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Impact of individual and perioperative factors in colorectal surgical site infections in Portugal

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Declaro que colaborei em todos os momentos dos trabalhos que compõem a presente tese, desde o desenho dos estudos e definição de objetivos até à análise estatística e interpretação dos dados. Redigi as versões iniciais de todos os artigos e participei ativamente na elaboração das suas versões finais.

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Background

Disease is a product of its context, whether historical, geographical or philosophical. It occurs in a particular time and space. The advances in health and science in the last two centuries have shifted mortality and disease patterns, in a process now known as the epidemiological transition. The dramatic decrease in the incidence rate and severity of infectious diseases and severity have led healthcare-associated infections to become centrally relevant to the quality of health services and the manner in which we, as a society, provide and protect health.

Healthcare-associated infections – infections arising in any patient after 48 hours of hospitalization and within 30 days after receiving care, or 90 days following certain surgical procedures – are the most frequent adverse events during healthcare delivery. They are associated with prolonged length of stay and a higher risk of death, within 30 days and one year, a burden which is more severe in high-risk populations such as patients admitted to intensive care units. They also pose a relevant direct economic burden, most of which has been deemed preventable through effective infection control programs. Nonetheless, healthcare-associated infections are heterogeneous, and ought to be considered separately. Among the commonest of these infections, surgical site infections are the costliest, the most frequent in surgical patients and are, most likely, underreported. Although they may affect any body part in which a surgery takes place, it is more frequent, more severe and has different causal organisms following colorectal surgery. This is particularly relevant in the Portuguese context. Although Portugal compares favorably to other European countries in most healthcare-associated infections, it is one of the worst performing countries both for laparoscopic and open colorectal surgery. Furthermore, there has been no improvement in surgical site infection incidence in this surgical group in the last decade, suggesting that something in the Portuguese context of colorectal surgery needs optimization.

Many risk factors have been associated with surgical site infection following colorectal surgery, including modifiable – those we may act upon acutely to improve outcomes – and non-modifiable – those we may act upon only in the longest run, often through transversal interventions. The former are relevant as optimal targets for public health interventions, to decrease the burden of this problem effectively and efficiently, whereas the latter are relevant to establish a baseline ratio that may serve as a reference for the optimal incidence rate one aims to achieve. Male sex, obesity, diabetes mellitus, American Society of Anesthesiologists classification above 3, urgent procedure, inflammatory bowel disease and wound classification superior to 2 have been summarized in a recent systematic review as non-modifiable risk factors, whereas cigarette smoking, operative time superior to 180 minutes, open surgery, stoma creation and blood transfusion have been summarized as modifiable risk factors, thus increasing the risk of surgical site infection in this particular surgery group. However, this is a simplification, since the risk of infection depends on many more (potential)

factors other than the patient and procedure-related risk factors enumerated above. In particular, research at the hospital level has been scarce and inconsistent where, to the best of our knowledge, no systematic review had been published. Also, available research appears to be of suboptimal quality. Colorectal surgery is performed in hospitals. People with similar overall characteristics who are subjected to surgery in different hospitals may have different health outcomes due to each hospital's context. Epistemologically, epidemiology of surgical site infections is multilevel and needs to consider both people and areas, with adequate statistical techniques. Finally, although risk factors are universal, their prevalence is not. To understand how to improve incidence rates, one needs to estimate the impact known risk factors have on surgical site infection. The highest the impact, the more that factor contributes to the current incidence level; health interventions should focus on risk factors with highest impact, so to decrease infection rate with optimal efficiency and effectiveness.

Other factors are better referred to as prevention strategies, even if the line separating them from the above may be thin. Prevention strategies include two general types: universal precautions, consisting of general measures aimed at decreasing the risk of any infection; and specific strategies, targeted towards surgical site infection. The most researched universal precaution is hand hygiene, whereas specific measures are usually bundled together to provide a synergic effect in the improvement of patient outcomes. Despite the heterogeneity of bundles implemented and researched throughout the world, they have been found to effectively decrease surgical site infection incidence in colorectal surgery, more so when all interventions included have solid evidence behind them. Surveillance – the process of ongoing and systematic collection, analysis and interpretation of health data – is also key in decreasing incidence rates. Its utility, however, depends critically on its quality. Consistency, sensitivity, and specificity are optimized through adequate case definitions, and comparability ensured when the same criteria is used similarly between hospitals. One key characteristic of optimal surveillance is representativeness, to ensure results are generalizable and provide a trustworthy image of the real phenomenon. Another key characteristic is timeliness, as feedback needs to occur in a time window that allows surgeons and preventionists to adapt interventions.

This thesis aims to understand the impact that risk factors and context have on the incidence of surgical site infection after colorectal surgery, in Portugal, to pinpoint targets for future health interventions. The following paragraphs shall describe the specific objectives of this work, along with the corresponding research that was conducted to answer each one.

1. *To review the available evidence on the association between healthcare-related characteristics and surgical site infection after colorectal surgery.*

A systematic literature search was conducted using PubMed, Scopus and Web of Science databases. The primary outcome of interest was surgical site infection after colorectal surgery. Studies were grouped into nine risk factors typologies: hospital size, ownership, affiliation, being an oncological hospital, safety-net burden, hospital volume, surgeon caseload, discharge destination and time since implementation of surveillance. A total of 4 703 records were identified and screened, of which 172 were reviewed and 16 included. Surgical site infection incidence ranged from 3.2 to 27.6%. Two out of five studies evaluating hospital size adjusted the analysis to individual and procedural risk factors and showed that larger hospitals were either positively associated or had no association with surgical site infection. Public hospitals did not present significantly different infection rates than private or non-profit ones. Hospital caseload showed mixed results. The heterogeneity of risk factors evaluated, methods and criteria did not allow a meta-analysis to be performed. Although few studies addressing hospital-level factors on surgical site infection following colorectal surgery were found, surgeon experience and the implementation of a surveillance system appear to be associated with better outcomes. Nonetheless, for hospitals and services to be efficiently optimized, more research addressing these variables is needed.

2. *To assess whether surgical site infection after colorectal surgery varies between hospitals, and what part of that variance may be due to contextual effects.*

Data were retrieved from the electronic platform of the Directorate General of Health, from 2015 to 2019. Eight individual and procedural characteristics were included as level-1 variables, all of them previously documented as risk factors for surgical site infection after colorectal surgery: age, gender, the American Society of Anesthesiologists Classification, wound classification, duration of surgery in minutes, absence of antibiotic prophylaxis, urgent operations and open surgery. Hospital characteristics were retrieved from publicly available data on the Portuguese public administration. These were included as level-2 variables: hospital group based on the case-mix index, previous participation in a quality improvement programme, being a reference centre for rectal cancer, nurse-to-bed ratio, occupancy rate and the geographical region of the hospital. Analysis considered a two-level hierarchical data structure, with individuals clustered in hospitals. To avoid overfitting, no models were built with more than one hospital characteristic. Cluster-level associations were presented through median odds ratio and intraclass cluster coefficient. Beta coefficients were used to assess contextual effects. A total of 11 219 procedures from 18 hospitals were included. Incidence of infection was 16.8%. The intraclass cluster coefficient for the null model was 0.09. Procedural variables explained 25% of variance, and hospital group (hospital dimension) explained another 17%. More than 50% of infection variance remained unaccounted for. After adjustment, heterogeneity between hospitals was still found, with a median odds ratio of 1.51, meaning that when a patient in a hospital with higher incidence rate is compared with a similar patient in a hospital with the same dimension, but with lower incidence rate, it has 1.50 times the risk of having an infection than the latter. After adjusting, it still makes a difference where surgery takes place. Therefore, procedural variables and hospital dimension should be taken into account when implementing prevention strategies. Future research should focus on compliance with preventive bundles and other process indicators in hospitals with significantly less surgical site infection in colorectal surgery.

3. *To estimate the representativeness of reported surgical site infection incidence by comparing the National Epidemiological Surveillance database with the gold-standard national database.*

The distribution of procedures whose data was collected for surveillance, retrieved from the database of the Directorate General of Health, was compared with all procedures performed in the country, available upon request *to Administração Central do Sistema de Saúde*. The analysis included procedures performed in public hospitals between 2015 and 2020. Representativeness was assessed per year, by including hospitals reporting at least 30 procedures for that given year, following European guidelines. The comparison considered demographic (sex and age), procedural (laparoscopic and urgent) and hospital (hospital group) risk factors. To avoid a large sample size fallacy, the effect size was used to compare datasets, presented in Cramer's V. Effect size is considered small between 0.1 and 0.3, medium between 0.3 and 0.5, and large above 0.5. Effect sizes were negligible for sex, age and open surgery. There was a small effect size in urgent procedures, both per year (V between 0.09 and 0.16) and for the entire period (V=0.14), as well as in hospital type, with V between 0.16 and 0.20, thus suggesting a small non-negligible bias in the surveillance database. Therefore, this database needs to be optimized to include more urgent procedures and hospitals that may better reflect the distribution of the hospital network in the country.

3.1 *To determine whether a classification model, using electronically available data, could improve the efficiency, completeness and representativeness of surveillance.*

Colorectal surgeries performed in a tertiary Portuguese hospital, between 2016 and 2018, were selected. Post-surgical antibiotic use, positive culture, C-reactive protein values, body temperature, leukocyte count, surgical re-intervention, admission to the emergency room and hospital readmission were retrieved. For representativeness, procedures subjected to surveillance were compared with procedures not included in surveillance. The capacity of each variable to divide procedures in high-risk and low-risk, where low-risk procedures are considered automatically as having no infection and high-risk are manually reviewed, considered the presence of surgical site infection as the gold standard. Sensitivity, specificity, positive and negative predictive values were estimated, with their respective 95% confidence intervals. The proportion of procedures flagged for manual review by each criterion was estimated. Little more than 50% of procedures were subjected to surveillance. Non-included procedures showed higher proportions of infection marks. Antibiotic use presented one of the highest sensitivities (89%) in colorectal surgery, the highest positive predictive value (22%) and flagged fewer procedures for manual review (48%). Surveillance at the hospital level has major limitations, underestimating the real incidence of infection. Antibiotic use appears to be the best criterion to select a sub-sample of procedures for manual review, improving the exhaustiveness and efficiency of the system.

4. *To estimate the impact of risk factors for SSI after colorectal surgery in SSI incidence in Portugal, using the population attributable fraction approach.*

Patients undergoing colorectal surgery in hospitals that reported colorectal surgeries every year between 2015 and 2019 were included. Among 42 reporting hospitals, 18 complied with the criteria, corresponding to 11 219 procedures. Risk factor prevalence was estimated using the surveillance database from the Directorate General of Health, which follows the methodology recommended by the European Centre for Disease Prevention and Control. American Society of Anesthesiologists classification, wound classification, open surgery, urgent operation, antibiotic prophylaxis, operation duration and male sex were included as risk factors. Measures of association were retrieved from published meta-analyses. Population attributable fractions were calculated using the Levin formula. To account for interaction between risk factors, communality of risk factors was used in a weighted-sum approach, providing a combined value that serves as a measure of the comprehensiveness of surveillance. The cumulative incidence of infection was 16.8%. The proportion of infection attributed to all risk factors was 61%. Modifiable variables accounted for 31% of procedures – the highest was laparotomy (17%) and the lowest was urgent operations (3%). Non-modifiable factors accounted for 29%, the highest being wound classification (14%). Therefore, a relevant proportion of infection remains unaccounted for by current surveillance indicators. Interventions focusing on shorter, less-invasive procedures may be optimally effective in reducing SSI incidence.

Conclusion

By considering that this is a modern health problem, this thesis helps to build the notion that future research and project implementation should take into account the setting in which it is being performed. Although hospital characteristics have seldom been researched in this scope and no single characteristic was significantly associated with infection in paper II, it was found that it still makes a difference in which hospital the surgery takes place, even after adjusting for major patient and perioperative risk factors. The review of literature suggests that surveillance appears to be associated with lower incidence rates; however, it is of suboptimal quality both at the local and central settings, as it fails to include a substantial proportion of urgent procedures, likely underreporting true incidence rates. The use of semi-automated methods, namely using postoperative antibiotic use in a classification model, was shown to improve efficiency, completeness and representativeness of surveillance by decreasing workload and focusing review on high-risk procedures. Current surveillance data explains approximately 60% of incidence rates, underlining the need to continue to research and understand the role other risk factors may pose on this infection.

Finally, this thesis elaborates on the most effective solutions that may be adopted in the short term, as the promotion and implementation of shorter, laparoscopic procedures, whenever possible, was found to be the most effective strategy to decrease the incidence of surgical site infection after colorectal surgery.

Introdução

A doença é um produto do seu contexto – histórico, geográfico ou filosófico. Ocorre num tempo e num espaço específicos. Os avanços na saúde e na ciência nos últimos dois séculos alteraram radicalmente os padrões de mortalidade e morbilidade, num processo conhecido como transição epidemiológica. A redução marcada na gravidade e na incidência de doenças infeciosas levaram a que as infeções associadas aos cuidados de saúde se tornassem centrais para a qualidade dos serviços de saúde e para a forma como nós, enquanto sociedade, fornecemos, promovemos e protegemos a saúde.

As infeções associadas aos cuidados de saúde – infeções que surgem num doente 48 horas após hospitalização e dentro de 30 dias após cuidados, ou 90 dias no caso de certos procedimentos cirúrgicos – são o evento adverso mais frequente nos cuidados de saúde. Estão associados a um aumento do tempo de internamento e a um aumento da mortalidade, uma carga que é ainda mais grave em populações de alto risco, como é o caso dos doentes admitidos em unidades de cuidados intensivos. Estas infeções também têm um peso económico relevante, a maior pate do qual foi considerado evitável através de programas de controlo de infeção efetivos. No entanto, as infeções associadas aos cuidados de saúde são heterogéneas, e devem ser consideradas separadamente. Dentro das mais comuns, a infeção do local cirúrgico é a mais cara, a mais frequente em doentes cirúrgicos e, para mais, subestimada. Ainda que possa afetar qualquer parte do corpo submetida a cirurgia, ela é mais frequente, mais grave e tem diferentes organismos causais após a cirurgia de colon e reto. Isto é particularmente relevante no contexto português. Apesar de Portugal se comparar favoravelmente com outros países europeus na maioria das infeções associadas aos cuidados de saúde, é um dos piores países no caso da infeção de local cirúrgico após cirurgia colo-retal, tanto no caso de laparotomia como laparoscopia. Além disso, a incidência desta infeção tem-se mantido constante na última década, sugerindo que algo no contexto nacional requer otimização.

Muitos fatores de risco foram associados a infeção do local cirúrgico após cirurgia colo-rectal, incluindo modificáveis – aqueles que podemos atuar a curto prazo para melhorar resultados em saúde – e não-modificáveis – aqueles que podemos atuar apenas a longo prazo, através de intervenções transversais. Os primeiros são alvos ótimos para intervenções em saúde que sejam efetivas e eficientes, ao passo que os segundos são relevantes para estabelecer uma referência da incidência ideal que desejamos alcançar. Sexo masculino, obesidade, diabetes, classificação da Sociedade Americana de Anestesiologistas, procedimentos urgentes, doença inflamatória intestinal e classificação da ferida foram sumariados numa revisão sistemática recente como fatores de risco não-modificáveis, enquanto o tabagismo, tempo de cirurgia, laparotomia, abertura de estoma e transfusão sanguínea foram descritos como fatores modificáveis. Contudo, isto é uma simplificação do verdadeiro risco, que depende de muitos mais fatores potenciais. Em particular, a investigação de características hospitalares tem sido parca e inconsistente, e nenhuma revisão sobre o assunto foi publicada. Além disso, os artigos publicados parecem ser de qualidade subótima. A cirurgia colo-retal é realizada em hospitais. Pessoas com características semelhantes que sejam submetidas a cirurgia em diferentes hospitais podem ter diferentes resultados em saúde, devido ao contexto hospitalar. Epistemologicamente, a epidemiologia da infeção do local cirúrgico é multinível e tem que considerar tanto as pessoas como os locais, com a estatística adequada. Finalmente, apesar dos fatores de risco serem universais, a sua prevalência é variável conforme o local. Para compreender como melhorar a incidência, é preciso conhecer o impacto que cada fator de risco tem nesta infeção. Quanto maior o impacto, maior a sua contribuição para a incidência atual. As intervenções em saúde devem focar-se nos fatores de risco com maior impacto, para que a redução da incidência seja feita com eficiência e efetividade ótimas.

Outros fatores são referidos como estratégias de prevenção, ainda que a linha que os separe dos demais seja fina. Estas estratégias incluem dois tipos: precauções universais, que consistem em medidas gerais para diminuir o risco de qualquer infeção; e estratégias específicas, dirigidas para a infeção de local cirúrgico. A precaução universal mais estudada é a higiene das mãos, ao passo que as medidas específicas são normalmente aglutinadas num feixe de prevenção, com um efeito sinérgico para melhorar os resultados em saúde dos doentes. Apesar da heterogeneidade dos feixes implementados pelo globo, foi demonstrado que eles são efetivos a diminuir a incidência de infeção de local cirúrgico na cirurgia colo-rectal, especialmente quando as intervenções incluídas têm evidência sólida. A vigilância – o processo contínuo e sistemático de coleção, análise e interpretação de dados de saúde – é também chave para diminuir a incidência. A consistência, sensibilidade e especificidade são otimizadas com definições de caso apropriadas, e a comparabilidade é garantida quando os mesmos critérios são utilizados em diferentes locais. Uma característica-chave de uma vigilância ótima é a representatividade, para garantir que os resultados são generalizáveis e que oferecem uma imagem fidedigna do fenómeno em estudo. Outra característica fundamental é ser atempada, já que o feedback deve ocorrer período temporal que permita a cirurgiões e profissionais do controlo de infeção atuar oportunamente.

Esta tese procura compreender o impacto que os fatores de risco e o contexto têm na incidência de infeção de local cirúrgico após cirurgia colo-retal, em Portugal, para identificar alvos de futuras intervenções em saúde. Os próximos parágrafos irão descrever os objetivos específicos deste trabalho, tal como a investigação que foi realizada para responder a cada um deles.

1. *Rever a evidência disponível sobre a associação entre características relacionadas com os cuidados de saúde e infeção de local cirúrgico após cirurgia colo-retal.*

Uma revisão sistemática da literatura foi realizada, utilizando as bases de dados da PubMed, Scopus e Web of Science. O outcome primário foi a infeção de local cirúrgico após cirurgia colo-retal. Estudos foram agrupados em nove tipologias: tamanho hospitalar, propriedade, afiliação, ser hospital oncológico, carga de rede de segurança, volume hospitalar, volume do cirurgião, destino da alta e tempo desde o início da vigilância. Um total de 4 703 entradas foram identificadas, das quais 172 artigos foram revistos e 16 incluídos. Incidência de infeção variou entre 3,2 e 27,6%. Dois de cinco estudos avaliando tamanho hospitalar ajustaram a análise para fatores individuais e da cirurgia, e mostraram que hospitais maiores estavam ou positivamente associados ou não tinham associação com este tipo de infeção. Hospitais públicos não apresentaram incidência significativamente diferente de privados. Volume hospitalar mostrou resultados mistos. A heterogeneidade dos fatores estudados, as metodologias e critérios não permitiram realizar nenhuma meta-análise. Apesar de termos encontrado poucos estudos, a experiência do cirurgião e a implementação de vigilância parecem estar associados a melhores resultados. De qualquer forma, para que hospitais e serviços sejam eficientemente otimizados, é necessária mais investigação neste campo.

2. *Aferir se a infeção de local cirúrgico após cirurgia colo-retal varia entre hospitais, e que parte da variância pode dever-se a efeitos contextuais.*

Dados foram retirados da plataforma eletrónica da Direção-Geral da Saúde, entre 2015 e 2019. Oito características individuais e relacionadas com a cirurgia foram incluídas como variáveis de nível 1, todas elas documentadas como fatores de risco para infeção de local cirúrgico após cirurgia colo-retal: idade, sexo, classificação da Sociedade Americana de Anestesiologia, cirurgias urgentes e laparotomia. As características hospitalares foram retiradas de dados públicos disponíveis em páginas eletrónicas da administração pública portuguesa. Estas foram incluídas como nível 2: grupo hospitalar baseado no índice de complexidade dos doentes, participação prévia num programa de melhoria da qualidade na área do controlo de infeção, ser um centre de referência para o cancro do reto, razão enfermeira-camas, taxa de ocupação das camas e região geográfica do hospital. A análise considerou uma estrutura hierárquica em dois níveis, com indivíduos agrupados em hospitais. Para evitar sobre-ajustamento, nenhum modelo foi construído com mais que uma característica hospitalar. Associações ao nível de cluster foram apresentadas através de odds ratio mediano e coeficiente de cluster intraclasse. Coeficientes beta foram usados para aferir os efeitos contextuais. Um total de 11 219 procedimentos de 18 hospitais foram incluídos. Incidência de infeção foi 16,8%. O coeficiente de cluster intraclasse para o modelo nulo foi 0.09. Variáveis associadas ao procedimento explicaram 25% da variância, e o grupo hospitalar (dimensão hospitalar) explicou mais 17%. Mais de 50% da variância ficaram por explicar. Após o ajustamento, heterogeneidade entre hospitais continuou a existir, com um odds ratio mediano de 1,51, o que significa que quando um doente num hospital com maior risco de infeção é comparado com um doente semelhante num hospital da mesma dimensão, mas com menor incidência, tem 1,5 vezes o risco de infeção do que o último. Após o ajuste, continua a fazer diferença onde é realizada a cirurgia. Desta forma, as variáveis individuais e da cirurgia e a dimensão hospitalar devem ser consideradas quando são implementadas estratégias de prevenção. Investigação futura deverá focar-se na adesão aos feixes de prevenção e outros indicadores de processo nos hospitais com menor incidência de infeção de local cirúrgico na cirurgia colo-retal.

3. *Estimar a representatividade da incidência de infeção de local cirúrgico reportada, comparando a base de dados da vigilância epidemiológica nacional com a base de dados de referência nacional.*

A distribuição dos procedimentos cujos dados forem recolhidos para vigilância, retirados da base de dados da Direção-Geral da Saúde, foi compara com todos os procedimentos cirúrgicos colo-retais realizados no país, disponível a pedido na Administração Central do Sistema de Saúde. A análise incluiu cirurgias realizadas em hospitais públicos entre 2015 e 2020. A representatividade foi aferida por ano, incluindo hospitais que reportaram pelo menos 30 procedimentos nesse ano, de acordo com orientações europeias. A comparação considerou fatores de risco demográficos (sexo e idade), processuais (laparoscopia e cirurgia urgente) e hospitalares (grupo hospitalar). Para não cair na falácia de tamanho amostral grande, a comparação entre bases de dados utilizou o Cramer's V. Este é considerado pequeno entre 0,1 e 0,3, médio entre 0,3 e 0,5, e alto acima de 0,5. O efeito medido pelo Cramer's V foi negligenciável para o sexo, idade e laparotomia. Houve um pequeno efeito nas cirurgias urgentes, quer por ano (V entre 0,09 e 0,16) quer para o período todo (V=0,14), assim como no grupo hospitalar, com V entre 0,16 e 0,20, assim sugerindo um pequeno viés não-negligenciável na base da vigilância. Assim, esta base de dados carece de otimização para incluir cirurgias urgentes e hospitais que reflitam melhor a distribuição da rede hospitalar no país.

3.1 *Determinar se um modelo de classificação, usando dados disponíveis eletronicamente, poderá melhorar a eficiência, completude e representatividade da vigilância.*

Cirurgias colo-retais realizadas num hospital terciário português, entre 2016 e 2018, foram selecionadas. Dados sobre antibioterapia pós-cirúrgica, cultura positiva, valores de proteína C-reativa, temperatura corporal, contagem de leucócitos, reintervenção cirúrgica, admissão num serviço de urgência e reinternamento hospitalar foram colhidos e considerados. Para aferir a representatividade, os procedimentos sujeitos a vigilância foram comparados com os procedimentos não incluídos na vigilância local. A capacidade de cada variável considerada poder dividir os procedimentos em alto e baixo risco, em que nos de baixo risco é assumido não existir infeção e nos de alto risco é efetuada vigilância manual, considerou a presença de infeção de local cirúrgico como referência. Sensibilidade, especificidade, valores preditivos positivos e negativos foram estimados, com respetivo intervalo de confiança a 95%. A proporção de procedimentos sinalizados para revisão manual por variável foi estimada. Pouco mais de 50% dos procedimentos foram sujeitos a vigilância. Procedimentos não incluídos mostraram proporções superiores de marcadores de infeção. Antibioterapia pós-cirúrgica apresentou umas das melhores sensibilidades na cirurgia colo-retal (89%), o valor preditivo positivo mais alto (22%) e sinalizou menos procedimentos para revisão manual (48%). Neste estudo, concluiu-se que a vigilância a nível hospitalar tem marcadas limitações, subestimando a real incidência de infeção. Antibioterapia parece ser o melhor critério para selecionar uma subamostra de procedimentos para revisão manual, melhorando a exaustividade e eficiência do sistema.

4. *Estimar o impacto dos fatores de risco para infeção de local cirúrgico após cirurgia colo-retal na incidência da infeção em Portugal, utilizando a fração atribuível populacional.*

Doentes submetidos a cirurgia colo-retal em hospitais que reportaram cirurgias vigiadas todos os anos entre 2015 e 2019 foram incluídos. Entre 42 hospitais, 18 cumpriram o critério, correspondendo a 11 219 procedimentos. Prevalência de cada fator de risco foi estimada utilizando a base de dados de vigilância da Direção-Geral da Saúde, que segue a metodologia recomendada pelo *European Centre for Disease Prevention and Control*. A classificação da Sociedade Americana de Anestesiologia, a classificação de ferida, laparotomia, cirurgias urgentes, antibioterapia profilática, duração da cirurgia e sexo masculino foram incluídos como fatores de risco. Medidas de associação foram recolhidas de meta-análises publicadas em revistas indexadas. As frações atribuíveis populacionais foram calculadas utilizando a fórmula de Levin. Para ter em conta a interação entre fatores de risco, utilizou-se a comunalidade de fatores de risco numa abordagem de pesos somados, que estima um valor combinado que serve como medida da abrangência da vigilância. A incidência cumulativa de infeção foi 16,8%. A proporção de infeção atribuída a todos os fatores de risco foi 61%. Fatores de risco modificáveis explicaram 31% dos procedimentos: o mais alto foi laparotomia (17%) e o mais baixo cirurgias urgentes (3%). Fatores não-modificáveis explicaram 29%, o maior sendo a classificação de ferida (14%). Assim, uma proporção relevante de infeção fica por explicar pelos indicadores de vigilância atuais. Intervenções que se foquem em procedimentos mais curtos e menos invasivos serão otimamente efetivos para reduzir a incidência de infeção de local cirúrgico.

Conclusão

Ao considerar que este é um problema de saúde atual, esta tese ajuda a construir a ideia que investigação futura e a implementação de projetos deve tomar em consideração o local na qual elas são realizadas. Apesar das características hospitalares terem sido infrequentemente consideradas na investigação no âmbito da cirurgia colo-retal e nenhuma característica ter sido associada com significância estatística a infeção no artigo II, ainda assim demonstrou-se que ainda faz diferença em que hospital decorre a cirurgia, mesmo após ajustar para fatores de risco individuais e peri-operatórios. A revisão da literatura sugere que a implementação de vigilância está associada a taxas de incidência mais baixas; contudo, a qualidade da vigilância é subótima quer a nível local quer a nível central, já que não consegue incluir uma proporção considerável de cirurgias urgentes, o que provavelmente levará a uma subestimativa da verdadeira incidência.

Por último esta tese desenvolve as soluções mais efetivas a serem adotadas no curto prazo, como a promoção e implementação de procedimentos laparoscópicos mais curtos, quando possível, que foram identificados como as estratégias mais efetivas para diminuir a incidência de infeção de local cirúrgico após cirurgia colo-retal.

INTRODUCTION

Disease is a deeply social process.[1] It is a product of its own historical, geographical and philosophical context. In the following pages, the historical background of disease, and infectious diseases in particular, will be outlined, justifying why this is the moment to tackle healthcare-associated infections (HAI). The overall epidemiology, risk factors and preventive measures of surgical site infections (SSI), a type of HAI, shall be addressed, with a focus on SSI following colorectal surgery. Acknowledging the national efforts to tackle this health problem in the last decade, research gaps will be identified that may help understand the features in the Portuguese context of healthcare delivery that may explain the reason SSI after colorectal surgery have a higher incidence in the country than anywhere else in comparable European countries.[2] This knowledge is essential to pinpoint optimal targets for future public health interventions aiming to decrease the incidence of this infection with maximal efficiency and effectiveness and, consequently, improving public health.

Historical background

In his science series Cosmos, Carl Sagan famously affirmed that to make an apple pie from scratch, one must first create the Universe. Hyperbolically, it reminded us that even the simplest things in existence depend on their global context; in this case, the laws of our Universe. More humbly, HAI – infections acquired by patients during their stay in an acute care setting[3] – imply the creation of healthcare and healthcare facilities, a creation which is not void of philosophical meaning.

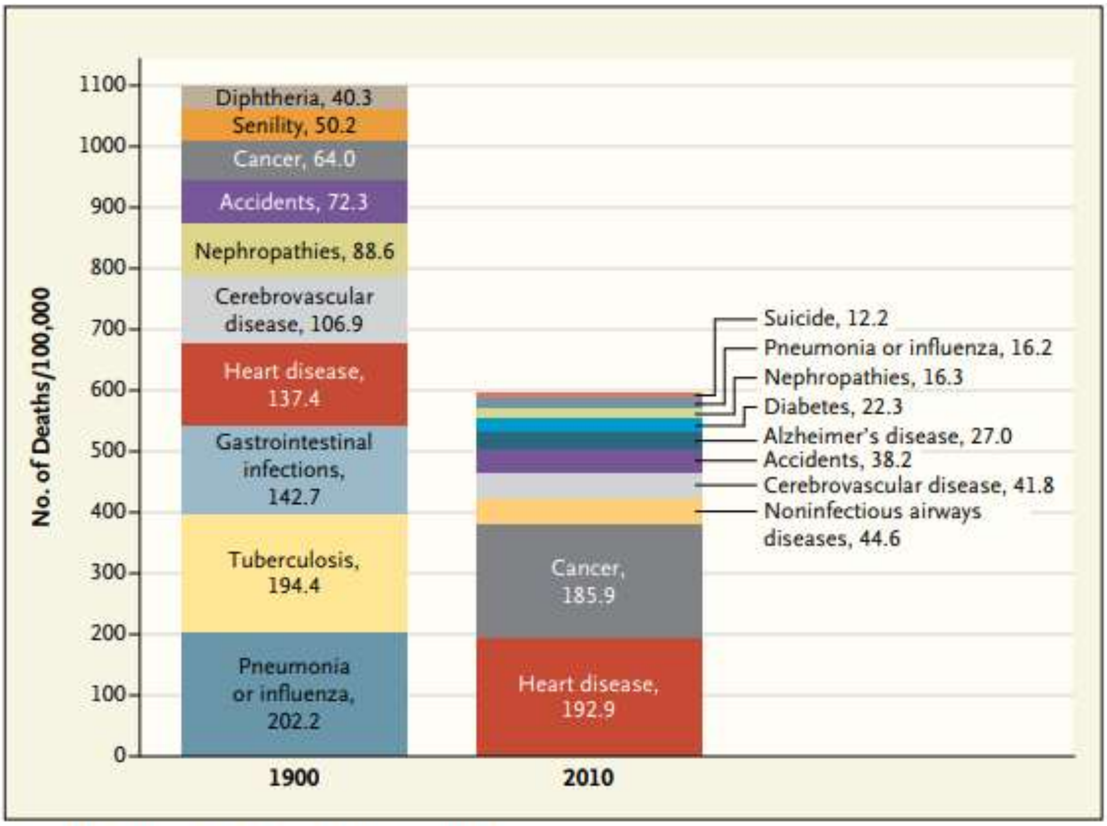
Although the concept of health and care date back to prehistoric societies, it was not until the advent of the Scientific Revolution in the 18th century that healthcare began to gradually take its modern form.[4] The revolution was not a single event, as it encompasses all the remarkable feats of extraordinary people that reshaped our society throughout the years. Relevantly, it did not occur spontaneously, nor arbitrarily. It occurred because a new philosophical paradigm had been popularized in Western societies: that reason was the primary source of authority. A powerful, original idea, that brought changes to virtually every sphere of life.[5] From this small seed sprung radical concepts – empiricism, liberalism, the hypothetico-deductive model, the modern state – that would alter the way each person looks at reality. These new ideas reshaped our Universe.

