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SPATIAL-TEMPORAL ANALYSIS OF NOSOCOMIAL INFECTIONS USING GEOGRAPHICAL INFORMATION SYSTEMS.

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To my family

Perseverance is not a long race; it is many short races one after the other – Walter Elliot

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List of publications

In compliance with Article 8 of the Decree-Law 388/70, this thesis was based on the following main publications:

1. Teixeira H, Magalhães A, Ramalho A, Pina M de F, Gonçalves H. Indoor Environments and Geographical Information Systems: A Systematic Literature Review. *SAGE Open* **2021**, 11(4) | (2020 Impact Factor = 1.356 / Social Sciences, Interdisciplinary, Q3 - 72/109) https://doi.org/10.1177/21582440211050379

2. Teixeira, H.; Freitas, A.; Sarmento, A.; Nossa, P.; Gonçalves, H.; Pina, M.d.F. Spatial Patterns in Hospital-Acquired Infections in Portugal (2014–2017). *International Journal of Environmental Research and Public Health* **2021**, *18(9)*, 4703 | (2020 Impact Factor = 3.390 / Public, Environmental & Occupational Health, Q1 - 41/176) https://doi.org/10.3390/ijerph18094703

3. Teixeira, H.; Norton, P.; Gonçalves, H.; Pina, M.d.F.; Development of a 3D GIS-based model of a Portuguese Hospital indoor space to support spatiotemporal analysis of events: application to COVID-19 cases among healthcare workers (Submitted).

4. Teixeira, H.; Sarmento, A.; Pina, M.d.F.; Gonçalves, H. Spatiotemporal analysis of Hospital-Acquired Infections in São João University Hospital (Portugal) (Under review).

Abbreviations

ASHR - Age Standardized Hospitalization Rates

CAOP - Portugal's Official Administrative Map

CDC - Centers for Disease Control and Prevention

DGS - Directorate-General of Health

EU - European Union

GIS – Geographical Information System

HAI - Hospital-acquired infection

ICU - Intensive Care Units

IoT - Internet of Things

IT - Information Technologies

MeSH - Medical Subject Headings

MRSA - Methicillin Resistant Staphylococcus Aureus

ML - Machine learning

OECD - Organization for Economic Co-operation and Development

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

SSI - Surgical Site Infection

WHO - World Health Organization

Abstract

The health care sector is one of the largest industries in Europe. Approximately 10% of European Union workers are employed in the health sector with a high proportion employed in hospitals. Health care is one of the most important social and economic components of modern society, and the effective use of Information Technologies (IT) in this industry is important to its success. The Organization for Economic Co-operation and Development (OECD) supports the widespread use of information and communication technologies in health care contexts since they can contribute to the reduction of operational costs of clinical departments through improvement of their efficiency in task performing and data processing, which will in turn result in increased levels of productivity. From a historical perspective, hospital-acquired infections (HAIs) represent the most frequent adverse events during healthcare delivery, which may result in prolonged hospital stays, long-term disability, increased resistance to antimicrobials or even death. As life expectancy increases, technology becomes more invasive, and with more patients on immunosuppressive therapy, the risk of infection also increases. The economic cost of this problem is immense, and the financial losses can be estimated conservatively at about 6 billion euros/year in Europe (direct costs) for 16 million days of inpatient extra time.

The purpose of this thesis is to explore the use of Geographical Information Systems (GIS) to analyze the patterns of HAIs on two scales of research: one global, with the analysis in Portugal; and one local with the creation and construction of an indoor GIS-based model to examine the cases within the São João University Hospital. Once built, the GIS will not be limited to the study of nosocomial infections but will be made accessible to the hospital for use in other epidemiological research, the analysis of workplace accidents, and the support of management and administrative decisions.

We started by understanding how to represent the indoor space of a hospital in a GIS-based model. We decided to analyze the evidence related to this thematic. To this end, we searched three scientific libraries, following the PRISMA statement guidelines. All phases were analyzed independently by two reviewers and agreement between them was calculated through the Kappa statistic. Subsequently, the included studies

were categorized into five groups: "indoor management", "indoor geospatial analysis", "indoor positioning", "indoor data acquisition" and "indoor spatial data models". The results show that research on the use of GIS in indoor spaces is still emerging, despite its huge potential to help data producers, researchers, or policymakers improve their work by providing scientific evidence for better decision support.

Afterwards, we described and analyzed the spatial patterns of Age Standardized Hospitalization Rates (ASHRs) of HAIs from 2014 to 2017 in Portugal, using data from the Portuguese Discharge Hospital Register. This study allowed us to understand that the incidence of HAI is not randomly distributed in the space (with the most representative adverse event recorded being nosocomial pneumonia), contributing to alerting the HAI control committees and warning analysts in surveillance systems within the clinical context, leading to well-informed decisions.

Later, to make available the study at a local scale of analysis a spatial database model has been developed (in a GIS environment) for the São João University Hospital. This approach presented the opportunity to explore the dynamics, patterns and phenomena that occur within walls. Besides, it demonstrates the potential to enable the administration of the hospital with a compelling tool, allowing it to develop a wide-ranging plan to assess resources allocation, or monitor and plan interventional measures.

Finally, data related to HAIs (the nosocomial pneumonia episodes) from the São João University Hospital were georeferenced using the GIS-based model, presenting practical examples. The results show that the identification of the spatial clusters of HAIs, may contribute in a decisive way to improving the surveillance system of nosocomial infection, and orienting the appropriate policies for infection control.

Resumo

O setor de saúde apresenta-se como uma das maiores indústrias da Europa, uma vez que aproximadamente 10% dos trabalhadores da União Europeia se encontram empregados aqui. Os cuidados de saúde são um dos pilares sociais e económicos mais importantes da sociedade moderna e o uso eficaz das Tecnologias da Informação é absolutamente crucial para o seu sucesso. A Organização para Cooperação e Desenvolvimento Económico (OCDE) sugere o uso generalizado deste tipo de tecnologias em contextos de saúde, uma vez que podem contribuir para a redução dos custos operacionais dos departamentos clínicos através da melhoria da sua eficiência na execução de tarefas e processamento de dados, o que, por sua vez, resultará em maiores níveis de produtividade.

Do ponto de vista histórico, as infeções hospitalares representam os eventos adversos mais frequentes durante a prestação de cuidados de saúde, o que pode resultar em hospitalizações prolongadas, incapacidade permanente, aumento da resistência aos antimicrobianos ou até morte. Conforme aumenta a esperança média de vida, a tecnologia se torna mais invasiva e, com mais pacientes em terapia imunossupressora, o risco de infeção também aumenta. O custo económico deste problema é imenso, e as perdas financeiras podem ser estimadas conservadoramente em cerca de 6 bilhões de euros / ano na Europa (custos diretos) por 16 milhões de dias de tempo adicional de internamento.

O objetivo desta tese é explorar a utilização de Sistemas de Informação Geográfica (SIG) para analisar os padrões de infeções hospitalares em duas escalas de investigação: uma global, com a análise em Portugal; e um local com a criação e construção de um modelo espacial baseado em SIG para examinar os casos que ocorrem no Hospital Universitário de São João. Uma vez construído, o SIG não se limitará ao estudo das infeções nosocomiais, mas será disponibilizado ao hospital para uso em outras pesquisas epidemiológicas, análise de acidentes de trabalho e apoio às decisões de gestão e/ou administrativas.

Inicialmente, para entender como representar o espaço interno de um hospital num modelo SIG, decidimos analisar a evidência científica relacionadas com a temática.

Para este fim, utilizamos três bibliotecas científicas, seguindo as diretrizes do PRISMA. Todas as fases foram analisadas de forma independente por dois revisores e a concordância entre eles foi calculada por meio da estatística *Kappa*. Posteriormente, os estudos incluídos foram categorizados em cinco grupos: "gestão interna", "análise espacial interna", "posicionamento interno", "aquisição de dados" e "modelos de dados espaciais internos". Os resultados mostraram que as pesquisas sobre o uso do SIG em espaços internos ainda são emergentes, apesar de seu enorme potencial para ajudar produtores de dados, pesquisadores ou formuladores de políticas a aprimorar seus trabalhos, fornecendo evidências científicas para melhor suporte à decisão.

De seguida, pretendemos descrever e analisar os padrões espaciais das taxas de hospitalização padronizadas por idade das infeções hospitalares ocorridas entre 2014 e 2017 em Portugal, utilizando dados das bases de registo de alta hospitalar. Este estudo permitiu compreender que a incidência deste tipo de infeção não está distribuída aleatoriamente no espaço (sendo o evento adverso mais representativo registado a pneumonia nosocomial), contribuindo para alertar as comissões de controlo de infeção, bem como os analistas dos sistemas de vigilância em contexto clínico.

Com o propósito de possibilitar o estudo numa escala de análise local, foi desenvolvido um modelo de dados espacial (em ambiente SIG), para o Hospital Universitário de São João. Esta abordagem apresentou-se como a oportunidade de explorar as dinâmicas, padrões e fenómenos que ocorrem dentro do edifício. Além disso, demonstra o potencial para habilitar a administração hospitalar com uma ferramenta capaz de permitir o desenvolvimento de um plano abrangente para avaliar a alocação de recursos, ou monitorizar medidas de intervenção. Por fim, os dados relativos às infeções (episódios de pneumonia nosocomial) ocorridos no Hospital Universitário de São João foram georreferenciados utilizando o modelo desenvolvido, e foram expostos exemplos práticos. Os resultados mostram que a identificação dos clusters espaciais, pode contribuir de forma decisiva para melhorar o sistema de vigilância da infeção hospitalar, e orientar as políticas adequadas para o seu controlo.

1. Introduction

Outline

This chapter presents the thesis background, the key words, and all relevant studies or theories. This review chapter allows for the identification of the main research gaps in this thesis topic, thus justifying the main and specific objectives.

Background

Hospital-acquired infections

Hospitals and health units are environments where both infected people and people at high risk of contracting infection assemble, representing a potential source of infection for other patients and health professionals [1]. However, some places within the hospital present a higher susceptibility to infection, such as newborn wards, burns wards, and intensive care, due to the larger concentration of patients in those places and their health condition [2].

A nosocomial infection, also known as hospital-acquired infection (HAI), is generally described as an infection acquired by a patient while receiving health care [3]. These infections normally develop throughout hospitalization and appear no earlier than 48 hours after admission. In the case of Surgical Site Infections (SSI), they can appear up to 30 days after getting health treatment [4]. Even though HAIs are more commonly identified in hospitalized inpatients, they also include infections discovered after discharge or occupational infections among health professionals [5].

Patients are exposed to a wide range of viruses, bacteria, and fungal pathogens throughout their hospitalization, which may result in the development of clinical illness [6]. This contact does not always result in infection since other factors impact the form and frequency of HAIs, such as the patient's susceptibility, comorbidities, age, and immunological state, among other factors [7]. The most common forms of nosocomial infections include urinary tract infections [8-10], bloodstream infections related to the central venous catheter [11-13], hospital-acquired pneumonia [14-16], intestinal infections by *Clostridium difficile* [17,18], and SSI [19,20].

HAIs are strongly associated with increased antibiotic resistance, resulting in longer hospital admissions, higher morbidity and mortality rates, and substantial costs for health systems and society [21-23]. Even though they are significant, the real impact of HAIs is unknown due to the complexity of the numerous surveillance systems and the lack of uniform diagnosis criteria across countries [24].

According to several studies [25-27], the HAI prevalence in developing countries fluctuates from 5.7% to 19.1% of all admissions, whereas in high-income countries, it varies between 5.7% and 7.5%. However, in some of these countries, the prevalence has been described to be as high as 12.0% [28].

In Portugal, nosocomial infections have an increasing importance, presenting the highest proportion of Methicillin Resistant Staphylococcus Aureus (MRSA) at European level [29]. A survey related to the prevention program for infection control covering the European countries in 2017 reported a prevalence of HAIs in Portugal of 7.8% [30,31].

On the other hand, the literature suggests that there is a lack of epidemiological data on HAIs in individual Portuguese Intensive Care Units (ICUs), making it difficult to compare data and provide a real understanding of any spatial differences in prevalence that may be associated with the area of influence of ICUs, according to the national referral system [32].

According to statistics from the Centers for Disease Control and Prevention (CDC), HAIs are directly or indirectly responsible for more than 98,000 deaths in the United States each year [3,33], while some studies reported 148,000 deaths yearly in Europe [21,34].

This represents a significant burden of infectious diseases in Europe, greater than the burden of other infections such as tuberculosis or influenza. However, regardless of this, hospitals take HAIs extremely seriously. Following the WHO recommendations, to reduce the effect of these infections, they have applied infection tracking and surveillance systems as well as consistent prevention measures, increasing the responsibility of all health actors [35].

Information technologies in healthcare

Representing one of the most important components of modern society, where approximately 10% of European Union (EU) workers are employed [36], healthcare providers worldwide are confronted with a single challenge: the requirement to improve patient outcomes while reducing costs. The digital transformation in healthcare and its utilization are now a reality and present as a fundamental option to increase the success and efficacy of its management [37].

The EU and the OECD are increasingly encouraging the adoption of Information Technologies (IT) in the healthcare sector, such as the Internet of Things (IoT), advanced analytics, machine learning (ML), artificial intelligence or GIS [38,39]. These ITs are being recognized as a key component in improving the levels of productivity.

Geographic information systems in epidemiology

A Geographical Information System can be described as a decision support system framework which is conceived to acquire, manage, explore, analyze, and visualize spatial and alphanumeric data [40].

Nowadays, geospatial data is familiar to practically everyone, offering considerable capabilities to assess the multidisciplinary of GIS and its multiparadigmatic qualities [41]. As an important technology tool, GIS has been used in epidemiology and health sciences research, mainly to produce disease mapping, geographical analysis of diseases, as well as associations between environmental factors, cluster analysis or rate smoothing, and spatial model exploration [42-44].

This type of system can help revealing patterns, trends and relationships that would be harder to discover if it were used other methods [45], triggering an understanding of how humans interact with their environment, promoting the creation of health prevention policies and measures [46].

Geographical information systems and indoor spaces

Considering its remarkable growth in the recent past, knowledge of spatial information has not changed throughout the years, with different GIS techniques being used and applied to geographical elements (such as neighborhoods, cities, and regions) of an external territory [47]. The georeferencing method is valuable in studies related to the spatialization of data in a geographic segmentation of a particular area. Data is referenced to a predefined coordinate system, which allows relationships to be built across various maps and databases [48]. However, at this point, it is meaningless to confine the term "place" to an outer area considering that 80% of people's daily lives are spent within buildings [49,50].

The basic concepts, models, and standards must be redefined to meet the indoor spatial application requests since findings suggest how this approach may be used to georeference and evaluate disease transmission or other health occurrences within physical structures related to healthcare [51-53]. Space characterization is an important effort to study and comprehend its complex relationships with more evidence of the impacts. In addition, the space must be illustrated and appropriately depicted, along with all associated information, and the topology concept must be integrated [54]. The raw data connected to these spaces must present a viable gathering method.

Due to the variety of complex infrastructures, such as hospitals or industrial centers, with a large daily traffic volume, an opportunity is presented here with the development of spatial database models [55].

Keywords

The thesis keyword list is presented in table 1.

