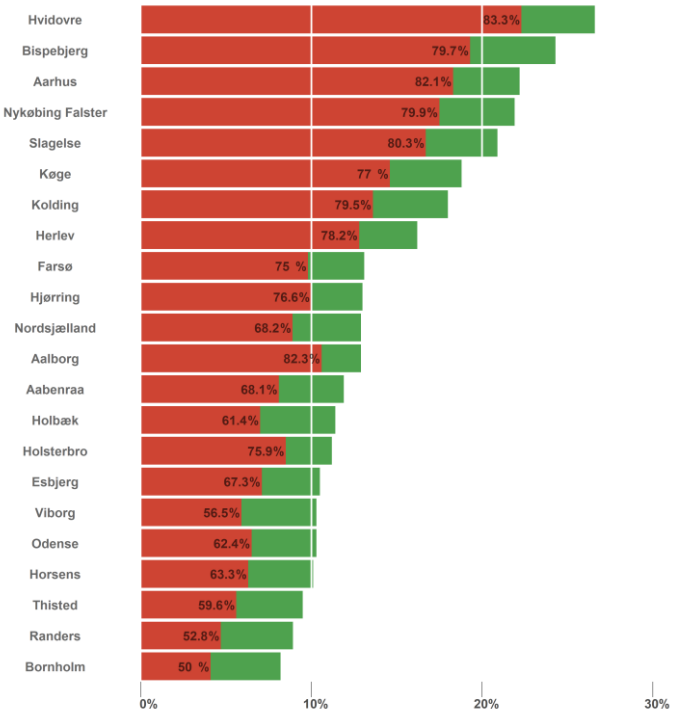
Supplementary figure 1: *League tables ranking hospitals for pneumonia.*
** Sex, age, comorbidity, BMI, surgery delay and operation type*



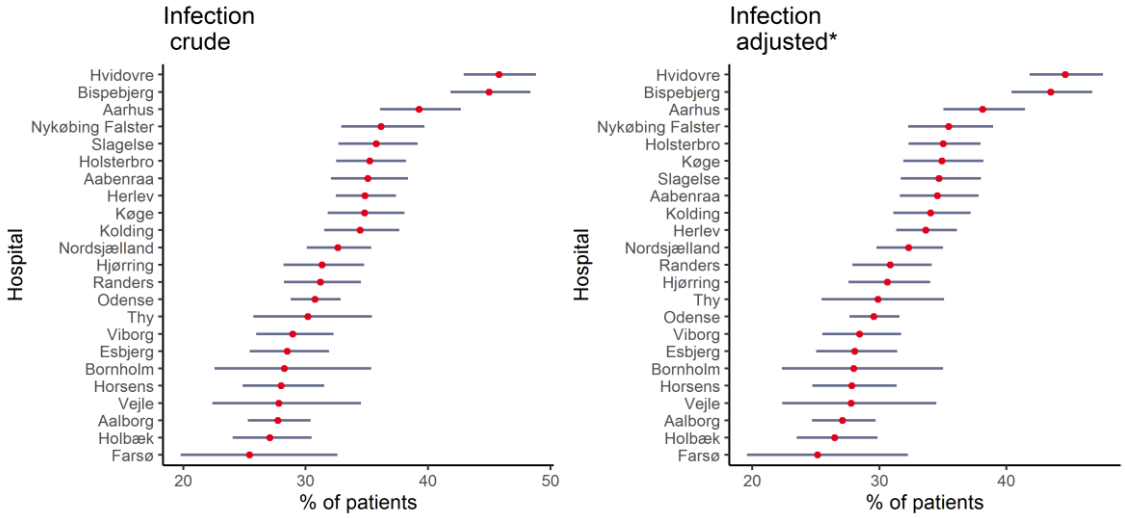
Supplementary figure 2: *League tables ranking hospitals for sepsis, excluding hospitals < 5 infections.*
** Sex, age, comorbidity, BMI, surgery delay and operation type*



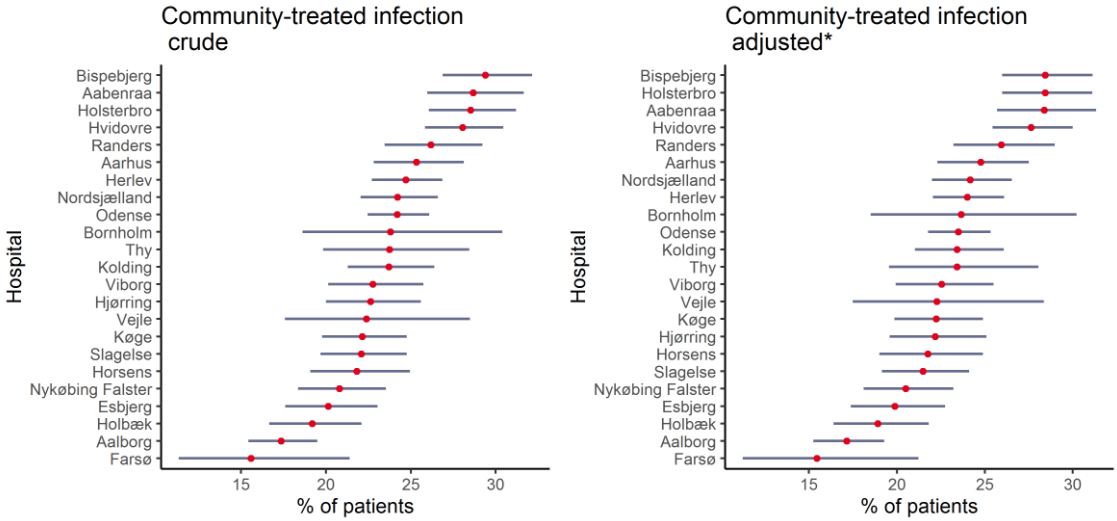
Supplementary figure 3: *Risk of infection detected during primary hospitalization (red). Risk of all infections (red + green). Percent of infections detected during primary hospitalization.*



Supplementary figure 4: *League tables ranking hospitals for hospital-treated and community-acquired infection as combined outcome.*
** Sex, age, comorbidity, BMI, surgery delay and operation type*



Supplementary figure 5: *League tables ranking hospitals for community-acquired infection with follow-up from discharge.*
** Sex, age, comorbidity, BMI, surgery delay and operation type*



Supplementary figure 6: *Infection incidence (green) and mortality (red) across hospitals. Adjusted for sex, age, comorbidity, BMI, operation delay and operation type.*