Health became something new. In the 19th century, knowledge in the field of health would surpass everything that had been achieved in the previous millennia. Vaccination was adopted by British armed forces in 1800 after Edward Jenner showed cowpox injection was effective to prevent smallpox. In 1854, John Snow found strong epidemiological support that the source of a cholera epidemic was the contaminated water from the river, which was distributed to homes in South London.[5] Semmelweis, often regarded as the first hospital epidemiologist, performed a step-by-step analysis of an outbreak and proved the effectiveness of hand hygiene on reducing surgical adverse events.[6, 7] Joseph Lister introduced the idea of sterile surgery, thus reducing postoperative mortality rates of amputations from 45% to 15%. Remarkably, these advances were made before Louis Pasteur's germ theory and Robert Koch's postulates on the role bacteria pose as infectious agents. The use of soap spread universally, as well as water treatment, sewer systems and the chlorination of public drinking water supplies. Gloves were introduced in surgical practice in 1890.[8] Concurrently, the field of sociology was born, and established the idea that knowledge on distribution of determinants of population health is epistemologically multilevel, as it needs to consider both people and their socio-geographical context.[9] During the second world war, already in the 20th century, the United States used the first dose of recently discovered penicillin to treat a septic patient.[10] Suddenly, old infectious acquaintances like tuberculosis or syphilis could be treated. The epidemiology of infectious diseases shifted.[11]

Hospitals followed on this overall reform. Originally linked to charitable services by religious orders, they gradually became part of municipal and national services as the power of the central State grew.[5] During the Crimean war, Florence Nightingale became the face of a new standard of hospital planning and community nursing.[7] Hospitals focused mainly on severe infectious diseases; tetanus, typhus, cholera or tuberculosis were frequent in virtually every hospital ward.[12] With aseptic techniques, hospital mortality started to improve.[8] Following the Second World War, the United States saw a hospital building boom. In Portugal, too, the hospital network developed, although yet linked to religious orders.[13] There was a shift in hospital epidemiology, as *Staphylococcus aureus* emerged for the first time as the predominant pathogen of HAI.[8, 14] The Centers for Disease Control and Prevention (CDC) was founded in 1946,[15] evolving from its previous role of malaria control, and the earliest infection control programs were implemented back in the 1950s, focusing mainly on environmental cleanliness.[8, 14]

These advances marked what has been deemed the epidemiological transition.[11] In the last 200 years, people have different diseases, doctors hold different ideas of them and even diseases carry different meanings in society.[1] Changes in demographical, sociological and economical determinants would bring a shift in mortality and disease patterns. Antibiotics, vaccination, improved nutrition, sanitation and social welfare were some of the main contributors to a dramatic reduction in infection disease morbidity and mortality,[5] and infections were gradually displaced by degenerative and chronic conditions as the primary cause of morbidity and death, as observed in figure 1. Humankind may have failed the *Boston Medical and Surgical Journal* expectation that by the 21st century all preventable diseases would have been eradicated, the cure for cancer discovered and eugenics superseded evolution in the elimination of the unfit.[16] Yet, the notion that many of today's medical issues are a consequence of our success still holds true. The past is now, perhaps more than ever, a foreign country.[17]

Figure 1. Top 10 causes of death: 1900 vs 2010.



Top 10 Causes of Death: 1900 vs. 2010.

Data are from the Centers for Disease Control and Prevention.

Figure retrieved from Jones D, Podolsky SH, Greene JA. The Burden of Disease and the Changing Task of Medicine. N Eng J Med 2012. 366(25): 2333-2338.

Due to its geographical position and cultural affinity, Portugal benefited from these advances. In the transition from 19th to the 20th century, Ricardo Jorge would become the founding father of the country's public health system,[18] advocating for health authorities at the district level and the professionalization of sanitary staff. In 1965, the National Program of Vaccination was launched, focusing initially on mass vaccination against poliomyelitis, growing in coverage until this very day.[19] The standardization of hospitals and medical careers would only be addressed in that decade, and the first draft of a national health service appeared in 1971. Despite the late advancements of the former regime, it was for the new democratic government to establish the present National Health Service (*Serviço Nacional de Saúde*, or SNS). This service is similar to the Beveridge model of the United Kingdom, which provides healthcare for every citizen through income tax payments. The universality and (tending) gratuity of healthcare was established, along with drug reimbursement.[13] For the first time in 900 years of history, private institutions and religious welfare services were no longer the main providers of health in the country.

The SNS philosophy is based on the notion of the State as the guarantor of the rights of its citizens, a philosophical concept which is historically modern. This social vision is shared by the majority of the Portuguese society, and it explains why most differentiated healthcare in Portugal has been part of the public sector for the last 40 years.

Today, our Universe is unfamiliar to what it had been since the dawn of humankind. And, as ibn Khaldun so beautifully put it many centuries ago, when there is a general change of conditions, it is as if the entire creation had changed and the whole world been altered.[20] Our success in the prevention, management and treatment of infectious diseases may have eradicated smallpox and decreased the negative social impact of other infections, yet other challenges lurked in the shadows. In industrialized countries – a definition with marked geographical and historical significance – HAI emerged as one of the main health problems, inherently linked to how care is delivered. Although the World Health Organization (WHO) has reported that HAI usually receive public attention only in the context of epidemics,[21] they are now one of the leading causes of death in the United States, surpassing AIDS or traffic accidents,[22, 23] even though the latter seem more present in the public conscience.

Geographically and historically, this is when and where HAI became responsible for a considerable proportion of morbidity and mortality. Philosophically, this is when the right to health is consecrated as a universal human right, whose protection is in the Portuguese Constitution, as part of an ideological evolution leading to the overall acceptance of the responsibilities of State towards its citizens.

This is when we have the knowledge, the motive, the will and the resources. This is the moment to tackle HAI.

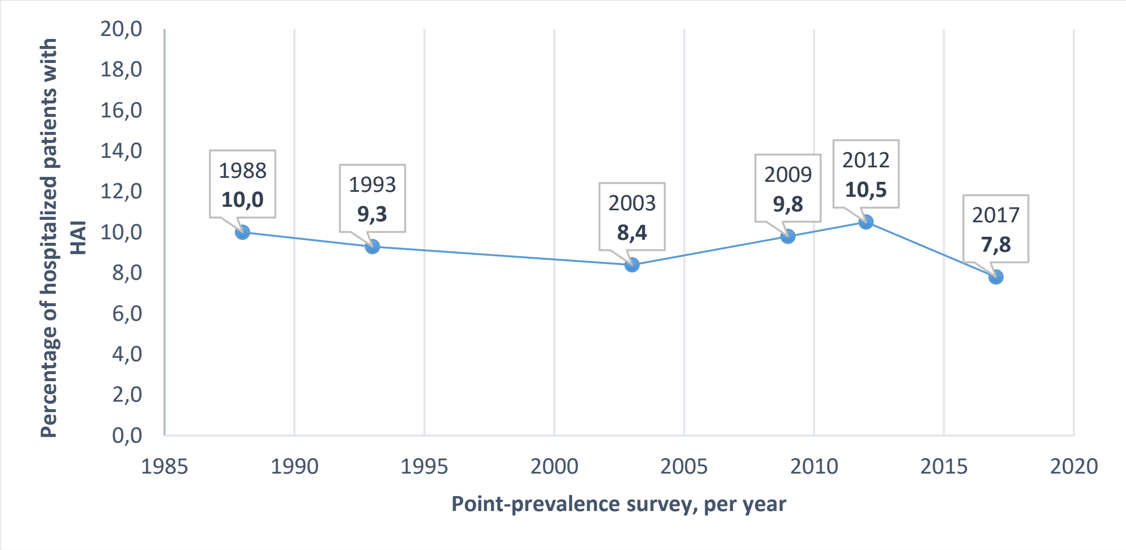
Healthcare-Associated Infections

As long as there has been some sort of hospital facility, there have been adverse events associated – notably, death.[8] Most adverse events were overlooked due to the severe nature of primary infectious diseases and the lack of effective tools for a better care. With the aforementioned epidemiological transition,[11] that is no longer true.

HAI refer to infections that arise in any patient 48 hours after hospitalization and within 30 days after receiving care, or 90 days following certain surgical procedures.[3] These criteria ensure that these are infections that were not present at admission and that may be accurately related with health delivery. The term HAI has been coined to account for the fact that these infections may affect patients in any setting they may receive care, yet most data on the burden of HAI is hospital-based.[21] Precise estimates on the prevalence and incidence of infection in nursing homes are difficult to obtain due to the heterogeneity in the characteristics of nursing homes and the elderly population they serve, and estimates are highly variant.[24-27]

HAI are the most frequent adverse event during healthcare delivery.[28] In 2008, the European Centre for Disease Prevention and Control (ECDC) reported that as many as 4 544 100 episodes of HAI affect patients every year in Europe, with a mean prevalence of 7.1% and 16 million extra-days of hospital stay.[29] In Portugal, HAI reported prevalence has been estimated at higher levels in the last 30 years, as observed in Figure 2, with little improvement.[30]

Figure 2. Prevalence of Healthcare-Associated Infections (HAI) per point-prevalence survey, in Portuguese hospitals



Data retrieved from the Point-prevalence survey in acute hospitals report, 2017
HAI, Healthcare-associated Infections

On any given day, about 1 in 31 hospital patients has at least one HAI (1 in 13 in Portugal).[30, 31] This poses a negative impact on both patients and health system alike. Patients with HAI have been found to have a higher risk of death within 30 days and at one year relative to those without them,[32] a problem aggravated by the increasing prevalence of multidrug-resistant organisms.[33] In one influential study, it was found that, in the United States, 1 in 17 patients who developed a HAI died due to it – that is to say, they died due to a condition they acquired while being treated for other health issues.[34] This burden is more severe in high-risk populations, such as patients admitted to intensive care units (ICU), approximately 30% of which are affected by at least one episode of HAI during their hospital stay.[35] The direct economic burden is estimated to be around 28 to 33 billion dollars a year in the United States alone, although most of that burden (25 to 30 billion) was considered to be preventable with effective infection control programs.[23, 36, 37] In Europe, these infections accounted for 7 billion dollars annually in direct costs alone.[29] The burden is several times higher in low-to-middle income countries, a reminder of the impact of context on health.[28, 38] Estimating costs, morbidity and mortality among high-risk patients with underlying diseases is challenging, and figures vary according to the study, setting or statistical approach.[21] Though we may not know the exact burden of these events, their impact and resonance in the population is undeniable, and the need to address it uncontroversial. Consequently, the prevention and control of HAI is considered a top priority for the CDC,[31] and antibiotic resistance has been deemed by the WHO as one of the major threats to global health, food security and development in the world.[39]

However, these data hide a more complex reality. HAI are heterogeneous and comprised of entities with diverse pathophysiology, risk factors, impact, treatment or prevention, justifying why they are approached individually in research. Most HAI are encompassed in four main types: Catheter-associated urinary tract infections (CAUTI), ventilator-associated pneumonias (VAP), central line-associated bloodstream infections (CLABSI), and SSI.

CAUTI account for as much as 40% of HAI internationally,[40] though that value drops to 27% in the European context.[29] They are caused by instrumentation of the urinary tract, and the only effective eradication is removal of the catheter, since antimicrobials struggle to destroy bacteria colonized in biofilms.[33] They are typically benign, with *Escherichia coli* identified as the main infecting microorganism, and complications are usually limited to some patients with potentially pathogenic virulent bacteria.[22] Hence, morbidity and mortality are low.[41] Patients in institutional care with long-term indwelling catheters, who are typically elderly with comorbidities, are the main population suffering from this specific type of HAI, which has seen a decline in its incidence in United States in recent years, most marked in non-ICU locations.[42]

VAP are a subtype of hospital-acquired pneumonias, which are the second most common HAI in Europe (24%),[29] although they rank third in the United States, behind SSI.[34] Nevertheless, they are the most lethal.[43] They occur after 48 hours of endotracheal intubation.[22] In a study from the United Kingdom and Ireland, the main invading organism was Methicillin-resistant *Staphylococcus aureus* (MRSA), although other pathogens of the human oral flora may be responsible.[44] In Portugal, incidence has dropped from 6.6 to 5.0 cases per 1000 intubation days between 2015 and 2020, a trend also found in the United States.[42, 45]

Although not as common,[29, 34] CLABSI substantially increase morbidity, mortality and hospital costs, and great attention has been paid to them worldwide.[46] Risk factors are related mainly to potential breaches on the catheters. Although any organism penetrating a central venous catheter may cause a CLABSI, *Staphylococcus aureus*, enterococci, *Candida* species and Gram-negative bacteria are the most commonly isolated organisms.[47] In the United States, between 2001 and 2009 there was a 58% reduction in the incidence of these infections, with estimates of 6 000 lives saved and 414 million dollars saved in potential excess healthcare costs.[48] From 2009 to 2016, progress has also been positive.[42] Portugal follows the same decreasing trend, and incidence density in 2020 was 0.7 bacteraemia per 1000 catheter-days.[45]

SSI is still one of the most frequent adverse events occurring in hospitalized patients and the commonest among surgical patients, besides being the most frequent cause for postoperative unplanned readmission.[29, 33, 34] Unlike other HAI, SSI are in-themselves heterogeneous, as the type of surgery determines the incidence of infection, its agents and associated risk factors.

Surgical Site Infections

Despite the extensive advances made since the times of Joseph Lister and Ignaz Semmelweis in infection control, with improved operating room ventilation, sterilization methods, barriers, surgical technique and antimicrobial prophylaxis, SSI continue to be a substantial cause of morbidity and death.[49] They are the costliest HAI and 75% of SSI-associated deaths were directly attributable to the SSI.[50, 51] Even though it is reported as constituting up to 20% of all HAI in Europe,[29] their incidence is most likely underreported, as most SSI become evident following discharge from the hospital and may go unnoticed.[36, 52]

Although SSI are broadly defined as infections occurring after surgery in the body part where surgery took place, they are furtherly divided in superficial incisional, deep incisional and organ/space, depending on the depth and tissue spaces involved. These SSI types have different diagnostic criteria, as may be observed in table 1.[3, 53] Most superficial infections may be managed in the outpatient setting, yet deep and organ/space SSIs require readmission.[54]

Table 1. Surgical Site Infection Criteria, according to the Centers for Disease Control and Prevention

Surgical Site Infection type	**Criteria that must be met**
Superficial incisional SSI	Date of event occurs within 30 days after any NHSN operative procedure (where day 1 = the procedure date) **AND** involves only skin and subcutaneous tissue of the incision **AND** patient has at least ***<u>one</u>*** of the following: purulent drainage from the superficial incision. organism(s) identified from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or nonculture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing. superficial incision that is deliberately opened by a surgeon, physician* or physician designee and culture or non-culture based testing of the superficial incision or subcutaneous tissue is not performed **AND** patient has at least one of the following signs or symptoms: localized pain or tenderness; localized swelling; erythema; or heat. diagnosis of a superficial incisional SSI by a physician or physician designee.
Deep incisional SSI	The date of event occurs within 30 or 90 days after the NHSN operative procedure

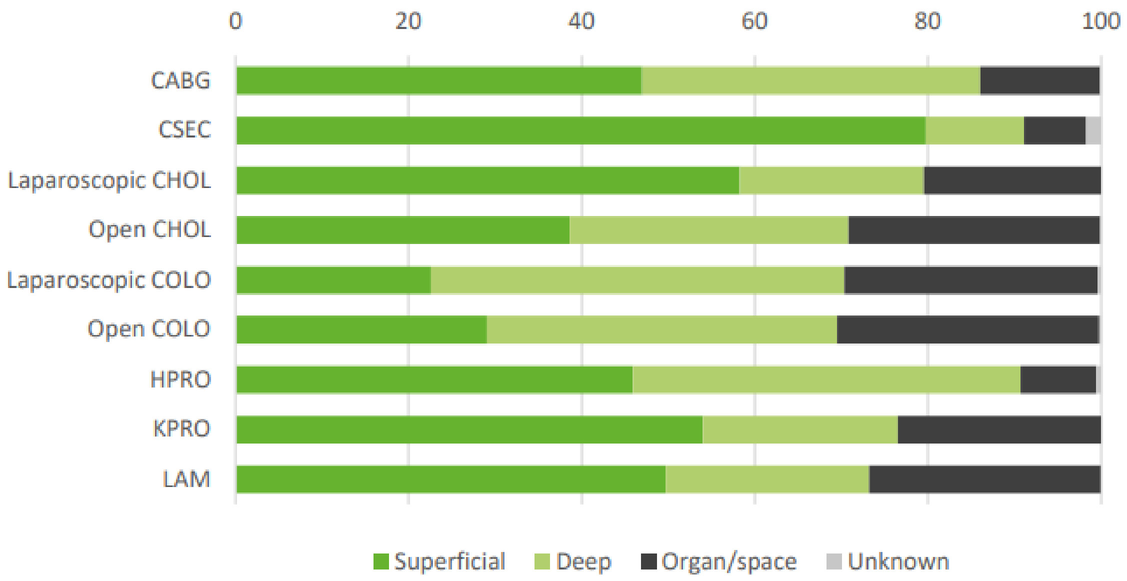
	(where day 1 = the procedure date) **AND** involves deep soft tissues of the incision (for example, fascial and muscle layers) **AND** patient has at least ***one*** of the following: purulent drainage from the deep incision. a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, physician or physician designee **AND** organism(s) identified from the deep soft tissues of the incision by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing) or culture or non-culture based microbiologic testing method is not performed. A culture or non-culture based test from the deep soft tissues of the incision that has a negative finding does not meet this criterion. **AND** patient has at least one of the following signs or symptoms: fever (>38°C); localized pain or tenderness. an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test.
Organ/Space SSI	Date of event occurs within 30 or 90 days after a NHSN operative procedure (where day 1 = the procedure date) **AND** involves any part of the body deeper than the fascial/muscle layers that is opened or manipulated during the operative procedure **AND** patient has at least ***one*** of the following: purulent drainage from a drain that is placed into the organ/space (for example, closed suction drainage system, open drain, T-tube drain, CT-guided drainage). organism(s) identified from fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not Active Surveillance Culture/Testing). an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection. **AND** meets at least one criterion for a specific organ/space infection site listed in the Surveillance Definitions for Specific Types of Infections.

CT, computer tomography. NHSN, National Healthcare Safety Network. SSI, Surgical Site Infection.

A close look at the above definitions may hint at some of the difficulties of applying these criteria in clinical practice. Superficial infections may be defined by the diagnosis of the physician alone, and deep infections may be diagnosed based on the deliberation of the surgeon as well. This subjectivity has been shown to result in poor interrater agreement among infection control specialists and surgeons in diagnosing SSI, making definitions difficult to apply.[55-58] This variability is a consequence of uncertainty. Recent data from colorectal surgery has shown that the exclusion of surgeon's diagnosis improves the reliability, accuracy and concordance of diagnosis across specialists.[59]

Besides the definition, SSI is complicated by the fact that it may affect any body part in which a surgery is performed. Focusing in Europe, where 13 countries – representing 648 512 surgical procedures from 1 639 hospitals – reported their figures to the ECDC, figure 3 and table 2 show how such heterogeneity reflects in the proportion of infection type (hence, severity) and overall SSI incidence.[2] Surgeries performed in different parts of the body – with different techniques and invasiveness – also translate in the distribution of microorganisms responsible for SSI, when those agents are successfully isolated (table 3). By being part of a continental network, these countries share a standardized methodology for surveillance and data reporting, making data comparable between them, as will be addressed opportunely.[53]

Figure 3. Type of Surgical Site Infection by surgical group in Europe, 2017



CABG: coronary artery bypass graft, CHOL: cholecystectomy, COLO: colon surgery, CSEC: caesarean section, HPRO: hip prosthesis surgery, KPRO: knee prosthesis surgery, LAM: laminectomy

Table 2. Percentage of Surgical site infections and incidence density of in-hospital surgical site infections by year and type of surgical procedure in Europe, 2017

Type of surgical procedure	Percentage of SSIs per 100 operations [intercountry range]	Incidence density of in-hospital SSIs per 1 000 post-operative patient-day [intercountry range]
Coronary artery bypass graft	2.6 [0.0-5.5]	1.2 [0.0-3.2]
Caesarean section	1.8 [0.5-5.3]	0.6 [0.1-1.7]
Laparoscopic cholecystectomy	1.5 [0.4-3.1]	1.0 [0.3-1.8]
Open cholecystectomy	3.9 [1.1-10.9]	3.5 [1.6-7.6]
Laparoscopic colon surgery	6.4 [0.0-12.5]	4.1 [0.0-8.4]
Open colon surgery	10.1 [4.1-16.9]	5.7 [2.8-11.1]
Hip prosthesis surgery	1.0 [0.4-2.2]	0.3 [0.2-0.9]
Knee prosthesis surgery	0.5 [0.2-2.7]	0.1 [0.1-0.5]
Laminectomy	0.8 [0.2-2.7]	0.4 [0.0-2.2]

Adapted from the Annual epidemiological report Healthcare-associated infections: surgical site infections, by the European Centre for Disease Prevention and Control, 2019.
SSI, Surgical Site Infection.

Table 3. Percentages of microorganisms identified in surgical site infections by surgery group, in Europe, 2017

Microorganisms	CABG	Laparoscopic CHOL	Open CHOL	Laparoscopic COLO	Open COLO	CSEC	HPRO	KPRO	LAM	TOTAL
Gram-positive cocci	50.6	30.7	38.5	26.7	31.4	52.5	67.1	72.6	66.2	51.6
Staphylococcus aureus	16.4	5.3	3.1	2.1	4.2	30.7	31.9	38.7	38.2	21.5
Coagulase-negative staphylococci	26.4	2.7	4.6	1.3	2.4	3.5	18.9	17.6	15.4	11.0
Enterococcus species	3.7	14.0	27.7	16.7	21.5	8.3	7.7	7.1	3.7	11.9
Streptococcus species	1.5	8.0	3.1	5.6	2.6	9.0	5.0	6.4	2.9	4.9
Other gram-positive cocci	2.6	0.7	0	1.1	0.7	1.0	3.7	2.9	5.9	2.2
Gram-positive bacilli	2.2	2.0	0	0.5	0.5	1.0	4.1	4.8	0.7	2.3
Gram-negative bacilli, Enterobacterales	32.3	44.7	50.8	50.8	46.6	25.7	19.3	15.5	17.6	30.7
Escherichia coli	5.2	25.3	32.1	31.7	22.5	13.7	6.9	4.6	5.1	13.9
Citrobacter species	1.9	2.7	6.2	3.2	1.8	0.7	0.6	0.7	1.5	1.4
Enterobacter species	5.6	4.7	4.6	6.3	7.2	3.0	3.0	2.4	1.5	4.4
Klebsiella species	6.7	7.3	10.8	5.6	7.2	2.9	2.3	2.4	2.9	4.4
Proteus species	5.6	2.7	1.5	2.4	2.4	3.9	4.0	2.2	4.4	3.3
Serratia species	3.7	0.7	1.5	0.3	0.8	0.3	1.5	1.5	0.7	1.2
Other Enterobacterales	3.7	1.3	3.1	1.3	4.7	1.2	1.0	1.5	1.5	2.2
Gram-negative non-fermentative bacilli	9.3	4.0	0	6.6	11.2	3.9	5.0	2.1	6.6	6.3
Acinetobacter species	1.1	0	0	0.3	0.2	0.2	0.4	0	0	0.3
Haemophilus species	0	0	0	0	0	0.3	0	0	0	0
Pseudomonas aeruginosa	6.7	3.3	0	5.8	8.8	1.0	3.6	1.9	6.6	4.7
Pseudomonadaceae family, other	1.1	0	0	0	1.8	1.2	0.9	0.2	0	1.0
Stenotrophomonas maltophilia	0	0.7	0	0	0	0.2	0	0	0	0
Other gram-negative non-fermentive bacilli	0.4	0	0	0.5	0.3	1.0	0.1	0	0	0.3
Anaerobes	0.7	9.3	1.5	8.7	4.4	13.5	2.9	3.1	5.1	5.2
Bacteroides species	0	1.3	1.5	6.9	3.2	1.2	0.2	0.3	0	1.7
Other anaerobes	0.7	8.0	0	1.9	1.1	12.3	2.7	2.8	5.1	3.6
Other bacteria	1.9	8.7	4.6	4.5	3.0	1.4	0.8	1.7	0.7	2.2
Fungi, parasites	2.6	0.7	4.6	2.1	2.7	1.5	0.5	0.2	2.2	1.5
Candida species	2.2	0.7	4.6	2.1	2.7	1.2	0.5	0	2.2	1.4
Other fungi or parasites	0.5	0	0	0	0	0.3	0	0.2	0	0.1

CABG: coronary artery bypass graft, CHOL: cholecystectomy, COLO: colon surgery, CSEC: caesarean section, HPRO: hip prosthesis surgery, KPRO: knee prosthesis surgery, LAM: laminectomy;
Adapted from the Annual epidemiological report Healthcare-associated infections: surgical site infections, by the European Centre for Disease Prevention and Control, 2019.

Colon surgery stands out as the surgery group with the highest incidence density and highest proportion of infection per 100 procedures. The proportion of superficial incisional SSI among all colon SSI is lower than for other surgery groups, suggesting that not only is this group more commonly complicated by infection, but that infection tends to be more severe. Although part of the explanation may lie on the invasiveness of colon surgical procedures, laparoscopic surgery still associates with higher rates of infection compared to other surgical groups, suggesting other explanations are needed.

Gram-positive cocci, especially *Staphylococcus aureus*, represent the majority of organisms isolated in cultures from surgical sites, in line with the epidemiological transition referred previously.[8, 14] Again, a closer look permits to observe phenomena that aggregate data occlude. In cholecystectomy and colorectal surgery, gut bacteria (*Enterococcus* and *Enterobacterales)* account for the vast majority of cases. S*taphylococcus aureus* represent but a minor fraction of SSI in these groups. This suggests that, in most cases, these infections are caused by endogenous agents, rather than transmitted from personnel. Noteworthy, the proportion of *Pseudomonas aeruginosa* lies between 5.8% and 8.8%, above other surgical groups. These multi-drug resistant ubiquitous bacteria live in soil, and usually opportunistically infect immunocompromised patients. Whether these agents represent endogenous (via colonization) or exogenous sources of infection remains controversial.[60]

Therefore, SSI following colon surgery differs in some ways from other SSI. It is more frequent, more severe and has different causal organisms. From 2013 to 2017, the ECDC reported a statistically significant decreasing trend for both open and laparoscopic colon surgery.[2] The future appeared to be bright. However, an ecological fallacy is to be avoided. Disease is context-dependent.[1] Is this magnitude equally elevated across countries? Is this decreasing trend true for every European country?

Table 4. Percentage of surgical site infections and incidence density per 1000 postoperative patient-days per country, 2017, for laparoscopic and open colon surgery

Country	Laparoscopic Colon Surgery		Open Colon Surgery	
	Percentage of SSIs per 100 operations [95% CI]	Incidence density of SSIs per 1000 postoperative patient-days [95% CI]	Percentage of SSIs per 100 operations [95% CI]	Incidence density of SSIs per 1000 postoperative patient-days [95% CI]
Austria	12.5 [5.0-25.8]		7.5 [5.0-10.7]	
France	7.8 [6.5-9.3]	5.5 [4.4-6.8]	7.4 [6.3-8.7]	3.9 [3.2-4.7]
Germany	5.3 [4.7-6.0]	2.5 [2.0-3.0]	9.4 [8.7-10.1]	3.9 [3.5-4.4]
Hungary	4.0 [1.6-8.1]	2.6 [0.7-6.6]	10.0 [7.2-13.6]	6.7 [4.6-9.6]
Italy	2.9 [2.2-3.9]	2.3 [1.6-3.1]	6.7 [5.8-7.7]	3.8 [3.2-4.4]
Lithuania	0.0 [0.0-61.5]	0.0 [0.0-65.9]	4.1 [1.3-9.6]	2.8 [0.8-7.1]
Netherlands	7.8 [6.8-8.9]	5.5 [4.6-6.6]	16.6 [14.4-19.0]	11.1 [9.4-12.9]
Norway	7.7 [6.4-9.2]	5.6 [4.3-7.2]	12.7 [11.0-14.6]	5.9 [4.8-7.1]
Portugal	11.5 [8.9-14.6]	8.4 [6.3-11.1]	16.9 [15.4-18.5]	10.7 [9.7-11.8]
UK-England			8.1 [7.2-9.2]	6.3 [5.5-7.1]
EU/EEA	**6.4 [6.0-6.9]**	**4.1 [3.8-4.5]**	**10.1 [9.7-10.6]**	**5.7 [5.5-6.0]**

CI, Confidence interval, EEA: European Economic Area, EU: European Union, SSI: Surgical site infection, UK: United Kingdom.
Adapted from the Annual epidemiological report Healthcare-associated infections: surgical site infections, by the European Centre for Disease Prevention and Control, 2019.

Regardless of the metric considered, it is clear that countries fare differently (table 4). Even if estimates may not be equally trustworthy, Portugal appears to be one of the worst performing countries both for laparoscopic and open colon surgery, in all cases with figures significantly higher than the European average. To make matters worse, between 2013 and 2019 there has been no countrywide improvement in SSI incidence in this surgical group.[45] Something in the Portuguese context needs optimization.

Risk factors for surgical site infection after colorectal surgery

Before we describe the Portuguese strategy on SSI prevention and control, it is vital to take a closer look at the factors that are associated with increased risk of infection and that are, thus, usually identified as targets for public health interventions.

The likelihood of developing a SSI depends on a complex interaction between host characteristics, surgical site tissue condition, presence of foreign material, degree of wound contamination and pathogenicity of the microorganism.[61] In their guidelines for the prevention of SSI back in 1999, the CDC called for an awareness that the risk of infection is influenced by characteristics of the patient, operation, personnel and hospital.[51] The distinction is not always obvious, nor does it need to be. The relevance of this statement is the recognition that surgeries are also context-dependent.

Risk factors may be divided in many ways. The classical division is the one provided by the CDC which, in practice, translates into patient-related risk factors and operation-related risk factors. They may also be divided into intrinsic (patient) and extrinsic (procedure, facility, pre and perioperative) factors.[50] However, from the point of view of a public health specialist, it is more useful to divide risk factors into modifiable – those we may act upon in the short run to improve the outcomes – and non-modifiable – those we may act upon only in the longest run, often through transversal interventions. Modifiable risk factors are acutely optimizable, and are usually the focus of intervention in the scope of surgery.[61] Non-modifiable require structural interventions focusing on health determinants. The most comprehensive systematic review of risk factors for SSI in colorectal surgery opted for the latter division and, in line with the objectives of this thesis, the same will be followed here.[62]

Non-modifiable risk factors

Although a plethora of published papers have addressed risk factors on colorectal surgery over the years, only in 2021 a comprehensive systematic review with meta-analysis was able to provide a clearer picture on non-modifiable risk factors, for which reviews were lacking.[62] Table 5 summarizes the findings on these risk factors.

Table 5. Non-modifiable risk factors for surgical site infection after colorectal surgery, summarized from the study by Xu et al (2021)

Risk Factors	No. of studies	I^2 (%)	RR (95%CI)
Male sex	8	59	1.30 (1.14-1.49)
Obesity	8	25	1.60 (1.47-1.74)
Diabetes mellitus	9	60	1.65 (1.24-2.20)
ASA score ≥3	10	0	1.34 (1.19-1.51)
Emergent surgery	7	40	1.36 (1.19-1.55)
IBD	3	63	2.12 (1.24-3.61)
Wound classification >2	7	86	2.65 (1.52-4.61)
Respiratory comorbidity	3	76	2.62 (0.84-8.13)
Neoplasm	5	81	1.24 (0.58-2.26)

ASA, American Society of Anaesthesiologists. CI, confidence interval. IBD, inflammatory bowel disease. RR, relative risk

The overall findings are that the magnitude of the relative risk (RR) is similar between risk factors, and that the heterogeneity found in the studies addressing each factor was considerably high, except for obesity and the American Society of Anaesthesiologists (ASA) score. Current evidence does not support the association between having a respiratory comorbidity or a neoplasm and developing a SSI following colorectal surgery.

The ASA Status Classification System is a score that was designed to assess and communicate a patient's pre-anesthesia medical comorbidities.[63] It ranges from 1 – a normal healthy patient – to 5 – a moribund patient who is not expected to survive without the operation. It takes into account not only the medical comorbidities, but whether those comorbidities – diabetes, hypertension, etc. – are controlled. Hence, it is a finer analysis of the patient's overall condition than any isolated comorbidity. The null heterogeneity found in the 2021 meta-analysis reinforces the confidence one may take on its estimate.[62]

For the purposes of that paper, obesity was defined as a body mass index (BMI) greater than 30 kg/m^2, following the WHO definition.[64] The result of this meta-analysis supports a previous finding of a systematic review that focused only on the association between obesity and SSI in colorectal surgery, using the same definition.[65] That systematic review found an odds ratio (OR) of 1.51, with a 95% confidence interval of 1.39-1.63 and an I^2 of 41%. Despite the heterogeneity and the fact that one single study had a weight of 46.5% in the first manuscript and two studies had a weight of 65.4% in the second, it may be worth noticing that all included studies found a positive association, nearly all of them with statistical significance. One other study in the Netherlands quantified the association beyond this binary definition, by stratifying weight into 5 categories. It found that the higher the BMI, the higher the risk, using normal BMI as reference (18.5-25 kg/m^2), both for laparoscopic and open colorectal surgery. Being underweight was associated with a higher risk of deep SSI in open surgery.[66] Diabetes mellitus had been previously found, in a systematic review, to increase the risk of SSI across multiple surgical procedures. However, colorectal surgery was one of the only two surgical groups where that increase was not statistically significant.[67]

The wound classification system was created by the CDC to assess the degree of contamination of a surgical wound at the time of the surgical procedure. Assigned by a person involved in the surgical procedure, it ranges from class 1 – clean wound – to 4 – dirty/infected wound.[49] The fact that male sex, ASA score, emergent surgery and wound classification were found to be associated with higher risk of SSI will be particularly relevant when we address how surveillance is performed in the Portuguese context.

Other non-modifiable risk factors have been suggested. Age may be the most widely studied, although results vary. Experts claim that a potential increased risk of SSI in older adults may be due to comorbidities and immunosuppression, rather than age itself and the physiologic changes associated. A lower risk on older adults has also been found, although it has been claimed it may be due to a bias similar to a healthy-worker effect, as only healthy older patients are submitted to surgery.[61] Malnutrition has also been suggested as a risk factor, addressed by the serological levels of albumin. It has been linked with both SSI and other complications, including death in patients with colorectal cancer.[68, 69] History of radiation or steroid therapy for inflammatory bowel disease has also been linked with increased of risk, due to underlying tissue damage.[70, 71] None of these risk factors has been supported by a systematic review of the literature.