Keyword	MeSH Tree Number	MeSH ID
Nosocomial Infections	C01.539.248, C23.550.291.875.500	D003428
Epidemiology	H02.403.720.500	D004813
Geographic Information Systems	L01.313.500.750.300.314, L01.470.750.750.462	D040362
Hospitals	N02.278.421	D006761
Spatio-temporal analysis	E05.318.740.933.500, N05.715.360.750.746.500, N06.850.520.830.933.500	D062211
Portugal	Z01.542.727	D011174

Table 1. Study keywords.

Study area

Figure 1 depicts the two primary levels of analysis included in this thesis: global (the mainland of Portugal) and local (São João University Hospital).

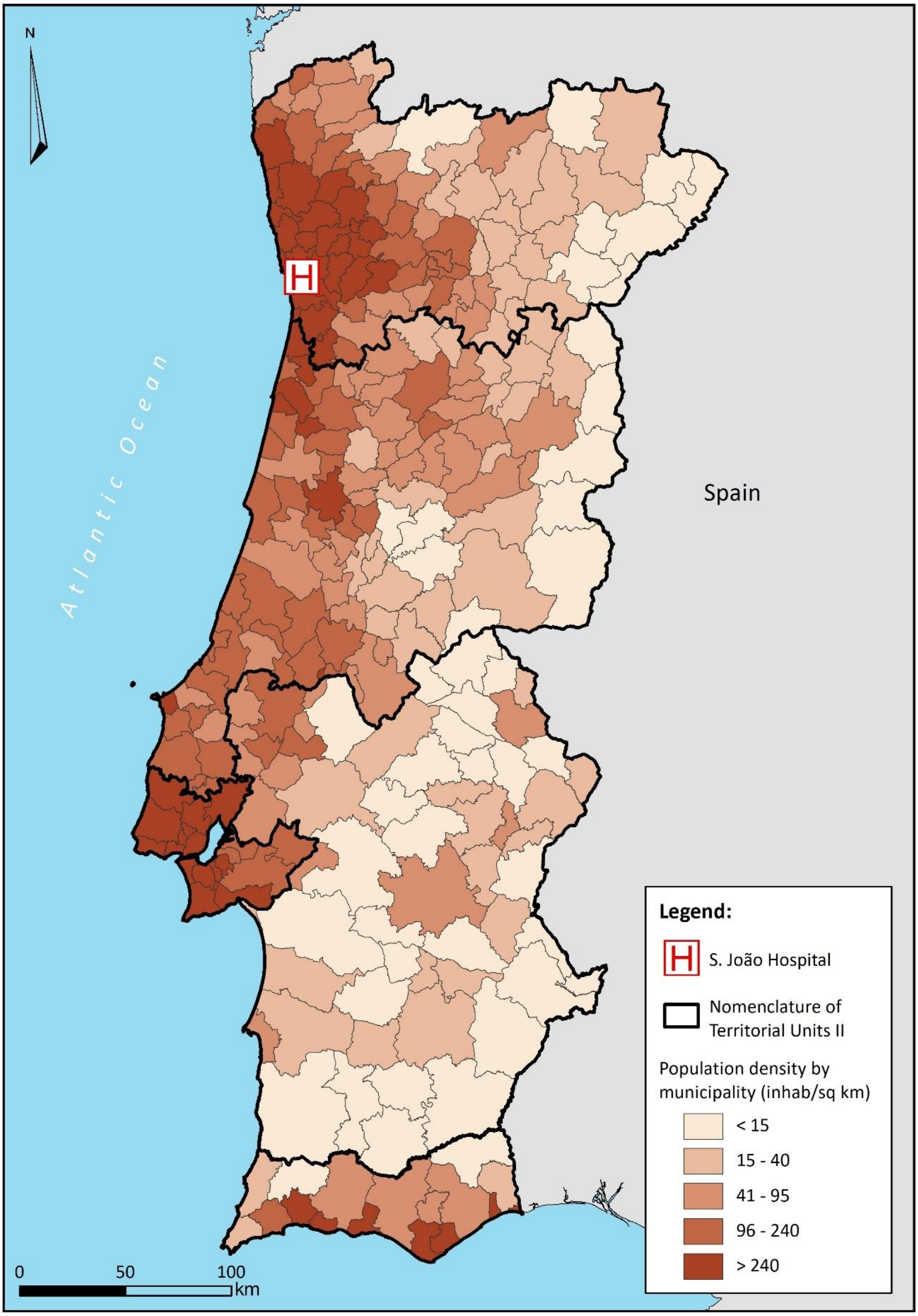


Figure 1. Study area framework and population density by municipality.

Portugal, with a total area of 89,102 km^2, is located on the Iberian Peninsula in southern Europe. In 2020, the mainland was forecasted to have 9,802,128 inhabitants (men accounting for 47.0% of the total), dispersed unevenly throughout five regions and 278 municipalities (with a population varying from 1,623 to 509,614 inhabitants). In 2020, the North, Center, and Lisbon Regions accounted for 88.4% of the Portuguese population, while Alentejo (7.1%) and Algarve (4.5%) accounted for significantly less.

With a high GINI index value (34.8 in 2020), Portugal is a developed country with one of the highest levels of wealth disparity in the Eurozone [56].

The national health system is universal, providing full coverage to all inhabitants (Appendix 1), regardless of socioeconomic, legal, or job status. It coexists with three systems: the public health service, health subsystems for specialized professions, and the private health sector [57]. Besides that, the hospital network, under the responsibility of the Portuguese Directorate-General of Health (DGS), must comply with the epidemiological surveillance plans for the prevention of nosocomial infections [30].

The São João University Hospital, originally inaugurated on June 24th, 1959, is based in the northwest of Portugal, particularly in the Porto municipality, and is the country's second main hospital. This hospital provides support to the residents of the municipalities of Porto, Maia, and Valongo (roughly 450,000 inhabitants) and serves as a reference for the entire northern region, in cutting-edge fields.

According to Meyers [58], we may classify this hospital as a complex structure because of the large number of people who work there (about 7000) and due to its official capacity of 1200 beds and 45 cots dispersed among the numerous medical and surgical services. Furthermore, 15,000 individuals each day circulate throughout the hospital, including health professionals, technicians, suppliers, patients, or visitors.

This level of detail (a building as a study area) creates a significant barrier for researchers. People and commodities interact more in such a limited location than in some cities across the country. Appropriate control of such structures is a crucial component of dealing with dynamic situations, and it promotes proper surveillance.

Aims

The main objective of this thesis is to explore the use of GIS to analyze the patterns of HAIs on two scales of research: one global, with the analysis in Portugal; and one local, with the creation and construction of an indoor GIS-based model to examine the cases within the São João University Hospital, from 2014 to 2017. Specific objectives are:

Chapter 1: Synthesis of the evidence related to GIS applied to indoor spaces.

A systematic review of the literature was carried out to identify and summarize information related to GIS utilization for modeling the indoor space or to analyze and comprehend the spatial phenomena that are occurring in this type of environment.

Chapter 2: Descriptive analysis of HAIs in Portugal.

To characterize and understand the spatial patterns of the age-standardized hospitalization rates (ASHRs) of HAIs and to describe and explore the existence of spatial clusters in mainland Portugal from 1 January 2014 to 31 December 2017, using secondary data.

Chapter 3: Development of a 3D GIS-based model to represent the São João University Hospital.

A GIS-based model was developed for the hospital building, where it was georeferenced the spatial and alphanumeric information related to each space, stored, and incorporated as graphic elements into the database. As a case study, we performed a scan statistic to detect COVID-19 emerging clusters (among healthcare workers) across the hospital services. This model will also be used for comprehension and analysis of health events and as a starting point for the 4th study, which will provide literature support for further work and decision support.

Chapter 4: Analysis of geographical patterns of nosocomial infection cases at São João University Hospital using the map obtained in Chapter 3 to identify high-risk areas.

Analyze spatiotemporal clusters of nosocomial infection (nosocomial pneumonia) cases based on the 3D GIS-based model obtained in Chapter 3 to identify high-risk areas, allowing for a better understanding of their dynamics. Consequently, this can improve the infection control surveillance system as well as the wellbeing of patients and health staff and reduce costs.

Outline

The remaining thesis is organized into five chapters that describe the work performed. The next four chapters correspond to the studies developed, where the first two are already published, the third is submitted, and the fourth is currently under review by the authors. The last chapter presents the general discussion and conclusions.

Methods and Materials

At this stage, we will simply mention the types of data and software that served as the basis for the elaboration of this thesis. The detailed methods will be revealed and discussed in each chapter. Regarding the types of data used in this work, we looked primarily at scientific evidence, digital data (including both spatial and alphanumeric information), and analogic data, as we can check in figure 2.

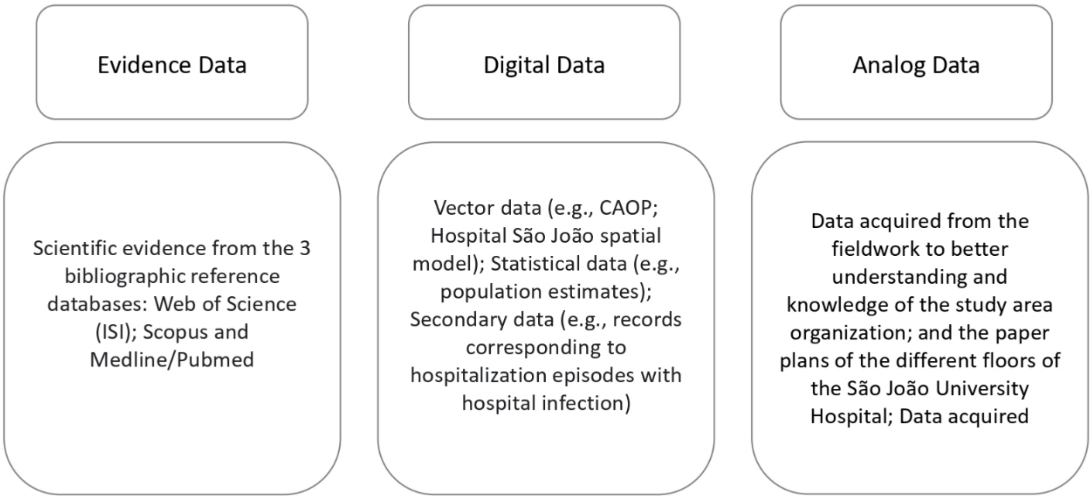
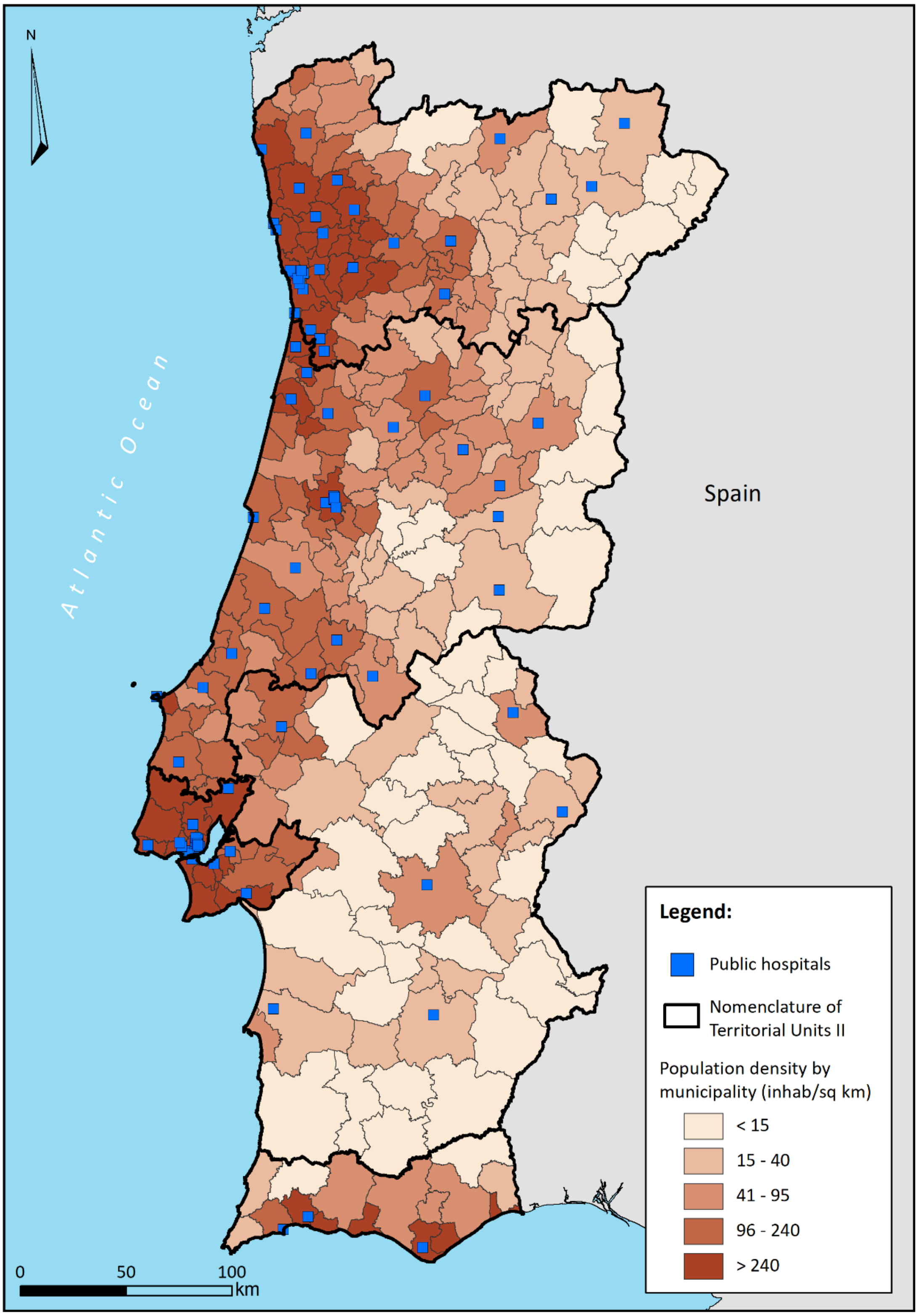


Figure 2. The different types of data that were used in the thesis.

For the elaboration and production of thematic cartography, data analysis and calculation, as well as cluster identification and patterns studies, some specific software packages were used, such as ArcGIS 10.5.1 (ESRI, Redlands, CA, USA), GeoDa 1.16.0.12 (University of Chicago, Chicago, IL, USA); SPSS (IBM, Armonk, New York, USA), and SaTScan 9.7 (Harvard Medical School, Boston, Massachusetts, USA).

Supplementary material



Appendix 1. National health system network location.