Modifiable risk factors are those whose acute optimization may decrease the likelihood of developing a SSI.[61] Several have been suggested and the line that separates these risk factors from preventive strategies is occasionally thin. While non-modifiable tend to refer to patient comorbidities, modifiable tend to refer to the surgical procedure. Returning to the comprehensive systematic review with meta-analysis published in 2021, five modifiable risk factors were found (table 6).

Table 6. Modifiable risk factors for surgical site infection after colorectal surgery, summarized from the study by Xu et al (2021)

Risk Factors	No. of studies	I^2 (%)	RR (95%CI)
Cigarette smoking	6	64	1.38 (1.14-1.67)
Operative time (≥180 min)	6	58	1.88 (1.49-2.36)
Open surgery	16	69	1.81 (1.57-2.10)
Stoma creation	8	69	1.89 (1.28-2.78)
Blood transfusion	5	74	2.03 (1.34-3.06)

ASA, American Society of Anaesthesiologists. CI, confidence interval. IBD, inflammatory bowel disease. RR, relative risk

As observed for most non-modifiable risk factors, the heterogeneity of estimates found in the included studies is substantial, always surpassing the 50% mark. Operative time and blood transfusion are markedly affected by the case-mix of the population. Open surgery is possibly the most researched risk factor in colorectal surgery, a good example of how SSI should be considered separately for each surgical group. Besides Xu *et al*,[62] at least other 8 systematic reviews with meta-analysis compared laparoscopy and open surgery.[72-79] Although the populations of these articles differed – from octogenarians to patients with colorectal cancer – they all concluded that laparoscopy was protective, with RR estimates ranging from 0.45 to 0.67. The exception was a 2010 systematic review on patients with ulcerative colitis, which found no association between laparoscopy and SSI in colorectal surgery.[77]

Systematic reviews abound for stoma creation, a risk factor which is highly specific of colorectal surgery. Yet, they tend not to focus on stoma creation *per se*. Three systematic reviews found that loop ileostomy may be associated with lower morbidity than loop colostomy for temporary decompression of colorectal anastomosis,[80-82] while one found no significance difference except for stoma prolapse.[83] Published systematic reviews agree that early preventive ileostomy is associated with overall improved morbidity, at the expense of higher SSI incidence rate, underlining that SSI policies should not disregard other coexisting risks.[84-86] Evidence also supports that purse-string closure is associated with better outcomes than linear skin closure.[87, 88]

Cigarette smoking may delay wound healing, thereby increasing the risk of SSI. Although smokers never truly become non-smokers, a randomized clinical trial has suggested that 4 weeks of abstinence prior to surgery may reduce the incidence of SSI.[50, 89]

Non-modifiable risk factors are relevant to establish a baseline ratio that may serve as a realistic and achievable target for prevention efforts. Modifiable risk factors are relevant as optimal targets for public health interventions in order to reach that target. However, it is important not to consider this division rock-solid. Some authors consider obesity and diabetes mellitus as modifiable risk factors, while others see them as non-modifiable.[61, 62]

Three of the described risk factors are used by the National Healthcare Safety Network (NHSN) of the United States to predict the risk of SSI: ASA Score (class 3 to 5), wound classification (contaminated or dirty) and operative time in minutes (> 75^{th} percentile, or 180 minutes). Each risk factor represents 1 point, and thus the NHSN risk index ranges from 0 (lowest risk) to 3 (highest risk). However, this risk index has been shown to yield poor predictive performance in most surgeries, particularly colorectal. Even with the addition of other variables – anesthesia, use of endoscope, medical school affiliation and bed size above 500, the c-index improved only slightly, from 0.56 to 0.59, meaning the goodness-of-fit of the model remained suboptimal.[90]

The risk factors reviewed in the former two subchapters share one thing in common – they are either patient-related or procedure-related risk factors. Nevertheless, this is a simplification of the true risk, which represents a myriad of events, as observable in Figure 4.[51, 91]

Figure 4. Fishbone diagram of the factors influencing the risk of Surgical Site Infection

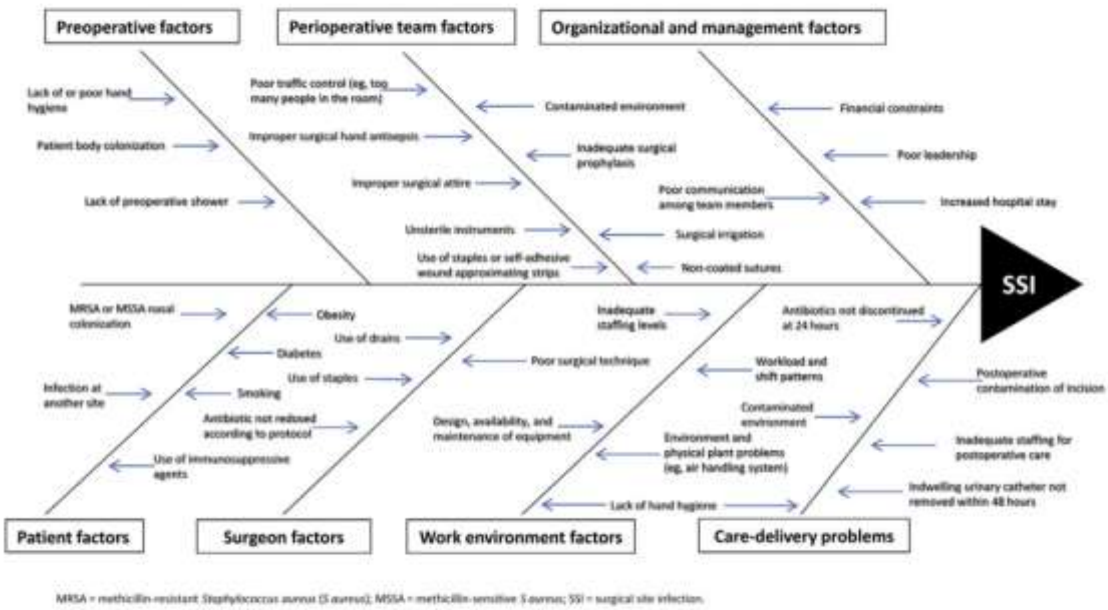


Diagram retrieved from Edmiston, C.E., Jr. and M. Spencer, *Going forward: preventing surgical site infections in 2015.* AORN J, 2014. **100**(6): p. 616-9.

One systematic review went beyond the activities performed perioperatively and compared short-term and oncological outcomes following colorectal resection performed by surgical trainees and expert surgeons. They found that expert-supervised trainees had better outcomes in non-oncological procedures, although they were unable to account for potential differences in case-mix complexity.[92] Other potential factors related to work environment, leadership and management may be challenging to address. One systematic review found 9 studies addressing the impact of single-patient rooms on the acquisition of HAI, compared to multi-bedrooms, and concluded that single-rooms were beneficial for infection control purposes.[93] Nevertheless, research at the structural level has been scarce and inconsistent.

Finally, some factors influencing the risk of infection are better referred to as prevention efforts, rather than risk factors, and will be addressed in the following chapter.

Preventive strategies

Preventive strategies may be divided in two general classes: universal precautions, in the sense that they are not directed at any particular infection, agent or patient, as they constitute a series of general measures to decrease the risk of infection; and specific strategies directed to decrease the risk of SSI. Furthermore, surveillance shall also be considered. Although it is reactive – it reports infections that already occurred and, hence, are no longer preventable – it provides vital data on optimal baseline levels of infection, and data on the impact interventions may have on infection incidence. Thus, it may succeed as a form of tertiary prevention.

Standard Precautions of Infection Control

Standard precautions of infection control (SPIC) are transversal. The underlying principle is that there are no risk patients, but risk procedures.[94] They are usually summarized in the following items: Patient placement and assessment for infection risk, hand hygiene, respiratory etiquette, use of personal protective equipment, safe disposal of care equipment, environment and waste (including sharps), safe management of linen and occupational safety.[94, 95]

The item that has been more widely researched is hand hygiene, dating back to Semmelweis,[6] which remains one of the central items in infection control.[96] It is effective not only against human skin flora, but also decreases the transmission of agents such as *Klebsiella*, a relevant microorganism isolated in SSI after colorectal surgery.[2, 97] Hand hygiene is recommended in 5 moments: before touching a patient, before aseptic procedures, after body fluid exposure, after touching a patient and after touching a patient surroundings.[94, 98, 99] Although the action may be easily understandable by the health workforce, compliance remains suboptimal throughout the world.[99, 100] In the Portuguese context, compliance ranged from 86% in the moment after body fluid exposure to 68% before touching a patient.[45] This reflects a tendency of healthcare workers to have a higher compliance in moments associated with an increased risk to themselves, rather than in those moments with an increased risk to patients.[99, 101] Compliance with hand hygiene is assessed by direct observation, which has been shown to yield low validity. A Hawthorne effect is likely overestimating true compliance, and everyday compliance may be grimier than reported.[101, 102] Although many interventions have been suggested to improve compliance, methodologically robust research is lacking to assess their effectiveness.[96, 103]

Approaches based on quantitative studies may be missing other dimensions that may help explain low compliance with hand hygiene. The WHO has underlined that low compliance results from a complex interaction between individual, institutional and community factors.[99] Qualitative literature identifies social norms and work environment characteristics – including colleagues' behavior, cues, resources, level of knowledge or organizational culture – as influences on hand hygiene compliance.[104] The consumption of antiseptic hand rub solutions has also been linked to their location,[93] supporting that behavioral economics may be a valuable ally in improving health outcomes and that context plays a major role in healthcare delivery. Nevertheless, universal measures apply for every HAI, not only SSI after colorectal surgery. Unless compliance with SPIC differs according to the ward and the professional – an institutional context – they do not justify why SSI after colorectal surgery appears to be more refractory to interventions than other HAI.

Specific Measures of Infection Control for SSI

SSI are necessarily related to surgical procedures. Hence, most interventions focusing on decreasing its incidence relate to the provision of safer and cleaner surgeries. The American College of Surgeons and the Surgical Infection Society (ACS/SIS) released in 2016 guidelines for the prevention of SSI, as have the CDC in 2017 and the WHO in 2018. These three guidelines represent the cornerstone of current evidence on the best practices associated with optimal SSI prevention.[50, 105, 106] Recommendations apply to all surgeries, except for bowel preparation, which is specific for colorectal surgery (table 7).

Table 7. Summary of recommendations for the prevention of surgical site infection in the three main guidelines

Interventions	ACS/SIS 2016	WHO 2018	CDC 2017
Glucose control	Recommended		
Skin preparation	Use alcohol-containing preparation		
Antibiotic prophylaxis	When indicated, and dictated by procedure and pathogens		
Intraoperative normothermia	Recommended		
Antibiotic sutures	Triclosan-coated sutures preferred		
Topical antibiotics	Not recommended		
Supplemental oxygen	Recommended if general anaesthesia		
MRSA Screening and decolonization	Context-dependent		No reference
Bowel preparation*	MBP and antibiotic preparation for elective colectomies		No reference
Hair removal	Avoid, if possible		No reference
Surgical hand scrub	No superior agent		No reference
Wound protectors	Recommended		No reference
Wound irrigation	No reference	Insufficient evidence	
Preoperative bathing	Insufficient evidence	Recommended	
Smoking Cessation 4-6 weeks prior to surgery	Recommended	No reference	
Wound closure	Purse-string closure preferred	No reference	
Gloves	Double gloves recommended	Insufficient evidence	No reference
Instruments	Use of new instruments for colorectal surgery recommended	Insufficient evidence	No reference
Wound care	Vacuum therapy for open colorectal and vascular cases, and daily wound probing for contaminated wounds	Negative pressure wound therapy recommended	No reference
Nutritional support	No reference	Recommended for underweight patients	No reference
Normovolemia	No reference	Recommended	No reference

ACS, American College of Surgeons. CDC, Centers for Disease Control and Prevention. MBP, Mechanical bowel preparation. MRSA, Methicillin-*resistant Staphylococcus aureus*. SIS, Surgical Infection Society. WHO, World Health Organization

*specific for colorectal surgery

Recommendations on safe surgery differ slightly, depending on the guidelines. The guidelines by the WHO are the only ones addressing nutritional support and normovolemia, while the ACS/SIS guidelines address smoking cessation prior to surgery. These guidelines also focus on different aspects of postoperative wound care, in which evidence is limited.

Although the WHO and the CDC recommend preoperative bathing, using either antimicrobial soap or chlorhexidine-impregnated cloth, they acknowledge that this is based on traditional good clinical practice. The ACS/SIS avoid taking a position, referring that evidence shows that, while routine preoperative bathing decreases skin surface pathogen concentration, there is no evidence that it decreases SSI incidence.[107]

There are seven interventions that gather consensus: perioperative glucose control and maintenance of normothermia, skin preparation (to be performed with an alcohol-containing preparation), antibiotic prophylaxis (with the choice of antibiotic depending on the procedure), perioperative oxygenation for patients undergoing general anesthesia with tracheal intubation, and topical antibiotics (not recommended). There also appears to be a consensus, when addressed, that mechanical bowel preparation (removal of solid stool) and antibiotic preparation (but not mechanical bowel preparation alone) is recommended in elective colectomies, that hair removal is to be avoided and that no superior agent is recommended for surgical hand scrub.

Mechanical bowel preparation is specific to colorectal surgery. After the publication of the above guidelines, a meta-analysis has sustained that mechanical bowel preparation and oral antibiotics associate with lowest risk of SSI, yet a review on best practices in bowel preparation for colorectal surgery defended that the combination has no benefits in terms of SSI, although oral antibiotic alone does.[108, 109] A systematic review published by Cochrane had already concluded there was no benefit from mechanical bowel preparation for either colon or rectal surgery.[110] Others suggest that oral antibiotic preparation has comparable effectiveness with and without mechanical bowel preparation, and the ACS/SIS guidelines do not recommend mechanical bowel preparation without the administration of oral antibiotics.[111] The debate on mechanical and antibiotic bowel preparation is still ongoing.[112] Nevertheless, even if evidence has suboptimal quality, mechanical bowel preparation is widely used by surgeons throughout the world, especially in rectal surgery where 95% of surveys' respondents have confirmed to use it routinely.[112-116]

The specificities of colorectal surgery are noted in other recommendations. Changing outer gloves and using new instruments for closure are recommended by the ACS/SIS guidelines for open colorectal surgery, and appear to be complied with.[112] Even if they acknowledge there is no research supporting such practices, they recommend them as common-sense conventional practices supported by expert consensus. The use of wound vacuum therapy (or negative pressure) is also recommended for particular procedures, amongst which is open colorectal surgery, based on a research paper with a sample of 254 patients.[117] However, a recent meta-analysis has challenged this view and claimed that standard dressing may be superior to negative pressure wound therapy.[118] Another recent systematic review has failed to demonstrate the effectiveness of high fraction supplemental oxygen in colorectal surgery, compared to low fraction.[119] A Cochrane systematic review on dressings for the prevention of surgical site infection recommended to base decisions about how to dress a wound following surgery on dressing costs, given the uncertainty of its effectiveness in reducing the risk of SSI.[120]

The large number of potential interventions and the differential evidence surrounding each one could drive surgeons away from prevention efforts, particularly those they may doubt to be beneficial. To accommodate for this, the Institute for Healthcare Improvement (IHI) developed the bundle concept in 2001 – a small set of evidence-based interventions for a defined population and care setting.[121] The agglutination of interventions with strongest evidence provide a synergic effect in the improvement of patient outcomes, namely SSI, with a straightforward measurement that makes it easy to adhere to. Their synergy depends on the compliance with the entire bundle. As missing one intervention is the same as failing to comply with the bundle, the latter is as strong as its weakest link. The rationale is not to just simply tie some interventions together, but to implement a culture of safety on patient care,[122] as total compliance needs to be sustained over the long-term.

Several studies have addressed the effectiveness of bundles in colorectal surgery. In 2013, the Mayo Clinic experience found a 50% reduction in SSI incidence with preoperative showering, antibiotic prophylaxis, chlorhexidine antisepsis, glove change before fascia closure, adherence to hand hygiene, dressing removal 48 hours after surgery, patient education and surveillance.[123] The Duke experience reduced superficial SSI from 19% to 6%, with a smaller and non-significant effect in organ/space infections. Costs increased, with no statistical significance. Their bundle included preoperative showering, mechanical bowel preparation with antibiotic preparation, chlorhexidine antisepsis, antibiotic prophylaxis, fascial wound protector, glove change, limited operating room traffic, maintenance of euglycemia and normothermia, removal of dressing 48 hours after surgery, daily wound irrigation and patient education.[124] The Cleveland Clinic experience, on the other hand, showed a significant reduction in overall (12% to 7%) and organ/space infections (6% to 2%), with no significant difference in superficial infections. Their bundled measures included mechanical bowel preparation and antibiotic preparation, preoperative bathing, chlorhexidine rub, antibiotic prophylaxis, wound edge protector, glove change after each intraoperative digital rectal exam and after anastomosis established, wound saline irrigation, dressing removal at 48 hours and postoperative surveillance.[125] Moreover, compliance with all components reduced not only SSI but also episodic costs.[126]

In Europe, results have shown a similar trend, even though adopted bundles have been more modestly sized. In the Netherlands, the prevention bundle for colorectal surgery was implemented in 2008, following the recommendations of the ECDC, and included antibiotic prophylaxis, avoidance of hair removal, maintenance of normothermia and hygiene discipline (such as limiting operating room door movements). It showed a 37%

risk reduction, with a 13% risk reduction for each point increase in compliance-level.[127] National bundles were also implemented in Piedmont, Italy, in 2008, where two papers from two different hospitals found a significant decrease in SSI incidence for colorectal surgery, even if they constructed their bundles with different evidence-based interventions.[128, 129]

It is claimed that it is the bundle approach that is successful, and hence the combination of interventions within the bundle may vary.[130] Through their improved culture of safety, nearly any combination of evidence-based measures would do, as they would be applied consistently by motivated teams. However, some bundles are more equal than others.[122] A randomized trial found an increase in SSI after colorectal surgery with the implementation of a bundle, consisting of maintenance of normothermia, supplemental oxygen, fluid restriction, use of wound protector and no mechanical bowel preparation.[131] The choice of interventions does matter.

To this day, three systematic reviews, with meta-analysis, have summarized the effectiveness of surgical care bundles in reducing SSI after colorectal surgery.[130, 132, 133] The main results are displayed in table 8.

Table 8. Main results of the effectiveness of prevention bundles in reducing surgical site infection after colorectal surgery, per systematic review

	Tanner 2015 [130]	Zywot 2017 [133]	Pop-Vicas 2020 [132]
Number of original studies	210	1775	1044
Number of studies in qualitative synthesis	16	37	40
Number of studies in quantitative synthesis	13	24	30
Overall quantitative sample size in patients (intervention/control)	8 515 (4 649/3 866)	17 619 (8 796/8 823)	20 701 (10 627/10 074)
Compliance rate range	2.9-92%	19-99%	19-92%
SSI in intervention groups	7.0%	9.3%	8.4%
SSI in control groups	15.1%	14.9%	15.5%
Effect (RR)	0.55 (0.39-0.77)	0.60 (0.50-0.72)	0.56 (0.48-0.65)
I^2	84%	71%	71%

RR, Relative Risk. SSI, Surgical site infection.

The overall number of included studies and, hence, sample size in patients increased relevantly between each publication, a proxy indicator of the interest this subject has received in recent years. All three systematic reviews summarize a similar effect, suggesting that the implementation of prevention bundles may reduce the incidence of

SSI after colorectal surgery by half. It is worth highlighting that, in every systematic review, no single included article had a weight superior to 10%. The reviews by Zywot and Pop-Vicas also estimated the effect of bundles for each type of SSI.[132, 133] They found that bundles were effective in reducing the incidence of both superficial and organ/space infections, with no apparent effect on deep infections. However, heterogeneity is tremendous, and the option to meta-analyse data is statistically doubtful. Heterogeneity was justified by different components in bundles in each study, as well as lack of data on implementation methods, hospital characteristics, baseline interventions and different types of colorectal procedures being performed. Heterogeneity is better understood by taking a close look at table 9, which summarizes the frequency – absolute and relative – of each bundled intervention in the papers included in each systematic review. The option to include only interventions from the ACS/SIS guidelines was made because only those were considered for the latter two reviews.[132, 133]

Table 9. Frequency of inclusion of each bundle intervention in the systematic reviews

ACS/SIS bundle intervention	Tanner 2015 [130] n (%)	Zywot 2017 [133] n (%)	Pop-Vicas 2020 [132] n (%)
Number of studies included	16	37	40
Antibiotic prophylaxis	14 (87.5)	18 (48.6)	40 (100)
Glycemic control	8 (50.0)	21 (56.7)	22 (55.0)
Intraoperative normothermia	9 (56.2)	20 (54.0)	32 (80.0)
Appropriate hair removal	9 (56.2)	18 (48.6)	20 (50.0)
Supplemental oxygen	3 (18.7)	6 (16.2)	7 (17.5)
Wound edge protector	2 (12.5)	7 (18.9)	11 (27.5)
Preoperative bathing with CHG	1 (6.3)	15 (40.5)	16 (40.0)
CHG in alcohol skin preparation	4 (25.0)	13 (35.1)	6 (15.0)
Glove/gown change	2 (12.5)	13 (35.1)	15 (37.5)
Restricted operating room traffic	2 (12.5)	0 (0.0)	5 (12.5)
Smoking cessation	1 (6.25)	2 (5.4)	4 (10.0)
MBP plus oral antibiotics	3 (18.7)	9 (24.3)	18 (45.0)
Removal of sterile dressing within 48 hours	2 (12.5)	16 (43.2)	16 (40.0)
MRSA screening	0 (0.0)	2 (5.4)	0 (0)

ACS, American College of Surgeon. CHG, chlorhexidine gluconate. MBP, Mechanical bowel preparation. MRSA, Methicillin-resistant *Staphylococcus aureus*. SIS, Surgical Infection Society.

The most commonly included interventions are those with the strongest evidence supporting them, and in which guidelines are consensual: maintenance of normothermia and glycemic control, appropriate antibiotic prophylaxis and hair removal. Adequate antibiotic prophylaxis has been shown by Cochrane to decrease SSI incidence in colorectal surgery from 39% to 13%.[134] Interventions recommended by guidelines but for which published evidence has provided mixed results are more rarely included. MRSA screening and decolonization is rarely considered, possibly reflecting the residual etiological role of *Staphylococcus aureus* as a causative agent of infection in this particular surgery.[2] The number of interventions present in each bundle ranged from 2 to over 11, which may have affected comparability, effect, but also compliance. Low compliance illustrates the difficulty of translation complex knowledge into clinical practice.[112]

The bundle concept is also integrated in the Enhanced Recovery After Surgery (ERAS®) Society care pathways, which are designed to reduce perioperative stress, maintain postoperative physiological function, and accelerate recovery after surgery, namely colorectal surgery. Their scope expands beyond SSI to address other outcomes such as postoperative ileus, pain or length of stay. Their 25-item checklist include numerous measures which do not affect SSI directly. Nevertheless, glycemic control, avoidance of hypothermia, antibiotic prophylaxis and skin preparation with chlorhexidine are all present with strong recommendations in their 2019 guidelines. Bowel preparation with oral antibiotics is preferred over bowel preparation alone, and there is no mention of supplemental oxygen.[135] The pathway has been suggested to decrease the incidence of SSI and to lead to healthcare cost savings,[136-138] although some papers have challenged this results.[139, 140]

In face of marked heterogeneity, even if results are mostly positive, it is vital to return to IHI to understand which criteria define an adequate surgical care bundle.[121] First, an effective bundle requires individual measures to have strong evidence. In the original article by Anthony *et al* in which the implementation of a bundle was associated with an increase in SSI incidence, they included two interventions (out of five) for which evidence is lacking, namely fluid restriction and omission of mechanical bowel preparation.[131] Secondly, the number of components should be limited: IHI suggests three to five components.[121] This links with a selection of the strongest evidence-based interventions, and it improves the practicality of the adoption of bundles. This is particularly relevant as full compliance has been shown to offer significantly higher protection than partial compliance in colorectal SSI rate.[141, 142] The more complex the bundle, the harder it is for healthcare professionals to comply. Lastly, selected measures need to be applied to every patient. In the Michigan study, Jaffe *et al* included minimally invasive surgery and short duration as components of a prevention bundle.[126] As it is not possible to perform a small laparoscopic procedure for every patient, these should not be part of a bundle of interventions.

The process of ongoing and systematic collection, analysis and interpretation of health data is called surveillance, and is essential for planning, implementation and evaluation of public health practice and timely dissemination of these data to those who need to know.[143] It is accepted that surveillance operates through two mechanisms: surveillance and feedback effects. Surveillance effect promotes better practices by promoting awareness among healthcare professionals that they are being observed. Feedback refers to the timely dissemination of analysed data, easily interpretable, that pinpoints processes and/or outcomes requiring optimization.[144-146]

As mentioned, hospital surveillance for HAI began in the post-second world war period, as the proliferation of hospitals and the improvement on general health brought these infections to the forefront of health problems.[8, 14] However, it was not until a few decades later that the effectiveness of intensive surveillance and prevention programs was established, in an influential study that concluded that such measures could prevent up to one-third of HAI,[147] leading to the recommendation by the CDC to implement surveillance as a key strategy for the prevention of HAI.[145] In the United States, hospitals report to a national surveillance system, called the NHSN, which was formed in 2005 as a combination of prior existing surveillance systems. In Europe, the European Council Recommendation of 9 June 2009 on patient safety recommended performing surveillance of the incidence of targeted infection types. The current HAI-Net protocol dates to 2016, and its main objective is to ensure standardization of definitions, data collection and reporting procedures for participating hospitals, in order to contribute to improve the quality of care. Beyond monitoring the burden and epidemiology HAI and, in particular, SSI, the network aims to validate risk factors and explore the correlation between structure and process indicators and the incidence of SSI throughout Europe, while allowing hospitals to benchmark their data to other hospitals with comparable methodology.[53] In the case of the HAI-Net, in which Portugal is included, the indicators used for SSI surveillance are the same regardless of the surgery, even if reports do differentiate incidence by surgical groups.[2, 53]

The first step of surveillance is data collection, which needs a clearly specified case definition, with objective criteria. In SSI, as observed earlier, the case definition mixes both clinical and laboratory criteria.[3, 53] Collection needs to be similar across hospitals for accurate benchmarking. In addition, guidance on data to be included in both the numerator and denominator of metrics are required, so that the second step of data analysis may be performed accurately. Although cumulative incidence and density of infection are the usual historical metrics used to summarise surveillance data, as is the case in Europe, the NHSN prefers to use the standardized infection ratio.[53, 148] The latter adjusts for patients with varying risk of infection, combining facility-level, patient-level and procedure-level information. Nevertheless, the adjustment approach is not without limitations, as it only allows for adjustment of readily available variables, which do not comprise all risk factors, and the inclusion of variables in the model is based on statistical parameters; hence, cut points may not be clinically relevant.[149] Other limitations, such as the difficulty of patients and hospital administrators to understand this metric and the fact that the reference baseline population that generates the "expected" number of cases quickly becomes outdated have limited the adoption of this metric elsewhere.[145] Nevertheless, infection rates have also been shown to yield limitations when comparing rates between countries.[150] It is also possible to use the days since the last infection, although such metric is usually reserved for situations in which incidence is particularly low.[145] Data analyses include not only fluctuations in described metrics but also changes in age and sex distributions, geographical locations or, for more sophisticated systems, at-risk groups.[151] Outside the scope of this introduction, surveillance may also act as a sensitive system for early detection of outbreaks.[145, 151] Importantly, surveillance data need to be displayed in a form that is easily interpretable for any interested party. The format in which data are shared, the frequency, the mechanism or the central message should all be carefully considered when disseminating data to stakeholders.

The utility surveillance data depends critically on its quality. A basic assumption on the data presented is that it represents the true nature of the phenomenon at hand. As one refers to the frequency of infection, one is truly referring to the *measured* frequency, which serves as an indicator of the *true* frequency of infection. Remembering Plato's allegory of the cave, one sees but the shadows. Case definitions need to be applied consistently and systematically for data to be interpretable, and laboratory testing methods need to be sensible and specific. Representativeness is key to ensure results are generalizable and applicable to the entire population. However consensual these characteristics may be, the WHO reports that HAI's true global burden remains unknown due to the difficulty in gathering data and the complexity and lack of uniformity of criteria for HAI diagnosis, even for countries with implemented surveillance systems.[21] There is a gap between scientific evidence and day-to-day practice.[112] One major limitation of surveillance is that the majority of SSI occur following discharge, a trend accelerated by ambulatory surgery, which usually miss detection.[52, 54] Another major limitation is that it is often performed manually by reviewing patient medical records. This process has been shown to be labour-intensive, time-consuming and prone to error, affecting the characteristics outlined in the beginning of the paragraph.[152-154] Often, the collection of data is so morose that data analysis, interpretation and dissemination are relegated to a secondary position.[145] Automated surveillance is a novel solution that has been suggested recently. Fully automated surveillance applies a standard definition using available data on electronic health records to detect infections, with no need for manual chart review. These systems are highly complex and limited to available data. They may not be applicable to every HAI. In the case of SSI after colorectal surgery, the most promising systems are semi-automated, which use data in electronic health records to select patients with high-risk of SSI for subsequent manual review.[152] Patients categorized as low-risk are assumed as having no SSI, and need no further review. These semi-automated systems have been shown to improve the exhaustiveness, representativeness, efficiency and accuracy of SSI counts, optimizing the process of data collection.[153-156]

Due to the significant resources required for SSI surveillance, it is often targeted to high-volume and/or high-risk procedures, amongst which is colorectal surgery.[61] When correctly implemented, one may expect SSI rates to artificially increase. Rigorous surveillance has been shown to be associated with higher SSI rates, thus demonstrating possible underestimation of current incidence, especially for superficial infections.[157-159] Quality matters, which is why surveillance programs need to be periodically evaluated, to ensure maximum effectiveness.[61] Nonetheless, throughout the years surveillance has been shown in different countries to effectively reduce SSI incidence following colorectal surgery.[160-162] In Spain, surveillance was shown to be effective when implemented concomitantly with a prevention bundle, even if feedback to surgeons remained low.[112, 163]

Infection prevention and control at the national level

Risk factors for SSI after a colorectal operation are universal, in the sense they apply to every patient submitted to surgery. The same is true for prevention strategies. However, table 4 shows that SSI incidence is not similar across comparable European countries. Something is amiss. The differential distribution of risk factors and implementation of the most robust prevention interventions may justify a substantial part of that variance.

As referred earlier, Portugal's health system (SNS) is inspired in the Beveridge model of the National Health Service of the United Kingdom. Succinctly, this is an universal health care system financed mainly through general taxation.[164] The private sector in this model is relatively small, mainly specializing in a narrow range of elective procedures.[165] Thus, most healthcare delivery is made through public hospitals and primary care providers. The adoption of a certain system rather than another is not arbitrary: it reflects a philosophical positioning in terms of the role of the State and is a direct consequence of each country's historical and geographical background.

SNS comprises 45 hospital centres distributed across continental Portugal. One of the central services of the Ministry of Health is the Directorate General of Health (DGS), which has administrative autonomy. Among its main intervention areas is the coordination and development of health programs, designed to tackle the identified health problems of the nation.[166] As resources are inherently limited, DGS pinpointed the 12 major health problems in the country. These major problems are the focus of the priority health programs, amongst which is Antimicrobial Resistance and Infection Prevention and Control Program (PPCIRA, in the Portuguese acronym).[167]

PPCIRA was created from the fusion of the infection prevention program and the antibiotic resistance program, back in 2013.[168] It presents a vertical structure where, besides the national coordination, there are also Regional and Local Units in each health regional administration and each healthcare delivery unit, be it in the primary, secondary or tertiary care. Infection control commissions are also mandatory in private and social healthcare delivery units.[169] The program's general objective is to reduce the incidence of HAI as well as the percentage of isolated microorganisms with antimicrobial resistance. Its strategies include health education on adequate use of antibiotics and infection prevention practices, epidemiological surveillance, and the normalization of procedures and clinical practice across settings.

In 2014, one of the first interventions of PPCIRA was the extension of the hand hygiene campaign to other components of SPIC, thus creating the Multimodal Strategy of Promotion of Standard Precautions of Infection Control. In the scope of this same strategy, it is recommended for every health unit to perform an annual internal audit to the quality of processes and structures central to SPIC. The audit analyses ten process patterns (patient placement, use of personal protective equipment, hand hygiene, respiratory etiquette, safe injection practices, worker safety, safe handling of textiles, laundry and residues, treatment of clinical equipment and environmental control) and two structure patterns (SPIC knowledge and resources). Between 2015 and 2020, there was a 6.5% increase in compliance with all ten SPIC components. Worker safety and safe handling of residues were the precautions with lowest compliance (82% and 86%, respectively).[45]

Following the prevention strategies outlined previously, DGS emitted a norm in 2015 to establish a prevention bundle for every surgery performed in continental Portugal. It included most of the consensual interventions from the guidelines: maintenance of perioperative normothermia and glucose control, antibiotic prophylaxis, chlorhexidine bath in the day of the surgery and the day prior to it, and avoidance of hair removal.[170] Unfortunately, no public data on bundle compliance is available.

In terms of surveillance, PPCIRA collects, analyses and interprets data from every hospital and reports to the ECDC under the HAI-Net protocol, as referred previously.[53] The network differentiates between surveillance in ICU and surveillance of SSI. Under the scope of this protocol, Portugal collects data not only on the incidence of and type of infection, but also on the risk factors with strongest evidence linking them to SSI. These include the patient's sex, ASA score, wound classification, urgent status, duration of surgery and whether it was performed laparoscopically, which comprise most risk factors summarized by Xu et al.[62] Comorbidities are lacking, as well as stoma creation, which is specific to colorectal surgery, and blood transfusion. The registry of whether antibiotic prophylaxis was given is also included. Internally, PPCIRA also implemented surveillance in neonatal intensive care units and surveillance of nosocomial bloodstream infections. Portugal also participated in the Second European Point-Prevalence Survey of HAI; disability-adjusted life years were estimated for each HAI, yet SSI was considered as a whole group, without taking into account the specificities of each surgery.