2. Indoor Environments and Geographical Information Systems

Teixeira H, Magalhães A, Ramalho A, Pina M de F, Gonçalves H. Indoor Environments and Geographical Information Systems: A Systematic Literature Review. *SAGE Open* **2021**, 11(4) | (2020 Impact Factor = 1.356 / Social Sciences, Interdisciplinary, Q3 - 72/109) https://doi.org/10.1177/21582440211050379

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Indoor Environments and Geographical Information Systems: A Systematic Literature Review

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Abstract

The increasing dissemination of geographic information systems (GIS) in recent years has broadened the availability and use of geospatial tools, mostly to analyze the spatial data of different territories. A territory can be viewed at different analysis scales, and some buildings are as complex as small cities, presenting the opportunity to use GIS to study the dynamics, patterns, and phenomena within a building. This study presents a systematic literature review of the relevant evidence focused on the utilization of GIS in indoor spaces. To this end, we searched in three scientific libraries following the PRISMA statement guidelines. All phases were analyzed independently by two of the authors and agreement between them calculated through the Kappa statistic. In total, 50 studies were included. A qualitative synthesis was performed, considering the assessment of data and heterogeneity of methodologies within the included articles. Subsequently, the studies were categorized into five groups: indoor management, indoor geospatial analysis, indoor positioning, indoor data acquisition, and indoor spatial data models. The results demonstrate that research on the use of GIS in indoor spaces is still emerging, despite its great potential to help and GIS users, data producers, researchers, or policymakers to improve their work, providing scientific evidence for decision support.

Keywords

systematic literature review, indoor spaces, geographical information systems

Introduction

A Geographical Information System (GIS) can be characterized as a decision support system framework which is designed to acquire, organize, manage, analyze, and visualize spatial and alphanumeric data (Duckham et al., 2003; Goodchild, 2009b, 2010). The first use of the term GIS was credited to Roger Tomlinson at the beginning of the 1960s, developing the ideas and knowledge that led to the tools used at present (Wing & Bettinger, 2003). In the late 1980s, specialists in a wide variety of scientific areas started to use GIS at a larger scale, due to the better accessibility of spatial information (Karimi & Akinci, 2009; Waters, 2018), and since maps became into powerful analytical devices, instead of being merely descriptive (Maliene et al., 2011; Teixeira & Pina, 2018). Indeed, they started to produce data and integrate additional analysis or comprehension tasks related to spatio-temporal clusters and statistical analysis into layers on top of a base map (Wieczorek & Delmerico, 2009). Nowadays, geospatial data is familiar to virtually everyone, providing vast potentialities to evaluate the GIS multidisciplinary and multiparadigmatic natures (Blaschke & Merschdorf, 2014).

Usually, other scientific areas than geography or cartography are ever more associated with these tools, such as health, computer vision, computational geometry, remote sensing, robotics, or architecture, for example, proving that there are no boundaries for GIS (Kumar & Shekhar, 2016; Obaidat & Al-kheder, 2006). Health researchers classically use GIS for processing, analyzing, and visualizing spatial data about diseases (Goodchild, 2009a). At the same time computer vision operators focus on the extraction process of highly accurate data, presenting spatial data inventory, introducing numerous analytical procedures, and developing advanced and sophisticated technical systems (Kistemann et al., 2002). Engineering or geometry usually integrate GIS data with a

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Building Information Model (BIM) mainly to analyze the existing spatial relationships, leading to tremendous improvements in efficiency, cost containment, and better decision-making (Kang & Hong, 2015; Zhang et al., 2009). Furthermore, some architects have used those tools to calculate isovists; such software can be applied to save and explore the spatial properties of the graphic structure inherent in space (Llobera, 2003).

Despite its incredible evolution in recent decades, the comprehension related to spatial information has not changed over time, with different GIS approaches, being applied and considering geographical features (such as neighborhoods, cities, and regions) of an external territory (Misra et al., 2020; Teixeira & Pina, 2018). However, at this moment, it is pointless to constrain the term "place" to an external territory since 80% of people's daily lives are being spent within indoor spaces (Deng et al., 2013). According to Santos (1996) definition, a territory is a space where people and processes interact, in which history, dynamics, and phenomena take place, and does not necessarily have to be open-air (Zlatanova et al., 2014). Space characterization is a critical advance, providing a better understanding of it (Mennis & Yoo, 2018), since space, which is being studied today, is no longer restricted to being outdoors but can also be extended to the indoors (Li, 2008).

Indoor space varies from outdoor space in many characteristics. Outer space can be defined as a portion of land which is not enclosed by some environment, while indoor space is typically bounded and constrained by an architectural structure (Goetz, 2012; Li, 2008; Vanclooster et al., 2012; Worboys, 2011; Zlatanova et al., 2020). Besides that, the basic concepts, models, and standards must be redefined to encounter the requirements of indoor spatial applications, without necessarily changing the approaches. An excellent example of a proposed standard spatial data model for indoor space is the IndoorGML since it represents all the properties addressed in the model, such as geometry, symbolic space, network topology, and spatial reference (Afyouni et al., 2012).

Although indoor spaces are already being the target of several research approaches, not many researchers are using GIS, and their theories and data models. The raw data related to these spaces, need to present a viable collection method, since it is needed to show and correctly represent the space, with all associated information and integrating the topology concept (Afyouni et al., 2012; Kang & Li, 2017).

Consequently, reproducing the traditional use of GIS—which is more oriented to analyze the geographical territory—into another type of space, such as buildings, is a challenging task which could be extremely interesting for researchers from a wide variety of study areas, triggering essential developments in some works; due to the variety of complex infrastructures, such as hospitals or industrial centers, for example, with a high circulation of persons per day (Goetz, 2012).

To our knowledge, no review of studies associated to GIS utilization in indoor spaces has been published so far. Given the lately interest and the practical demand for it, in this paper, we aim to carry out a systematic review of the literature to identify and summarize the scientific evidence related to GIS utilization to modeling the indoor space or to analyze and comprehend the spatial phenomena which is occurring in this type of environment.

Our contributions are as follows: (1) we gave an overview of the applied methods for evaluating the GIS utilization in indoor spaces; (2) we identified the included papers and extracted its mains outcomes; (3) we grouped the studies and constructed an index co-occurrence of the included articles keywords; and (4) we discussed the results and highlighted the challenges and opportunities for future works.

Materials and Methods

To provide insights into various aspects of GIS applications to explore the distribution of events and dynamics happening within the indoor spaces, we evaluated and filtered a wide variety of publications based on a systematic literature review process. Even though this review process was initially associated to the medical research area, it has been used lately into another studies areas, such as GIS, for example (Klonner et al., 2016; Steiger et al., 2015; Unrau & Kray, 2019). It was applied to ensure that the selection of the included documents was based on clear eligibility criteria, making it less subject to bias, in order to answer the study specific question, providing methods that can be systematically described and reproducible (Randolph, 2009; Torraco, 2005).

The systematic literature review was performed independently by two of the authors (HT and AM), according to the guidelines presented by the PRISMA Statement (Moher et al., 2009), to carry out a critical and comprehensive qualitative review.

Eligibility Criteria

The included studies satisfied the following criteria:

(1) Original research papers which address the issue of the utilization of GIS in indoor spaces/environments.
(2) Studies analyzing data from indoor spaces of buildings, such as factories, companies, hospitals, malls, and universities.
(3) Studies providing indoor modeling/navigation techniques.
(4) Indoor Positioning studies using wireless sensors or GPS devices.
(5) Data acquisition studies using robots or deployed devices.

Studies were excluded for the following reasons:

(1) Studies using GIS methods applied to external physical territories, such as land-use, river basins, rivers, seismicity, and natural hazards.
(2) Original papers focusing on demographic data and, or the evolution of urban growth using 3D models of cities and landscapes such as CityGML—the interior of the building is the goal of this review analysis, not the set of buildings.
(3) Building Information Model (BIM) papers—despite the two technologies being complementary (GIS and BIM), BIM are often seen as the new generation of CAD tools and the paper focus is the GIS and its application to the indoor spaces.
(4) Non-original articles, non-peer-reviewed books of conference proceedings, dissertations, and studies that are providing duplicated information.

These eligibility criteria were considered in the four phases of the systematic review, which are described in the following subsections.

Identification Phase

The selection of terms to search for the articles is an essential process, since it, determines the number of studies found. For choosing the set of query terms, we used the subsequent strategy. First, we created a list of all reasonable terms, and two rounds of tests with the various terms were carried out. In these rounds, the terms were quantitatively analyzed, and the confirmation of related relevant studies was observed. There were no missings for the selection. Subsequently, the terms were tested in a single expression and "placing and removing" terms from the search expression, to identify whether there are chances of loss of relevant articles. Tests were performed for the composition of the three domains: GIS, indoor and spatiotemporal analysis. As well, the defined criteria were applied to build the query, and it was calibrated using MEDLINE (MeSH), as it offers an extensive dictionary of indexing terms (MeSH terms). The query string was used, with no restriction regarding the language of publication: ("GIS" OR "Geographic* Information System*" OR "Geographic* Information Science*" OR "Global Positioning System*" OR "Geographic* mapping" OR "Mapping" OR "Georeferencing") AND ("building*" OR "edifice*" OR "premise*" OR "facility" OR "indoor" OR "indoor modeling" OR "indoor navigation" OR "inside" OR "hospital*") AND ("Spatio Temporal" OR "Spatio-Temporal" OR "Spatial Temporal" OR "Spatiotemporal" OR "Geoanalysis"), which was applied to SCOPUS, Web of Science, and MEDLINE databases, from inception to April 30th, 2020.

Screening Phase

Eligibility criteria were assessed by reading titles and abstracts resulting from the search expression. In this phase, the authors (HT and AM) independently screened the database, searching all retrieved articles, titles, and abstracts by peer review. The resolution of divergences was solved by the consensus method, and concordance evaluation was measured using the Kappa statistic with corresponding 95% confidence interval (CI). Cohen's kappa coefficient (κ) is a statistic utilized to measure inter-rater reliability (and intra-ratter reliability) for qualitative (categorical) items, in the case of this study, "INCLUDE" or "EXCLUDE." It is a more robust measure than the simple percentage calculation of agreement (Kraemer, 2014). The reproducibility process was evaluated to ensure the transparency of the employed methods, allowing any user to address the same question and identify the same set of studies to reach a similar general conclusion.

Eligibility Phase

After the screening phase, all potential candidate articles were evaluated in full-text format. In this phase, the same authors (HT and AM) scrutinized the entire text of the studies to ensure their eligibility, using the criteria defined for inclusion or exclusion. Furthermore, the authors checked the reference lists of each eligible study, searching for any which were omitted in the database search. Once again, a concordance evaluation measure was evaluated through the Kappa statistic with corresponding 95% CI, and the divergences were solved by consensus. A record of the reasons for exclusion was also drawn up at this stage and then, the final list of included articles for qualitative synthesis was completed.

Data Extraction and Subgroup Criteria

The evaluation findings in the reviewed publications covered an extensive range of GIS usability in indoor spaces with different levels of detail. We classified the included publications into five categories, according to their applied analyses and findings, as described in the following.

(1) Indoor management: studies related with network analysis (including route planning optimization, optimal service areas, or carrying out location-allocation (Kamilaris & Ostermann, 2018)); emergency response analysis studies (allowing quicker and adequate decision-making in both offline and real-time contexts (Chiu & Liu, 2008; Franzese & Liu, 2008)); and facility management or multicriteria decision support studies (Chakhar & Mousseau, 2017; Crossland, 2017; Worboys, 2011).
(2) Indoor geospatial analysis: studies using spatial analysis methods to find patterns or detect anomalies, and

test hypotheses and theories (Goodchild, 2008, 2009a) within indoor environments; and visualization technique studies to comprehend and study several features and dynamics occurring within complex indoor spaces (Yuan, 2008).

(3) Indoor positioning: studies using this type of technique to track an individual's movement (Youssef, 2015); estimating the location of target objects from observation of data collected by a set of sensing devices or sensors (Caron et al., 2008; Kanaan et al., 2008; Yang & Li, 2008); and location-based service studies using geographic data to provide information to users, supporting additional information related to that location such as a point of interest or a street address (Francica, 2008).

(4) Indoor data acquisition: studies about indoor data collection and modeling (including automatic extraction techniques (Heipke, 2008), or information acquirement through Wi-Fi, GPS, automata cellular data, and sensors (Kalogeraki & Soheili, 2008; Rolf, 2001)); and studies using the human–robot interaction approach to enlarge the semantic information related to indoor GIS.

(5) Indoor spatial data models: studies related to the development of spatial data models, enabling the representation of the indoor environments using GIS (Afyouni et al., 2012; Hughes et al., 2014).

After categorization, we analyzed the qualitative data collection approaches used in the different studies and their aims, methodological lines, and main findings.

Results

Search and Study Selection

As a result of our database search, a total of 1,533 articles were returned; of these, 986 were from Scopus, 452 from Web of Science (WOS), and 95 from Pubmed®. After the removal of duplicate articles, 1,036 scientific articles were obtained (Figure 1).

Two of the authors (HT and HM) independently examined all titles and abstracts according to relevance and, after the application of eligibility criteria, most of the studies ($n=958$) were excluded.

An agreement meeting between the two reviewers was held at the end of this phase. Concordance evaluation by Kappa statistic resulted in .562 (95% CI=0.452–0.671), which indicates moderate agreement; thus, the analysis of eligibility for inclusion was carried out, with full-text reading. The second phase started with 78 articles which were wisely scrutinized independently by the two reviewers based on the eligibility criteria. We excluded 49 studies after full-text analysis, for the following reasons: 31% focused on spatio-temporal analyses, but not within indoor spaces; 23% of the articles did not model GIS in an indoor space; 20% used robotics, but not to acquire data related to indoor spaces; 16% of the articles contained exclusion criteria features, such as the evolution of urban growth or the utilization of GIS methods for external territories; and 10% were excluded due to the unavailability of a full text, even after contact with the author.

Twenty-one studies were added after the cross-reference analysis, resulting in a total of 50 articles. In the same way, we performed a concordance evaluation that resulted in Kappa=.894 (95% CI=0.778–1.000). After reading the articles in their full text-format and the consensus meeting between the reviewers, articles were selected for the extraction phase. The included studies characteristics are presented in Table 1, as detailed by authorship, year, country, setting, primary outcome, and subgroup assignment. From the 50 articles included in the qualitative synthesis, 12 were developed in North America, 22 in Europe, and 16 in countries and territories from Asia and Australia. The settings used in several studies ranged from public service buildings ($n=11$), offices ($n=12$), university buildings ($n=17$), or even fictional models ($n=6$) and others ($n=4$).

An association between the terms appearing most commonly within the 50 included studies were made, using the VOS viewer software (Figure 2).

Checking the Figure 2 we realize that the words "GIS," "Three-dimensional," "indoor space" and "spatio-temporal" are those that have a stronger correlation, representing the searched domains that we intend to study and understand in the first place.

Subgroup Analysis

At this point, a descriptive synthesis is given to explain the different study methodologies by subgroup (Figure 3).

Indoor management. This subgroup represents 24% ($n=12$) of the studies identified in this review. A reasonable number of articles emphasized emergency evacuation or rescue, using GIS to plan for this type of situation adequately. Kwan and Lee (2005) employed an integrating solution based on a decision support system for management of emergency response, providing the automatic calculation of shortest routes in a navigable three-dimensional GIS. The work developed by Pu and Zlatanova (2005) presented a new concept of evacuation route calculation for indoor spaces using three-dimensional models, take into consideration dynamic factors such as human movements or environmental problems. The study developed by Lee and Kwan (2014) had an emphasis on the construction of an optimal route, for emergency response and evacuation within the indoor space of a building. The authors Liu and Zlatanova (2015) carried out navigation and routing study based on an approach to compute indoor paths avoiding obstacles, allowing the user to create navigation networks with different dimensions. Wu

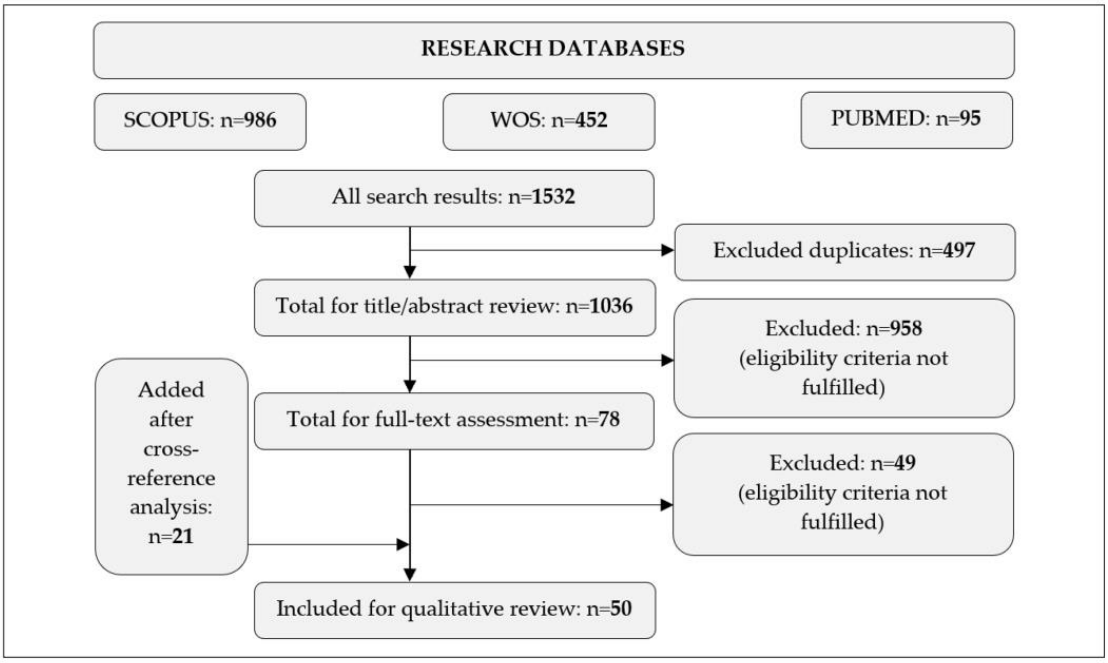

Figure 1. Article inclusion flowchart.

and Chen (2012) elaborated a study based on fire-fighting search and rescue route analysis providing an emergency response support system. Tang and Ren (2012) represented, within a uniform framework, a GIS-based simulation model to generate an entire evacuation process automatically. Some studies (Chen et al., 2019; Schabus & Scholz, 2015; Schabus et al., 2017; Scholz & Schabus, 2017) focused on smart manufacturing, using GIS to perform indoor space analysis, allowing for understanding and optimization of the systems, data, and processes (Schabus & Scholz, 2015; Schabus et al., 2017). Scholz and Schabus (2017) worked on the construction of an optimal path calculation inside a manufacturing environment. Chen et al. (2019) established a GIS-based index system, which was used to address energy-saving issues, allowing for optimal operation and management of space heating and cooling systems in indoor spaces, thus supporting decisions. Finally, the articles developed by Dao et al. (2012) and Zhou et al. (2015) emphasized the creation of an optimal service area within multistory buildings, with the goal of the placement of emergency medical devices. They are using improved three-dimensional visualization techniques and the indoor network, to support the location planning of such devices.

Indoor geospatial analysis. This subgroup represents 14% ($n=7$) of studies identified in this review. Bhattacharya et al. (2015) developed an algorithm which calculates line count inference and spatio-temporal density estimation to predict places of interest inside buildings in an automatic manner. Wan et al. (2017) established an operational framework based on people's constant activities, using Global Positioning System (GPS) to collect information in both indoor and outdoor environments, allowing for the calculation of activity patterns and creating valuable data about people's life routes. Yuan (2007) used cellular automata to simulate the movements of walkers inside a gallery building, allowing for the spatial-temporal analysis of their patterns. Kho et al. (2006) implemented a GIS-based software for infection control within hospital wards. Therefore, the authors were able to realize and conclude that this technology should be used as a nosocomial infection surveillance tool. Lake et al. (2015) developed several hazard maps related to workplace noise. They intend to identify patterns and areas of higher risk with the view to potentially help noisy working environments by clearly indicating where the high-risk places are located, thus protecting its workers. Qi and Du (2013) presented an experimental analysis method which includes automatic pre-processing, activity space characterization, trajectory segmentation, visualization, and density estimation using GPS. Vanclooster et al. (2012) defined a new measure (exitability) for indoor contexts, quantifying the quality of access to exits. This exitability measure calculates the accessibility not based on exclusively geometrical parameters, but also the movements of people.

Table 1. Characteristics of Included Studies, Detailed by Authorship, Year, Territory, Setting, Main Outcome, and Subgroup Assignment.

Author	Year	Territory	Setting	Primary outcome	Subgroup
Chen et al.	2019	China	University building	GIS-based system for management of heating and cooling systems within buildings, providing optimal energy-saving	Indoor management
Dao et al.	2012	USA	University building	Optimal location-allocation modeling of medical devices (automated external defibrillators) within a building	
Kwan and Lee	2005	USA	Office building	Emergency management information systems based on GIS for spatial decision support	
Lee and Kwan	2014	Korea	University building	Optimal route and building evacuation system, for emergency response	
Liu and Zlatanova	2015	The Netherlands	Hospital building	The creation of a navigation network (indoor path) that considers user dimension and obstacles	
Pu and Zlatanova	2005	The Netherlands	University building	Optimal route and building evacuation system, for emergency response	
Schabus and Scholz	2015	Austria	Office building	GIS application at indoor production line environments, to understand and optimize production processes	
Schabus et al.	2017	Austria	Office building	A problem-solving methodology applied to support decisions at indoor manufacturing environments	
Scholz et al.	2017	Austria	Office building	Development of an ad-hoc network to calculate the "optimal" transportation paths in indoor manufacturing environments	
Tang and Ren	2012	China	Office building	GIS-based simulation model which incorporates human behaviors and building geometry to support intelligent decisions	
Wu and Chen	2012	Taiwan	Service building	Optimal route and building evacuation system, for emergency response and fire-fighting search	
Zhou et al.	2015	USA	Service building	Optimal location-allocation planning based on GIS and three-dimensional visualization techniques	
Bhattacharya et al.	2014	Australia	University building	The development of an algorithm to correct GPS measurements and find places of interest within the indoor space	Indoor geospatial analysis
Kho et al.	2006	USA	Hospital building	An animated GIS to employ spatial analysis of nosocomial infections within a hospital ward	
Lake et al.	2015	USA	Office building	Hazard map production for facilities with different spatio-temporal variability under various sampling strategies	
Qi and Du	2013	USA	University building	An integrated GIS desktop-based visual interface for the pre-processing and spatiotemporal analyses of trajectories within indoor spaces	
Vanclooster et al.	2012	Belgium	University building	Understanding the accessibility in new indoor environments with a proposed accessibility measure (exitability)	
Wan et al.	2016	USA	University building	Presented an integrated methodology using GPS data within the indoor space to obtain detailed human activity information	
Yuan	2007	USA	Service building	Indoor geographic dynamics visualization and analysis using agent-based modeling	
Ai et al.	2020	China	Service building	Development of a large-scale fingerprint database, providing a location-based service for indoor localization	Indoor positioning
Anjana et al.	2016	India	Office building	Presented a smart positioning system allowing personalized energy management within the indoor space of buildings	
Cheng et al.	2019	USA	Residential building	Indoor positioning technology based on ultrasound to measure the air quality inside buildings	
Coumans	2018	Austria	Office building	GIS-based framework with indoor positioning of smart production environments to support human-machine interactions	
Goetz	2012	Germany	Office building	Indoor location-based services: utilization of crowdsourced indoor geodata to generate a 3D indoor routing web application	
Panta and Sèdes	2016	France	Fictional model	Presented a platform for querying indoor spatio-temporal data by hybrid trajectories generated by deployed location sensor networks	

(continued)

Table 1. (continued)

Author	Year	Territory	Setting	Primary outcome	Subgroup
Będkowski et al.	2016	Poland	Service building	The application of an intelligent mobile system (using SLAM algorithms) to improve spatial support and security inside buildings	Indoor data acquisition
Ishikawa et al.	2005	Japan	Service building	Application of a remote-controlled robot for data collection and segmentation to develop a 3D GIS geometric model	
Mitsou and Tzafestas	2007	Greece	University building	Mobile-robots utilization to map dynamic indoor environments, through a temporal occupancy structure grid.	
Pang et al.	2018	China	Service building	Presenting a theoretical method for information extraction related to complex building environments based on boundary calculation	
Rituerto et al.	2014	Spain	University building	Presented a semantic topological map for the indoor spaces analysis using a catadioptric system (robot)	
Schaffernicht et al.	2017	Sweden	Fictional model	Presented an approach that combines collected data from mobile robots and wireless sensors to handle spatial and temporal interpolation	
Wang et al.	2015	China	Fictional model	Presented a grassroot navigation system (Easy Pop) to generate pathway mapping for indoor spaces	
Wong et al.	2010	USA	Office building	Association between SLAM and robotic wireless sensor networks to map a dynamic indoor environment	
Xiong et al.	2017	China	University building	Presented a free multi-floor indoor space data extraction for large and complex buildings	
Zlatanova et al.	2014	The Netherlands	Non-applicable	Utilization of three-dimensional approaches for indoor space subdivision for the purpose of indoor navigation	
Becker et al.	2009	Germany	Fictional model	Presented a multilayered space model for indoor navigation	Indoor spatial data models
Becker et al.	2008	Germany	Fictional model	A model which contains two dual graphs for navigation in indoor space	
Billen and Zlatanova	2003	Belgium	Fictional model	Utilization of a framework model based on 3D topology	
Hussein et al.	2012	Denmark	Service building	Implementation of a unified model to represent the outdoor and indoor spaces based on collected data through receptor deployment	
Goetz and Zipf	2011	Germany	Service building	Presented an advanced spatial model which represents indoor environments with topologic, semantic, and metric information	
Ikeda et al.	2007	Japan	University building	Development of an indoor spatial model for emergency response based on sensors data	
Lee	2007	USA	University building	Presented a three-dimensional navigable data model to represent the micro-spatial built environments	
Lee	2008	USA	University Building	Presented a three-dimensional data model for emergency response in urban areas	
Meijers et al.	2005	The Netherlands	University building	Implementation of a three-dimensional GIS-based model to represent the indoor space for emergency response	
Saygi et al.	2018	Turkey	Service building	Development of an approach based on GIS for a 3D spatial model with the purpose of archiving building's chronological information	
Song et al.	2019	China	Fictional model	Construction of a building fire simulation model based on GIS to support management and decision-making	
Song et al.	2016	China	University building	A new spatial data model approach that can be used for pedestrian route analysis in a micro-spatial environment	
Tashakkori et al.	2015	Australia	Service building	Presented a 3D indoor–outdoor model to assist rescuers in planning for emergency responses in a timelier manner	
Xu et al.	2013	China	Service building	An indoor GIS application model to simulate fire disasters	
Zlatanova et al.	2013	The Netherlands	Office building	A framework model which supports indoor localization and navigation allowing automatic subdivision of indoor space	

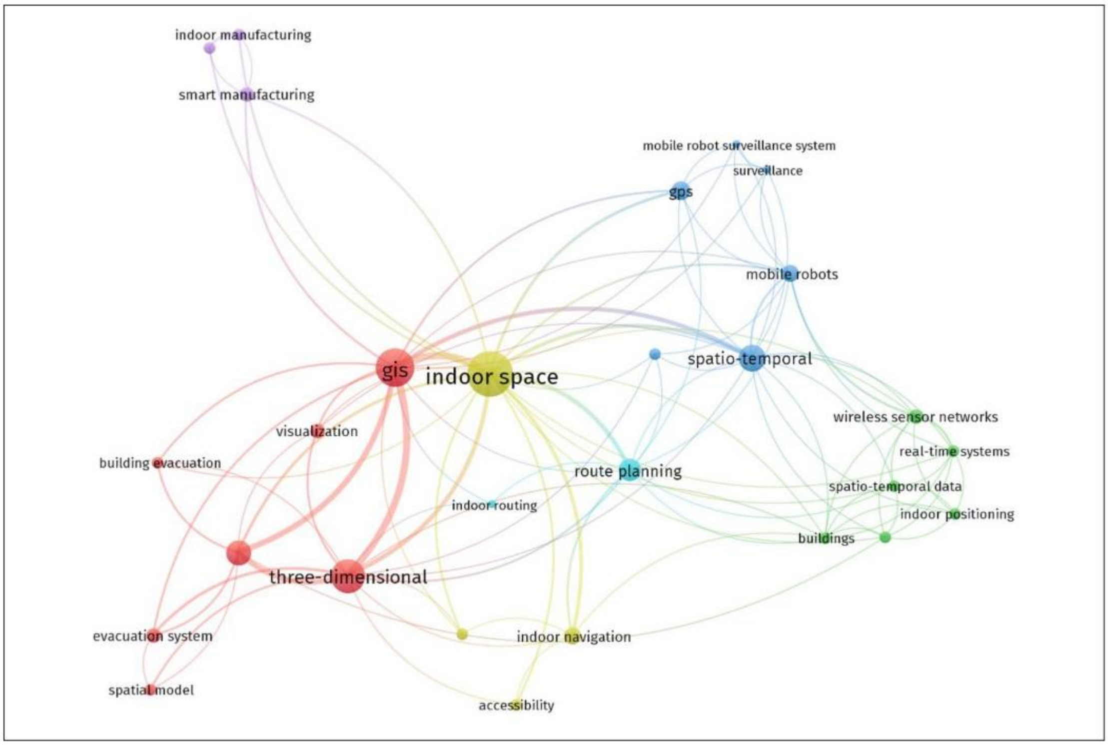

Figure 2. Co-occurrence of index or author keywords. The colors represent the clusters created based on co-occurrence of keywords, and the size of the circles represents the number of articles. The minimum occurrence of the words plotted was 5.

Indoor positioning. This subgroup represents 12% ($n=6$) of studies selected in this review. Ai et al. (2020) proposed a fast fingerprint construction, to allow the information collection that only requires sparse sampling of the received signal strength of the space, based on indoor localization. The study made by Coumans (2018) emphasized the human–machine interaction in smart production environments for indoor positioning, production asset monitoring, orientation, location-based management, and operational safety, as well as the situational perception of personnel and machines. Cheng et al. (2019) utilized a random walk approach to identify the spatial distributions of smoke intrusion based on an indoor positioning technique. Energy sustainability is essential to effective management (Kumar, 2019), and for that reason, Anjana et al. (2016) implemented a system within a building based on smart positioning, to fulfill that purpose.