In 2015, *Fundação Calouste Gulbenkian* promoted a 3-year national challenge to decrease the incidence of 4 HAI: SSI (in colorectal surgery and orthopaedic surgery), CLABSI, CAUTI and VAP. Hospitals were eligible to participate if they applied and had a minimum of 200 hospital beds, an adult ICU, a general surgery and/or orthopaedics service and an internal medicine service. It was promoted in 12 selected hospitals, through a collaborative approach with the scientific support of IHI, and was named *Stop! Infeção Hospitalar* (Stop! Hospital Infection).[171] The vision behind this approach is that evidence exists on optimal practices, yet there is a gap between scientific evidence and clinical practice.[112, 121] Through a series of local visits to discuss local contexts, learning sessions and implementation and measurement of the most effective prevention strategies, the challenge succeeded in its goal of decreasing in over 50% the incidence of each HAI included. The exception was, precisely, colorectal surgery.[171] This challenge is to be revived in 2023 with the same goals. In this context, the SSI bundle was redesigned. It maintains the previous peri-operatory interventions (antibiotic prophylaxis, avoidance of trichotomy, skin preparation and glycaemia and normothermia control) and adds three pre-operatory (MRSA screening, preoperative bath with chlorhexidine and oral antibiotic preparation) and two post-operative measures (glycaemia and normothermia control and aseptic technique in dressing management).[170] Antibiotic preparation is specific to elective colorectal surgery, acknowledging the specificities of these procedures.

Addressing SSI in a specific context

Disease occurs in specific contexts, in time and space. Portugal is in a decisive moment in its history of infection prevention. The new health law, approved in late 2019, reaffirmed the centrality of SNS in the overall health system. It restated the duty of society to contribute to health protection in every policy and activity sector. The COVID-19 pandemic is finally controlled. Although it has improved compliance with all SPIC and brought the need to tackle infectious diseases to the political debate, its impact on surveillance, SSI incidence and overall practices is undetermined.[172-176] Three years after the onset of the pandemic, infection preventionists are now ready to refocus their efforts on HAI. The previous pages have analysed known risk factors and preventive strategies in the field of this particular SSI. To understand their role in the Portuguese context, one needs to go beyond association metrics and assess how these and other factors occur locally.

Hospital-level characteristics, in particular, have been consistently overlooked over the years, even though the CDC acknowledged their potential role as early as 1999.[51] Systematic reviews abound for both operative risk factors and comorbidities, as presented. To the best of our knowledge, no systematic review had been published, however, on hospital-level risk factors in SSI following colorectal surgery. This is an essential step to understand which hospital characteristics have the strongest evidence as risk factors, and which require further research.

Research on hospital characteristics in the field of SSI after colorectal surgery is not only scarce, but of suboptimal quality. Colorectal surgery is performed in hospitals. People with similar overall characteristics who are subjected to surgery in different hospitals may have different health outcomes due to each hospital's context. If SSI incidence may be correlated within hospitals, then analysis using common regression methods underestimate contextual effects.[177] Previously, one established that disease is a deeply social process.[1] Epistemologically, knowledge on distribution and determinants of population health – epidemiology – is multilevel, as it needs to consider both people and areas.[9] Hence, it is vital to assess whether SSI incidence does vary between hospitals, and which hospital characteristics explain such variance, using the adequate multilevel regression analysis.

Another key point in establishing context is by addressing surveillance. Disease measurement depends critically on the quality of the surveillance system. Consistency, sensitivity, and specificity are optimized through adequate case definitions, and comparability ensured when the same criteria is used similarly between hospitals. Despite the limitations of the current CDC definition of SSI, it is used universally. One of the key characteristics of optimal surveillance is the representativeness of data, to ensure generalizability and applicability. As the European network admits, for practical purposes, that a hospital may report as few as 30 procedures and/or perform surveillance for only three months each year, it is highly relevant to analyse whether reported figures on colorectal surgery are representative of the true phenomenon, or whether a selection bias may be present. Hence, it is vital to compare reported figures under PPCIRA surveillance to those reported nationally to *Administração Central do Sistema de Saúde* (ACSS), which are used to systematically characterize hospital morbidity. Another key characteristic of optimal surveillance is timeliness.[145] In every national setting, surveillance implies the manual review of patient charts for the occurrence of SSI and the registry of relevant data. This process is not only labour-intensive and prone to error and inter-observer variability, but it is also time-consuming.[152, 178]. Even though the application of semi-automated surveillance has been increasingly and successfully tested throughout the world,[154, 179] it requires customization in each setting to maximally support hospital surveillance efforts.[180] Therefore, it is relevant to understand whether, and how, data registered in current electronic health records in Portugal allows the adaptation and implementation of semi-automated methods.

Although risk factors are universal and their association is expected to be the same regardless of the setting, their prevalence is not. One may use both association and prevalence to estimate the population attributable risk and population attributable fraction (PAF) of each risk factor to assess their impact on SSI following colorectal surgery. Theoretically, the higher the PAF of a specific risk factor, the larger the decrease in SSI if one targets that risk factor in health interventions. Risk factors with strongest evidence of association are collected under the scope of HAI-Net and are readily available to be analysed. Using a weighted-sum approach, it is also possible to assess the impact of all risk factors combined, thus providing an estimate of the comprehensiveness of current surveillance indicators to explain incidence rates. It would be highly relevant to extend this analysis to the compliance with preventive strategies, both SPIC and prevention bundles. Unfortunately, required data are not available.

In his influential book *Meditations on Quixote*, Ortega y Gasset famously wrote that “I am I and my circumstance”. This notably socio-philosophical idea is usually quoted as such, yet it gains more power when one considers the entire sentence: “I am I and my circumstance, and if I do not save it, I do not save myself."[181] The same is true in epidemiology. One needs to know his context deeply, to know where to target preventive efforts to decrease SSI with maximum efficiency and effectiveness. By improving one's circumstances, one improves himself.

The aim of this thesis is to understand the impact that risk factors and context have on the incidence of surgical site infection after colorectal surgery, in Portugal, to pinpoint targets for future health interventions (Figure 5).

1. To review the available evidence on the association between healthcare-related characteristics and surgical site infection after colorectal surgery.

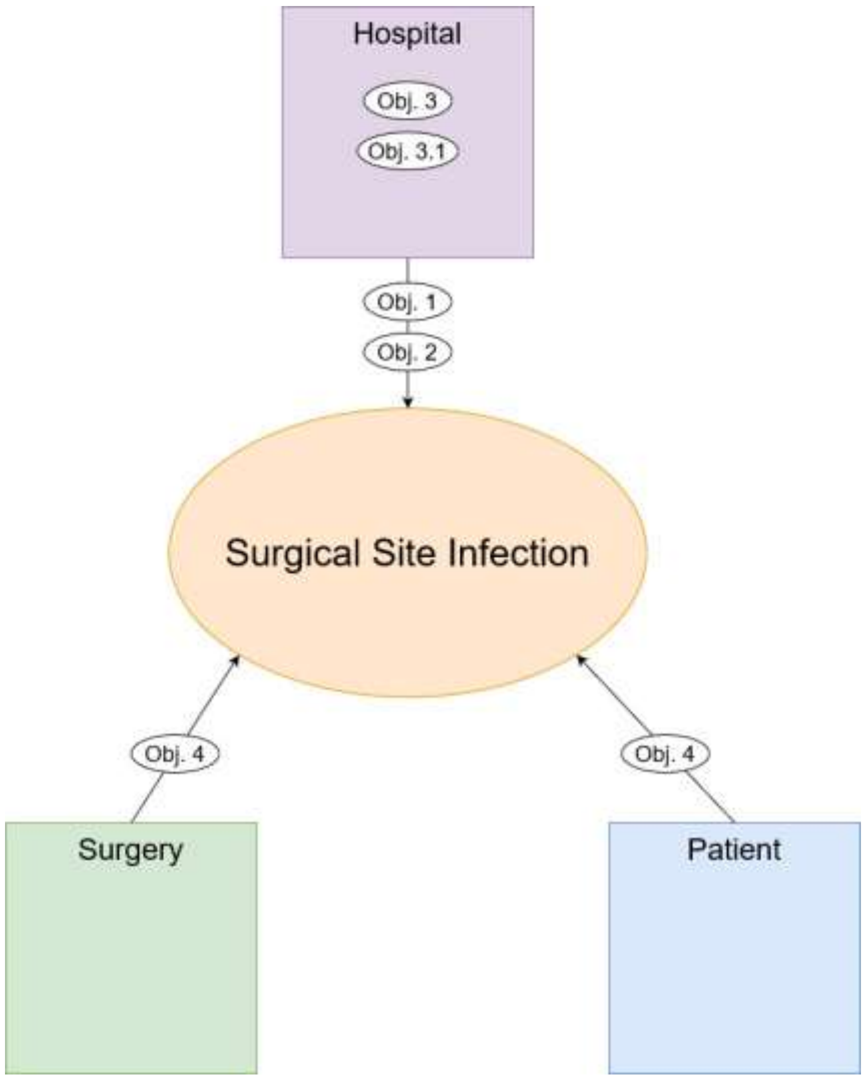
2. To assess whether surgical site infection after colorectal surgery varies between hospitals, and what part of that variance may be due to contextual effects.

3. To estimate the representativeness of reported surgical site infection incidence by comparing the National Epidemiological Surveillance database with the gold-standard national database.

    3.1 To determine whether a classification model, using electronically available data, could improve the efficiency, completeness and representativeness of surveillance.

4. To estimate the impact of risk factors for SSI after colorectal surgery in SSI incidence in Portugal, using the population attributable fraction approach.

Figure 5. Simplified concept map of risk factors for surgical site infection after colorectal surgery



The National Surveillance Database

At every Portuguese hospital, surveillance is performed following the European methodology under the HAI-Net protocol.[53] Accordingly, for each admission for surgery, the main surgeon or other trained physician fills a sheet, with identification data and surgery data, as outlined in table 10. Some relevant variables not included may be calculated using the variables below, such as age and duration of operation.

Table 10. Operation, patient and infection data retrieved in the surveillance of surgical site infections, according to the HAI-Net protocol

Variable group	Variable	Variable type
Patient Data	Date of Birth	Date
	Gender	Categorical
	Date of Hospital Admission	Date
	Date of Discharge	Date
	Outcome from hospital	Binary (Dead or Alive)
Operation Data	Date of Operation	Date
	Time of Beginning of Surgery	Hour
	Time of Ending of Surgery	Hour
	Procedure ICD code	Numerical
	Urgent Operation	Binary
	ASA Classification	Categorical
	Antibiotic Prophylaxis	Binary
	Wound Contamination Class	Categorical
	Multiple Operations	Binary
	Endoscopic Procedure	Binary
	Implant in Place	Binary
	Number of operating room door openings during operation	Numerical
Infection Data	Surgical Site Infection	Binary
	Infection Type	Categorical

ASA, American Society of Anaesthesiologists. ICD, International Classification of Diseases

Surgery codes use the International Classification of Diseases (ICD) ninth or tenth revisions, as recommended by the ECDC. Codes for both revisions referring to colon or rectal surgery are available on Annex I. There is also room to register up to 3 identified microorganisms and respective resistance profile per patient and when the bacteriological exam was performed. Likewise, up to six antibiotics may be registered per patient, with respective date of beginning, days of antibiotic use, dosage and route of administration. These include both prophylactic and therapeutic antibiotics. Although the European protocol provides potential hospital data to be collected by participating hospitals, most are not available in the Portuguese context. Apart from where surgery took place (hospital and service), variables such as hospital type, hospital size, alcohol hand-rub consumption per year in surgical ward/units, patient-days per year in surgical wards/units and the presence of a system for root cause analysis are not centrally available.

Data retrieved in each hospital is sent, collected and aggregated at the national level, in the electronic platforms of DGS. Participating hospitals are required to routinely collect patient and unit-based variables for a minimum of three months and/or 30 surgical procedures, each year.[53] The dataset uses the surgical procedure as the unit of measurement, registering all variables as different columns. For each procedure, corresponding to a line, there is an associated process and episode code, to ensure that there are no repetitions. The resulting sheet includes data on all procedures subjected to surveillance for SSI: colorectal surgery, cholecystectomy, caesarean section, cardiac surgery, hip and knee arthroplasties and laminectomy.

From 2015, when systematic collection of data was initiated, until mid-2018, the national dataset consisted of a single spreadsheet containing all data. From then onwards, in response to an operating system that was unable to be updated, a new software was developed. Although data collection remained the same across hospitals, it translated into a different dataset. Namely, the variables "Multiple Operations" (binary as "yes" or "no") and "Operating Room door openings" (numerical variable) are only present in the updated version, even though no door openings were registered throughout the study period.

Antibiotic, infection and resistance data began to be registered in different pages of the spreadsheet, linkable by ID of the procedure, surgery date, hospital and infection. Under this revised organization, there were no more quantitative limitations on antibiotic, microorganisms and resistances registrations. Infection data began to register whether diagnosis was made during admission or post-discharge, and, in case of the latter, which post-discharge surveillance method was used, as suggested by the European protocol.

In former dataset, there was column named "Antibiotic", which was categorically set as either "therapeutic" or "prophylactic". Hence, every time a procedure had this variable set as "therapeutic", it was not immediately clear whether prophylactic antibiotic had been administrated, as if the two were mutually exclusive. In the most recent dataset, the column "Antibiotic" was substituted for one named "Prophylactic Antibiotic", with "Yes" or "No" as possibilities of registration. Hence, regardless of the use of therapeutic antibiotics, from 2018 onwards there is a clear variable stating whether antibiotic prophylaxis was administrated or not. Following the same rationale as the resistance data, antibiotic data registered in a different sheet now include every antibiotic administrated to each patient in each given episode, with no upper limit on the number of antibiotics.

The referred changes improved the dataset accuracy on antibiotic prophylaxis, improved the comprehensiveness of data on antibiotic use and resistances and provided additional data on infection diagnosis. However, it made more difficult to join both datasets and make sure each variable is addressing the exact same construct. The alterations here mentioned were performed using the software R, version 4.0.0, which created a new spreadsheet without changing the original datasets. The libraries used for these procedures were ‘*openxlsx*’, ‘*readxl*’, ‘*tidyr*’ and ‘*dplyr*’.

The first step was to rename variables, to ensure variables addressing the same construct had the exact same column name. Two variables required additional standardization. In the first dataset, there was a column named “type”, referring to whether surgery had been “programmed” or “urgent”, while in the second the variable was named “Urgent procedure”, filled in a binary form. The final database was standardized using the second model, thus rearranging the former categorical variable into the binary one. The other variable requiring such standardization was already addressed, referring to antibiotic prophylaxis. For every line where it was unclear whether antibiotic prophylaxis had been given, it was considered as “Yes” if either cefoxitin in a single dose or the combination of metronidazole and gentamicin, in a single dose, were administrated, following national norms.[170] For cases where there was no evidence of antibiotic prophylaxis without a clear indication that it was not provided, they were classified as ‘missing’. Other data standardization referred to human input error. ICD-9 codes usually have 2 digits, a dot, and then 1 or 2 digits. In some cases, the cells had a colon separating the numbers. These sorts of issues were also uniformed.

Datasets were combined using the *merge* function in R. A novel binary variable was created, identifying procedures occurring in hospitals that were participating or had participating in *Stop! Infeção Hospitalar*. For each procedure which had a surgery code included in the ones provided in Annex I were classified as either COLON or RECTAL surgeries. Using the subset function of R, the final dataset would include these procedures exclusively. Duplicates were removed using date of birth, sex, date of surgery and hospital where surgery took place. For cases where date of birth was not available, the variable “ID” was used instead. Finally, the merged dataset was combined with the antibiotic, microorganism and resistance spreadsheets using the *left_join* function.

The final database comprised 18 366 procedures performed nationwide, from 2015 to 2020.

The classification of diagnosis and procedures in each hospital admission, grouping them in diagnosis-related groups (GDH in the Portuguese acronym) is essential to characterize hospital production and morbidity. It is a fundamental activity in which hospitals invest significant resources, as hospital financing is based in the distribution of their GDH. This classification is termed clinical coding, which began in the 1989 in SNS hospitals and has used the ICD 9th revision and, from 2017, 10th revision. It is performed in hospitals by trained physicians, using a systematic and standardized approach that ensures that data refers to the effective clinical characteristics of the population, expressed in their medical records. Data from each hospital is reported and stored in a central database managed by ACSS, and it serves as the gold-standard for hospital productivity in the country.

To carry out objective 3, data was retrieved from this national database. Colon and rectal procedures were selected using codes available on Annex I, and were provided in two separate sheets. Each line corresponded to a group of patients in a given age quinquennium, hospital, year and sex. One column provided the count of colon and rectal procedures in that group, and a second column provided the count of urgent colon and rectal procedures in the same group. Laparoscopic procedures, either referring to colon or rectal surgery, were provided in a separate sheet, following the same rational: each line referring to a group of patients in a given age quinquennium, hospital, year and sex, where one column provided the count of laparoscopic procedures in that group, and a second column provided the count of urgent laparoscopic procedures. Although the ASA score was requested, it is not part of the morbidity characterization of hospital admissions.

Dataset was edited using Microsoft Excel, creating a new spreadsheet without changing the original datasets. The working dataset considered each line as a hospital, in a given year. Using the SUMIFS function, columns counted the number of colon and rectal procedures, laparoscopic, urgent operations, patients of male sex and patients aged 65 years-old or over.

PAPERS

Paper 1

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Antimicrobial Resistance and Infection Control

REVIEW

Open Access

Beyond the operating room: do hospital characteristics have an impact on surgical site infections after colorectal surgery? A systematic review

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Abstract

Background: Hospital characteristics have been recognized as potential risk factors for surgical site infection for over 20 years. However, most research has focused on patient and procedural risk factors. Understanding how structural and process variables influence infection is vital to identify targets for effective interventions and to optimize health-care services. The aim of this study was to systematically review the association between hospital characteristics and surgical site infection in colorectal surgery.

Main body: A systematic literature search was conducted using PubMed, Scopus and Web of Science databases until the 31st of May, 2021. The search strategy followed the Participants, Exposure/Intervention, Comparison, Outcomes and Study design. The primary outcome of interest was surgical site infection rate after colorectal surgery. Studies were grouped into nine risk factor typologies: hospital size, ownership affiliation, being an oncological hospital, safety-net burden, hospital volume, surgeon caseload, discharge destination and time since implementation of surveillance. The STROBE statement was used for evaluating the methodological quality.

A total of 4703 records were identified, of which 172 were reviewed and 16 were included. Studies were published between 2008 and 2021, and referred to data collected between 1996 and 2016. Surgical site infection incidence ranged from 3.2 to 27.6%. Two out of five studies evaluating hospital size adjusted the analysis to patient and procedure-related risk factors, and showed that larger hospitals were either positively associated or had no association with SSI. Public hospitals did not present significantly different infection rates than private or non-profit ones. Medical school affiliation and higher safety-net burden were associated with higher surgical site infection (crude estimates), while oncological hospitals were associated with higher incidence independently of other variables. Hospital caseload showed mixed results, while surgeon caseload and surveillance time since implementation appear to be associated with fewer infections.

Conclusions: Although there are few studies addressing hospital-level factors on surgical site infection, surgeon experience and the implementation of a surveillance system appear to be associated with better outcomes. For hospitals and services to be efficiently optimized, more studies addressing these variables are needed that take into account the confounding effect of patient case mix.

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Keywords: Characteristics, Colorectal surgery, Facilities, Hospital, Review, Surgical site infection, Surveillance

Background

Surgical site infection (SSI) is the third most common healthcare-associated infection (HAI) [1], and it is known to have a high impact on hospital length of stay, expenditure, surgical morbidity and mortality [1–3]. According to the latest report from the European Centre for Disease Prevention and Control, open colon surgery was the procedure associated with the highest risk of SSI (10.1 per 100 operations) followed by laparoscopic colon surgery (6.4 per 100 operations) [4]. Given its burden, efforts have been made to identify modifiable risk factors. In their guideline for the prevention of SSI in 1999, the Centers for Disease Control and Prevention (CDC) acknowledged that the risk of SSI is influenced by the characteristics of the patient, procedure, personnel and hospital [5]. Based on the same rationale, the National Healthcare Safety Network (NHSN), the North American surveillance system for HAI, combine facility, patient and procedure-level variables in their SSI risk adjustment models to predict the number of expected infections [6]. However, most research has focused on patient and procedural risk factors. Similarly, preventive interventions—either isolated or in a bundle—have focused exclusively on optimizing patient condition and delivering the surgical procedure as safely as possible [7–10]. Hospital characteristics have been consistently overlooked. Even though most may be deemed as non-modifiable, they are proxy indicators of unmeasured variables, such as cleanliness, structural and organizational characteristics, staffing or training [11], all of which may be potential targets for improvement. Better structural resources and better processes should provide better outcomes. Thus, understanding how structural and process variables may influence SSI is vital to pinpoint effective interventions and to optimize healthcare services.

The aim of this study was to systematically review the published literature regarding the association between hospitals' characteristics, including services provided, and SSI incidence after colorectal surgery.

Methods

Search strategy

The search strategy followed the Participants, Exposure/Intervention, Comparison, Outcomes and Study (PE/ICOS) design [12]. PubMed, Scopus and Web of Science databases were searched, with no date limit, using the following query: (colorectal OR colon OR rectal) AND (surgical site infection OR wound infection OR skin infection) AND (effect OR risk OR association OR impact OR relation* OR influence OR outcome). All sources were last searched on May 31st, 2021, and backward citation tracking was conducted for all included articles. This systematic review was undertaken using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines [13] but was not registered in the PROSPERO database.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) articles written in English, Portuguese, Spanish, Italian, French or German, (2) not a review article, editorial, comment, guideline or descriptive study, (3) patients submitted to colorectal surgery, (4) analysis of risk factors representing hospital characteristics, services or organization (no patient or procedure-related risk factors), (5) SSI as an outcome and (6) studies with odds ratio (OR) or relative risk (RR), or raw data allowing the estimation of those measures of association.

Data extraction

RM and BP independently reviewed titles and abstracts of all records retrieved from electronic searches, applying the aforementioned criteria. Any disagreements were solved through a consensus discussion, or involving SC. Full texts and supplement material (when available) of all identified studies were then reviewed by the same researchers. Given that all included studies were observational, the STROBE checklist was used for evaluating their methodological quality [14]. This is a checklist of 22 items that should be included in reports of observational studies. Each sub-item was graded as 1, if the study reported them as recommended; 0, if the sub-item was missing from the study; or 0.5, if the sub-item was included but only partially met the recommendation. As some sub-items could be non-applicable, the maximum score ranged from 24 to 30.

Data on first author, publication year, language, study design, country, recruitment period, surgical procedures considered, procedure codes used, databases used, type and criteria of SSI and study size were retrieved. Missing data was registered as such, and no assumptions were made. Nonetheless, authors were contacted to retrieve necessary data when studies fulfilling the inclusion criteria had missing data. When applicable, information on whether the hospital had an infection control team and whether surveillance included post-discharge diagnosis were also retrieved.

The primary outcome of interest was SSI rate after colorectal surgery, whether superficial incisional, deep incisional or organ/space, as defined by the CDC [10]. Measures of association and their respective 95% confidence interval (CI) were retrieved, or estimated when raw data was available.

Studies were grouped in nine risk factor typologies: hospital size, for those studies that estimated the association between hospital's number of beds and SSI; hospital ownership, when the analysis focused on whether hospitals were public, private or non-profit; medical school affiliation, for the comparison of teaching versus non-teaching hospitals; Oncological hospitals, for studies researching whether a hospital being a specialized oncological center had an impact on SSI incidence; safety-net burden, defined as the proportion of patients a hospital treats who are either uninsured or insured by Medicaid, an American state program that helps with healthcare costs for people with limited income and resources; hospital volume of procedures, when the risk factor analyzed was the number of colorectal procedures performed at each hospital; surgeon volume of procedures, when the risk factor was the number of colorectal procedures performed per surgeon, rather than per hospital; post-discharge destination, analyzing if patients discharged to their homes had different outcomes when compared to those discharged to skilled facilities; and surveillance time, for studies estimating the impact of surveillance programs over the years on SSI rates.

Results

A total of 4703 records were identified through the databases' search, after duplicates were removed, of which the full text of 172 was reviewed, and 16 were included in our systematic review (Fig. 1). No additional article was included following backward citation tracking. Six studies were from the United States (U. S.), two from Italy, two from Spain, one each from Australia, China, Germany, the Netherlands and Switzerland, and one was an international study conducted across Australia, Singapore, South Korea and 12 European countries. Apart from the Dutch study, published in 2008, the remaining 15 were published in the last decade, between 2011 and 2021, with data collected between 1996 and 2016. The 16 studies included comprised 1,314,608 colorectal procedures, and are described in detail in Table 1. SSI incidence ranged from 3.2 to 27.6%, and the methodological quality score varied between 11 and 25.

Figure 2 summarizes the main findings per hospital determinant. Six studies [11, 15–19] addressed structural variables—hospital size, ownership, affiliation and being an oncological hospital. Two out of the five evaluating hospital size adjusted their analysis for patient and procedural risk factors, finding that larger hospitals were either associated with higher SSI [16] or had no association [18]. In Germany, ownership type was not associated with SSI following colon procedures [18]. In the U. S., crude estimates suggest that hospitals with medical school affiliation were associated with higher incisional and organ/space SSI [11] compared with hospitals without that affiliation, whilst oncological hospitals in the same country were associated with higher superficial SSI incidence (but not organ/space) compared to non-specialized hospitals, independently of patient demographics, procedural risk factors and surgical complexity [19].

Five studies addressed how hospital or surgeon caseload associates with SSI. Hospital volume was defined as the annual volume of colorectal surgeries performed in hospitals [20], the average annual number of rectal procedures [21] or the colectomy case volume only [22]. All presented crude estimates, each reaching a different conclusion (Fig. 2). One study concluded that less experienced surgeons were associated with more postsurgical complications—SSI and others [23], while in the other no significant difference was found between high and low volume surgeons, though medium volume surgeons had significantly less SSIs than high volume ones [24]. Crude analysis suggests that higher safety-net burden may be associated with increased SSI rates [22], and the study evaluating post-discharge destinations found no difference in SSI rates between patients discharged home versus patients discharged to skilled facilities, after adjusting for 19 endogenous and exogenous risk factors [25].

The impact of surveillance over time on SSI rates was evaluated in four studies. In a large international study from 2019, each additional year of surveillance was associated with a lower SSI frequency, using the former year as reference. Additionally, participating in a surveillance network for over five years was associated with lower SSI rates [26]. The same conclusions were found in Italy, in the same year [27], although in the Netherlands, in 2008, no association was found [28]. Contrarily to these findings, one study using data from the Swiss surveillance system showed that time from the start of surveillance to the operation was significantly associated with higher SSI rates in colorectal surgery [29]. All surveillance analyses were adjusted for patient and procedure variables, and are shown in Table 1; Fig. 2.

Discussion

Although it has been recognized for over 20 years that hospital characteristics may be associated with SSI [5], as they have been shown with other adverse events [30–32], we found few studies addressing them. SSI rates also showed a wide range in incidence, though most use the CDC criteria, suggesting that case identification, as

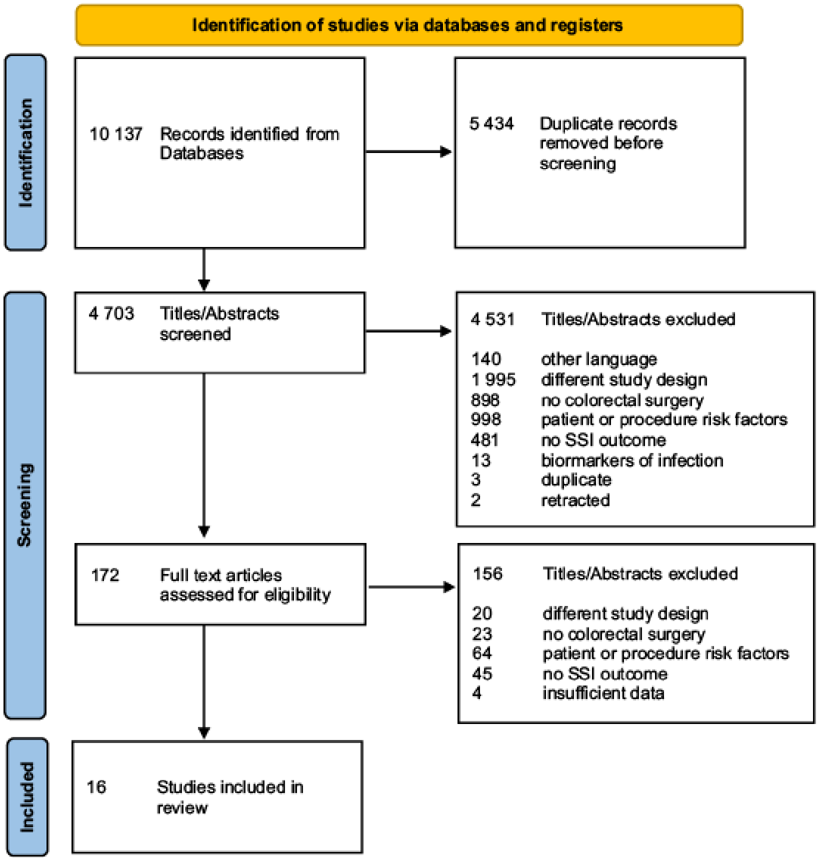

Fig. 1 Flow diagram of the study selection process

well as follow-up time, may be markedly different across settings, a major issue to be addressed given that SSI incidence is commonly used as a quality indicator for benchmarking between institutions and countries. Moreover, most data retrieved by this review is based on crude estimates, and needs to be interpreted with caution.