The indoor system, implemented in one algorithm, can determine a person's exact position, and can suitably control nearby electrical applications, thus saving energy. The study of Panta and Sèdes (2016) contributed to the understanding of a comprehensive framework related to sensor networks deployed within indoor spaces and usage of their generated information. Goetz (2012) used crowdsourced information associated with indoor spaces to develop a three-dimensional routing web app, allowing for the exploration and computation of routes and room visualization within an indoor space.

Indoor data acquisition. This subgroup represents 20% ($n=10$) of the studies identified in this review. Several studies focused on human–robot interactions, allowing for the acquisition of indoor topological data as performed inside a building, resulting in the generation of dynamic maps. Będkowski et al. (2016) used mobile robots and the simultaneous localization and mapping (SLAM) algorithm to acquire three-dimensional data, to map the indoor space of some buildings, as well as perform and optimize specific security tasks. Mitsou and Tzafestas (2007) presented an innovative way to map dynamic indoor environments using mobile robots and a temporary occupancy grid. One of the advantages of this procedure is that it allows the extraction of information related to moving or static objects. However, the authors admit that the SLAM algorithm would be an asset for the work and will integrate it in future works. Rituerto et al. (2014) developed an augmented topological mapping solution based on omnidirectional vision and using the catadioptric image. Schaffernicht et al. (2017) used mobile robots to

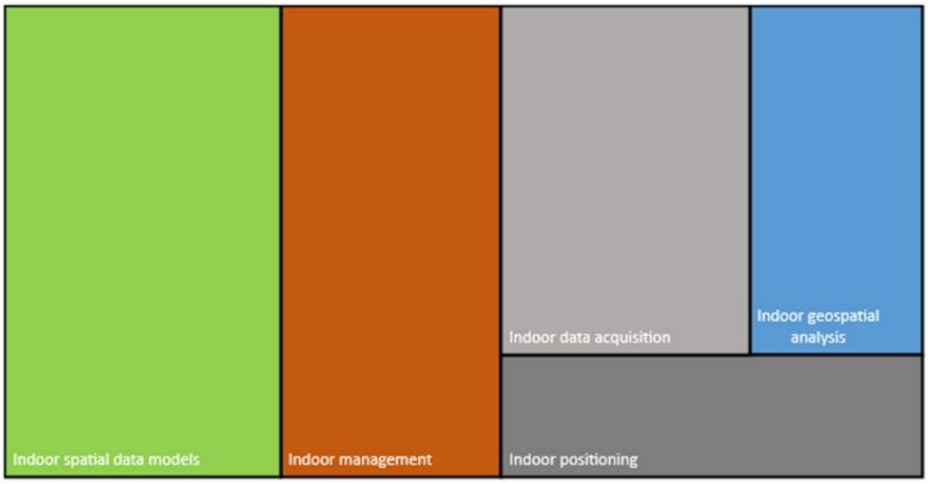

Figure 3. Treemap visualization of the of articles by category, after the full-text screening.

close the gap of the resulting measurements between learned local interpolation models and sensor nodes in indoor environments. Ishikawa et al. (2005) used a system based on mobile robot mapping three-dimensional data segmentation for exploration and surveillance of disaster areas. Wang et al. (2015) studied a navigation and pathway mapping approach based on Wi-Fi or cellular signals which, according to the logical map constructed, allows for guiding users to points of interest. Wong et al. (2010) used an approach based on SLAM association with robotic wireless sensor nodes network for data collection and mapping of indoor spaces. Xiong et al. (2017) converted indoor spaces into grids and automatically extracted the data from a building model. Nonetheless, the granularity of discrete grids determines the precision of indoor space modeling. This new method of extraction is commonly used in complex building models, with the right boundaries and structures. Zlatanova et al. (2014) presented an overview of approaches for indoor space subdivision for the purpose of indoor navigation, classifying the type of navigation (grid or graph), and provide its analysis. Pang et al. (2018) analyzed complex indoor environments in detail, presenting a new approach based on space boundary calculation for data extraction and reconstruction of such buildings.

Indoor spatial data models. This subgroup intended to select the studies related to the development of spatial data models to represent the indoor space. Fifteen articles were identified, representing 30% of the total articles included in the review. Several models were produced to be used at emergency response. The study produced by Lee (2007) focused on the application of a three-dimensional navigable data model, based on a spatio-temporal optimal route algorithm (the Dijkstra algorithm) for emergency response. Another study elaborated by Lee (2008) had an emphasis on the analysis of three-dimensional geospatial information models to manage emergency systems and improve the decision-making process. Ikeda et al. (2007) constructed an indoor spatial model for emergency response, based on sensors collected data. Song et al. (2019) developed a combinatorial spatial data model based on GIS to represent the indoor space of a building. The main goal was to provide enough information through fire simulation scenarios and analysis to support the decision-making process in case of emergency response. Tashakkori et al. (2015) elaborated a three-dimensional spatial data model to represent the indoor space of buildings, to provide fast response for fire-fighting rescue and route analysis in emergency case. Meijers et al. (2005) implemented a three-dimensional GIS-based indoor model, to be able to perform the calculation of the most accessible evacuation routes in case of a calamity. Xu et al. (2013) proposed a spatiotemporal-oriented three-dimensional model to represent the indoor space, which could be used to simulate indoor fire disasters in different scenarios. However, not all the presented models by the different grouped studies were made for emergency response. The study published by Billen and Zlatanova (2003) highlighted some concepts related to spatial relationships and cadaster techniques through the modeling and application of topology to develop a three-dimensional GIS model of buildings. Hussein et al. (2012) developed a flexible and expressive model capable of space plan segmentation to represent outdoor and indoor spaces based on data collection by receptor deployments. Song et al. (2016) employed a grid-based graph data model through a rasterization process, enable to represent the pedestrian routes within micro-spatial spaces, such as indoor environments. Goetz and Zipf (2011) developed an advanced model which represents indoor environments with topologic, semantic, and metric information (room labels, door accessibilities, stairways, or lifts) that allows nearly length-optimal routing in complex building structures. The work of Zlatanova et al. (2013) emphasized on the extraction process of indoor space information model through identifying the boundaries from three-dimensional data. This framework focusses specifically on physical and conceptual units of indoor space, which supports its localization and navigation. The works developed by Becker et al. (2009, 2008) emphasis on the construction of a multilayered space model, in which every single form of logical and physical feature is mapped in its space layer, with a novel concept since different semantic criteria can be applied to it. This model can be used for route planning, tracking and location. Finally, Saygi et al. (2018) carried out the implementation of an information management platform model to represent the indoor space of historical buildings, to provide better and well-informed decisions, such as the planning of restoration projects.

Discussion

This study provides a detailed review by screening several techniques and procedures to represent and model indoor spaces, which have broad applicability and can be vital and decisive for GIS users, data producers, and policymakers. The selected papers ($n=50$) presented a publication year median of 2014, thereby bringing relevant information that should not be overlooked. From these papers, data collection approaches and primary outcomes were extracted, and a subgroup analysis (five categories were identified—Figure 3) was performed. The qualitative synthesis presented was fundamental to organize and summarize the gathered scientific evidence.

Indoor management contemplates studies using GIS technologies to comprehend the indoor spaces of buildings (inside and out) at a single location, providing resource exploration management, and process optimization (Chakhar & Mousseau, 2017; Chiu & Liu, 2008; Crossland, 2017; Franzese & Liu, 2008; Kamilaris & Ostermann, 2018; Worboys, 2011). The 9/11 terrorist attacks triggered the development of several studies (Kwan & Lee, 2005) concerned with the utilization of emergency response techniques in micro-spatial environments using the existing proposed standard models. These types of studies are presenting some interesting possibilities for analysis, such as scenario simulation, victim tracking and rescue, facility and resource vulnerability, real-time data delivery, data availability, and air monitoring (Kevany, 2011). The limitations of this type of approach have been identified, as it is necessary to identify the affected rooms and floors by the emergency. The verification of the occupation area is a fundamental task since it is needed to allow the system to calculate, in a viable way, a safe evacuation route (Zhou et al., 2015).

Regarding the indoor settings of production or working places, the three-dimensional visualization techniques are being used to perform optimization of the systems, routes, data, and processes, allowing better management of the associated costs, security, and action performance (Scholz & Schabus, 2017; Worboys, 2011; Zhou et al., 2015). Nonetheless, limitations have been described; for example, the amount of data and the complexity of the geometric and topological models used might favor the non-use of the system at its full potential. This process often leaves opportunities to gain a more detailed understanding of the unexploited problem (Zhou et al., 2015). In summary, the articles included in this group, intended to apply extended uses to the pre-existing models, valuing the spatial-temporal analysis to contribute for an efficient management of these spaces. The visualization, interpretation and validation approaches are the most used to optimize and enhance the expected results.

Although the "indoor geospatial analysis" subgroup might be considered the one with the most significant margin of development, it is currently under-explored with relation to the other categories. The reason for this fact may be interconnected with data availability and the lack of experience of researchers in geospatial studies that analyze the phenomena occurring within the indoor spaces. In this type of study, understanding the dynamics, movements, behaviors, and interactions of people within buildings is a fundamental condition, leading to the development of solutions which are essential for the existing problems (Goodchild et al., 2007; Yuan, 2007). Despite the heterogeneity present in the included studies, their applied mapping skills were the same, using data model representation, visualization, and simulation (Kho et al., 2006). In fact, a benefit that emerges from this type of studies is the creation of indoor space scenario models, which offers one of the most thoughtful possibilities for analysis, as the outcomes give clues that make the process of data inspection easier, helping to identify potential problems and generate solutions (Yuan, 2007, 2008). Of the several studies included in this subgroup, only one addressed the utilization of GIS to comprehend the spatial epidemiology of health data (Kho et al., 2006). This situation provides an unprecedented opportunity for health researchers, allowing the development of more studies associated to disease patterns within physical structures, such as hospitals or health facility buildings (Kistemann et al., 2000, 2002), contributing to a more complete and efficient analysis (Olimpio & Smith, 2009). The main limitations regarding spatial analysis in indoor spaces are usually related to the quality and quantity of available data, which typically leads to complex and multifaceted challenges (Vanclooster et al., 2012; Worboys, 2011). In brief, and according to the included studies, the spatial analytical functions that emphasis on discovering and learning the relationship between these spaces and the phenomena occurring there are the most applied approaches, although they vary through the scale of the study object.

More than 80% of people's daily lives are spent within an indoor space, and the requirements of indoor positioning technologies have demonstrated to be very important in this context area, as GPS and other satellite technologies lack precision or fail inside multistory buildings (Deng et al., 2013). It has been noted that indoor positioning technologies have entered a period of significant change and development, providing a technological leap to ensure public security and significant economic and social benefits (Li et al., 2007). With the view to collect data related to person or object positions within an indoor space, some authors used methodologies based on fast fingerprint database networks (Ai et al., 2020; Li et al., 2007); while other built an indoor positioning framework to support human–machine interaction (Coumans, 2018). Even though the indoor positioning methods were developed to solve the limitations of GPS within indoor spaces, no technology is completely perfect (Jun et al., 2013). The diffusion of indoor positioning is still limited, considering its potential, requiring complementary research (especially in the performance field). The most used approach by the authors is related to track locations inside buildings through the indoor positioning system (IPS).

The fourth subgroup focused on the acquisition of data related to the indoor context, using devices such as mobile robots (with SLAM algorithm), wireless sensors, remote-sensing techniques, or smartphones (Będkowski et al., 2016; Rituerto et al., 2014; Wang et al., 2015). These processes generated vast amounts of spatial information, allowing the acquisition of topological data and the process of indoor mapping (Lee, 2008). We are aware that the included articles in this group do not represent the current field insight associated with indoor acquisition since there are many other methods to extract information. However, their results and primary outcomes should not be ignored. More than a few techniques have been developed during the last years, such as the laser scan to obtain a "cluttered point cloud" (Díaz-Vilariño et al., 2015; Lehtola et al., 2017; Nikoohemat et al., 2018, 2020) to perform the three-dimensional reconstruction. This method allows the detection of all the elements that are present within a building. Walls, doors, obstacles, and access to the stairs are the essential information to be attained in this process (Nikoohemat et al., 2020). Yet, like any other method, it also has some limitations, since processing a large amount of data to reconstruct such space is not a minor task and needs expert knowledge and sophisticated software and hardware (Nikoohemat et al., 2020). Also, in many situations, the process of data achievement (which is involved in several specific procedures) depends on human evaluation, to validate the entire process (Kanaan et al., 2008; Peersman, 2014).

Finally, the last group contemplates studies where the conception of spatial data models to represent the indoor space were the main goal. Most of the studies found, focus on emergency response as a main motivation (Lee, 2007; Song et al., 2019; Tashakkori et al., 2015). Despite the reason, the authors implemented different techniques and approaches to build their indoor space models. This is an essential work for field development, presenting relevance and being an opportunity to complement the identified problem related to the lack of support in software packages for indoor data collection (Park et al., 2020).

Nevertheless, the evolution occurring with indoor spatial data modeling, with published papers being using approaches that vary from the GIS utilization (Meijers et al., 2005; Saygi et al., 2018; Xu et al., 2013) or sensors and receptor deployments that collected the needed data (Hussein et al., 2012; Ikeda et al., 2007), have been complemented with the recent standard (OGC, 2012, 2014). This model, developed by the open geospatial consortium (OGC), the IndoorGML, provides a basis, that can be extended to meet the requirements of any indoor spatial application (Nagel et al., 2010; Zlatanova et al., 2016). Therefore, as we said above, this model is only the start of something that should be part of today's science since only a few works have been done for assessing its potential and discovering how to apply it in practice (Kang & Li, 2017; Nagel et al., 2010; Park et al., 2020).

The scope of our study was clearly defined, and we have shown that, indeed, there are several studies using distinct GIS approaches related to the indoor spaces. The presented possibilities of analysis are vast, with papers focusing on facility management, occupational data pattern analysis, emergency simulation, route navigation, indoor modeling, indoor positioning, or optimal resource allocation. Notwithstanding these studies presenting numerous advantages, there were transversal limitations to all articles. Ethical and legal issues can appear in these types of studies; especially if people's privacy is put at risk, leading to social issues such as reactions ranging from uneasiness to a plain refusal to adopt the technology. Even though the risk of bias and effect measurement analysis is frequently applied in this type of study (i.e., systematic reviews), the authors did not use it, as the objective of this work was to summarize the evidence, and not to evaluate measures of the results.

Study Limitations

This study, as a systematic review, present some important limitations since only considers peer-reviewed articles from the selected databases (Scopus, ISI, and Pubmed). Gray literature (not indexed) and other indexed databases or conference proceedings books were not investigated, where may usually present a fair amount of information showing a potential insight related to the most recent developments of the field. Besides, at the time of the search strategy creation for this review, the authors tried to guarantee the quality of the results making it fair and less subject to bias, through a greater rigor of the publications to answer the starting investigation question. However, given the considerable heterogeneity or lack of terms used by authors and indexing services, some studies may not have been included. Finally, this article does not pretend to be another state of art study about the scope "indoor," but to give useful peer-reviewed evidence related to GIS applications to the indoor space.