Public or private ownership had no apparent association with SSI after colorectal surgery in the German setting, although public hospitals had significantly less SSI after hip prosthesis following arthrosis [18]. A paper from Switzerland, albeit not providing sufficient data for the estimation of measures of association—and thus failing to meet our inclusion criteria—claimed private hospitals had fewer SSI after colorectal surgery [33]. In Australia, a study reported that private hospitals invest significantly less than public institutions in surveillance resources, emphasizing the possible underreporting of infections in the former setting [34]. While the meaning of private and public hospitals is similar throughout the world, the population served, the types of procedures performed, the structural and processual characteristics of hospitals and the financial incentives may differ

Table 1 Characteristics of all included studies

First author, year, country	Description	Study design and PICO	Study results
Abbas 2019 [26] Multiple countries English	Large-scale international study to determine the time-trend of surgical site infection (SSI) incidence in SSI surveillance networks. Networks identified through systematic literature review were provided with standardized data template	Cohort *Population* Colorectal surgery (no source) *Intervention* Surveillance over time 1) One-year increase in surveillance time 2) X years of surveillance *Comparison* 1) Year One in surveillance time 2) X-1 years of surveillance *Outcome* SSI rate (no source) *STROBE Score* 25 in 29	*Study size*: 320 1 23 10 networks included 8.5 (IQR 7–11) median years of surveillance *Relative Risk* Intervention 1) 1) 2 years 0.92 (0.89–0.96) 2) 3 years 0.90 (0.87–0.94) 3) 4 years 0.91 (0.87–0.95) 4) 5 years 0.86 (0.83–0.90) 5) 6 years 0.92 (0.87–0.96) 6) 7 years 0.84 (0.79–0.89) 7) 8 years 0.86 (0.80–0.92) Intervention 2) 1) X = 3 - 0.98 (0.94–1.02) 2) X = 4 − 1.00 (0.96–1.05) 3) X = 5–0.95 (0.91–0.99) 4) X = 6–1.06 (1.01–1.12) 5) X = 7–0.92 (0.86–0.98) 6) X = 8–1.02 (0.04–1.11)
Angel García 2020 [17] Spain English	Study data from nine public hospitals in Murcia, Spain, from January 2006 to December 2015. The study developed two risk-adjustment models based on multiple logistic regression, without considering hospital bed size as a candidate variable	Cohort *Population* Colorectal surgery (ICD-9) *Exposure* 1) Bed size > 500 2) Bed size 250–500 *Comparison* Bed size < 250 *Outcome* SSI (ICD-9 codes) *STROBE score* 17 in 24	*Study size* 6 325 423 SSIs (7.32%) *Odds ratio (OR) (overall SSI, univariate analysis)* 1) 0.54 (0,41–0,72) 2) 0.95 (0.74–1.23)
Du 2019 [16] China English	Multicenter surveillance of radical resection of colon and rectal carcinoma in 26 tertiary hospitals in 14 cities, from January 2015 to June 2016 Surveillance made by infection control professionals until discharge, using a real-time nosocomial infection surveillance system, and by telephone 30 days postoperatively	Cohort *Population* Radical resection of colon and rectal carcinomas (ICD-9) *Exposure* Beds < 2500 *Comparison* Beds ≥ 2500 *Outcome* SSI (CDC 1992) *STROBE score* 11 in 30	*Study size* 5 729 3 406 radical resection of colon carcinoma 2 323 radical resection of rectal carcinoma 206 SSIs (3.60%) 87 SSIs after colon resection (2.55%) • 32 superficial (0.94%) • 19 deep (0.56%) • 36 organ space (1.06%) 119 SSIs after rectal resection (5.12%) • 53 superficial (2.28%) • 26 deep (1.11%) • 40 organ space (1.72%) *OR (Multivariable analysis for overall SSI)* 0.644 (0.451–0.921) resection of colon carcinoma 0.513 (0.356–0.739) resection of rectal carcinoma

Table 1 (continued)

First author, year, country	Description	Study design and PICO	Study results
El Aziz 2020 [25] United States English	Six-year longitudinal study using the American College of Surgeons—National Surgical Quality Improvement Program (ACS-NSQIP) database, an American quality improvement program gathering abstract patient information through predesigned data extraction sheets manage by trained data abstractors from all participating institutions SSIs assessed in-hospital before discharge and after discharge until post-operative day 30 ORs adjusted for age > 80 years old, gender, race, body mass index, diabetes mellitus, current smoker within one year, dyspnea, functional health status prior to surgery, history of severe chronic obstructive pulmonary disease, ascites, congestive heart failure in 30 days before surgery, hypertension requiring medication, dialysis, disseminated cancer, open wound infection, steroid use for chronic condition, > 10% loss bodyweight in the last six months, bleeding disorders, transfusion > 1 unit red blood cells 72 h before surgery, pre-operative albumin and hematocrit, diagnosis, extent of resection, operative approach, diversion, operation time, any surgical complication before discharge, any medical complication before discharge, days from operation to discharge	Cohort *Population* Elective surgery for colon or rectal cancer, using Current Procedural Terminology (CPT) codes *Exposure* 1) Discharge to skilled facility 2) Discharge to rehabilitation center 3) Discharge to separate acute care *Comparison* Discharged home *Outcome* SSI (ACS-NSQIP 2016) *STROBE score* 21 in 27	*Study size* 108 617 3476 total SSIs (3.2%) 1396 superficial SSIs (1.3%) 349 Deep SSIs (0.3%) 1915 organ space SSIs (1.8%) *ORs (overall SSIs, adjusted)* 1) 1.02 (0.87–1.20) 2) 1.03 (0.81–1.31) 3) 1.25 (0.74–2.09)
Furuya-Kanamori 2017 [20] Australia English	New South Wales Admitted Patient Data Collection contains data on all admitted patient services provided by public and private hospitals in the region Subset population of adult patients who underwent colorectal surgery between January 2002 and December 2013 The annual volume of colorectal surgery in public hospitals was categorized into tertiles, per surgical procedure: low-volume hospitals performed < 45 procedures/year, mid-volume performed 45–115 procedures/year and high-volume performed > 115 procedures/year Outcome includes in-hospital infection only	Cohort *Population* Colorectal surgery (ICD-10, Australian Modification) *Exposure* 1) Mid-Hospital Volume 2) High-Hospital Volume *Comparison* Low-Hospital Volume *Outcome* Surgical site infection (ICD-10) *STROBE score* 20.5 in 28	*Study size* 58 096 cases from 59 hospitals Incidence: 9.64% (9.40–9.88%) *OR (overall SSI, crude analysis)* 1) 1.23 (1.08–1.40) 2) 1.50 (1.34–1.69) When risk-adjusted SSI rates per 1000 admissions were examined, low-volume hospitals performed better for colorectal procedures (91.7 for low, 96.7 for mid and 96.7 for high-volume public hospitals)

Table 1 (continued)

First author, year, country	Description	Study design and PICO	Study results
Manilich 2013 [23] United States English	Single-center study, with exclusion of outpatient surgical cases. 30-day follow-up by letter or phone call Surgeon volume determined by the number of procedures in each major category that a surgeon performed in 2 years—colorectal surgical procedure as the unit of analysis	Cohort *Population* Major abdominal or transanal colorectal surgery (no source) *Exposure* Surgeon volume < 20 procedures *Comparison* Surgeon volume ≥ 20 procedures *Outcome* SSI (ACS-NSQIP) *STROBE score* 23 in 29	*Study size* 3 552 cases by 15 surgeons 300 incisional SSIs (8.4%) *OR (overall SSI, adjusted OR)* 1.38 (1.06–1.79)
Mannien 2008 [28] Netherlands English	Data from 1996 to 2006 from the Dutch National Nosocomial Surveillance Network. Hospital participation is voluntary. Hospitals can annually decide which surgical procedures to include, and post-discharge surveillance is strongly recommended OR adjusted for post-discharge surveillance, American Society of Anesthesiologists (ASA) classification, wound contamination class, duration of surgery, duration of preoperative hospitalization and emergency procedure	Cohort *Population* Colectomy (no source) *Intervention* Surveillance 1) 1-year increase in surveillance time to operation *Comparison* 1-less year in surveillance time to operation *Outcome* SSI (CDC 1992) *STROBE score* 18.5 in 27	*Study size* 3 031 370 SSIs (12.2%) *OR (overall SSI, adjusted)* 1) 0.92 (0.83–1.02)
Merkow 2013 [19] United States English	Multicenter study using centers participating in the ACS-NSQIP, that collects comprehensive data from > 500 hospitals, including 51 National Cancer Institutes Age, race, ASA class, functional status, preoperative albumin level, hypertension, chronic obstructive pulmonary disease, chemoradiation, disseminated cancer and case complexity were all significantly different at baseline. Adjustment for differences in patient demographics and risk factors, as well as surgical complexity	Cohort *Population* Colorectal cancer surgery (CPT) *Exposure* Oncological Hospital 1) National Cancer Institute *Comparison* Non-oncological hospital *Outcome* SSI (ACS NSQIP) *STROBE score* 18.5 in 28	*Study size* 52,265 from 310 hospitals Incidence 7.7% superficial SSIs 4.8% deep or organ/space SSIs *OR (adjusted)* Superficial: 1.35 (1.08–1.70) Deep or organ/space: 1.17 (0.98–1.40)

Table 1 (continued)

First author, year, country	Description	Study design and PICO	Study results
Schröder 2018 [18] Germany English	Data from surgical site infection module of the German national nosocomial infection surveillance system, the component for surgical site infections, which is patient based and voluntary. SSI following laparoscopic colon resection from 145 hospitals (44 public, 65 non-profit and 36 private) and following open colon resection in 159 (45, 67 and 37, respectively)	Cohort *Population* Colon procedures (national codes) *Exposure* Public ownership Non-profit ownership Bed size < 400 *Comparison* Private ownership Bed size < 400 *Outcome* SSI *STROBE score* 19 in 29	*Study size* 28,291 • 19 453 open colon procedures • 8838 laparoscopic colon procedures *ORs (overall SSIs, multivariate analysis)* 1.12 (0.86–1.47) for public ownership 0.85 (0.66–1.09) for non-profit ownership 0.81 (0.51–1.29) for bed size < 400
Serra-Aracil 2011 [15] Spain English	Multicenter study of 19 public hospitals in Catalonia, Spain, between June 2007 and March 2008 Colon operation defined as any resection above the peritoneal reflection. Rectal operation defined as any resection below the same point. Inclusion criteria were the application of all preventive measures and rectal cancer operations with oncologic resections. Outpatient visit after 30 days	Cohort *Population* Elective operations for colon or rectal cancer *Exposure* 1) > 500 beds 2) 250–500 beds *Comparison* < 250 beds *Outcome* SSI (CDC 1992) *STROBE score* 18 in 29	Study Size: 611 383 colon cancer operation 89 total SSIs (23.2%) • 49 superficial SSIs (12.8%) • 8 deep SSIs (2.1%) • 32 organ space SSIs (8.4%) 228 rectal cancer operation 63 SSIs (27.6%) • 31 superficial SSIs (13.6%) • 13 deep SSIs (5.7%) • 19 organ space SSIs (8.3%) *OR (univariate analysis)* Colon cancer operations Overall SSI 1) 0.48 (0.25–0.95) 2) 0.41 (0.17–0.95) Incisional SSI 1) 0.36 (0.18–0.76) 2) 0.26 (0.09–0.68) Organ/space SSI 1) 1.25 (0.41–5.68) 2) 1.52 (0.39–7.80) Rectal cancer operations Overall SSI 1) 0.69 (0.30–1.67) 2) 0.68 (0.24–1.94) Incisional SSI 1) 0.89 (0.35–2.63) 2) 0.90 (0.27–3.13) Organ/space SSI 1) 0.51 (0.16-2.00) 2) 0.49 (0.08–2.54)

Table 1 (continued)

First author, year, country	Description	Study design and PICO	Study results
Spolverato 2019 [21] Italy English	Data from National Italian Hospital Discharge Dataset, from January 2002 to November 2014 Adult patients only Hospital volume calculated as the average annual number of rectal cancer procedures performed at each hospital, during study period, divided into tertiles (respectively 1–12, 13–31, > 31 surgeries/year) Main outcome is failure to rescue, defined as the mortality rate among patients with complications, which is why there is no adjusted analysis specifically for SSI; however, low-volume hospitals, in multivariable analysis, are associated with higher rate of failure to rescue and any complication, when compared with high volume hospitals	Cohort *Population* Major surgical procedure for primary rectal cancer (ICD-9) *Exposure* 1) High-volume hospital 2) Intermediate-volume hospital *Comparison* Low-volume hospital *Outcome* SSI (ICD-9) *STROBE score* 20.5 in 30	*Study size* 75 280 3.9% SSI incidence *OR (overall SSI, crude analysis)* 1) 0.99 (0.90–1.08) 2) 0.95 (0.87–1.04)
Staszewicz 2014 [29] Switzerland English	Data collected from 1998 to 2010 from the Swissnoso consortium, a voluntary participation surveillance network of Swiss public hospitals OR adjusted for age, sex, ASA Score ≥ 3, delay from admission to operation > 2 days, emergency, antibiotic prophylaxis, contamination class ≥ 3, multiple procedures, laparoscopy, duration > T, re-intervention for non-infectious complications	Cohort *Population* Colectomy (no source) *Intervention* Surveillance 1) time to operation *Outcome* SSI (CDC 1992) *STROBE score* 18 in 28	*Study size* 7411 1349 SSIs (18.2%) 555 superficial SSIs (7.5%) 308 deep SSIs (42%) 486 organ/space SSIs (6.6%) *OR (overall SSI, adjusted)* 1.05 (1.03–1.07)
Tserenpuntsag 2014 [11] United States English	Multicenter study of 174 New York State hospitals, with mandatory surveillance of SSIs following colon procedures through the NHSN, including post-discharge detection of SSI. Authors used 2009–2010 data of an audit of the surveillance program, performed by trained program staff certified in infection control If a small bowel procedure, kidney transplant, liver transplant, or bile duct, liver pancreatic or rectal procedure was performed through the same incision, and it was not clear which procedure was associated with infection, the SSI was attributed to 1 of the above listed procedures	Case-control *Population* Colon procedures, using ICD-9 codes *Exposures* Teaching hospitals Bed size > 500 *Comparison* Nonteaching hospitals Bed size ≤ 500 *Outcome*: SSI (CDC 1992) *STROBE Score*: 18.5 in 28	*Study Size*: 2 656 cases from 175 hospitals 698 SSIs identified • 355 superficial incisional • 343 deep incisional and organ space *ORs (overall SSI, bivariable analysis)*: Teaching hospitals: 1.88 (1.55–2.95) for superficial 1.86 (1.45–2.39) for deep incisional and organ space Bed size: 2.32 (1.82–2.95) for superficial incisional and 2.08 (1.54–2.80) for deep and organ space

Table 1 (continued)

First author, year, country	Description	Study design and PICO	Study results
Vicentini 2019 [27] Italy English	32 Piedmont hospitals (primary, secondary and tertiary) participating in the voluntary Italian surveillance system for SSIs, using data from January 2009 to December 2015 Surveillance must be performed at least 6 months/year or a minimum of 50 procedures must be monitored Surveillance time is equivalent to the number of years of participation in a surveillance program	Cohort *Population* Colon surgery (ICD-9) *Intervention* Surveillance 1) Participating in surveillance program for over 5 years 2) 1-unit increase in the number of monitored procedures 3) 1-year increase in surveillance time *Comparison* 1) No participation in surveillance network *Outcome* SSI (ECDC) *STROBE score* 16 in 27	*Study size* 6 060 595 SSIs (9.83%), 172 post-discharge 370 incisional SSIs (6.13%) 96 deep SSIs (1.59%) 97 organ/space SSI (1.60%) *RR (overall SSI)* 1) 0.64 (0.46–0.90) 2) 0.99 (0.98-1.00) 3) 0.93 (0.89–0.97)
Wang 2021 [22] United States English	Safety-net hospitals are mandated to treat patients regardless of their ability to pay, and consequently carry a high safety-net burden (SNB), defined as the proportion of patients who are either uninsured or Medicaid-insured. Hospitals were stratified into tertiles of low, medium and high SNB Data from State Inpatient Databases (2009–2014) Hospital volume stratified into quartiles by colectomy case volume Adult patients only	Cohort *Population* Colectomy (ICD-9) *Exposure* 1. High safety-net burden 2. Medium safety-net burden 3. Hospital volume—4th quartile 4. Hospital volume—3rd quartile 5. Hospital volume—2nd quartile *Comparison* 1. Low safety-net burden (1–2) 2. Hospital volume—1st quartile (3–5) *Outcome* SSI (ICD-9) *STROBE score* 21.5 in 30	*Study size* 459 568 29 117 SSIs (6.3%) *OR (overall SSI, crude analysis)* 1. 1.35 (1.31–1.40) 2. 0.97 (0.94-1.00) 3. 0.51 (0.50–0.53) 4. 0.64 (0.62–0.66) 5. 0.70 (0.68–0.73)
Yi 2018 [24] United States English	Administrative databases used for colorectal surgical patients discharged in years 2013 and 2014, in a hybrid tertiary referral central with 8 campuses and 2247 beds. Over 80% of study patients were from campuses with high colorectal surgery volume Volume of surgery determined by the actual number of patients operated on per surgeon. High volume surgeon with case volume of more than 34 cases in the last 2 years, medium volume with case volume between 14 and 34, and low volume with fewer than 14 cases	Cohort study *Population* Colorectal procedures (ICD-9) *Exposure* Medium-volume Surgeon Low-volume Surgeon *Comparison* High-volume Surgeon *Outcome* SSI (no source provided) *STROBE Score* 16,5 in 27	*Study size* 1 190 cases by 44 surgeons *ORs (overall SSI, adjusted)* 0.23 (0.08–0.65) for medium-volume surgeons 0.39 (0.09–1.71) for low-volume surgeons

ACS-NSQIP, American College of Surgeons-National Surgical Quality Improvement Program; ASA, American Society of Anesthesiologists; CDC, Centers for Disease Control and Prevention; CPT, Current Procedural Terminology; ECDC, European Centre for Disease Prevention and Control; ICD, International Statistical Classification of Diseases and Related Health Problems; IQR, interquartile range; NHSN, National Healthcare Safety Network; OR, odds ratio; SNB, safety-net burden; SSI, surgical site infection considerably between countries, precluding the external validity of these conclusions.

The most analyzed hospital characteristic was hospital size. Only two studies [16, 18] provided adjusted ORs for patient and procedure factors, and both considered different cutoff points than their counterparts, who used 500 beds [11, 15, 17], as proposed by the NHSN risk adjustment methodology [6]. One found no evidence of association using 400 beds as a cutoff, though it did find an association between hospital size and all device-associated and ventilator-associated infection, central venous catheter-bloodstream infection, infection by *Clostridioides difficile* and methicillin-resistant *Staphylococcus aureus* [18]. The other concluded that larger hospitals have significantly higher SSI after colorectal surgery, yet it used 1500 and 2500 beds as cutoffs, so the finding may yield no meaning in most countries of the world [16]. Comparisons among countries are also limited for oncological hospitals. While most countries dispose of specialized hospitals in cancer care, National Cancer Institutes are specific to the U. S., as they have a different payment mechanism than other American hospitals and are exempt from reporting all process-of-care and outcome measures to the Centers for Medicare & Medicaid Services [35]. Previously defined safety-net burden is also U. S.-specific. In this case, associations may also be strongly affected by patient case mix. The authors did find a significant association between high burden and in-hospital mortality and general complications, but, unfortunately, no adjusted analysis was conducted disaggregated at the SSI level [22]. Although no difference was found for SSI, discharge to skilled facilities was associated with higher respiratory morbidity, sepsis and vascular thromboembolism [25]. It has been suggested that most SSIs occur after discharge and, thus, may be affected by post-care variables [36], yet we found no other study addressing them.

The three papers on hospital volume [20–22], defined by specific colorectal procedures, provided crude data only. Furthermore, two used ICD-10 to detect in-patient SSI [20, 21], probably underreporting SSI incidence since administrative data has been shown to have limited accuracy for the detection of SSI [37]. Regarding surgeon caseload, the study failing to find an association acknowledged that the small number case may have been insufficiently robust [24].

The positive impact of surveillance on SSI has been widely documented, although many studies focus on total or non-colorectal procedures [38–40], not accounting for the specificities of each SSI. It is accepted that surveillance may decrease SSI rates through two mechanisms: feedback and/or surveillance effect, similar to the Hawthorne effect [41]. At the same time, an artificial increase in the SSI rate may occur, due to changes in case identification, including better registry of previously unreported infections and active post-discharge case finding [36, 42], and due to changes in case mix over time [43]. This artificiality is well supported by a recent study that found a positive correlation between infection rates and audit quality [33], following the biblical sermon: "seek, and ye shall find" [44]. Two papers found that each one-year increase in surveillance time was associated with reduced SSI after colorectal surgery, while one paper failed to find any association. Both positive effects were marginal [0.93 (95%CI 0.89–0.97) in one study [27] and 0.84 (0.79–0.89) in the best year of the other [26]], and could have limited clinical relevance. Relevantly, the influence of the surveillance effect and better case finding tends to wane over time. Hence, both papers concluding that the impact of surveillance is better noticed after the fifth year of its implementation support the impact of feedback on SSI incidence [26, 27]. Longer time trends may be needed to obtain more accurate results, even if an independent effect may exist by hospitals joining surveillance networks at a later point in time, benefiting from national efforts and overall better practices [26]. As opposed to this, one paper found that the longer the time from surveillance to procedure, the higher the SSI rate after colorectal surgery, as well as after appendectomy and knee arthroplasty [29]. Influencing these disparate findings is the fact that some surveillance networks make it mandatory for hospitals to participate, while others have voluntary participation. In the latter, there may be a selection bias similar to a healthy-worker effect, as hospitals in networks tend to allocate more resources towards surveillance when compared to non-included hospitals [26]. On the other hand, participants in voluntary systems are more interested and have more time available for

(See figure on next page.)

Fig. 2 Main findings of included studies, by hospital determinant. Each column refers to a single study. The number on top of each column is the STROBE classification of the study, and the number below is the year it was published. **a** maximum STROBE score of 29, **b** maximum STROBE score of 24, **c** maximum STROBE score of 28, **d** maximum STROBE score of 30, **e** maximum STROBE score of 27. Black columns refer to adjusted associations, grey refer to crude. Full columns refer to overall SSI as outcome, horizontal strips refer to superficial infection and diagonal strips to deep and organ/space infections

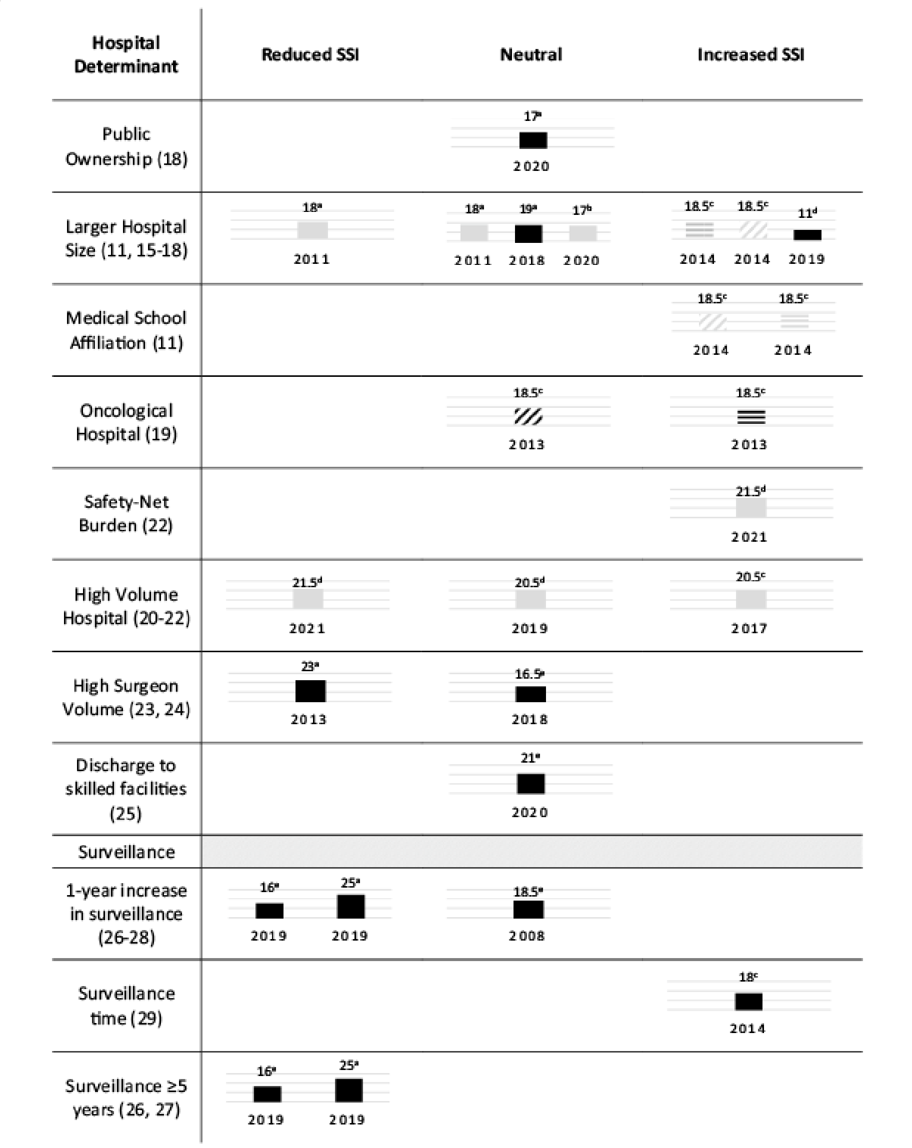

Fig. 2 (See legend on previous page.)

surveillance, and thus are more likely to produce more accurate data [45].

To the best of our knowledge, no systematic review has been published regarding the association between hospital characteristics and SSI. Our search strategy aimed at maximum sensitivity, focusing on three major databases that retrieved a large volume of initial results. It is unlikely that relevant papers were not retrieved as all included studies were written in English and no additional manuscript was found through backward citation. By focusing on SSI after colorectal surgery, we excluded papers evaluating surveillance on SSI as whole. Using the STROBE statement, we found that most papers failed to address how missing data was handled (14 in 16), and to clarify the study's design in the title or abstract (13 in 16). While study limitations were almost ubiquitously described, they tended to lack the description of the direction and magnitude of identified biases. Due to the heterogeneity found across studies, even when analyzing the same risk factor, we were unable to quantitatively combine study findings in a meta-analysis. Many relevant healthcare delivery variables were not reviewed as we failed to find any study addressing them—that would be the case of nurse staffing, rurality or whether hospitals had an infection control team. Many hospital factors may be highly correlated, as teaching hospitals tend to be larger, urban and have a higher caseload. Healthcare delivery—and its outcomes—is also dependent on regional and national regulations, incentives and the health literacy of the population. Finally, we addressed colorectal surgery as a whole, because most colorectal surgeons perform both colon and rectal procedures. However, they appear to have different SSI rates and, quite possibly, different risk factors [39], and thus it would be relevant to consider studying them as different entities in the future.

Conclusions

Although there is a paucity of studies addressing hospital-level factors on SSI, surgeon experience and the implementation of surveillance appear to be associated with better outcomes. In order for hospitals and services to be efficiently optimized, more studies addressing these variables are needed that take into account the confounding effect of patient case mix.

Abbreviations

CDC: Centers for Disease Control and Prevention; CI: Confidence Interval; HAI: Healthcare-Associated Infection; ICD10: International Statistical Classification of Diseases and Related Health Problems, 10th Revision; NHSN: National Healthcare Safety Network; OR: Odds Ratio; RR: Relative risk; SSI: Surgical site infection; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology.; U. S.: United States.

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Authors' contributions

RM and BP were responsible for data acquisition and application of inclusion criteria. RM was responsible for data analysis and drafted the work. All authors contributed to the conception and design of the work, interpretation of data and substantial revision of each draft. All authors approved the submitted version, and agree both to be accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved and documented. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The protocol of this study was submitted and approved by the Ethics Committee of Instituto de Saúde Pública da Universidade do Porto (CE20171), in November 2020. No informed consent was deemed necessary.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Paper 2

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Hospital context in surgical site infection following colorectal surgery: a multi-level logistic regression analysis

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SUMMARY

Background: Surgical site infections (SSIs) are associated with poor health outcomes. Their incidence is highest after colorectal surgery, with little improvement in recent years. The role of hospital characteristics is undetermined.

Aim: To investigate whether SSI incidence after colorectal surgery varies between hospitals, and whether such variance may be explained by hospital characteristics.

Methods: Data were retrieved from the electronic platform of the Directorate General of Health, from 2015 to 2019. Hospital characteristics were retrieved from publicly available data on the Portuguese public administration. Analysis considered a two-level hierarchical data structure, with individuals clustered in hospitals. To avoid overfitting, no models were built with more than one hospital characteristic. Cluster-level associations are presented through median odds ratio (MOR) and intraclass cluster coefficient (ICC). Beta coefficients were used to assess the contextual effects.

Findings: A total of 11,219 procedures from 18 hospitals were included. The incidence of SSI was 16.8%. The ICC for the null model was 0.09. Procedural variables explained 25% of the variance, and hospital dimension explained another 17%. More than 50% of SSI variance remains unaccounted for. After adjustment, heterogeneity between hospitals (MOR: 1.51; ICC: 0.05) was still found. No hospital characteristic was significantly associated with SSI.

Conclusion: Procedural variables and hospital dimension explain almost half of SSI variance and should be taken into account when implementing prevention strategies. Future

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research should focus on compliance with preventive bundles and other process indicators in hospitals with significantly less SSI in colorectal surgery.
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Introduction

Among the most common healthcare-associated infections, surgical site infections (SSI) are associated with increased morbidity, mortality, and expenditure [1–3]. Their incidence is particularly high after colorectal surgery, with little to no improvement in recent years [4,5]. The US Centers for Disease Control and Prevention (CDC) acknowledged in 1999 that the risk of SSI is influenced by patient and procedure risk factors, but also by hospital characteristics [6]. Nonetheless, most contemporary research on SSI after colorectal surgery has focused on the former two [6,7].

A few papers have addressed hospital determinants of SSI after colorectal surgery, namely public versus private ownership, hospital size, teaching status, or volume of procedures [8–10]. However, to test such hypotheses, multi-level regression analysis, which investigates whether a given health phenomenon has a contextual dimension, by disentangling the within-cluster effects from the between-cluster effects, is the most adequate statistical technique [11,12]. In doing so, one may obtain a better understanding of the underlying heterogeneity in data than is possible from conventional regression analysis [13]. Although a few published papers on the field of infection control and prevention have used this approach, they either focused on other outcomes or intended to improve the prediction of SSI [14–18].

Optimal outcomes require optimized processes and ad-equate resources. Thus, understanding how much of SSI incidence may be due to contextual effects is essential to optimize healthcare delivery. Contextual variables may be modifiable and, therefore, emendable. Others may reflect unmeasured variables such as hospital hygiene and organizational characteristics [9]. Although some may be unmodifiable, they may aide to understand systematic and structural differences between hospitals, to establish a baseline ratio that may serve as a realistic and achievable target for prevention efforts and to design strategies focusing on minimizing the effect of those hospital characteristics.

Thus, the aim of this research was to investigate whether SSI incidence after colorectal surgery varies between Portuguese hospitals, and whether such variance may be associated with procedural risk factors and/or hospital characteristics.

Methods

The electronic platforms of the Portuguese Directorate General of Health include the database of the National Epidemiological Surveillance of hospital-acquired infections in intensive care units, bloodstream infections, *Clostridium difficile* infections, and SSI following colorectal surgery, cholecystectomy, caesarean section, cardiac surgery, hip and knee arthroplasties, and laminectomy. As Portugal is part of the Healthcare-Associated Infection Surveillance Network (HAI-Net) of the European Centre for Disease Prevention and Control (ECDC), participating hospitals are required to routinely collect patient and unit-based variables for a minimum of three months and/or 30 surgical procedures [19]. The dataset uses the surgical procedure as the unit of measurement, registering all variables as different columns. Until mid-2018, the dataset consisted of a single spreadsheet containing all data. From then onwards, in response to an operating system that could not be updated, new software was developed. The dataset changed its structure, and antibiotic use and SSI data, such as SSI type and date, micro-organism isolation, and resistance profile, began to be registered in separate sheets, linkable by the ID of the procedure, surgery date and hospital.

Our analysis included only those procedures performed in hospitals that reported colorectal surgeries every year, from 2015 to 2019, to ensure that the same population was being analysed throughout the study period. No private nor oncological hospitals were included, because they failed to report consistently throughout the study period. Therefore, from a total of 42 reporting hospitals, of which 35 were state-owned, 18 hospitals were included.

Ethics

The protocol of this study was submitted and approved by the Ethics Committee of Instituto de Saúde Pública da Universidade do Porto (CE20171), in November 2020. No informed consent was deemed necessary.

Procedure-level characteristics

Eight individual characteristics available in the SSI database were included as level-1 variables, all of them previously documented as risk factors for SSI after colorectal surgery: age, gender, the American Society of Anesthesiologists (ASA) Physical Status Classification, wound classification, duration of surgery in minutes, absence of antibiotic prophylaxis, urgent operations, and open surgery. The ASA Physical Status Classification, designed to assess a patient's pre-anaesthesia medical comorbidities, was dichotomized and a score of ≥ 3 (referring to patients with severe systemic disease) was considered a risk factor, as well as wounds classified as III or IV, denoting contaminated and dirty wounds, in line with the National Healthcare Safety Network risk index [7,20,21]. Duration of surgery was limited to 180 min [7]. The absence of antibiotic prophylaxis was considered a risk factor. Until mid-2018, antibiotic use was registered as either prophylactic or therapeutic, whereas afterwards antibiotic prophylaxis had a 'Yes' or 'No' column. Antibiotics used in every procedure, either prophylactic or therapeutic, were registered in separate columns. For all cases in which it was unclear whether antibiotic prophylaxis was administered, we considered that it had been administered if either cefoxitin, or metronidazole and gentamicin, in a single dose, were given, following national norms [22]. Age was rescaled, so that the odds ratio (OR) relates to a 10-year increase.

Other procedure-level characteristics available were dismissed, namely the number of door openings and the execution of multiple operations, which were not systematically registered in our setting.

Hospital-level characteristics

Six hospital characteristics were included as level-2 variables: the hospital group based on the case-mix index (CMI), previous participation in a quality improvement programme (*Stop! Infeção Hospitalar*), being a reference centre for rectal cancer, nurse-to-bed ratio, occupancy rate, and the geographical region of the hospital.

The CMI is a global coefficient of hospital production that aims to reflect the relativity of one hospital towards the others, in terms of its proportion of patients with complex pathologies and, consequently, higher resource consumption. The Central Health System Administration (ACSS) divides hospitals in five groups, determined by hierarchical clustering after principal component analysis. From groups B to E there is an overall increase in hospital dimension, both in size (number of surgical beds) and production (number of surgeries performed, discharged patients/year, etc.), group F referring to oncological institutes. Data on methodological approach by ACSS is available online [23]. Supplementary Table S1 lists the characteristics of each CMI group in terms of absolute process and resource variables, which were retrieved from *Portal Transparência*, a digital platform of the Portuguese government presenting publicly available data from the public administration [24].

Stop! Infeção Hospitalar was a three-year national challenge (2015—2018), promoted by *Fundação Calouste Gulbenkian*, that sought to decrease the incidence of four types of healthcare-associated infections, including SSI after colorectal surgery. It occurred in 12 selected hospitals, through a collaborative approach with the scientific support of the Institute for Healthcare Improvement [25]. Hospitals were eligible to be included if they applied and had a minimum of 200 beds to participate in the programme.

From 2015 onwards, the Directorate General of Health recognized highly differentiated centres in rectal cancer as reference centres. During the study time-period, 21 hospital centres had been recognized; however, only six fulfilled the inclusion criteria of our study.

The nurse-to-bed ratio was calculated as the proportion of nurses with active employment contract divided by the number of beds used in surgical specialties' admission. The occupancy rate was defined as the proportion between the total days of admission in the year and the capacity of the hospital. Both were divided in tertiles, from highest (1st tertile) to lowest (3rd tertile) [26]. Data were retrieved from *Portal Transparência*. The geographical region in which surgery took place, available on our database, was also included. Mainland Portugal is divided in five health regions. Hospitals that consistently reported colorectal surgeries were distributed among three of them — *Alentejo*, *Norte* and *Lisboa e Vale do Tejo*.

Statistical analysis

Analysis considered a two-level hierarchical data structure, in which individuals are clustered in hospitals. The presence of SSI in the 30 days after colorectal surgery was defined as the outcome, following the ECDC criteria [19]. Variance of the outcome between hospitals is given by τ^2, in which higher values indicate greater heterogeneity.

As proposed by Oakes, several multi-level logistic regression models were fitted to measure both individual and hospital-level variables on SSI [27]. We started by assessing hospital-to-hospital differences in SSI, by fitting fully unconditional random-effects models with random intercepts at the hospital level (Model 1). In this model, we estimated the intraclass cluster coefficient (ICC), representing the proportion of total observed individual variation in SSI that is attributable to between-hospital variation, calculated as

$$\tau^2 / (\tau^2 + (\pi^2 / 3))$$

where π refers to the mathematical constant 3.141592. The higher the ICC, the more relevant is the contextual dimension. Model 2 adjusted for the level-1 variables described above. The remaining models were fitted to adjust separately for each hospital characteristic. To avoid overfitting, given the uneven distribution of hospital characteristics per hospital group (Supplementary Table II), no models were built with more than a single level-2 variable. Thus, for each level-2 variable a different model was fitted and the ICC estimated, as well as the proportion of hospital variance that could be explained by the addition of each respective hospital variable, using model 1's variance as reference.

The OR and respective 95% confidence interval (CI) for operative variables were computed for model 2. Since these ORs are cluster-specific measures of association, cluster-level associations are presented through the median odds ratio (MOR), ICC, and proportion of explained variance. MOR is defined as the median value of the OR between the hospital at highest risk and the hospital at lowest risk, when randomly picking two subjects with the same covariates from different hospitals [28]. It shows the extent to which the individual probability of having an SSI is determined by the hospital and, hence, formally quantify the magnitude of the general contextual effect [13]. Beta coefficients and respective *P*-value were used to assess the contextual effects of hospital characteristics.

All tests were two-tailed. Analysis was performed using R, version 4.1.1, using the 'lme4' library. Confidence intervals were estimated for ICC and MOR using the 'stats' library. The simulated random effects of the clustering of hospitals on SSI incidence, in OR, were plotted, both for the null model and the best explanatory model.

Results

A total of 11,219 out of 18,363 procedures (61%) were included. SSI incidence was 16.8%. The baseline characteristics of our sample are described in Table I. Procedures were balanced throughout the years, and the majority were performed in the same geographical region. Only one group D hospital was included.

The estimated variance of the random effects in the null model was 0.3203, corresponding to an ICC of 0.09, suggesting that almost 10% of SSI incidence may be attributable to between-hospital variation. The estimated intercept was −1.681, meaning that, at an average hospital, the probability of infection was 15.7%. The addition of individual variables explained 25% of the variance, corresponding to an ICC of 0.07.

Table I
Baseline characteristics

Variable type	Variable	Procedures	Hospitals
Operative characteristics	Male sex	6416 (57.2%)	
	Age, median [IQR]	70 [60–78]	
	ASA score >2	5126 (47.1%)	
	Wound class >II	3219 (29.2%)	
	Urgent operation	2193 (19.6%)	
	Operation time ≥180 min	3559 (31.7%)	
	Open surgery	8501 (76.1%)	
	Lack of prophylactic antibiotic	641 (6.5%)	
	Colorectal procedures, per year		
	2015	1813 (16.2%)	
	2016	2373 (21.2%)	
	2017	2545 (22.7%)	
	2018	2150 (19.2%)	
	2019	2338 (20.9%)	
Hospital characteristics	Hospital groups		
	B	1471 (13.1%)	4 (22.2%)
	C	4671 (41.6%)	8 (44.4%)
	D	892 (8.0%)	1 (5.6%)
	E	4185 (37.3%)	5 (27.8%)
	Participation in *Stop!*	6216 (55.4%)	9 (50.0%)
	Reference centre	1687 (15.0%)	6 (33.3%)
	Nurse-to-bed ratio		
	1st tertile	4352 (38.8%)	6 (33.3%)
	2nd tertile	3263 (29.1%)	6 (33.3%)
	3rd tertile	3604 (32.1%)	6 (33.3%)
	Occupancy rate		
	1st tertile	4197 (37.4%)	6 (33.3%)
	2nd tertile	3874 (34.5%)	6 (33.3%)
	3rd tertile	3148 (28.1%)	6 (33.3%)
	Geographical region		
	A	890 (7.9%)	2 (11.1%)
	B	3494 (31.1%)	5 (27.8%)
	C	6785 (60.5%)	11 (61.1%)
	SSI: total	1888 (16.8%)	
	2015	324 (17.9%)	
	2016	420 (17.7%)	
	2017	432 (17.0%)	
	2018	338 (15.7%)	
	2019	374 (16.0%)	

IQR, interquartile range; ASA, American Society of Anesthesiologists; SSI, surgical site infection.

Male sex, age, duration of surgery >180 min, and lack of antibiotic prophylaxis were significantly associated with SSI (Table II).

Hospital group and participation in *Stop! Infeção Hospitalar* explained a higher proportion of the remaining variance (17% each). Being a reference centre for rectal cancer had no effect on the outcome (Table III). The MOR for the models with the best explanatory variables – hospital group and participation in *Stop!* – was 1.51. Hence, the risk of a colorectal procedure being complicated with an SSI in hospitals with higher risk of infection is 1.5 times the risk in hospitals with lower incidence, for a randomly selected similar patient in a hospital within the same CMI group. The ICC in this model was 0.05.

The simulated random effects of the clustering of hospitals on SSI incidence is plotted in Figure 1, in OR. After the best

Table II
OR (95% CI) for operative characteristics with surgical site infection after colorectal surgery

Operative characteristics	OR (95% CI)
Male sex	1.22 (1.09–1.37)
Age	1.04 (1.00–1.08)
ASA score >2	1.00 (1.00–1.00)
Wound class >II	1.00 (1.00–1.01)
Urgent operation	0.99 (0.98–1.01)
Operation time ≥180 min	1.44 (1.27–1.61)
Open surgery	1.00 (1.00–1.01)
Prophylactic antibiotic	1.28 (1.04–1.59)

OR, odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists.

Table III
Clustering effects of hospital characteristics (level-2 variables), each adjusted for procedural (level-1) variables

Models	Explanation	τ^2	PCV	ICC (95% CI)	MOR (95% CI)
1	Null model	0.32 (0.13–0.55)	ref	0.09 (0.04–0.14)	1.72 (1.42–2.03)
2	Includes procedural variables	0.24 (0.08–0.44)	0.25	0.07 (0.02–0.12)	1.60 (1.31–1.88)
3	Model 2 plus hospital groups	0.19 (0.04–0.31)	0.42	0.05 (0.01–0.08)	1.51 (1.21–1.69)
4	Model 2 plus participation in *Stop!*	0.19 (0.04–0.30)	0.42	0.05 (0.01–0.08)	1.51 (1.21–1.69)
5	Model 2 plus reference centre	0.24 (0.09–0.43)	0.25	0.07 (0.03–0.12)	1.60 (1.33–1.87)
6	Model 2 plus nurse-to-bed ratio	0.24 (0.07–0.40)	0.27	0.07 (0.02–0.11)	1.59 (1.29–1.83)
7	Model 2 plus occupancy rate	0.24 (0.07–0.40)	0.27	0.07 (0.02–0.11)	1.59 (1.29–1.83)
8	Model 2 plus geographical region	0.21 (0.06–0.34)	0.36	0.06 (0.02–0.09)	1.54 (1.26–1.74)

τ^2, estimated variance of the distribution of the random effects; CI, confidence interval; PCV, proportion of explained variance (%), corresponding to the proportion of between-hospital variance that could be explained by added variables of each model; ICC, intracluster correlation coefficient; MOR, median odds ratio.

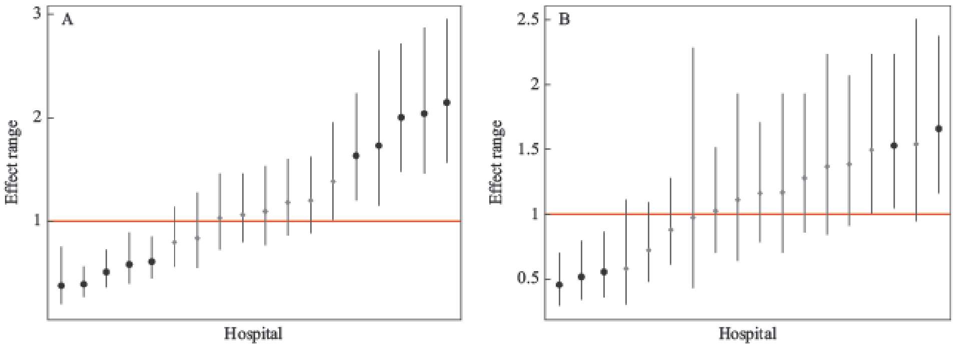

Figure 1. Simulated random effects of the clustering of hospitals on surgical site infection (SSI) incidence, converted to odds ratio. (A) Null model. (B) Model with level-1 variables and hospital group (level-2). Effect is presented in odds ratio, between each hospital and the overall average. Hospitals whose SSI incidence is significantly different from the average are highlighted in bold.

explanatory variables are included, most of the clustering effect is indistinguishable from zero, yet three hospitals remain significantly below the mean OR of ≥2. No hospital characteristic was found to be significantly associated with SSI, when adjusted for procedural risk-factors (Supplementary Table III).

Discussion

This study found a small, yet non-negligible heterogeneity in SSI incidence across Portuguese hospitals. Without adjustment, almost a tenth of observed variance could be attributable to between-hospital differences. Although participation in *Stop! Infeção Hospitalar* explains the same proportion of variance as hospital CMI groups (17%), the former is not so evenly distributed across the sample. In fact, they may all be addressing approximately the same construct — hospital dimension (Supplementary Table II). Such correlation is not necessarily a selection bias, as it corresponds to the philosophy of the executive commission, whose selection criteria included a bed size of at least 200 beds [25].

The variability of SSI after colorectal surgery is partly explained by procedural risk factors and by the hospital group; nonetheless, >50% of SSI variance remains unaccounted for. In the best model, the MOR was 1.51, which implies that — even taking into account the known procedural risk factors and the hospital dimension — it still makes a difference where surgery takes place. Similar patients in different hospitals have different SSI risks. Likewise, the ICC of the model with operative variables and hospital groups is 0.05, meaning that even adjusting for those factors a residual part (5%) of the variance is attributable to between-hospital differences. These differences are most likely due to unavailable variables. Our previous study suggested that the volume of colorectal surgeries per surgeon and the time since the implementation of surveillance were associated with decreased SSI incidence in colorectal surgery, and may help explain part of the remaining difference [29]. It is also plausible that variables such as the cleanliness of operating rooms, the quality of wound management or other hard-to-collect variables may be relevant in the risk of this infection [18]. These unmeasured variables may also justify the impact of geographical region on SSI variance, as there is no other plausible biological explanation for this effect. However, the compliance to standard precautions for infection control and to prevention care bundle may be the most relevant missing variables. Care bundles consist of a set of simple, strong evidence-based practices that, when implemented in a combined and consistent manner, improve patient outcomes, with a higher impact than the addition of each intervention effect. They have been shown to decrease SSI after colorectal surgery up to 45% [30–32]. In Portugal, the care bundle for the prevention of SSI consists of a preoperative bath with chlor-hexidine, antibiotic prophylaxis, avoidance of trichotomy, and the maintenance of perioperative normothermia and glycaemia [33]. Although other interventions have been suggested to optimize surgical care, the success of care bundles relies as much in specific elements included as in high compliance rates with the entire bundle and the implementation process itself [30,34]. Suboptimal compliance rates may well justify why Portugal has the highest SSI incidence after colorectal surgery in Europe [5]. Future research focusing on the systematic differences between the hospitals with significantly lower SSI incidence and the remaining hospitals, as highlighted in Figure 1, may provide a deeper insight into these differences. Nevertheless, no model included multiple hospital-characteristics, which limits our ability to fully understand the total remaining variance in each model. In larger cluster sizes, it may be possible to adjust for more level-2 variables without the risk of overfitting, and to better apprehend how different hospital characteristics relate to one another.

The association of hospital characteristics, namely hospital dimension and resources, and the incidence of adverse events, in general, and SSI following colorectal surgery, in particular, has been previously reported [8,9,35]. It has also been reported that a minimum of 40 clusters are needed to accurately estimate small fixed effects with small intercept variances, meaning the lack of significance of hospital variables in our study could reflect a type II error due to insufficient statistical power [36]. This potential effect is highly relevant in terms of hospital management. More robust data are required to truly denote which hospital determinants affect SSI.

To the best of our knowledge, this is the first study to consider two-level structured data in the analysis of hospital-level risk factors for SSI after colorectal surgery, and one of the first in the field of infection control. The methodology used to collect the variables is comparable with other European settings. We addressed an understudied topic in SSI prevention, and we have also included relevant hospital variables that have not been previously studied, but that may require a keener attention. Hospital CMI groups may be a better-suited indicator to address the reality of hospitals than the more commonly used bed size, especially given that the division between groups is not arbitrary but based on robust principal components analysis [8,9,23].

This study has some limitations regarding indicators. Hospitals are recognized as a reference centre for rectal cancer only, which corresponds to a small proportion of colorectal surgery. A centre of excellence for rectal cancer is not, necessarily, a centre of excellence for all colorectal surgery. Other limitations arise from unavailability of data. Comorbidities were unavailable and, thus, were not considered in our analysis. Nonetheless, most comorbidities — obesity, smoking habits, alcohol use, diabetes — are indirectly expressed in the ASA physical status classification [20]. Other procedural variables, such as mechanical bowel preparation, are not part of the ECDC mandatory indicators and were, thus, unavailable. Unfortunately, a few national hospitals did not report procedures consistently throughout the time-period, which meant that oncological hospitals and two geographical regions could not be analysed in our paper, and only one group D hospital was included. Although a selection bias is possible, the option to analyse only consistent hospitals rather than the entire database made our subpopulation stable and comparable over the study period. Procedures from hospitals that reported only sporadically may not be representative of the overall procedures from those hospitals, as the motive behind this sporadicity is unknown.

In conclusion, although no hospital characteristic was significantly associated with SSI after colorectal surgery, hospital dimension and procedural variables helped to explain almost half of the proportion of SSI variance and should be taken into account when implementing prevention strategies. Future research should focus on compliance with preventive care bundles and other process indicators in hospitals with significantly less SSI in colorectal surgery.

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Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2022.11.004.

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Paper 3

Malheiro R, Correia S, Silva G, Lebre A, Paiva JA, Peleteiro B. Surveillance in surgical site infection in colorectal surgery: what are we missing? (*submitted*)

Surveillance in surgical site infection in colorectal surgery: what are we missing?

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Abstract

We proposed to assess the representativeness of surveillance of surgical site infection after colorectal surgery in Portugal, by comparing the distribution of procedures whose data was collected for surveillance with the distribution of all procedures performed in the country.

Our analysis included procedures performed in public hospitals between 2015 and 2020. The distribution of data in the national database was compared with the distribution in the surveillance database by demographic, procedural and hospital risk factors. Effect size was used to compare the datasets, presented in Cramer's V.

Effect sizes were negligible for male sex, age and open surgery. There was a small effect size in urgent procedures, both per year (V between 0.09 and 0.16) and for the entire period (V=0.14), as well as in hospital type, with (V between 0.16 and 0.20).

Surveillance needs to be optimized to better reflect the population at risk in the country.

Keywords

Colorectal surgery, Effect size, Representativeness, Surgical site infection, Surveillance

Introduction

As surveillance is a critical component in any strategy aiming to decrease the burden of healthcare-associated infections, the European Centre for Disease Prevention and Control harmonised the methods for surveillance in continental hospitals, leading to the implementation of the Healthcare-Associated Infection Surveillance Network (HAI-Net).[1] In surgical patients, the most frequent healthcare-associated infection is surgical site infection (SSI), a complication associated with increased morbidity and mortality.[2] Its incidence is highest in colorectal surgery.[3]

One of the fundamental characteristics of an ideal surveillance system is representativeness.[4] According to the HAI-Net protocol, data collection is recommended for a minimum of three months and/or for 30 surgical procedures of a certain type, per year.[1] However, no recommendation is provided to ensure that the collection is random. Even if involuntarily, hospitals may be collecting data on procedures that do not reflect their overall practice. This is highly relevant, as a biased sample of procedures means low-quality denominator data, which hampers the reliability of incidence figures.[4] A previous study in a tertiary hospital in Portugal showed that elective procedures were more likely to have data collected for surveillance than urgent procedures.[5] However, whether this is extensible to the remaining national hospitals remains unknown.

Hence, we proposed to assess the representativeness of surveillance of SSI after colorectal surgery in Portugal, by comparing the distribution of procedures whose data was collected for surveillance with the distribution of all procedures performed in the country.

Methods

Administração Central do Sistema de Saúde (ACSS) is a public institute that is responsible for the integrated management of the resources of the Portuguese National Health System. Through the formation and employment of physicians as clinical coders, ACSS is able to systematically and transversally characterize hospital morbidity for all patients admitted to public hospitals. Its dataset is considered to be the complete database for hospital care in Portugal. Data is not available for researchers disaggregated at the individual level, but rather as counts of patients with certain variables, per year and hospital centre.

Surveillance data at each hospital is reported nationally to the Directorate General of Health, which is responsible to manage the national surveillance database. The dataset uses the surgical procedure as the unit of measurement, registering all variables as different columns. As Portugal is part of HAI-Net, hospitals are required collect data for a minimum of three months and/or for 30 surgical colorectal procedures, per year, regardless of size or resources.[1]

Our analysis included colorectal procedures performed in public continental hospitals between 2015 and 2020. Hospitals outside the National Health System were excluded. Baseline characteristics of each final database are presented in figure 1. Representativeness was assessed per year, by including hospitals reporting at least 30 procedures for that given year. The distribution of data in the national database was compared with the distribution in the surveillance database by demographic (sex and age, cut-offed at 65 years), procedural (open surgery and urgent surgery) and hospital risk factors (hospital group). The latter is based on the case- mix index, a global coefficient of hospital production that aims to reflect the relativity of one hospital towards the others, in terms of its proportion of patients with complex pathologies and, consequently, higher resource consumption. From groups B to E there is an overall increase in hospital dimension, both in size and production, while group F refers to oncological institutes.

Effect size was used to compare the datasets, as they reflect the magnitude in difference of proportions and are not directly affected by sample size. [6, 7] The effect size presented is *Cramer's V*, which may be used for multi-category variables. Effect size is considered small between 0.1 and 0.3, medium between 0.3 and 0.5, and large above 0.5.[8] Analysis was performed using R, version 4.1.1.

Results

Surveillance database includes 23.8% of colorectal procedures performed, with a slightly higher proportion of patients older than 65. The proportion of open surgeries and urgent procedures were higher in the ACSS database. Hospital groups were unevenly distributed across groups. In the ACSS database, over half procedures were performed in groups C and D, whereas in the surveillance database over half procedures were reported for groups C and E.

Effect sizes were negligible for male sex, age and open surgery (figure 2). There was a small effect size in urgent procedures, both per year (V ranging between 0.09 and 0.16) and for the entire period (V=0.14), as well as in hospital type, with V ranging from 0.16 to 0.20.

Discussion

The findings of this study suggest that there is a small non-negligible bias in the surveillance database, which has proportionally less urgent procedures reported and a hospital type distribution that does not reflect the countrywide distribution. Hence, SSI incidence could be underestimated. Although infection cases were unavailable for comparison, incidence proportions may only be comparable if the denominator is derived from a representative sample. Therefore, efforts to improve surveillance should be directed towards these limitations. Patients in surveillance database were demographically representative of patients submitted to colorectal surgery countrywide, and had a similar proportion of open surgeries.

One study in Norway has also assessed the representativeness of national SSI surveillance considering sex, age and hospital type, although it did not include colorectal surgery nor procedural risk factors, and used chi-squared analysis. Their system also showed no demographic differences, while hospital type distribution was significantly different in the first years and gradually became similar between surveillance and national databases, except for cholecystectomy.[9] The study also addressed completeness, which is not a requirement for an effective surveillance system.[4] Even if total completeness would ensure representativeness, it would not be efficient nor realistic, given that resources are inherently limited.

The inclusion of demographic variables, procedural risk factors and hospital characteristics allowed to test multiple dimensions affecting the risk of SSI in colorectal surgery. To the best of our knowledge, this is the first study in the field of surveillance analysis in SSI to account for large sample size fallacy. Nonetheless, this study has some limitations. Nationally, data on SSI incidence and other risk factors were unavailable, whereas the surveillance database does not include comorbidities, and thus other relevant risk factors could not be analysed. Therefore, other risk factors may be unevenly distributed between databases. Data are not linked and were compared aggregately, meaning there is no absolute certainty that the surveillance database is a subset of the national one.

Conclusion

Surveillance needs to be optimized to include more urgent procedures and hospitals that may better reflect the distribution of the hospital network in the country.

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Conflict of interest: None declared.

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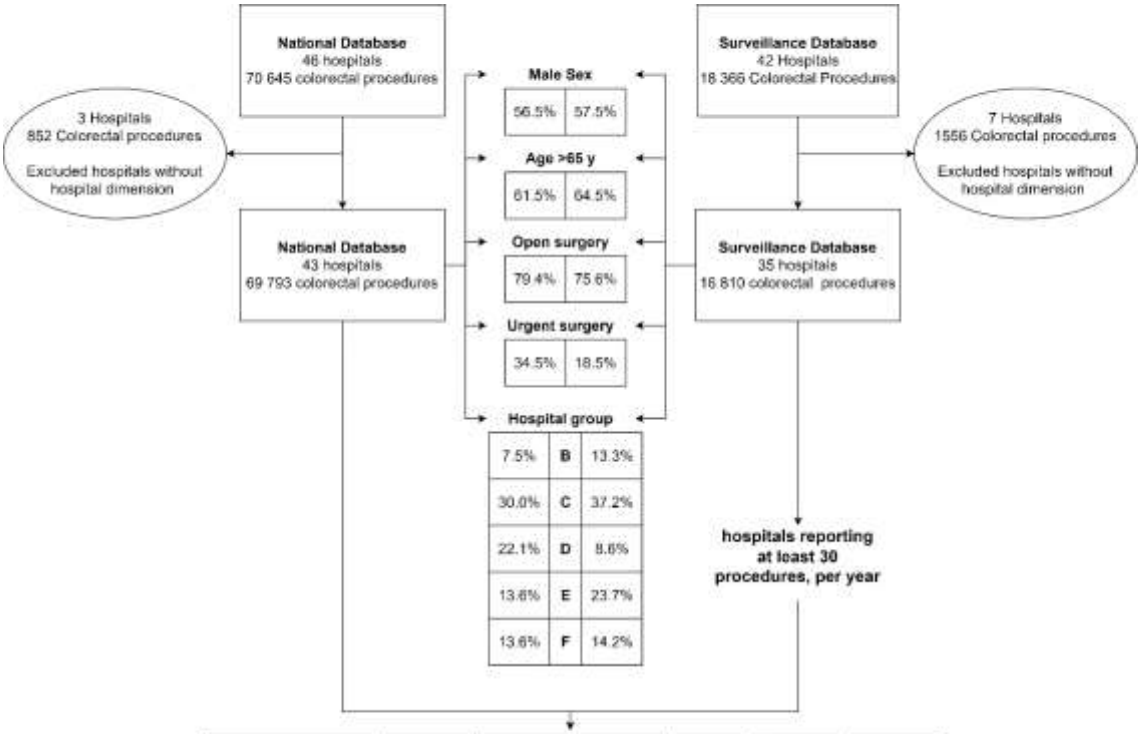
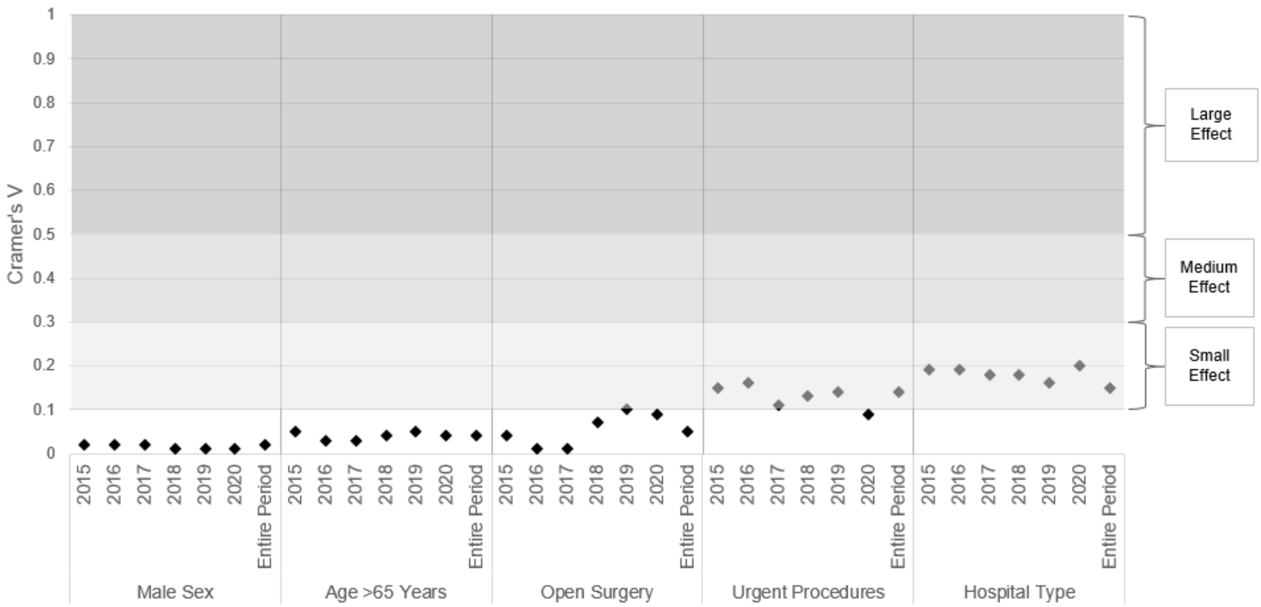
Figure 6. Flow chart of procedures subgrouping, for analysis



Year	2015	2016	2017	2018	2019	2020
No hospitals	21	24	23	23	22	17
No procedures National database	7 781	8 009	6 563	5 936	5 704	4 156
No procedures Surveillance database	2 893	3 415	3 098	2 731	2 869	1 503

Figure 7. Effect size, given by Cramer's V, per year



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Validation of a semi-automated surveillance system for surgical site infections: Improving exhaustiveness, representativeness, and efficiency

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ABSTRACT

Objectives: To assess whether electronic records data could improve the efficiency, exhaustiveness, and representativeness of SSI surveillance by selecting a group of high-risk patients for manual review.

Methods: Colorectal surgeries (2016–2018) and cholecystectomies (2017–2018) were selected. Post-surgical antibiotic use, positive culture, C-reactive protein (CRP) values, body temperature, leukocyte count, surgical re-intervention, admission to the emergency room, and hospital readmission were retrieved. For representativeness, procedures registered in HAI-Net were compared with non-included procedures, and the validity of each variable (or combination) was tested considering the presence of SSI as the gold standard. The proportion of procedures flagged for manual review by each criterion was estimated.

Results: Little more than 50% of procedures were included in HAI-Net (SSI risk: 10.6% for colorectal and 2.9% for cholecystectomies). Non-included procedures showed higher proportions of infection markers. Antibiotic use and CRP >100 mg/dl presented the highest sensitivity for both surgical groups, while antibiotic use achieved the highest positive predictive value in both groups (22% and 21%, respectively) and flagged fewer colorectal procedures (47.7%).

Conclusions: Current SSI surveillance has major limitations. Thus, the reported incidence seems unreliable and underestimated. Antibiotic use appears to be the best criterion to select a sub-sample of procedures for manual review, improving the exhaustiveness and efficiency of the system.

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Introduction

Surgical site infection (SSI), one of the most common types of healthcare-associated infection (HAI) worldwide, is associated with significant morbidity, mortality, and costs (Zimlichman et al., 2013; Umscheid et al., 2011). Despite their huge burden, they are not inevitable: as many as 55% may be preventable (Umscheid et al., 2011). The magnitude of SSI was the rationale for their inclusion in the Healthcare-Associated Infection Surveillance Network (HAI-Net) in 2009, which harmonized the European methodology for the surveillance of HAIs in order to improve the quality of care and compare the implementation of key preventive measures between hospitals and between EU/EEA countries (European Centre for Disease Prevention and Control, 2017).

Surveillance usually implies manual review of patient charts for the occurrence of SSIs (Mulder et al., 2019; Trick, 2013). Unsurprisingly, it is known to be labour-intensive, time-consuming, and prone to error and inter-observer variability (Mulder et al., 2019; Trick, 2013; Chalfine et al., 2006; van Mourik et al., 2018; Woeltje, 2013; van Mourik et al., 2013; Gubbels et al., 2017; Cho et al., 2018). Some hospitals actually select only a few surgeries to survey (Cho et al., 2018), based on their frequency and risk of

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infection, but the exhaustiveness and, more importantly, the representativeness of this process is often unknown.

Nowadays, the large amount of data in electronic health records provides the opportunity to improve surveillance both qualitatively and financially. One solution is to automate part or the entire process (van Mourik et al., 2018; Woeltje, 2013). Fully automated surveillance applies a standardized definition using available electronic data (van Mourik et al., 2018) to detect SSIs, without the need for manual review. These systems may be complex to implement; additionally, it may not be possible to extract and incorporate relevant characteristics. Semi-automated surveillance, on the other hand, uses data stored in electronic records to select patients with a higher probability of SSI for subsequent manual review. Patients with a low probability are assumed as having no SSI and do not undergo further review (van Mourik et al., 2013; Gubbels et al., 2017).

This latter model has been increasingly tested throughout the world (Chalfine et al., 2006; Hu et al., 2015; Streefkerk et al., 2016; Trick et al., 2004; Woeltje, 2013). It provides objective and consistent definitions across time and institutions for benchmarking purposes, expands current surveillance to include all surgeries, is less time-consuming, and is less affected by human error (van Mourik, 2018; Streefkerk et al., 2016, 2014; Trick et al., 2004). However, it requires validation in each setting, as it needs to be customized to maximally support hospital surveillance efforts (van Mourik et al., 2015).

The aim of this study was to assess the exhaustiveness of current surveillance of SSIs in Centro Hospitalar Universitário S. João (CHUSJ), and to determine whether a classification model could improve the efficiency of the entire process, through the implementation of a semi-automated surveillance system for SSIs after colorectal surgery and cholecystectomy, using electronically available parameters.

Methods

Study setting and design

This study was conducted in the Hospital Epidemiology Centre, part of CHUSJ, a 1105-bed tertiary care public university hospital in Porto, Portugal. In 2012, an in-house business intelligence platform was developed called HVITAL, which links and correlates data from different sources on every hospital encounter. CHUSJ integrates the HAI-Net SSI protocol and focuses SSI prevention activities on colorectal surgeries, cholecystectomies, and hip and knee arthroplasties. Colorectal surgery and cholecystectomy were selected for this study because they have the highest incidence rates of SSI nationwide.

Currently, surgeons are asked to complete a paper form for all colorectal and cholecystectomy procedures coded according to the International Classification of Diseases Ninth Revision (ICD-9; Supplementary material File 1). The form has all relevant information for infection control purposes, namely diagnosis of infection, in accordance with the HAI-Net SSI protocol (European Centre for Disease Prevention and Control, 2017). However, the form is frequently incomplete, meaning that in practice, infection preventionists (IPs) manually review nearly all medical records of patients who undergo colorectal surgery or cholecystectomy. Data collected are then registered on the HAI-Net electronic platform, which is managed on a national basis. Surveillance is highly dependent on the availability of surgeons to enter all required data. The shortage of human resources is, thus, a limitation step in the exhaustiveness and timeliness of the system, which results in a smaller number of procedures included. Moreover, elective and emergent surgeries may differ in the availability of data (e.g. incision time), which is mandatory for the inclusion of the procedure, and it is not entirely known if this results in a selection bias regarding the included procedures.

Participants

For the current analysis, the same eligibility criteria used for HAI-Net surveillance were considered: all colorectal and cholecystectomy procedures coded according to ICD-9 (Supplementary material File 1) and registered in the administrative data source SONHO. Local surveillance was implemented in different time periods, so all colorectal surgeries between January 1, 2016 and December 31, 2018 and all cholecystectomies between September 1, 2017 and December 31, 2018 were eligible.

Ambulatory procedures were not included because they are not presently subject to SSI surveillance. Re-interventions, i.e., eligible procedures that were performed up until 30 days after a previous similar surgery, were also excluded.

Data selection

For each procedure, nine parameters were retrieved for analysis: antibiotic use, positive culture, C-reactive protein (CRP) values >50 mg/dl and >100 mg/dl, body temperature, leukocyte count (all these in the current hospitalization); surgical re-intervention, admission to the emergency room, and hospital readmission.

These parameters were selected based on a literature review and IP experience (Abbas et al., 2019; Chalfine et al., 2006; Gerbier-Colomban et al., 2012; Perdiz et al., 2016; Song et al., 2008; Streefkerk et al., 2016; Trick et al., 2004). The presence of each parameter (dichotomously classified as present/absent) was limited to 30 days after each procedure, following the European Centre for Disease Prevention and Control (ECDC) case definition (European Centre for Disease Prevention and Control, 2017). For antibiotic use, temperature (data source: nursing registries – SClinico Enfermagem), and laboratory and microbiological culture results (data source: Clinidata), a positive result was considered if it occurred within 3–30 days after the procedure.

Antibiotic use considered all drugs administered during the hospitalization and included in category J01 of the Anatomical Therapeutic Chemical (ATC) classification. Erythromycin and neomycin, as well as single-dose antibiotics, were excluded, as they indicate prophylactic use. Positive cultures included all isolates identified in blood, peritoneal fluid, and drain fluid. Positive cultures with no specific place of identification were also considered, because of non-standardized registry practices. Well-known community-associated organisms and organisms associated with latent infections were excluded, meeting the ECDC criteria for SSI (European Centre for Disease Prevention and Control, 2017). Two values were considered to test CRP: 50 mg/dl and 100 mg/dl, according to the experience of the IPs. The cut-off considered for body temperature (38 °C) followed the ECDC criteria for SSI (European Centre for Disease Prevention and Control, 2017). Due to possible registry errors, no temperature value above 42 °C was considered positive. Leucocytosis was defined as a leukocyte count $>11 \times 10^9/l$.