Future Directions and Conclusions

Thus far, we have presented the different studies in a brief comparative way, highlighting its main outcomes, strengths, and weaknesses, clarifying in what they succeed at. However, the future directions of this type of research area may not be entirely evident. Even though it is known that GIS tools initially appeared to be applied to the external territory, they can undoubtedly be used to study the indoor spaces, as supported by the articles included in the present study. Nevertheless, we identified five main themes (subgroups), some already emphasized by the reviewed studies and others that resulted from this systematic literature search. The concept of space is increasingly drawing the attention of researchers from several scientific areas, with new approaches and methodologies about shapes and patterns emerging for graphical representation. Besides, the indoor spaces of buildings turn out to be bigger and more complex due to the fast urbanization (Kang & Li, 2017), thus requiring efficient and optimal management. It was realized that there is a lack of complex building maps and models, and an absence of a gold standard methodology to obtain this type of data. We pointed in this review several ways to acquire the information about the indoor spaces, being also essential to enhance the problems that might be associated with the process, such as topology errors, or base map problems. Another valid concern which can possibly appear, is related to the internal security of the buildings, since that when giving access to the indoor maps, it is clearly necessary to define who has access to it.

Despite the massive demand for this type of study, and with a few commercial services already available, such as Google Indoor Maps and ESRI ArcGIS Indoors, we still need a basic indoor spatial theory support to create a core of information and model forms for this subject. The studies are showing a lot of new techniques, and methodologies, but still more are needed, specifically considering the plumbing or ventilation systems, since it allows another type of approaches and considerations.

To the best of our knowledge, this is the first systematic review focused on the utilization of GIS in the analysis of indoor spaces. Since most part of the studies included in this review focus on the indoor spaces of university buildings or even fictional models (n=23), it supports the idea that this approach is clearly in its first steps, and that research is still incipient and considerably less developed when compared with the utilization of GIS to study external spaces.

The introduction of the smart city concept has created an opportunity (Misra & Kumar, 2020), raising the awareness of researchers to the potential of GIS for the analysis of indoor spaces, providing a literature support for further work to evaluate the proposed visual models in real-world decision support environments.

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Supplementary material

Section/topic	#	PRISMA 2020 Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Pages 2 and 3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Not Applicable
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 5 and 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Pages 7, 8 and 9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Pages 8 and 9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 8 and 9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Not Applicable

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Not Applicable
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not Applicable
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not Applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not Applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Pages 9, 10 and 11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Not Applicable
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Pages 12 to 18
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not Applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not Applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not Applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Pages 18 to 24
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 24
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Pages 24 to 26
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Title page

Appendix 1. Prisma 2020 Checklist.

3. Spatial Patterns in Hospital-Acquired Infections in Portugal

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Article

Spatial Patterns in Hospital-Acquired Infections in Portugal (2014–2017)

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Abstract: Background: Hospital-Acquired Infections (HAIs) represent the most frequent adverse event associated with healthcare delivery and result in prolonged hospital stays and deaths worldwide. Aim: To analyze the spatial patterns of HAI incidence from 2014 to 2017 in Portugal. Methods: Data from the Portuguese Discharge Hospital Register were used. We selected episodes of patients with no infection on admission and with any of the following HAI diagnoses: catheter-related bloodstream infections, intestinal infections by *Clostridium difficile*, nosocomial pneumonia, surgical site infections, and urinary tract infections. We calculated age-standardized hospitalization rates (ASHR) by place of patient residence. We used empirical Bayes estimators to smooth the ASHR. The Moran Index and Local Index of Spatial Autocorrelation (LISA) were calculated to identify spatial clusters. Results: A total of 318,218 HAIs were registered, with men accounting for 49.8% cases. The median length of stay (LOS) was 9.0 days, and 15.7% of patients died during the hospitalization. The peak of HAIs (n = 81,690) occurred in 2015, representing 9.4% of the total hospital admissions. Substantial spatial inequalities were observed, with the center region presenting three times the ASHR of the north. A slight decrease in ASHR was observed after 2015. Pneumonia was the most frequent HAI in all age groups. Conclusion: The incidence of HAI is not randomly distributed in the space; clusters of high risk in the central region were seen over the entire study period. These findings may be useful to support healthcare policymakers and to promote a revision of infection control policies, providing insights for improved implementation.

Keywords: hospital-acquired infections; spatial epidemiology; age-standardized hospitalization rates; spatial autocorrelation; Portugal

1. Introduction

A nosocomial infection, also known as hospital-acquired infection (HAI), is defined as an infection acquired by a patient while receiving health care [1,2]. These infections are usually developed during hospitalization and manifest no earlier than 48 h after the hospital admission or up to 30 days after receiving health care, in the case of Surgical

Site Infections (SSI) [3]. Despite HAIs being more frequently identified in hospitalized inpatients, they also include infections detected after discharge or occupational infections among the health staff [4]. Usually, HAIs are caused by bacterial, viral, or fungal pathogens, where the most common types include the bloodstream infections related to the central venous catheter [5–7], hospital-acquired pneumonia [8,9], intestinal infections by *Clostridium difficile* [10,11], the SSI [12,13], and urinary tract infections associated with catheter use [14,15].

Hospital-acquired infections represent one of the most frequent adverse events during healthcare delivery; they may result in prolonged hospital stays, long-term disability, increased resistance to antimicrobials, or even death [16,17]. Despite their relevance, the real burden of HAIs remains unknown due to the complexity of the various surveillance systems and the lack of uniform diagnosis criteria from country to country [18]. According to several studies, the prevalence of HAIs in middle-income countries ranges from 5.7% to 19.1% of all hospitalizations, whereas in developed countries, it varies between 5.7% and 7.5% [19–22]. However, in some high-income countries, the prevalence has been reported to be as high as 12.0% [23]. According to data provided by the Portuguese Directorate-General of Health in the scope of the report of the 2nd European survey on the prevention program for infection control in 2017, the prevalence of HAIs in Portugal was around 7.8%, showing a decreasing trend since 2012 [24,25]. Nonetheless, the literature indicates, for the Portuguese case, an absence of epidemiological data on HAIs in individual Portuguese Intensive Care Units (ICUs), which makes it difficult to compare data and impairs the understanding of any spatial differences in prevalence, which may be associated with the area of influence of the ICUs, according to the national referral network [26].

Moreover, HAIs are directly or indirectly responsible yearly for more than 148,000 deaths in Europe and around 98,000 in the USA [2,27,28]. Despite these numbers, hospitals take hospital-acquired infections very seriously. To reduce the impact of these infections, several hospitals worldwide have implemented infection tracking and surveillance systems as well as solid prevention strategies [29]. Prevention and minimization of HAIs are the responsibility of all health actors and include infection control programs, infection control committees, and staff training [30,31].

Regarding surveillance, several hospitals have used data from health information systems, such as hospital discharge registers, as an automated alternative instrument to complement diagnosis and to improve process efficiency and precision [32–34]. Although the accuracy of administrative coded data is affected by coding process subjectivity and the variability of distinct coding versions [35–38], the information based on this type of data is internationally recognized [34,39]. Its use has been successfully applied for several research purposes, including to assess some HAIs [39–41].

The use of hospital discharge data for the assessment and description of HAIs as well as inference about these infections can give important clues about their trends and patterns. To our knowledge, no studies have provided a descriptive analysis of HAIs in Portugal or in other European countries using administrative data of hospitalizations. Our study aims to fill this gap, describing the spatial patterns of the Age Standardized Hospitalization Rates (ASHRs) of HAIs and exploring the existence of spatial clusters in mainland Portugal from 1 January 2014 to 31 December 2017.

2. Materials and Methods

2.1. Study Area

The study area is mainland Portugal, located on the Iberian Peninsula in southwestern Europe, with a land area of 89,102 km^2. The mainland was estimated to have 9,792,797 inhabitants in 2017 (43.0% aged 50 and over), distributed heterogeneously throughout five regions and 278 municipalities (with a population varying from 1634 to 509,515 inhabitants). The North, Center, and Lisboa Regions held 88.8% of the Portuguese population in 2017, while Alentejo (7.3%) and Algarve (4.5%) had much lower proportions.

Portugal is a developed country, despite presenting a high GINI index value (32.1 in 2017), meaning that the inequality of wealth distribution is one of the highest in the European region [42].

The national health system is universal, allowing global coverage to all residents despite their socioeconomic, legal, or employment status. It contains three coexisting systems: the national health service, the health subsystems for specific professions, and the private health sector [43].

2.2. Study Design

We carried out a retrospective and observational population-based ecological study using secondary data from public hospital admissions. The respective geographic and temporal units of analysis were the municipality and the calendar year for the period of 1 January 2014 to 31 December 2017.

2.3. Data Sources

We obtained hospitalization data from the Portuguese Hospital Discharge Register, managed by the Central Administration of the Health System (ACSS) of the Portuguese Ministry of Health. These data refer to hospital admissions in public hospitals and are provided for research upon request. Each record corresponds to one hospital admission and contains the following information: sex (male or female); age and date of birth; municipality of the patient's residence; external causes of injury, coded according to the International Classification of Diseases (ICD); principal diagnosis (and secondary diagnoses) coded according to the ICD; medical or surgical interventions (also represented with ICD codes); type of admission (unplanned admissions—admissions through the emergency department); dichotomy (yes/no) indicator of infection Present On Admission (POA) indicator; which hospital is providing the care; outcome (for example, discharge home, discharge to another hospital, deceased); Length of Stay (LOS); geographic units of the patient's place of residence; and Diagnosis Related Groups variables. Registers were coded according to ICD version 9, Clinical Modification (ICD-9-CM) for the years 2014 and 2015 as well as a significant part of 2016, and ICD version 10-CM was used for the remaining period. More detailed information about the variables used can be found in Table S1. In the studied period, no such data were available for the Portuguese archipelagos of the Azores and Madeira, and therefore they were not included in this study.

For the study period, population estimates were obtained from the National Institute of Statistics (INE) [44], which were aggregated by municipality, sex, and 5-year age groups.

2.4. Data Selection

Given the nature of the studied condition and the accuracy of the coding systems used, a review analysis was conducted, using the best available scientific evidence [33,39,40], to obtain a consensual list of codes to characterize the most common HAI contexts. The codes were organized by context and validated through discussions with physicians and specialists in the fields of medical coding and infection control, considering both coding systems. Table 1 shows the selected diagnoses in our analysis.

Table 1. ICD-9-CM/ICD-10-CM codes used to identify HAI episodes.

Hospital-Acquired Infections	ICD-9-CM Codes			ICD-10-CM Codes		
Catheter-related bloodstream infections	038.12 041.12	038.11 996.62	041.11 999.3x	A41.01 B95.62	A41.02 T80.2-	B95.61 T82.7-
Infection by *Clostridium difficile*	008.45			A04.7-		
Nosocomial Pneumonia	480x 483x 487.0	481 485 997.3x	482x 486	A48.1 J10.0- J13 J16-	B01.2 J11.0- J14 J17	B05.2 J12- J15- J18-
Surgical site infection	483x 487.0 996.6x 998.5x 999.39	485 569.61 997.3x 998.6	486 682x 996.7x 999.34	J10.0- J13 J16- O86.0- T84.5 T88.0-	J11.0- J14 J17 T81.4- T84.6 T88.8-	J12- J15- J18- T81.8- T84.7 Z48.8-
Urinary tract infection	590.1x 590.9 599.0	590.2 595.0 996.64	590.8x 595.4 997.5	N10 N30- N99.89	N15- N30.81 T83.5-	N16 N39.0

We selected all in-patient episodes with a discharge date between 1 January 2014 (first year with available POA indicator) and 31 December 2017 (latest available and validated data) from the Portuguese Hospital Discharge Register with any HAI suggested diagnosis through the ICD code, combined with a negative POA indicator.

Each hospitalization was considered an independent episode. We excluded episodes with a LOS of less than three days to conform with the HAI definition. Episodes with more than 180 days (n = 246, 0.07%) were excluded due to prolonged hospitalizations that may be associated with lack of social support (e.g., older adults without a place in a nursing home).

The Charlson Comorbidity Index (CCI) was calculated through the identification of specific comorbidities using secondary diagnosis. The CCI categorizes comorbidities of patients based on the ICD diagnosis codes [45,46]. A weight is assigned to each comorbidity group based on resource use and adjusted mortality risk. The index score results in the sum of all weights. A score of zero means that no comorbidities were found, while a higher score indicates a higher chance of developing a weak general health status, which would require the consumption of more resources [47]. More detailed information can be found at Freitas et al. [48].

2.5. Data Analysis

Geographic Information Systems (GISs) and spatial statistical techniques were used to analyze the data. Due to the high differences observed in HAI incidence by age groups, data were analyzed globally and according to the following categories: youth (0–19 years), adults (20–64 years), and elderly (65 or more years). Descriptive statistics, such as the median (interquartile range) for the quantitative variables and the absolute (relative) frequencies for the categorical variables, were calculated for each sociodemographic and clinical characteristic using IBM SPSS Statistics 26 for Windows (IBM Corp., Armonk, NY, USA).

The age-standardized hospitalization rates (ASHRs) of HAIs, per municipality and year, were calculated using the direct method, with the European population as standard [49] and five-year age groups (from 0 to 100 or more). To overcome the statistical instability caused by the Problem of Small Numbers [50] in municipalities with a small population, we used the empirical Bayes (EB) method (Equation (1)) [51] to smooth the local risk. This approach is a statistical estimation based on the observed data, where the degree of "smoothing" is calculated according to a weight that varies from 0 to 1 as a function of the population size and the variability of the ASHR in the neighborhood.

Therefore, for municipalities with large populations and thus not affected by the statistic instability, the weight is close to 1, meaning that the adjusted rates are like the observed rates. On the other hand, the lower the weight, the less we "trust" in the observed rates (because they can be artificially high due to the Small Number Problem); therefore, they are smoothed to the average of the neighbors [52].

$$\text{EB ASHRi} = (\text{ASHRi} \times Wi) + \left(\text{ASHR}_{\text{neighorhood}} \times (1 - Wi)\right) \quad (1)$$

ASHRi= age standardized hospitalization rate in the municipality i
Wi= weight in municipality i

ASHR $_{\text{neighorhood}}$ = neighborhood age standardized hospitalization rate

We used first order neighborhoods calculated using the "queen contiguity" method, which considers as neighbors all the municipalities that share at least one vertex. After defining the neighbors of each municipality, we summed the cases and population of each neighbor and calculated the $\text{ASHR}_{\text{neighorhood}}$ using the direct method and European standard population as described before. In summary, the estimated EB ASHR better describes the risk in a municipality by smoothing the artificially high observed ASHR caused by few cases in a small population.

Using the EB ASHR, we calculated the Moran's Index according to Equation (2) [53], to measure the presence of spatial autocorrelation. The Moran index is a global indicator of autocorrelation, where a score close to zero means that there is no autocorrelation, with events arising randomly in space. A score near −1 or 1 represents a strong (negative or positive) autocorrelation, implying a spatial dependency in the event occurrence. However, when dealing with many areas, different local spatial associations may occur. Therefore, we also computed the Local Index of Spatial Autocorrelation (LISA) using Equation (3) [54].

$$I = \frac{n \sum w_{ij} (z_i - \overline{z})(z_j - \overline{z})}{S_o \sum_i (z_i - \overline{z})^2} \quad (2)$$

$$I_i = \frac{z_i \sum_{j=1}^{n} w_{ij} z_j}{\sum_{j=1}^{n} z_j^2} \quad (3)$$

where n = number of areas; z_i = value of the variable considered in area; $\overline{z}$ = the variable's average value in the study area; w_{ij} = elements of a well-balanced matrix, based on spatial proximity; z_j = variable value of the considered j area.