Surgical re-intervention was considered if, in the time set, there was another procedure registered at the hospital with the same patient ID, regardless of the procedure. Similarly, regardless of complaint or diagnosis, all admissions to the emergency room and all hospital readmissions were considered. All of these data are recorded in the administrative software SONHO.

The outcome was defined as the presence of SSI after each surgical procedure, as registered in HAI-Net.

From HAI-Net, the patient ID, episode number, and date of surgery were collected for data linkage purposes. The type of infection, whether it was superficial, deep, or organ/space, was also collected. In addition, administrative data such as patient sex and age, and type of procedure (emergent or scheduled) were retrieved.

There was no need for informed consent due to the purely observational and retrospective nature of this study. Confidentiality was assured by establishing the database in a hospital computer, protected by password, only accessible by the authors of the study. The protocol for this investigation was approved by the CHUSJ Ethics Committee.

Analysis

The observation unit was the procedure. In the case of a surgery including simultaneous colorectal and cholecystectomy procedures, the surgery was included twice in the analysis, once per procedure group.

All of the analyses were stratified by type of surgical procedure.

The database was linked with data reported to HAI-Net using the patient ID and surgery date. Some procedures included in HAI-Net were not linkable to the database. These were manually reviewed, and if a registry error was identified, it was corrected and subsequently included. Others were not linkable at all (Figure 1).

To test the representativeness of the current surveillance system, eligible reviewed procedures, defined as those included in HAI-Net, were compared with non-reviewed ones, i.e. eligible procedures not included in HAI-Net, using the parameters described above and the type of surgery.

The description of the categorical parameters was made through absolute and relative frequencies, while the only numeric parameter, age, was described through the mean and standard deviation. For comparisons between groups, the Pearson Chi-square test was used for the categorical parameters and the Student t-test was used for age; the significance level was set at 5%.

Within the eligible and reviewed procedures, the validity of each parameter was tested considering the presence of SSI recorded in HAI-Net as the gold standard. The validity of a combination of different parameters that, alone, presented higher sensitivity was also tested, namely antibiotic use or positive culture; antibiotic use or body temperature above 38 °C; antibiotic use or positive culture or body temperature above 38 °C; antibiotic use or CRP value above 100 mg/dl; and CRP value above 100 mg/dl or body temperature above 38 °C.

The sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated with their respective 95% confidence intervals (CI). Validity was tested considering all SSIs or only deep or organ/space SSIs. The latter was only tested for colorectal procedures, due to the larger sample size.

Among all colorectal procedures eligible for surveillance, the number and proportion of medical records that would have been flagged for manual review if each criterion (or combination) was implemented was estimated. This analysis was limited to colorectal procedures due to the larger sample size and higher incidence.

Microsoft Excel 2016 and R version 3.5.3 were used for the data analysis.

Results

A total of 1330 colorectal procedures were considered for the analysis (Figure 1). Of these, 743 (56%) were also included in the HAI-Net database. Similarly, 679 cholecystectomies were eligible, of which 408 (60%) were included in the HAI-Net database.

Within the eligible and reviewed procedures, the risk of an SSI after a colorectal surgery was 10.6% (deep or organ/space 7.9%) and after a cholecystectomy was 2.9% (deep or organ/space 2.2%).

As observed in Table 1, eligible non-reviewed colorectal procedures presented significantly higher proportions of antibiotic use, positive cultures, and leucocytosis. The mean age was significantly lower. Even more pronounced differences were observed in cholecystectomies. In both surgical groups, the proportion of emergent interventions was significantly lower in included procedures. Emergent colorectal surgeries presented higher proportions of antibiotic use, positive cultures, CRP values, leucocytosis, and re-interventions than elective procedures (Supplementary material Table S1).

In colorectal procedures (Table 2), CRP values and antibiotic use achieved the highest sensitivity (95% CI ranging between 79% and 97%). However, the PPV of antibiotic use was 22% (95% CI 18–27%), higher than CRP. Nearly half (45%) of colorectal surgery procedures

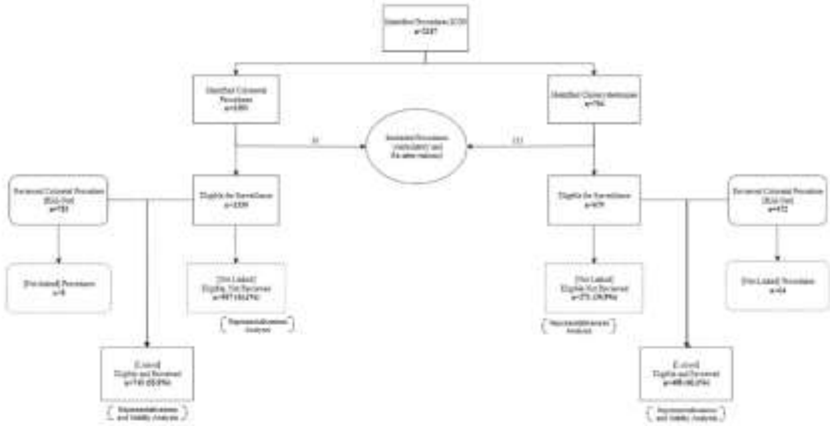

Figure 1. Flow chart of procedure selection for analysis.
Eligible: all procedures coded according to ICD-9 and registered in the administrative data source SONHO; HAI-Net: database of reviewed procedures sent to HAI-Net; Linked: procedures that were both coded according to ICD-9 and present in the HAI-Net database; Reviewed: procedures for which it was known whether an SSI had occurred or not.

Table 1
Characteristics of eligible procedures, according to their inclusion in the current surveillance system, by surgical group.

Colorectal surgeries, n (%)				Cholecystectomies, n (%)		
Parameters	Eligible and reviewed n = 743	Eligible not reviewed n = 587	p-Value	Eligible and reviewed n = 408	Eligible not reviewed n = 271	p-Value
Female	331 (44.5)	253 (43.1)	0.636	289 (70.8)	144 (53.1)	<0.001
Age (years), mean ± SD	65.8 ± 14.1	60.5 ± 21.9	<0.001	57.2 ± 15.9	56.8 ± 18.0	0.732
Emergent intervention	84 (11.1)	160 (27.3)	<0.001	30 (7.4)	91 (33.6)	<0.001
Antibiotic use	312 (42.0)	323 (55.0)	<0.001	53 (13.0)	75 (27.7)	<0.001
Positive culture	120 (16.2)	122 (20.8)	0.035	8 (2.0)	13 (4.8)	0.062
CRP >50 mg/dl	555 (74.7)	444 (75.7)	0.741	74 (18.1)	92 (33.9)	<0.001
CRP >100 mg/dl	407 (54.8)	335 (57.1)	0.435	52 (12.7)	70 (25.8)	<0.001
Leukocytes >11 × 10^9/l	207 (27.9)	232 (39.5)	<0.001	22 (5.4)	43 (15.9)	<0.001
Body temperature >38 °C	217 (29.2)	171 (29.1)	1.000	21 (5.1)	34 (12.5)	0.001
Re-intervention	143 (19.2)	115 (19.6)	0.929	4 (1.0)	15 (5.5)	0.001
Hospital readmission	84 (11.3)	49 (8.3)	0.090	18 (4.4)	7 (2.6)	0.303
Admission to ER	160 (21.6)	127 (21.6)	1.000	43 (10.5)	75 (27.7)	<0.001
SSI	79 (10.6)			12 (2.9)	–	
Deep or organ/space SSI	59 (7.9)			9 (2.2)	–	

CRP, C-reactive protein; ER, emergency room; SD, standard deviation; SSI, surgical site infection.

Table 2
Sensitivity and PPV of each parameter for the detection of SSI in colorectal procedures.

Colorectal procedures			
All (SSI: n = 79)	Flagged for manual review, n (%)	n [Sensitivity, % (95% CI)]	PPV, % (95% CI)
Antibiotic use	635 (47.7)	70 [89 (79–95)]	22 (18–27)
Positive culture	242 (18.2)	55 [70 (58–79)]	46 (37–55)
CRP >50 mg/dl	999 (75.1)	73 [92 (84–97)]	13 (10–16)
CRP >100 mg/dl	742 (55.8)	73 [92 (84–97)]	18 (14–22)
Leukocytes >11 × 10^9/l	440 (33.1)	44 [56 (44–67)]	21 (16–27)
Body temperature >38 °C	388 (29.2)	60 [76 (65–85)]	28 (22–34)
Re-intervention	258 (19.4)	43 [54 (43–66)]	30 (23–38)
Hospital readmission	133 (10.0)	17 [22 (13–32)]	20 (12–30)
Admission to ER	287 (21.6)	23 [29 (19–40)]	14 (9–21)
Deep or organ/space SSI (SSI: n = 59)			
Antibiotic use	–	90 (79–96)	17 (13–22)
Positive culture	–	75 (62–85)	37 (28–46)
CRP >50 mg/dl	–	90 (79–96)	10 (7–12)
CRP >100 mg/dl	–	90 (79–96)	13 (10–17)
Leukocytes >11 × 10^9/l	–	61 (47–73)	17 (12–23)
Body temperature >38 °C	–	73 (60–84)	20 (15–26)
Re-intervention	–	58 (44–70)	24 (17–32)
Hospital readmission	–	22 (12–35)	15 (9–25)
Admission to ER	–	31 (19–44)	11 (7–17)

CI, confidence interval; CRP, C-reactive protein; ER, emergency room; PPV, positive predictive value; SSI, surgical site infection.

with at least one post-surgical isolate had an SSI, but the sensitivity of this parameter was 70% (95% CI 58–79%). For each criterion, more than 90% of the negative results were true non-infected patients (Supplementary material Table S2).

When the analysis was repeated for deep or organ/space SSIs, values did not change significantly, nor did specificity or NPV.

The sensitivity and specificity of each parameter was very similar in cholecystectomies. Even though the incidence of infection is much smaller in these procedures, the PPVs were equivalent to those observed for colorectal surgeries (Table 3 and Supplementary material Table S3).

When considering the different combinations (signalling procedures as high-risk if at least one of the parameters was present), no improvement in the overall sensitivity and PPV was observed. Antibiotic use and CRP values increased the sensitivity of other parameters, but the PPV of the combination decreased (Figure 2).

When applied to all 1330 colorectal surgeries performed in this period, the criterion that would flag fewer procedures for manual review was antibiotic use, followed closely by antibiotic use or positive culture (Table 4). Both resulted in around half of the procedures to be reviewed. In contrast, antibiotic use coupled with CRP values flagged more procedures as high-risk.

Discussion

This study showed that current surveillance of SSIs in CHUSJ is neither exhaustive nor representative: almost half of the procedures are not currently part of the surveillance database, and non-reviewed procedures showed a higher proportion of proxies of infection, meaning that surveillance, as it is, seems to

Table 3
Sensitivity and PPV of each parameter for the detection of SSI in cholecystectomies.

Cholecystectomies All (SSI: n = 13)	n [Sensitivity, % (95% CI)]	PPV, % (95% CI)
Antibiotic use	11 [92 (62–100)]	21 (11–34)
Positive culture	4 [33 (10–65)]	50 (16–84)
CRP >50 mg/dl	10 [83 (52–98)]	14 (7–23)
CRP >100 mg/dl	10 [83 (52–98)]	19 (10–33)
Leukocytes >11 × 10^9/l	5 [42 (15–72)]	23 (8–45)
Body temperature >38 °C	6 [50 (21–79)]	29 (11–52)
Re-intervention	1 [8 (0–38)]	25 (1–81)
Hospital readmission	5 [42 (15–72)]	28 (10–53)
Admission to ER	6 [50 (21–79)]	14 (5–28)

CI, confidence interval; CRP, C-reactive protein; ER, emergency room; PPV, positive predictive value; SSI, surgical site infection.

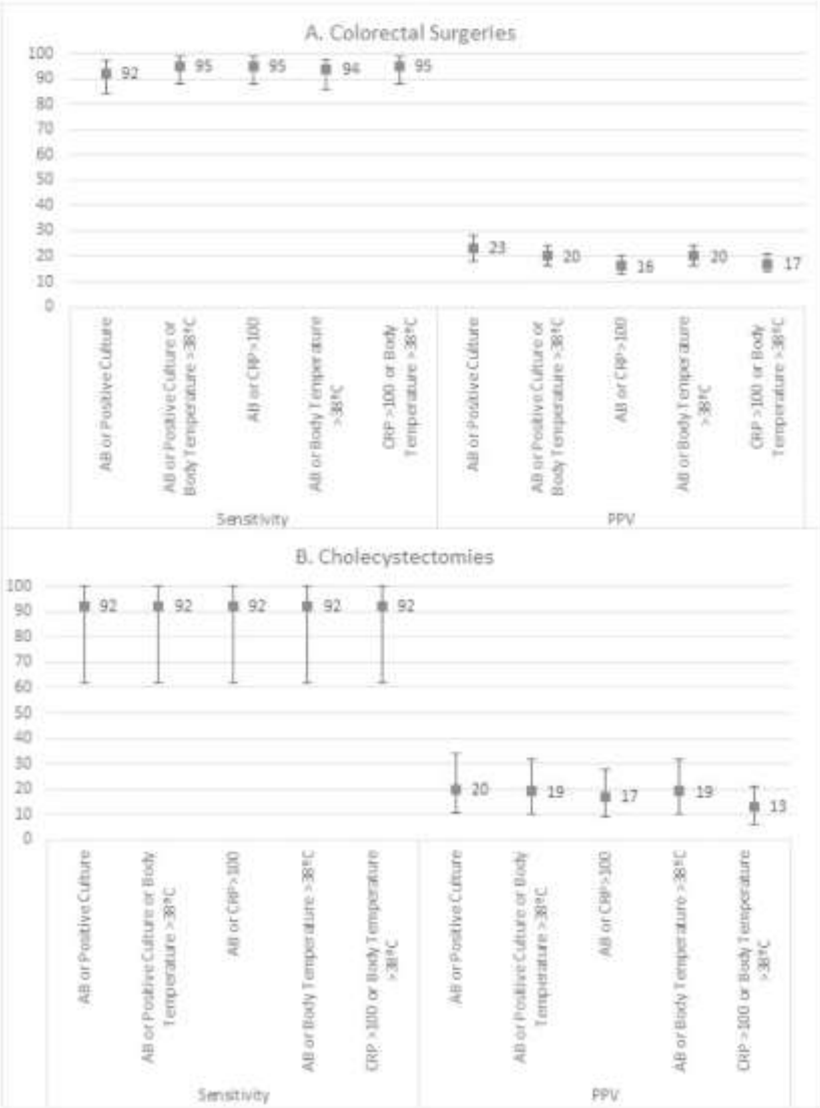

Figure 2. Sensitivity and positive predictive value (PPV) of the combined criteria studied for colorectal surgeries (A) and cholecystectomies (B), with respective confidence intervals.

systematically miss procedures with a higher risk of infection. Thus, current incidence estimates are not reliable and may be underestimated.

It was observed that emergent surgeries had a considerably higher risk of infection, but were less likely to be reviewed. This may be related to differences in the electronic registry of data, namely in variables that are considered mandatory to record for a surgery in the surveillance platform (e.g., incision time). Moreover, the coverage and quality of surveillance data is currently affected by the lack of human resources allocated to surveillance, namely physicians. During this time period, due to strike action by health professionals, there was an insufficient number of available

Table 4
Number of procedures flagged by each criterion when applied to all colorectal surgeries.

Parameter	Identified procedures for manual review	
	n	%
Antibiotic use	635	47.7
Antibiotic use or positive culture	644	48.4
Antibiotic use or temperature >38 °C	729	54.8
Antibiotic use or positive culture or temperature >38 °C	736	55.3
CRP >100 mg/dl	742	55.8
CRP >100 mg/dl or body temperature >38 °C	798	60.0
Antibiotic use or CRP >100 mg/dl	859	64.6

CRP, C-reactive protein.

clinicians to perform all routine care activities, so surveillance could not be assured. This resulted in 5 months during which colorectal surgeries were not subjected to SSI surveillance. Although these factors may seem very context-specific, both the shortage of resources and missing data are common reasons for the lack of quality of surveillance performed in different hospitals worldwide (Chalfine et al., 2006; van Rooden et al., 2020; Almeida, 2016). Unless every hospital is willing to adapt to a more efficient performance paradigm of surveillance, it is expected that the quality of SSI surveillance will decrease in the future, due to the steady increase in surgical procedures. Making use of current available electronic data is a way of improving surveillance systems.

In this study, antibiotic use, CRP values, and combined parameters all presented a sensitivity to detect infection cases of close to 90%, with overlapping confidence intervals. However, the same antibiotics are given for different types of infection, and CRP is a marker of inflammation that is not exclusive to infection, which decreases their specificity and PPV. Similarly, the validity of a positive culture might have been affected by the inclusion of many results from non-specified microbiological samples, following the conclusion of van Rooden that the identification of SSI frequently disregards culture samples (van Rooden et al., 2020).

Nevertheless, antibiotic use (with or without the presence of a microbiological isolate) seems to be the best criterion to select a sub-sample of procedures for manual review of the medical records. Antibiotic use, starting 3 days after surgery, by identifying 48% of eligible procedures, would decrease by half the number of cases to be reviewed. Although other variables are required in the surveillance system, these may easily be retrieved from existing information systems.

Rather than just saving time, the use of antibiotic as a classification tool is likely to improve the representativeness and exhaustiveness of surveillance, since the number of procedures to review manually becomes manageable, with no need to exclude any surgery within each surgical group. Furthermore, as the true incidence of SSI is probably higher than that observed in this study, the PPV and the efficiency of the process are also probably underestimated. This is particularly relevant in a setting where incidence rates still rely heavily on surgeon feedback, as surgeons have been reported to detect far fewer SSIs than their IP counterparts (Pham et al., 2016; Rosenthal et al., 2010). In fact, the impact of a semi-automated process is expected to be smaller in a setting where surveillance is only dependent on IPs.

Considering the lower value of the 95% CI, antibiotic use may have a sensitivity of just 79%, meaning that one in five infections could go undetected with antibiotic use as a selection criterion. In absolute terms, this would represent five infections a year, which would clearly be compensated by the better efficiency of surveillance and the probable truer report of SSI incidence.

This study was affected by the quality of the HAI-Net database used as the gold standard. This database originated from conventional SSI surveillance, which is dependent on manual chart review. Hence, many input errors are present, and it is possible that some cases of SSI may have gone undetected. The information system, while allowing for a swift identification of target procedures, assuring that all are included, is specific to this hospital. Thus, we possibly failed to exclude re-interventions if the first procedure was performed elsewhere. Also, the existence of pre-existing infections as an indication for surgery was not assessed. However, by considering as high-risk patients those who started antibiotic therapy 3 or more days after surgery, the semi-automated system is likely to have excluded those with pre-existing infections.

Although other studies have argued in favour of considering antibiotic use or microbiological results (Cho et al., 2018; Perdiz et al., 2016; Streefkerk et al., 2016; Trick et al., 2004; Woeltje, 2013), in the present study differences were negligible. Some studies have used the order for a microbial culture, rather than its result, as a surrogate for a clinical suspicion of infection (Cho et al., 2018; Branch-Elliman et al., 2014). However, these data are not so easily available in our system; antibiotic use can be used as a surrogate for such an order because of the high probability of beginning empirical antibiotic therapy when a suspicion of infection arises. The addition of more complicated variables has been shown not to improve overall accuracy (Branch-Elliman et al., 2014), and the marginal improvement in sensitivity does not offset the associated reduction in the PPV (van Rooden et al., 2020), which is particularly relevant when implementing the electronic system in clinical practice.

Nevertheless, all criteria need to be validated prospectively before implementation. In addition, it could be relevant to study the optimal cut-off values of parameters such as CRP in the future. In routine practice, antibiotic use and positive culture are easily extracted from HVITAL, in contrast to CRP values and body temperature, hence system adaptation would be smoother.

Time saved with the application of this semi-automated system was not measured due to the retrospective nature of the study. Estimates vary according to hospital setting and surveillance criteria (Rosenthal et al., 2010; Streefkerk et al., 2016; Trick et al., 2004; Woeltje, 2013), and depend not only on the number of selected procedures but also on the complexity of each chart. Regardless of each setting estimate, a systematic review concluded that the adoption of this type of system has almost always contributed to a decrease in IP staff time and has never increased it (Russo et al., 2018). Time saved may be used to improve the exhaustiveness of the process, to expand surveillance to other procedures, or to reallocate resources to monitor SSIs in the outpatient setting, which unfortunately is systematically overlooked (Chalfine et al., 2006; Gerbier-Colomban et al., 2012; van Rooden, 2020; Streefkerk et al., 2016; Trick et al., 2004; Woeltje, 2013).

In conclusion, current surveillance methods rely heavily on surgeon feedback and manual input of data, resulting in a very inefficient process. Frustratingly, it is not providing clinicians or decision-makers with reliable outputs of infection and risk.

Antibiotic use, with or without positive culture, may be used to improve the system exhaustiveness, representativeness, and efficiency in a semi-automated method of surveillance, with a sufficiently high sensitivity that is accepted in clinical practice. This is particularly relevant in settings where surveillance is embedded with surgeon feedback, where the benefit of adopting this method is expected to be even higher than if surveillance was embedded with IPs. In the future, artificial intelligence might be the solution to fully automate the entire process.

Funding

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Ethical approval

The protocol of this study was submitted to and approved by the Ethics Committee of Centro Hospitalar Universitário São João (n° 96/19), and was authorized by the President of the Hospital Administration Board. No informed consent was deemed necessary.

Availability of data and material

All data presented here are accessible upon contact with the main author of the study.

Code availability

Not applicable.

Conflict of interest

None.

Appendix A. Supplementary data

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Paper 5

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SHEA

Original Article

Surveillance of surgical site infection after colorectal surgery: comprehensiveness and impact of risk factors

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Abstract

Objective: The incidence of surgical site infection (SSI) is highest after colorectal surgery. We assessed the impact of risk factors for SSI using the population attributable fraction (PAF).

Design: Retrospective cohort study.

Setting: Portuguese hospitals performing regular surveillance.

Patients: We identified patients who underwent colorectal procedures in hospitals that reported colorectal surgeries every year between 2015 and 2019. Among 42 reporting hospitals, 18 hospitals were included.

Methods: Risk-factor incidence was estimated using the National Epidemiological Surveillance platform from 2015 to 2019. This platform follows the methodology recommended by the European Centre for Disease Prevention and Control. American Society of Anaesthesiologists (ASA) physical classification, wound classification, open surgery, urgent operation, antibiotic prophylaxis, operation time, and male sex were included as risk factors. Measures of association were retrieved from published meta-analyses. PAFs were calculated using the Levin formula. To account for interaction between risk factors, communality of risk factors was used in a weighted-sum approach, providing a combined value that serves as a measure of the comprehensiveness of surveillance.

Results: Among 11,219 reported procedures, the cumulative SSI incidence was 16.8%. The proportion of SSI attributed to all risk factors was 61%. Modifiable variables accounted for 31% of procedures; the highest was laparotomy (16.8%), and urgent operations (2.7%) had the lowest value. Nonmodifiable factors accounted for 28.7%; the highest was wound classification (14.3%).

Conclusions: A relevant proportion (39%) of SSI remains unaccounted for by current surveillance. Almost one-third of SSI cases have potentially modifiable factors. Interventions focusing on shorter, less invasive procedures may be optimally effective in reducing the SSI incidence.

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Surgical-site infection (SSI) is a surgical complication associated with increased morbidity, mortality, and costs.[1,2] Although SSI may occur following any surgical procedure, the highest incidence is observed after colorectal surgery.[3,4] Because surveillance is considered an important component of strategies implemented to reduce SSI,[5] the European Centre for Disease Prevention and Control (ECDC) harmonized the methods for SSI surveillance in European hospitals in 2000 and implemented of the Healthcare-Associated Infection Surveillance Network (HAI-Net) in 2008. Since then, increasing numbers of hospitals from each country have adhered to it. In their latest annual report, the incidence of SSI following colorectal surgery decreased only slightly across the European region, with Portugal leading the European incidence of SSI following open colon surgery.[3] The SSI incidence in the country, however, has not decreased since 2013.[4] From 2015 to 2018, Portugal adopted a 3-year challenge named *Stop Infeção Hospitalar!* to decrease the incidence of 4 types of healthcare-associated infection (HAI): central-line-associated bloodstream infection, catheter-associated urinary tract infection, ventilator-associated pneumonia, and SSI. This program urges the adoption of the best practices based on the highest-quality evidence available. In the 12 participating institutions, accounting for 19 hospitals, decreases have occurred in all types of HAI except SSI in colorectal surgery.[6]

Targeted approaches are needed to decrease the burden of this infection. The effectiveness of interventions depends on the vulnerability and magnitude of the selected target to be addressed.

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The HAI-Net protocol requires hospitals to routinely collect patient and unit-based indicators such as demographic data, standardized operative procedure codes and procedure-related risk factors. The latter represent known risk factors for infection and are used for benchmarking between institutions.[7] Although many original articles have reported estimates of the association between risk factors and SSI following colorectal surgery, few have considered their impact.[8–11] Two studies estimated the impact for abdominal surgery as a whole,[8,9] and, to the best of our knowledge, none has included an adjustment for the interaction between risk factors; they have all analyzed a single determinant. Hence, the comprehensiveness of these variables in explaining SSI incidence is yet to be determined. Even though variables include nonmodifiable risk factors, which are unsuitable targets for interventions, their relative contribution to infection may assist hospitals in determining a baseline optimal incidence and in setting achievable and realistic goals for prevention.

We assessed the impact of risk factors for SSI after colorectal surgery collected in the scope of European surveillance, in Portuguese hospitals. Using the population attributable fraction (PAF), it is possible to determine how much of the incidence may be attributed to a specific risk factor. By accounting for the nonindependence of risk factors, we intended to provide more accurate estimates and to provide a combined PAF value to serve as a measure of the comprehensiveness of current surveillance indicators.

The protocol of this study was submitted and approved by the Ethics Committee of Instituto de Saúde Pública da Universidade do Porto (CE20171), in November 2020. No informed consent was deemed necessary.

Methods

Population and data source

Data on the number of colorectal procedures and SSI were retrieved from the electronic platforms of the Portuguese Directorate General of Health, which include the database of the National Epidemiological Surveillance of hospital-acquired infections in intensive care units; bloodstream infections; *Clostridioides difficile* infections; and SSI following colorectal surgery, cholecystectomy, caesarean section, cardiac surgery, hip and knee arthroplasty, and laminectomy. Portugal is part of HAI-Net, and surveillance is performed similarly across different settings. Hospitals are required to routinely collect patient and unit-based indicators such as demographic data, operation codes under the *International Classification of Diseases, Ninth Revision*, compliance with prevention bundle, antibiotic use and antimicrobial resistance, and procedure-related risk factors, following a standardized data set provided by the ECDC. Data collection is performed retrospectively because infection preventionists manually review each surgical procedure to retrieve procedural data and infection outcome. Data collection is recommended for a minimum of 3 months and/or 30 surgical procedures per year.[7] The data set uses the surgical procedure as the unit of measurement, registering all variables as different columns. Until mid-2018, the data set consisted of a single spreadsheet containing all data. Thereafter, although there was no change in the HAI-Net protocol nor in surveillance practices, the data-set structure changed with a new software developed in response to an operating system that was unable to be updated. Antibiotic use, SSI type, microorganism isolation, and resistance profile began to be registered in separate sheets, linkable by the identification number of the procedure, surgery date, and hospital.

In our analysis, we included only those procedures performed in hospitals that reported colorectal surgeries each year, from 2015 to 2019, to ensure that the same population was being analyzed throughout the study period. All included hospitals were state-owned general hospitals. Procedural variables collected under HAI-Net were included in the final analysis. Nonmodifiable risk factors included the American Society of Anesthesiologists (ASA) physical status classification, wound classification, urgent operation, and male sex. Modifiable risk factors included the duration of operation, open surgery, and the use of prophylactic antibiotic. Age, the number of operating room door openings, multiple operations, and implant in place were not considered because we could not find any systematic review establishing their significant association with the outcome. Data on compliance with the prevention bundle were unavailable.

Definitions

We defined SSI following the ECDC criteria in the HAI-Net protocol.[7] ASA classification was designed to assess and communicate a patient's preanaesthesia medical comorbidities. A score of 1 refers to a normal healthy patient, and a score of 6 refers to a declared brain-dead patient.[12] In line with most literature,[13,14] we considered as a risk factor an ASA score of 3 or above, referring to patients with severe systemic disease.

We considered the Centre for Disease Control and Prevention (CDC) classification of the cleanliness and condition of wounds, given its widespread use and ability to help predict the likelihood of surgical site infections, postoperative complications, and reoperation.[15,16] We considered a wound class III or IV as a risk factor, in line with the ECDC risk index.[7]

Duration of surgery was cutoff at 180 minutes, and all surgeries beyond that time were considered risk factors.[13] The absence of antibiotic prophylaxis was considered a risk factor. In Portugal, cefoxitin in a single dose is the mandatory antibiotic for colorectal surgery, except when the patient is allergic to penicillin with high risk of anaphylaxis, in which case metronidazole and gentamicin are the indicated antibiotics, in a single dose.[17] Male sex was considered a risk factor, as were urgent operations and open surgery.

Measures of association

Reports published until January 26, 2022, were identified by searching PubMed. Measures of association were retrieved from published systematic reviews with meta-analyses (Table 1).[13,18] In the case of antibiotic prophylaxis, because it was studied as a protective factor, we considered the inverse of the published relative risk (RR).

Statistical analysis

The PAF for each risk factor was calculated using the Levin formula.[19] We applied adjusted relative risk estimates to these formulas. The formula assumes independence of risk factors, which may be false in this case, so we used a weighted-sum approach, which allowed for full interaction between exposure and covariates,[20] where weight was defined as 1 minus is the proportion of variance shared with the other risk factors, was calculated via principal component (ie, communality), following the example of previous articles in the field of dementia prevention.[21–24]

Weighting was also considered for the estimation of individual adjusted PAF. The formulas used are available as a supplement (Supplementary Methods online).

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Table 1. Articles from which Measures of Association were Retrieved

First Author	Year	Comparison	RR	No. studies
Nelson	2014	Antibiotic use vs no antibiotic/placebo use	0.34 (0.28–0.41)	2455
Xu	2021	Male sex vs female sex	1.30 (1.14–1.49)	8
		Emergent vs elective surgery	1.36 (1.19–1.55)	7
		Wound classification >II vs ≤II	2.65 (1.52–4.61)	7
		Operative time ≥180 vs <180 minutes	1.88 (1.49–2.36)	6
		ASA score >2 vs ≤2	1.34 (1.19–1.51)	10
		Open surgery vs laparoscopy	1.81 (1.57–2.10)	16

Note. ASA, American Society of Anaesthesiologists; RR, relative risk.

To deal with potential heterogeneity in the data, a sensitivity analysis was performed considering only the hospitals that participated in *Stop Infeção Hospitalar!* whose data were potentially more reliable.

Statistical analyses were performed using Microsoft Excel 2016 (Microsoft, Redmond, WA) and IBM SPSS Statistics, version 27 (IBM, Armonk, NY). We applied a significance level of 0.05.

Results

Consequently, among 42 reporting hospitals reporting 16,569 procedures, 18 hospitals were included, representing 11,219 colorectal procedures reported nationwide (68%) (Fig. 1). Most patients were male (57.2%), and the median age was 70 years. The overall cumulative incidence of SSI was 16.8%. The prevalence of each characteristic, RR and overlap of variance are presented in Figure 2. Overlap was calculated for 10,572 procedures, following case-wise deletion of procedures missing at least 1 risk factor. Deleted procedures (median age, 71 years; interquartile range [IQR] 61.5–79; 58.7% of males) were demographically similar to included procedures (median age, 70 years; IQR, 60–78; 57.1% of males), with no marked differences in operation times: median, 140 minutes (IQR, 94–190) versus median, 145 minutes (IQR, 100–200). Deleted procedures (those with at least 1 missing risk factor), however, had a slightly higher proportion of patients with an ASA score of 3 or above (50.7% of patients with ASA scores >2 vs 47.4%). Overlap in variance ranged from 24% for open surgery to 63% for male sex.

The proportion of SSI attributed to all risk factors was 61.1%. Modifiable variables accounted for 31.3% of incidence, and nonmodifiable variables accounted for the remaining combined PAF. The modifiable risk factor with highest adjusted PAF was open surgery (16.8%), and the prevalence of this factor has been decreasing in recent years (Table 2). The nonmodifiable risk factor with highest adjust PAF was wound class superior to II (14.3%). Respectively, lack of prophylactic antibiotic (4.9%) and urgent operations (2.7%) were the risk factors with lowest PAF score (Fig. 2).

When considering only the hospitals that participated in *Stop Infeção Hospitalar!*, values did not change significantly. Overall adjusted PAF remained at 60.2%, with 31.5% attributed to modifiable risk factors and 28.7% attributed to nonmodifiable factors. Open surgery (17.3%) and wound class > II (13.2%) remained the variables with the highest impact, whereas urgent operation (2.7%) and lack of prophylactic antibiotic (4.2%) were the variables with the lowest estimates (Table 3).

Discussion

Our findings suggest that the risk factors traditionally used for colorectal surgery SSI surveillance in the European setting account for ~60% of its incidence. Ergo, a substantial proportion of SSI incidence is explained by variables that are not present in the current methodology. Modifiable risk factors may be responsible for at least 31% of SSI incidence. Of the 3 strongest risk factors with highest impact on SSI following colorectal surgery, 2 factors were potentially modifiable. Interventions focusing on adopting techniques that are less invasive and that provide shorter surgeries may be optimally suited for prevention. The use of laparoscopy has been steadily increasing in recent years, both nationally (Table 2) and internationally,[25,26] and its progressive introduction has been shown to work as a protective factor not only for overall and incisional SSI but also for organ-space SSI.[27] These results suggest that although these risk factors cannot be entirely eliminated, there is still a considerable margin to decrease their prevalence and, thus, their impact on SSI incidence. Nonmodifiable variables estimates are mainly dependent on the wound classification, in which the estimate has low precision. Urgent operations and lack of antibiotic prophylaxis, although relevant risk factors for SSI, had the lowest PAFs due to their low prevalence.

Our results suggest that unmeasured risk factors may be responsible for 40% of incidence, a high enough value to warrant close attention. The HAI-Net protocol determines the collection of the same variables for all surgical procedures to guarantee comparability, yet risk factors may be surgery specific. The closing technique of ileocolic anastomosis have been shown to be associated with SSI and could be relevant to monitor, even if it applies solely to colorectal surgery. In contrast to most other surgery types, SSI after colorectal procedures is mainly attributed to endogenous gut bacteria.[3] Therefore, all operative factors associated with more invasive procedures or delayed wound healing are expected to have a considerable impact on SSI incidence and could be considered. Comorbidities are also not directly included in the HAI-Net protocol. Even if comorbidities are unlikely to be acutely modifiable prior to surgery, knowing their impact would help to ascertain the acceptable baseline level for each setting, considering the patient case mix. Nonetheless, most comorbidities (ie, obesity, smoking habits, alcohol use, diabetes) are indirectly expressed in the ASA classification.[12] Comorbidities such as diabetes, which are usually studied in a dichotomous manner,[13] are evaluated as well-controlled factors or are not in the preoperative assessment and, thus, better represent the overall status of the patient. Because many comorbidities tend to be present in the same patients, an adjusted PAF would most likely yield low estimates for each individual factor. A weighted PAF of 6% for the ASA score may suggest that regardless of the how comprehensive a surveillance system may be on the patient's medical history, its impact on SSI incidence may be low. Even so, patient and procedural variables may not tell the full story. Some part of the missing picture may be attributable to hospital characteristics, such as availability of surveillance, or surgeon caseload volume. However, robust studies providing accurate estimates are still lacking.[28]

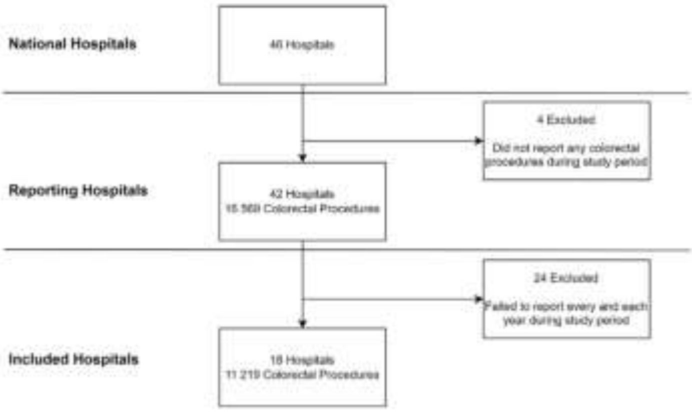

Fig. 1. Flow chart of included hospitals.

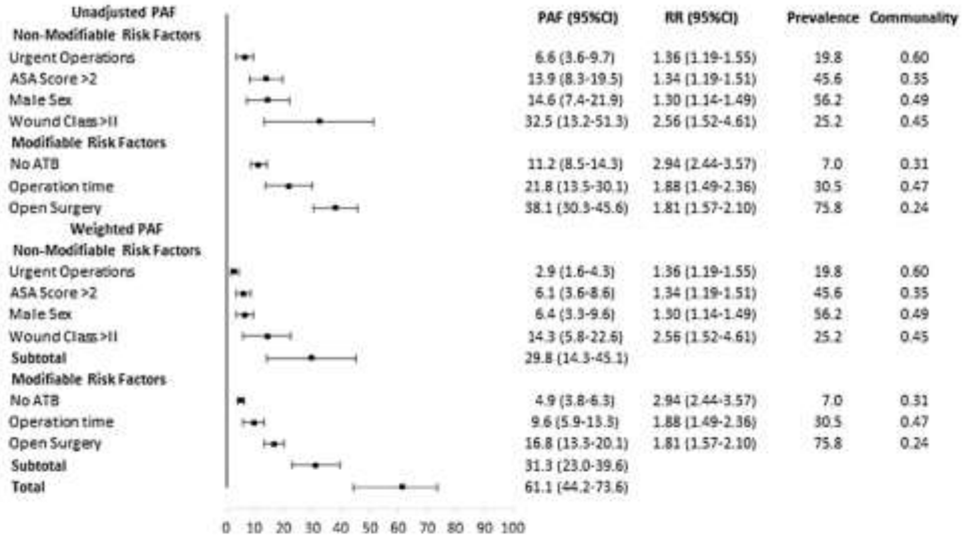

Fig. 2. Population attributable fraction, relative risk, prevalence and communalities for patients submitted to colorectal surgery in Portugal, between 2015 and 2019. Note. ASA, American Society of Anaesthesiologists; ATB, Antibiotic; CI, Confidence Interval; PAF, Population Attributable Fraction; RR, Relative Risk.

Nevertheless, compliance with prevention care bundles may be the most relevant missing variable. Care bundles consist of a set of simple, strong evidence-based practices that, when implemented in a combined and consistent manner, improve patient outcomes, with a higher impact than the addition of each intervention effect.[29] Although they have been shown to decrease SSI after colorectal surgery up to 45%, their success is deeply dependent on compliance with the entire bundle.[30,31] Suboptimal compliance rates may justify Portugal's place in SSI incidence at the European level and are strong candidates for the unexplained remaining incidence we found.[3]

Our secondary analysis of hospitals participating in *Stop Infeção Hospitalar!* showed that, for engaged hospitals, measured variables explain a lesser proportion of infection. Surveillance may decrease SSI rates through feedback and surveillance effect, which may justify why participating hospitals, with more robust surveillance teams, have a higher proportion of infection attributed to unmeasured risk factors.[32] Nonetheless, the difference was not significant. Although we acknowledge that no surveillance network can include every single risk factor for infection, it is vital to understand which variables are relevant enough to warrant inclusion in future updates of the protocol.

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Table 2. Use of Open Surgery Over Time, and Respective Population Attributable Fraction

Year	2015	2016	2017	2018	2019
Prevalence open surgery	79.7	81.6	82.3	72.5	65.7
Population attributable fraction	39.2	39.7	40.0	36.9	34.7

Table 3. Population Attributable Fraction (PAF) for Patients Undergoing Colorectal Surgery in Hospitals Participating in *Stop Infeção Hospitalar!*

Risk Factor	Overall (N=6,212)	Missing, No. (%)	RR (IQR)	Communality (N=6,105)	Weighted PAF % (IQR)	PAF % (IQR)
Nonmodifiable						
Sex, male	3,575 (57.6)		1.30 (1.14–1.49)	0.68	6.8 (3.4–10.1)	14.7 (7.5–22.0)
ASA score >2	2,696 (43.9)	64 (1.0)	1.34 (1.19–1.51)	0.37	6.0 (3.5–8.4)	13.0 (7.7–18.3)
Wound class >II	1,512 (24.4)	6 (0.1)	2.65 (1.52–4.61)	0.39	13.2 (5.2–21.6)	28.7 (11.2–46.8)
Urgent operation	1,080 (17.4)	7 (0.1)	1.36 (1.19–1.55)	0.60	2.7 (1.5–4.0)	5.9 (3.2–8.7)
Subtotal nonmodifiable					28.7 (13.6–44.2)	
Modifiable						
Operation time ≥80 minutes	1,941 (31.3)		1.88 (1.49–2.36)	0.33	9.9 (6.1–13.8)	21.6 (13.3–29.8)
Open surgery	4,582 (74.2)	35 (0.6)	1.81 (1.57–2.10)	0.22	17.3 (13.7–20.7)	37.5 (29.7–44.9)
No antibiotic prophylaxis	300 (5.2)	429 (6.9)	2.94 (2.44–3.57)	0.28	4.2 (3.2–5.4)	9.1 (7.0–11.8)
Subtotal modifiable					31.5 (23.0–39.9)	
Total (overall)					60.2 (43.3–73.0)	
Surgical site infection	947 (15.2)					

Note. ASA, American Society of Anaesthesiologists. PAF, population attributable fraction. RR, relative risk; IQR, interquartile range.

To the best of our knowledge, this is the first study to address the impact of risk factors in the context of SSI in colorectal surgery and the first in the infection prevention and control field to adjust estimates for nonindependence of risk factors. The weighted-sum approach also allows the estimation of a combined PAF that is interpretable as a measure of the combined impact of the risk factors considered, which is a known limitation of unadjusted impact measures. Although it has been described previously as a method of adjusting PAF for confounding, the ideal weight remains a matter of discussion.[20,33] The use of communalities is a novel solution that has only recently been used in the field of Alzheimer's disease and dementia.[23,24] It allows researchers to account for interaction between risk factors and provides a more robust, even if conservative, estimate than simply applying adjusted relative risk using the Levin or Miettinen formula, both of which have been shown to yield tremendous bias.[20,33] In our analysis, there was no obvious heterogeneity of variables, with all variables sharing some variance with the others. No variable was redundant, and all were usually defined by a communality >90%.[34]

Our sample size, the use of national data following the European methodology of surveillance, and the use of measures of association published in peer-reviewed meta-analysis are study characteristics that strengthen the external validity of our findings. Nonetheless, variations are expected in different settings. Prevalence estimates are setting dependent and may justify a differential impact elsewhere. Open surgery is still more prevalent in our setting than in other European countries,[25,26] and the same is true for the ASA score.[35]

Notably, hospitals are not required to provide data for all performed procedures. Hence, potential selection bias may occur for procedures registered in national databases. Likewise, the variance overlap was calculated for 83% of our sample, which could have affected its representativeness. Most of the excluded procedures were missing data on antibiotic prophylaxis due to the changes in the data set outlined earlier. Although missing procedures were demographically similar to included procedures, differences in proxies of infection, such as the ASA score and the operation time, meant that included procedures had a higher risk of infection. We were unable to determine whether this had any influence in the values estimated. Nonetheless, our sensitivity analysis provided communalities in approximately the same relative position for each risk factor, with only minor changes in weighted PAF values. Other missing data, such as the proportion of laparoscopic surgeries that ended up as open surgeries, were unavailable.

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In conclusion, variables routinely collected under the ECDC HAI-Net protocol explain 60% of SSI incidence after colorectal surgery, meaning that a relevant proportion of SSIs remains unaccounted for by current surveillance indicators. Interventions focusing on shorter, less invasive procedures may be optimally effective in reducing the burden of infection.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2023.40

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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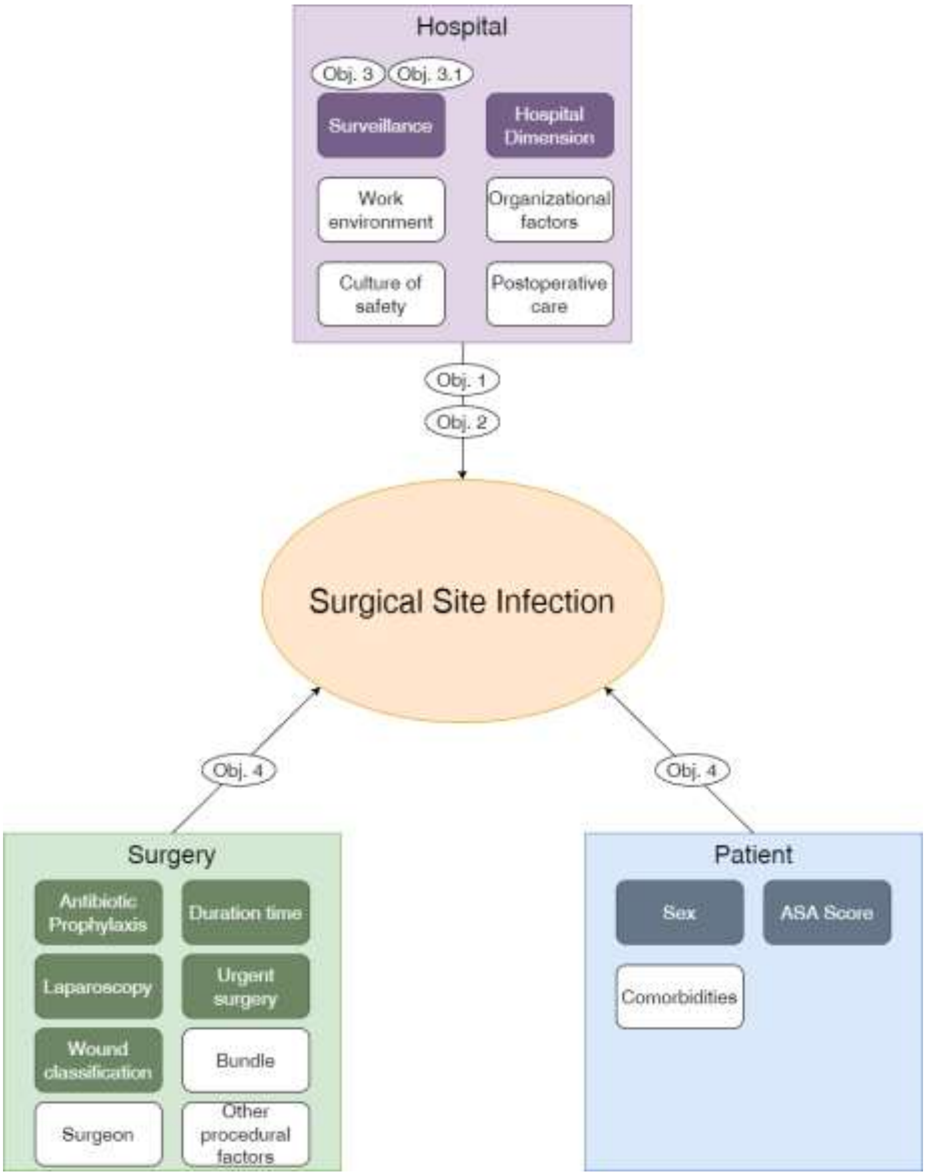
DISCUSSION AND CONCLUSIONS

The aim of this thesis was to assess the impact that patient and perioperative risk factors, including contextual risk factors, have on SSI after colorectal surgery in Portugal, in order to understand what is driving the incidence of this HAI to be the highest in Europe and, consequentially, to identify targets for future public health interventions. Conceptually, the factors influencing SSI may be grouped in patient, surgery and hospital-related risk factors, as observed below (Figure 6).

Figure 6. Concept map of risk factors for surgical site infection after colorectal surgery.



Hospital-related risk factors have seldom been researched, and the heterogeneity in risk factors considered and methodologies used limit the external validity of findings. The implementation of surveillance of SSI, however, appears to be associated with lower incidence rates, especially after the five-year mark (paper I). In the Portuguese setting, the contextual effect on SSI was shown to be relevant. Although no single variable was significantly associated with infection, it was found that it still makes a difference in which hospital the surgery takes place, even after adjusting for the major patient and perioperative risk factors and for the hospital dimension, in terms of size and production (paper II). Surveillance is suboptimal, both at the local and central setting, as it fails to include a substantial proportion of urgent procedures and, centrally, it fails to provide a representative sample in terms of the distribution of the hospitals, per dimension (papers III-IV). The use of semi-automated methods of surveillance, namely using postoperative antibiotic use in a classification model, has been shown to improve the efficiency, completeness and representativeness of overall surveillance by decreasing workload and focusing manual evaluation on high-risk surgeries (paper IV). Risk factors routinely collected under the HAI-Net protocol explain 60% of SSI incidence, thus underlining the need to continue to understand the role of other risk factors such as the hospital characteristics, bundle adhesion or colorectal-directed variables, namely the mechanical bowel preparation with or without antibiotic preparation or the type of ostomy performed, when applicable. The modifiable risk factors with highest impact on SSI incidence after colorectal surgery were open surgery and duration of surgery superior to 180 minutes, suggesting that the promotion and implementation of shorter, laparoscopic procedures, whenever possible, is the most effective intervention (paper V).

This thesis adds to previous research by taking into account the context – geographical, historical, cultural – of disease.[1] On the one hand, context in terms of hospital characteristics that may influence the risk of SSI after colorectal surgery. The query in the systematic review was designed to ensure maximum sensitivity, in order to include any potential risk factor researched. Its conclusions supported the need to contribute to the discussion with new evidence. The approach selected, using a multilevel logistic regression, was a necessary consequence of the nature of the identified problem. Colorectal surgery is performed in hospitals, and its complications are multilevel in the sense they are dependent on both the procedure and where it takes place. Therefore, the analysis of risk must take into consideration variables that may not be directly linked with comorbidities and the surgery itself. Although this methodology is robust, has been described extensively and is ideal to consider contextual and clustering effects,[177, 182, 183] it has been underused in the field of infection control.[184-188] The inclusion of process indicators such as bed occupancy rate and nurse-to-bed ration were a novelty, as process is usually focused on hospital and surgeon volume.[189] Hospital dimension was considered as both a structural and process indicator, given its close relationship with hospital production and bed size. Although it may translate better than bed size in clinical practice, it loses comparability across different settings.

On the other hand, context was taken into account in terms of local distribution of universal risk factors. As surveillance had been identified as a protector factor, it became necessary to address whether national surveillance was providing reliable, accurate data. The study acknowledged the limitations of excessive statistical power,[190] and provided insight into the specific limitations of surveillance, warranting that criticism was met by a constructive solution. Testing a semi-automated method also shed light into future solutions on the field. It considered readily available variables in the hospital setting, rather than conceptual indicators that could be unobtainable, which facilitates its swift implementation, with no need for revolutionary and undesirable changes in routine care. However, it is designed to suit a specific hospital, and adaptation in a different setting would requires local research and validation.

The measures of impact considered were able to determine clearly defined targets for prevention efforts to decrease SSI in colorectal surgery with maximum efficiency and effectiveness. Its original strength lies in the use of a weight-sum approach in the estimation of PAF. Although it has been described for over twenty years,[191] it has infrequently been used. The use of the individual variance as a weight is an innovative solution that promises to provide an estimation of the comprehensiveness of risk factors to explain a certain health problem.[192, 193] The idea that risk in SSI has a multifactorial nature is supported by finding that routinely collected individual and procedure risk factors fail to explain approximately 40% of its incidence. If one considered the prevalence of urgent procedures as reported in the national production database, its adjusted PAF would increase to approximately 6%, thus having no major impact on the conclusions. This finding link with the previous finding that even with hospital dimension, over half of SSI variance remains unexplained. Here, too, semi-automated surveillance may be part of the solution, by providing professionals with the necessary time to tackle these needs. Hospital context may help explain part of the missing picture; however, data suggests that other candidates ought to be sought and researched, namely bundle adhesion, postoperative care, leadership or organizational factors.

The work is not without limitations. As discussed in the individual papers, there is an unbalanced report of colorectal procedures across Portuguese hospitals throughout time. More than half of hospitals failed to report yearly from 2015 to 2019, and only one hospital of dimension D did so. The motives behind this are unclear, and any hypothesis would be pure speculation. Although it is true that data collection is burdensome and most hospitals do not meet the minimum recommended resources to implement effective surveillance and infection prevention[194], it does not justify the differential report, as many hospitals with those limitations are able to comply. Relevantly, the shortcomings of national surveillance on the accurate distribution of the hospital network likely decrease the ability of the multilevel analysis to find significant clustering effects, a probable type II error due to a potential reporting bias. The influence on the estimation of impact is likely residual, as discussed. Bundle adhesion was originally intended to be included, but data was unavailable. Other conceptual dimensions that are not directly related to hospital size – leadership, organization, culture of safety – are unmeasured and how much impact they may have on SSI incidence after colorectal surgery remains unknown. Comorbidities were assessed by the ASA Score. It is a classification that considers the patient holistically, and may be more clinically relevant in terms of risk than individual comorbidities. However, when one claims that 6% of incidence may be attributable to the patient condition, it is not explicit whether that percentage may be attributable to a single factor. For public health practice, that question would only be crucial if – or when – the impact of the patient's condition on its SSI risk is considerably higher.

In conclusion, by considering that this is a modern health problem – an unintended consequence of the tremendous success humankind has had in the field of infection prevention and control – and that there is a cultural and technical ability to optimize results, this thesis helps to build the notion that future research and project implementation should take into account the setting in which it is being performed. It elaborates on the most effective solutions that may be adopted in the short term. Future challenges are already peeking through the uncertainty of tomorrow. As PPCIRA, with the technical support of IHI and *Fundação Calouste Gulbenkian* is implementing a second collaborative project to decrease HAI incidence rates in the country, the opportunity arises to assess the impact it may have on bundle adhesion and SSI incidence in colorectal surgery, and to evalute the complex interaction between process and outcome indicators. It may also be an unique opportunity to estimate savings in cost of reducing these infections in a Beveridge-style health system. By bringing 24 hospitals together, it may also aide to assess infection prevention in practices, by inquiring participating hospitals on how data collection, analysis, interpretation and dissemination is performed in each setting. The variability of procedures for each step is essential to understand how standardized is the practice of infection preventionists. Although it is import for hospitals to have autonomy to adapt practices to their local sensibilities and to direct resources to local problems that may not be shared with other hospitals, nevertheless minimal standardization is vital. Without it, there may be no improvement. Automated methods may be a drive to improve standardization, comprehensiveness and liberate professionals to perform other prevention duties, namely in postoperative care, in which evidence is lacking. Validation studies are required in each setting, using the knowledge of other European countries that have led the path in this field and which have provided a roadmap for effective implementation.[195]

This research contributes to the knowledge on the complex interaction between patient, procedure and context. It also proposes actions to improve the care to those in need. Back to Ortega y Gasset, those actions may be a powerful tool to optimize the circumstances of SSI in colorectal surgery and, with it, to save ourselves.[181]

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ANNEXES

Annex I – Colorectal surgery codes used in this research

CID-9 codes:

Colon				Rectum
17.31	45.41	45.83	46.22	48.25
17.32	45.49	45.90	46.23	48.35
17.33	45.50	45.91	46.24	48.40
17.34	45.51	45.92	46.31	48.42
17.35	45.52	45.93	46.39	48.43
17.36	45.61	45.94	46.41	48.49
17.39	45.62	45.95	46.43	48.50
45.00	45.63	46.01	46.51	48.51
45.01	45.71	46.02	46.52	48.52
45.02	45.72	46.03	46.71	48.59
45.03	45.73	46.04	46.72	48.61
45.15	45.74	46.10	46.73	48.62
45.26	45.75	46.11	46.74	48.63
45.31	45.76	46.13	46.75	48.64
45.32	45.79	46.14	46.76	48.65
45.33	45.81	46.20	46.93	48.69
45.34	45.82	46.21	46.94	48.74

CID-10 codes

Colon						Rectum	
0D180KN	0D1A4ZH	0D1H4J4	0D1M07M	0D7N4DZ	0DBN0ZX	0D1807P	0D1N0ZP
0D1607L	0D1A4ZK	0D1H4JH	0D1M07N	0D7N4ZZ	0DBN0ZZ	0D1807Q	0D1N47P
0D160JL	0D1A4ZL	0D1H4JK	0D1M0J4	0D9C00Z	0DBN4ZX	0D180JP	0D1N4JP
0D160KL	0D1A4ZM	0D1H4JL	0D1M0JM	0D9C0ZX	0DBN4ZZ	0D180JQ	0D1N4KP
0D160ZL	0D1A4ZN	0D1H4JM	0D1M0JN	0D9C0ZZ	0DBNFZZ	0D180KP	0D1N4ZP
0D1647L	0D1B07H	0D1H4JN	0D1M0K4	0D9C40Z	0DCC0ZZ	0D180KQ	0D9P00Z
0D164JL	0D1B07K	0D1H4K4	0D1M0KM	0D9C4ZX	0DCC4ZZ	0D180ZP	0D9P0ZX
0D164KL	0D1B07L	0D1H4KH	0D1M0KN	0D9C4ZZ	0DCE0ZZ	0D180ZQ	0D9P0ZZ
0D164ZL	0D1B07M	0D1H4KK	0D1M0Z4	0D9E00Z	0DCE4ZZ	0D1847P	0D9P40Z
0D1807H	0D1B07N	0D1H4KL	0D1M0ZM	0D9E0ZX	0DCF0ZZ	0D1847Q	0D9P4ZX
0D1807K	0D1B0JH	0D1H4KM	0D1M0ZN	0D9E0ZZ	0DCF4ZZ	0D184JP	0D9P4ZZ
0D1807L	0D1B0JK	0D1H4KN	0D1M474	0D9E40Z	0DCG0ZZ	0D184JQ	0DBP0ZX
0D1807M	0D1B0JL	0D1H4Z4	0D1M47M	0D9E4ZX	0DCG4ZZ	0D184KP	0DBP0ZZ
0D1807N	0D1B0JM	0D1H4ZH	0D1M47N	0D9E4ZZ	0DCH0ZZ	0D184KQ	0DBP4ZX
0D180JH	0D1B0JN	0D1H4ZK	0D1M4J4	0D9F00Z	0DCH4ZZ	0D184ZP	0DBP4ZZ
0D180JK	0D1B0KH	0D1H4ZL	0D1M4JM	0D9F0ZX	0DCK0ZZ	0D184ZQ	0DDP4ZX
0D180JL	0D1B0KK	0D1H4ZM	0D1M4JN	0D9F0ZZ	0DCK4ZZ	0D1A07P	0DQP0ZZ
0D180JM	0D1B0KL	0D1H4ZN	0D1M4K4	0D9F40Z	0DCL0ZZ	0D1A07Q	0DQP4ZZ
0D180JN	0D1B0KM	0D1K074	0D1M4KM	0D9F4ZX	0DCL4ZZ	0D1A0JP	0DSP0ZZ
0D180KH	0D1B0KN	0D1K07K	0D1M4KN	0D9F4ZZ	0DCM0ZZ	0D1A0JQ	0DSP4ZZ
0D180KK	0D1B0ZH	0D1K07L	0D1M4Z4	0D9G00Z	0DCM4ZZ	0D1A0KP	0DSQ0ZZ
0D180KL	0D1B0ZK	0D1K07M	0D1M4ZM	0D9G0ZX	0DCN0ZZ	0D1A0KQ	0DSQ4ZZ

0D180KM	0D1B0ZL	0D1K07N	0D1M4ZN	0D9G0ZZ	0DCN4ZZ	0D1A0ZP	0DTP0ZZ
0D180ZH	0D1B0ZM	0D1K0J4	0D1N074	0D9G40Z	0DME0ZZ	0D1A0ZQ	0DTP4ZZ
0D180ZK	0D1B0ZN	0D1K0JK	0D1N07N	0D9G4ZX	0DME4ZZ	0D1A47P	0DTQ0ZZ
0D180ZL	0D1B47H	0D1K0JL	0D1N0J4	0D9G4ZZ	0DMF0ZZ	0D1A47Q	0DTQ4ZZ
0D180ZM	0D1B47K	0D1K0JM	0D1N0JN	0D9H00Z	0DMF4ZZ	0D1A4JP	0DTR0ZZ
0D180ZN	0D1B47L	0D1K0JN	0D1N0K4	0D9H0ZX	0DMG0ZZ	0D1A4JQ	0DTR4ZZ
0D1847H	0D1B47M	0D1K0K4	0D1N0KN	0D9H0ZZ	0DMG4ZZ	0D1A4KP	
0D1847K	0D1B47N	0D1K0KK	0D1N0Z4	0D9H40Z	0DMH0ZZ	0D1A4KQ	
0D1847L	0D1B4JH	0D1K0KL	0D1N0ZN	0D9H4ZX	0DMH4ZZ	0D1A4ZP	
0D1847M	0D1B4JK	0D1K0KM	0D1N474	0D9H4ZZ	0DMK0ZZ	0D1A4ZQ	
0D1847N	0D1B4JL	0D1K0KN	0D1N47N	0D9K00Z	0DMK4ZZ	0D1B07P	
0D184JH	0D1B4JM	0D1K0Z4	0D1N4J4	0D9K0ZX	0DML0ZZ	0D1B07Q	
0D184JK	0D1B4JN	0D1K0ZK	0D1N4JN	0D9K0ZZ	0DML4ZZ	0D1B0JP	
0D184JL	0D1B4KH	0D1K0ZL	0D1N4K4	0D9K40Z	0DMM0ZZ	0D1B0JQ	
0D184JM	0D1B4KK	0D1K0ZM	0D1N4KN	0D9K4ZX	0DMM4ZZ	0D1B0KP	
0D184JN	0D1B4KL	0D1K0ZN	0D1N4Z4	0D9K4ZZ	0DMN0ZZ	0D1B0KQ	
0D184KH	0D1B4KM	0D1K474	0D1N4ZN	0D9L00Z	0DMN4ZZ	0D1B0ZP	
0D184KK	0D1B4KN	0D1K47K	0D5C0ZZ	0D9L0ZX	0DQC0ZZ	0D1B0ZQ	
0D184KL	0D1B4ZH	0D1K47L	0D5C4ZZ	0D9L0ZZ	0DQC4ZZ	0D1B47P	
0D184KM	0D1B4ZK	0D1K47M	0D5E0ZZ	0D9L40Z	0DQE0ZZ	0D1B47Q	
0D184KN	0D1B4ZL	0D1K47N	0D5E4ZZ	0D9L4ZX	0DQE4ZZ	0D1B4JP	
0D184ZH	0D1B4ZM	0D1K4J4	0D5F0ZZ	0D9L4ZZ	0DQF0ZZ	0D1B4JQ	
0D184ZK	0D1B4ZN	0D1K4JK	0D5F4ZZ	0D9M00Z	0DQF4ZZ	0D1B4KP	
0D184ZL	0D1E074	0D1K4JL	0D5G0ZZ	0D9M0ZX	0DQG0ZZ	0D1B4KQ	
0D184ZM	0D1E07E	0D1K4JM	0D5G4ZZ	0D9M0ZZ	0DQG4ZZ	0D1B4ZP	
0D184ZN	0D1E0J4	0D1K4JN	0D5H0ZZ	0D9M40Z	0DQH0ZZ	0D1B4ZQ	
0D1907L	0D1E0JE	0D1K4K4	0D5H4ZZ	0D9M4ZX	0DQH4ZZ	0D1E07P	
0D190JL	0D1E0K4	0D1K4KK	0D5K0ZZ	0D9M4ZZ	0DQK0ZZ	0D1E0JP	
0D190KL	0D1E0KE	0D1K4KL	0D5K4ZZ	0D9N00Z	0DQK4ZZ	0D1E0KP	
0D190ZL	0D1E0Z4	0D1K4KM	0D5L0ZZ	0D9N0ZX	0DQL0ZZ	0D1E0ZP	
0D1947L	0D1E0ZE	0D1K4KN	0D5L4ZZ	0D9N0ZZ	0DQL4ZZ	0D1E47P	
0D194JL	0D1E474	0D1K4Z4	0D5M0ZZ	0D9N40Z	0DQM0ZZ	0D1E4JP	
0D194KL	0D1E47E	0D1K4ZK	0D5M4ZZ	0D9N4ZX	0DQM4ZZ	0D1E4KP	
0D194ZL	0D1E4J4	0D1K4ZL	0D5N0ZZ	0D9N4ZZ	0DQN0ZZ	0D1E4ZP	
0D1A07H	0D1E4JE	0D1K4ZM	0D5N4ZZ	0DBC0ZX	0DQN4ZZ	0D1H07P	
0D1A07K	0D1E4K4	0D1K4ZN	0D7C0DZ	0DBC0ZZ	0DSE0ZZ	0D1H0JP	
0D1A07L	0D1E4KE	0D1L074	0D7C0ZZ	0DBC4ZX	0DSE4ZZ	0D1H0KP	
0D1A07M	0D1E4Z4	0D1L07L	0D7C4DZ	0DBC4ZZ	0DSH0ZZ	0D1H0ZP	
0D1A07N	0D1E4ZE	0D1L07M	0D7C4ZZ	0DBE0ZX	0DSH4ZZ	0D1H47P	
0D1A0JH	0D1H074	0D1L07N	0D7E0DZ	0DBE0ZZ	0DSK0ZZ	0D1H4JP	
0D1A0JK	0D1H07H	0D1L0J4	0D7E0ZZ	0DBE4ZX	0DSK4ZZ	0D1H4KP	
0D1A0JL	0D1H07K	0D1L0JL	0D7E4DZ	0DBE4ZZ	0DSL0ZZ	0D1H4ZP	
0D1A0JM	0D1H07L	0D1L0JM	0D7E4ZZ	0DBF0ZX	0DSL4ZZ	0D1K07P	
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0D1A0KH	0D1H07N	0D1L0K4	0D7F0ZZ	0DBF4ZX	0DSM4ZZ	0D1K0KP	
0D1A0KK	0D1H0J4	0D1L0KL	0D7F4DZ	0DBF4ZZ	0DSN0ZZ	0D1K0ZP	
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0D1A0KM	0D1H0JK	0D1L0KN	0D7G0DZ	0DBG0ZZ	0DTC0ZZ	0D1K4JP	
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0D1A0ZN	0D1H0KK	0D1L47L	0D7H4DZ	0DBH4ZX	0DTG0ZZ	0D1L0ZP
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0D1A47L	0D1H0KN	0D1L4J4	0D7K0ZZ	0DBK0ZZ	0DTH0ZZ	0D1L4KP
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0D1A47N	0D1H0ZH	0D1L4JM	0D7K4ZZ	0DBK4ZZ	0DTK0ZZ	0D1M07P
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0D1A4KN	0D1H47N	0D1M074	0D7N0ZZ	0DBMFZZ	0DTNFZZ	0D1N0KP