The LISA identifies areas where the ASHR is significantly correlated with the ASHR of their neighbors [55]. Based on LISA results, four types of clusters were identified: high-high (areas of high ASHR, with neighbors also with high ASHR), high-low (areas with high ASHR surrounded by areas with low ASHR), low-high (areas with low ASHR surrounded by areas with high ASHR) and low-low (areas of low ASHR, with neighbors also with low ASHR). The GeoDa 1.16.0.12 software (University of Chicago, Chicago, IL, USA) was used to calculate the Moran Index and LISA, and ArcGIS 10.5.1 (ESRI, Redlands, CA, USA) was used to map the results.

2.6. Ethics Statement

The secondary data from the Portuguese Hospital Discharge Register was obtained following the current Portuguese legislation. The availability of these anonymized data does not require specific approval from ethical committees. The global research was approved since it did not include samples or experiments on humans or their personal information.

3. Results

During the study period, and according to the selected criteria, there were 320,288 episodes of hospitalizations with one or more HAIs. Of the total, 2070 episodes (0.65%) were disregarded because of missing information related to the patient residence municipality, leaving 318, 218 episodes of the analyzed population. Median (Interquartile range—IQ) age was 77.0 years (20.0) for men and 81.0 years (17.0) for women.

3.1. Profiles of HAI Cases and Their Sociodemographic and Clinical Characteristics

The yearly average number of episodes of HAI was 79,555, corresponding to approximately 1525 cases per week. The yearly number of hospitalizations with HAI exhibited an increase from 2014 to a peak in 2015 (n = 81,690), representing 9.4% of the hospital admissions, followed by a decrease until a global minimum in 2017, with an HAI incidence of 90.0 cases per 1000 admissions (Figure 1).

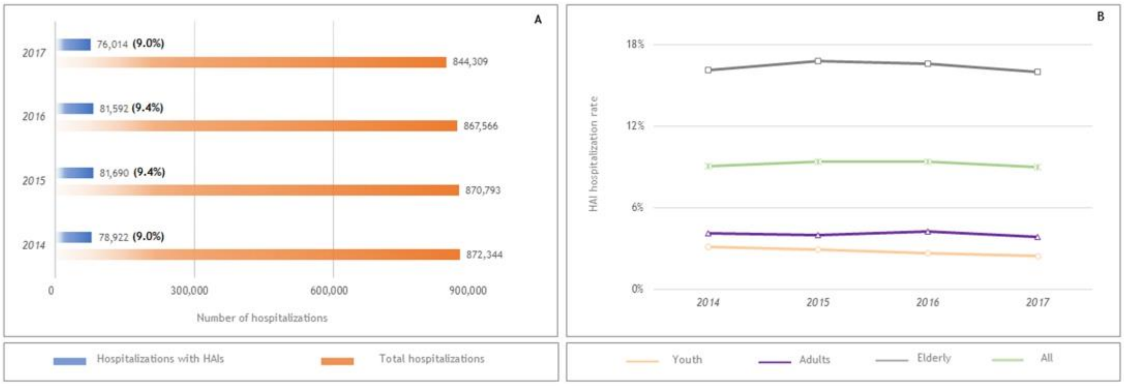

Figure 1. (**A**)Yearly number of hospitalizations with Hospital Acquired Infections and the total number of hospital admissions. (**B**) HAI hospitalization rate per age category.

This pattern was also observed within each age category. Within the whole study period, youth (0–19 years) accounted for 4.7%, whereas adults (19–64 years) and elderly (65 or more years) accounted for 18.1% and 77.2%, respectively. Regarding the distribution of cases by sex, men accounted for 49.8%. The age range was 0–109 years, with a median (IQ) age of 79.0 (20.0). The median length of stay was 6.0 (5.0) days for the youth and 10.0 days (10.0) for the elderly; 94.3% of patients were admitted urgently, while 5.7% were admitted in a scheduled way (Table 2).

Table 2. Sociodemographic and clinical characteristics of patients admitted in mainland Portuguese public hospitals with HAIs.

		Age Category		
Characteristics	**Total**	**Youth**	**Adults**	**Elderly**
Total HAI hospitalizations, *n* (%)	318,218 (100.0)	14,851 (4.7)	57,700 (18.1)	245,667 (77.2)
Age, (years), Median, (IQR)	79 (20.0)	2 (7.0)	54 (15.0)	82 (11.0)
Length of stay (LoS), (days), Median, (IQR)	9 (10.0)	6 (5.0)	10 (11.0)	10 (10.0)
Sex, *n* (%)				
Men	158,552 (49.8)	7921 (53.3)	33,822 (58.6)	116,809 (47.5)
Women	159,666 (50.2)	6930 (46.6)	23,878 (41.4)	128,858 (52.5)
Charlson comorbidity index, *n* (%)				
0	80,401 (25.3)	12,934 (87.1)	22,736 (39.4)	44,731 (18.2)
1–2	137,858 (43.3)	1751 (11.8)	21,054 (36.5)	115,053 (46.8)
3–4	63,897 (20.1)	110 (0.7)	6868 (11.9)	56,919 (23.2)
>4	36,062 (11.3)	56 (0.4)	7042 (12.2)	28,964 (11.8)

Table 2. *Cont.*

Characteristics	Total	Youth	Age Category Adults	Elderly
Destination after discharge, *n* (%)				
Residence	248,069 (78.0)	14,250 (96.0)	48,349 (83.8)	185,470 (75.5)
Hospital transfer	7484 (2.4)	421 (2.8)	2408 (4.2)	4655 (1.9)
Discharge against medical advice	881 (0.3)	23 (0.2)	505 (0.9)	353 (0.1)
Transfer to continuous care	11,697 (3.7)	58 (0.4)	1676 (2.9)	9963 (4.1)
Deceased	50,087 (15.7)	99 (0.7)	4762 (8.3)	45,226 (18.4)
Admission type, *n* (%)				
Scheduled	17,916 (5.6)	1280 (8.6)	6525 (11.3)	10,111 (4.1)
Unplanned	300,181 (94.4)	13,569 (91.4)	51,133 (88.6)	235,479 (95.9)
Others	121 (0.0)	2 (0.0)	42 (0.1)	77 (0.0)
Admissions by NUT II, *n* (%)				
North	100,933 (31.7)	4851 (32.7)	19,922 (34.5)	76,160 (31.0)
Center	87,719 (27.6)	3266 (22.0)	12,651 (21.9)	71,802 (29.2)
Lisboa Region	94,190 (29.6)	5422 (36.5)	19,768 (34.3)	69,000 (28.1)
Alentejo	22,944 (7.2)	718 (4.8)	3211 (5.6)	19,015 (7.8)
Algarve	12,432 (3.9)	594 (4.0)	2148 (3.7)	9690 (3.9)
Hospital-acquired infections context [1]				
Total, *n* (%)	**340,125 (100.0)**	**15,074 (4.4)**	**60,608 (17.8)**	**264,443 (77.7)**
Catheter-related bloodstream infections	19,581 (5.8)	1448 (9.6)	6435 (10.5)	11,698 (4.4)
Intestinal infection by *Clostridium difficile*	3822 (1.1)	49 (0.3)	609 (1.0)	3164 (1.2)
Nosocomial pneumonia	197,188 (58.0)	10,957 (72.7)	33,064 (54.6)	153,167 (57.9)
Surgical site infection	11,883 (3.5)	522 (3.5)	5795 (9.6)	5566 (2.1)
Urinary tract infection	107,651 (31.7)	2098 (13.9)	14,705 (24.3)	90,848 (34.4)

[1] The patient may acquire more than one type of HAI during hospitalization.

There were 50,087 patients (15.7%) who died during their stay, while the majority (78.0%) were discharged home. The elderly age category had the highest percentage of deaths (18.4%) during their hospital admission, while the youth presented the lowest, with 0.7%.

The North region, with a higher concentration of inhabitants, had a higher frequency of HAIs, with 100,933 (31.7%) cases. All age groups reflect these general values, except for youth in the Lisboa region, where the highest frequency was registered (36.5%) when compared with the others.

There were differences in the Charlson comorbidity index (CCI) for the HAI inpatients between the different age groups. Most of the youth (87.1%) did not have any pre-existing conditions, while in the opposite direction, 60.6% of the adults and 81.8% of the elderly registered at least one or more comorbidities.

Nosocomial pneumonia was the most common HAI in all age categories, with 197,188 hospitalizations (58.0%); urinary tract infections were the second most common, with 107,651 hospitalizations (31.7%). Overall, intestinal infection by *Clostridium difficile* was the least frequent, with 3822 (1.1%) episodes.

A minority of in-hospital deaths in patients with an infection acquired after surgery was verified (5.0%). Unsurprisingly, the lethality was higher for patients with nosocomial pneumonia, with 18.5% deceased during their hospital admission.

Although admissions of patients with intestinal infection by *Clostridium difficile* represented the least frequent event (1.1%), the data showed that 16.6% presented a fatal outcome (Table 3). In summary, almost all HAI contexts present a lethality above 10%.

Table 3. Frequency of HAI hospitalizations by context, outcome (alive or deceased during the hospital stay), and in-hospital lethality rate (IL).

Hospital-Acquired Infections	Total *n* (%)	Alive *n* (%)	Deceased *n* (%)	IL (%)
Catheter-related bloodstream infections	19,581 (5.8)	16,845 (5.9)	2736 (4.9)	14.0
Infection by *Clostridium difficile*	3822 (1.1)	3186 (1.1)	636 (1.1)	16.6
Nosocomial pneumonia	197,188 (58.0)	160,762 (56.4)	36,426 (65.8)	18.5
Surgical site infection	11,883 (3.5)	11,296 (4.0)	587 (1.1)	5.0
Urinary tract infection	107,651 (31.7)	92,707 (32.6)	14,944 (27.0)	13.9

The surgical site infection context was the most frequent (54.3%) among patients without comorbidities (Table 4), whereas urinary tract infections were the most common among patients with at least one comorbidity (77.7%). On the other hand, catheter-related bloodstream infections were the most frequent in patients with three or more pre-existing pathologies (36.9%).

Table 4. Overall frequencies of HAI contexts between 2014 and 2017 by CCI classes.

Hospital-Acquired Infections	0	1–2	3–4	>4
Catheter-related bloodstream infections	5398 (27.6)	6964 (35.5)	4101 (20.9)	3128 (16.0)
Infection by *Clostridium difficile*	929 (24.3)	1592 (41.7)	823 (21.5)	478 (12.5)
Nosocomial pneumonia	47,862 (24.3)	90,414 (45.8)	38,779 (19.7)	20,133 (10.2)
Surgical site infection	6453 (54.3)	3480 (29.3)	948 (8.0)	1002 (8.4)
Urinary tract infection	24,013 (22.3)	45,178 (42.0)	24,338 (22.6)	14,122 (13.1)

3.2. Spatial Distribution of Hospitalization Rates by Municipality

The spatial distribution of the ASHRs of HAIs by 100,000 inhabitants per municipality and by year is shown in Figure 2. Substantial spatial disparities were verified, with ASHR values in the range of 256.0–846.8 episodes/100,000 inhabitants in 2014, and 306.3–1109.2 episodes/100,000 inhabitants in 2015, with the highest rates in the central region of the country and lower in the south.

Between 2014 and 2015, the ASHR increased; however, from 2015 to 2017, we observed a global decrease throughout the mainland. In particular, the mean (standard deviation) of episodes per 100,000 inhabitants was 490.8 (78.4) in 2015 and 435.5 (72.2) in 2017. Moreover, the proportion of municipalities in the two highest quintiles decreased from 41.0% in 2015 to 20.9% in 2017. Despite this reduction, during the study period, the municipalities in the north and central region had consistently higher ASHRs than those in the south.

The Moran index was moderate to high in the studied period, being higher in 2016, with a value of 0.627 ($p < 0.05$), meaning that the ASHR does not occur randomly in the space. Spatial clusters of high and low ASHR were identified with LISA analysis (Figure 3). The most significant high-high clusters were located mainly in the center region of the country, with some smaller high-high clusters found in the north. A total of three low-risk clusters were identified between 2014 and 2015, while between 2016 and 2017, the number of low-risk clusters increased to four and six, respectively, despite a size reduction.

The largest low-risk cluster was situated in the southern municipalities, while a smaller low-risk cluster was concentrated in the northeast. No clusters were identified in the Lisboa region during the study period. Geographic disparities remained when data were analyzed by categories of age (Figure S1), with the ASHR variability higher in the older age categories (ranging between 1281.4 and 4886.4 cases per 100,000 inhabitants). The adults had ASHR values ranging from 99.5 to 571.1 cases per 100,000 inhabitants, while the youth had values between 26.2 and 997.6. In terms of the LISA, when compared to the other two age groups (adults and the elderly), the youth had a slightly different pattern, with higher clusters in the eastern area of the country and lower clusters of cases on the coast over the four years. More detailed information about the values per year ASHR and the Moran index can be found in Supplementary Tables S2 and S3.

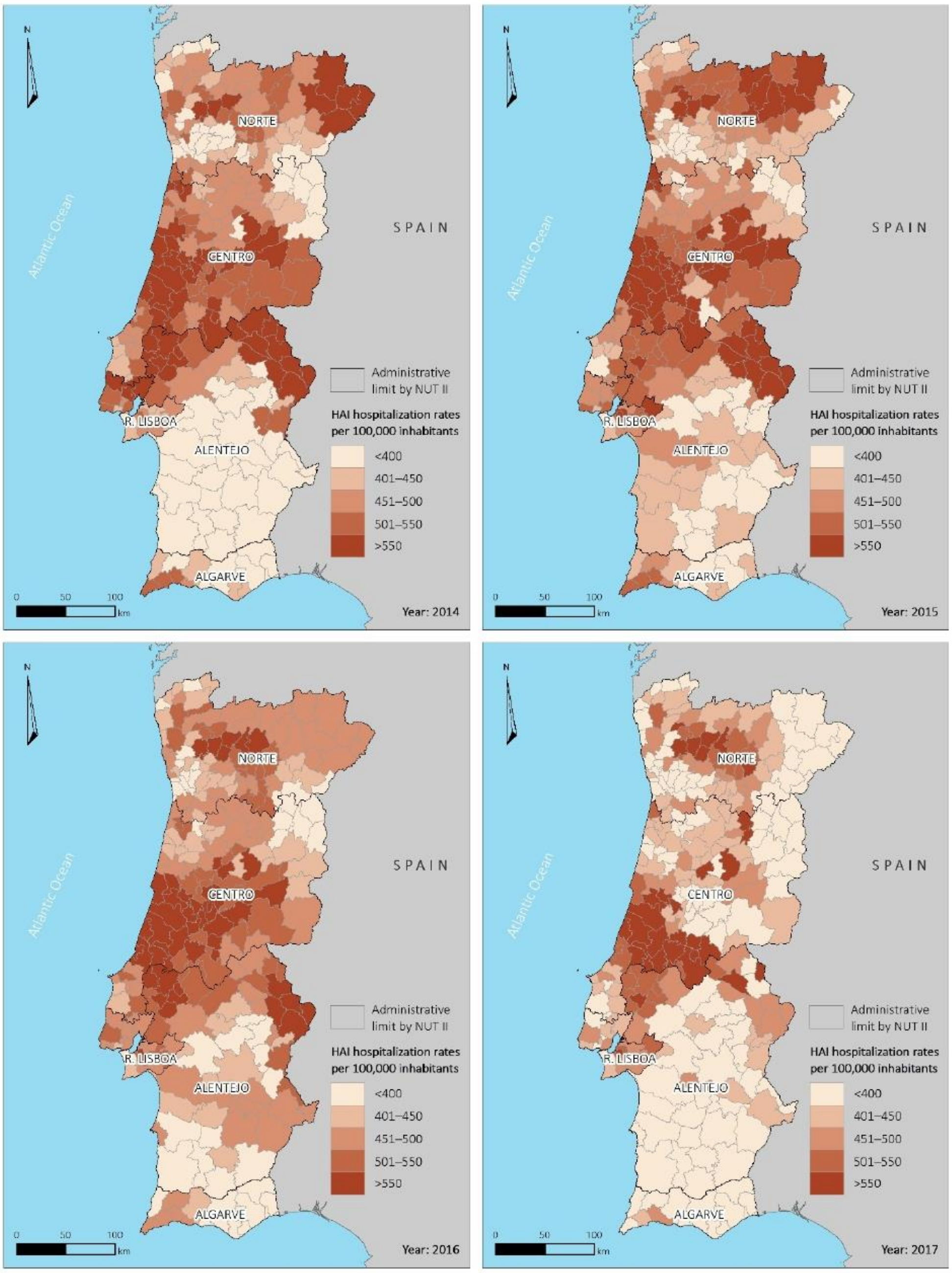

Figure 2. Spatial distribution of age-standardized HAI hospitalization rates per 100,000 inhabitants, per municipality, for the period 2014–2017.

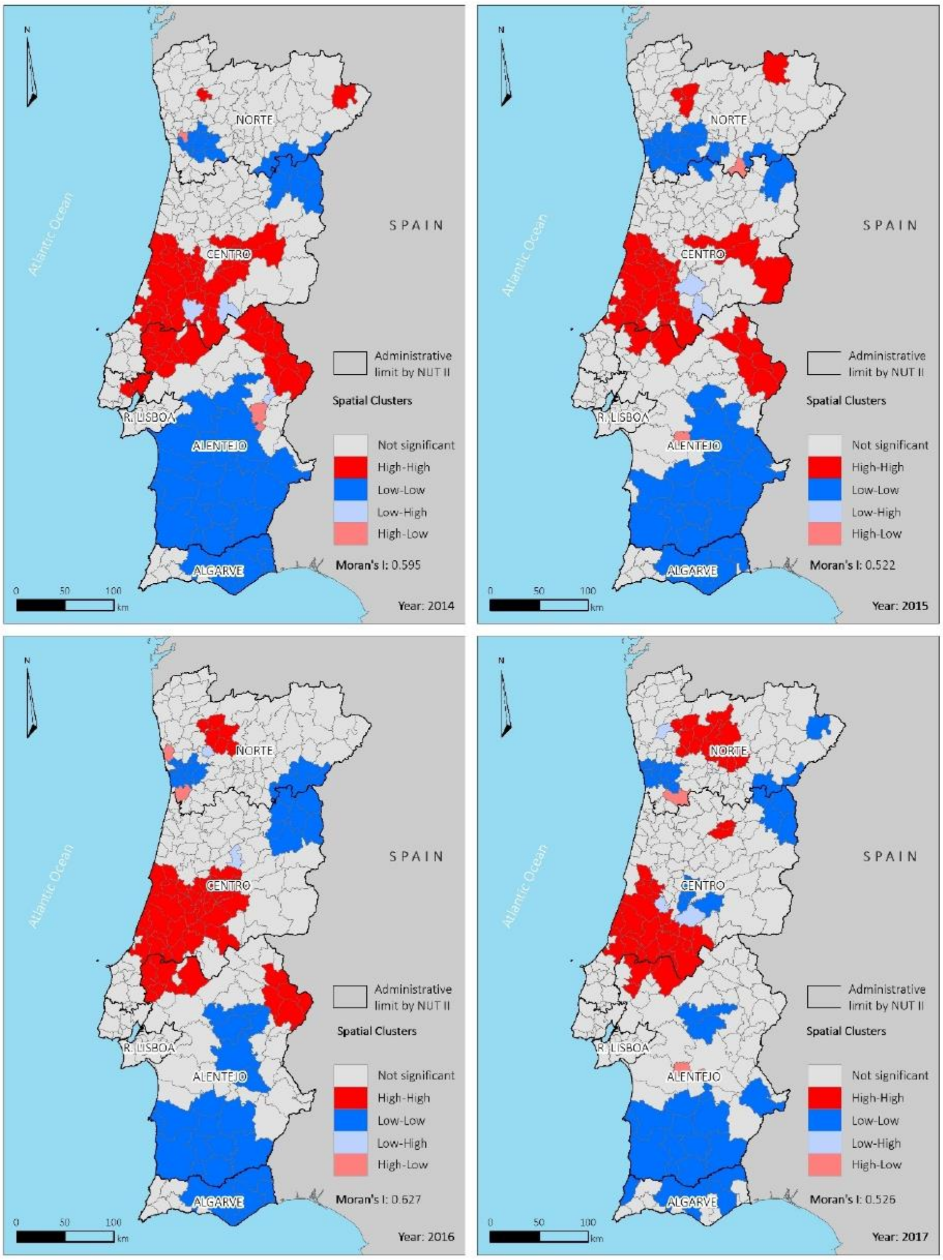

Figure 3. The spatial clusters of ASHR by municipality for the period 2014–2017.

4. Discussion

To the best of our knowledge, this is the first nationwide population-based ecological descriptive study of HAIs for all age groups in mainland Portugal and in Europe. This retrospective four-year study analyzes hospital admission episodes of patients who acquired a nosocomial infection, based on data collected from a national hospital discharge register gathering information from public hospitals. The geographic distribution, the incidence, and the characteristics of hospitalized patients are described for the first time. Our findings show that the incidence of HAI is not randomly distributed in space; there are strong inequalities, with high-risk clusters remaining in the central region throughout all the study periods.

As expected, the older age category was the most vulnerable, with the results showing a higher incidence of HAIs in patients 65 years of age or older. Findings in previous studies [18,19,56] have shown that people in this age group with infection have increased morbidity and mortality than younger individuals.

The average HAI incidence by year for all age categories fluctuated between 9.0% and 9.4% during the study period, which is in line with previously published findings for developed countries [1,23,57]. The year 2015 was the worst compared with the others within the study period, registering the highest number of cases, while the year 2017 registered the lowest number of cases. The improvement during the study period could be explained by the implementation of several plans and guidelines in the Portuguese public hospitals, such as the "STOP infeção hospitalar" (STOP hospital infection) project, promoting basic infection control precautions, and improvement of epidemiological surveillance [25], reflecting the results over a more extended period.

The observed median length of stay in this study for the individuals within the older age categories was 10.0 days. According to some studies, acquiring HAI implies an average increase of 5 (18) days within the hospitalization period [58–61], meaning that if patients had not acquired the infection, they would spend fewer days in the hospital.

An observation of the average hospitalization length of stay (Figure 4) for the four years, spatially distributed, shows some territorial randomization of this variable for values up to 13 days. However, we can observe some patterns of spatial distribution for lengths of stay >14 days, with more significant persistence in the southern part of the country, namely in the Algarve region, where high values are persistent over the four years, as well as in some municipalities in northern Alentejo (Portalegre district) and in some municipalities in the coastal area, located north of Lisboa. Empirically, higher values of the ageing index or longevity index could justify a longer duration of hospitalizations in the northern Alentejo area, also admitting a more remarkable number of comorbidities, but this justification is not valid for the Algarve and the coastal area north of Lisboa. It would be helpful in the future to investigate this variable broken down by hospital reference unit to check potential association patterns.

As expected, a higher CCI score was related to longer stays, possibly due to the length of time needed to evaluate and manage pre-release comorbidities and the longer time needed for recovery.

Nosocomial pneumonia was the most frequent adverse event among all HAIs, consistent with the findings reported by the Portuguese authorities [62]. Pneumonia is considered a severe problem associated with healthcare for in-patients of all ages, particularly for the youngest, who representing three quarters of the total HAI cases identified.

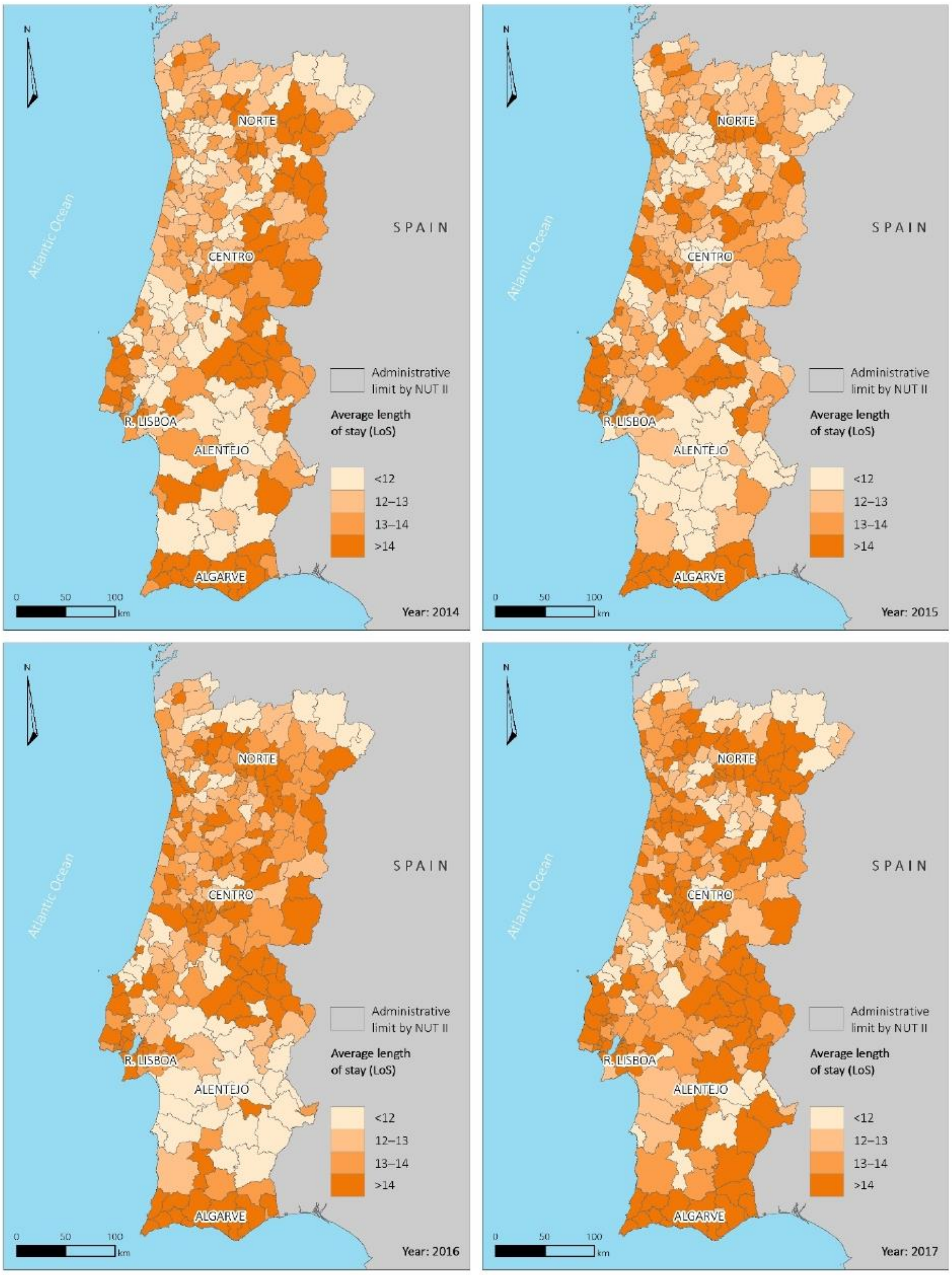

Figure 4. Spatial distribution of average length of stay of HAI hospitalization per municipality for the period 2014–2017.

This may be closely linked to the use of ventilators in neonates and children, as stated in some studies [63–65]. Older people also have high percentages of pneumonia acquired in the hospital context, but the reasons may differ from other age categories. Several studies [66–68] have shown that older people have more factors of weakness, including comorbidities and other associated pathologies, which decrease their immunity and make them more vulnerable. In addition, more prolonged hospitalizations due to HAIs can consequently increase antibiotic resistance and the presence of multidrug-resistant bacteria for all patients [69]. In addition to the specificity of the demographic, clinical, and physiological characterization (comorbidity index), in the case of hospital-acquired pneumonia, the literature warns of the importance of some risk factors that, in certain situations, could be present before hospitalization: prior antibiotic treatment (previous 30 days), structural lung disease, residence in assisted living facilities/nursing homes, long-term dialysis, diabetes mellitus and immunosuppression [26,70], gastrointestinal medication (suppression of gastric acid: use of antagonists H2), and proton pump inhibitors. In addition, the poor condition of the oral cavity is a risk factor to be taken into account. In Portugal in the last six years, the high consumption of antibiotics has been the subject of awareness campaigns organized by the health authority, intending to reduce their consumption and the associated resistance. The National Program for the Prevention and Control of Infections (2017) recognized that, despite the effort to reduce the consumption of these drugs, the global consumption of antibiotics at the primary health care level remains high (21.6 daily doses per thousand inhabitants), though it is below the European average (21.9) [24]. The risk factors identified above, some of which are common to other investigated HAIs—namely urinary tract infections—indicate that medication use before a hospital episode needs to be controlled when the patient is still in the community. This constitutes a less common approach; for the most part, control recommendations fall exclusively within the hospital context, with a strong emphasis on the aseptic issues associated with clinical procedures.

4.1. Spatial Asymmetries

The age-standardized HAI hospitalization rates were higher in the municipalities of the central region and a few municipalities of the northern region, with some clusters within the high-risk group.

Without more detailed studies to understand the causes of such geographical patterns, it can be challenging to try to justify these patterns. It is essential to point out that this perspective of analysis does not mean that the hospital infection occurred in that region; only the municipality of residence of the patient who had been infected in the hospital environment after admission was specified, which is why we calculated the ASHR for 1000 hospitalizations as well (Figure S2). When comparing both approaches, a similar ASHR pattern distribution is shown, but the spatial clusters are considerably smaller (Figure S3). However, this cluster analysis can provide relevant insights and suggest some of the factors that could be associated with these differences, specifically for the most elderly. This includes hospitalizations for chronic diseases that would initially be preventable [71,72], reducing the number of hospital infections (since they should not be hospitalized; patients would benefit from other types of outreach care, even in a home setting, including home hospitalization).

Furthermore, the quality of the population's access to primary healthcare and the optimization of the service performance could be determining factors [73–75] as it could prevent people being admitted to a hospital with greater vulnerability and a higher risk of susceptibility to infection. Another important factor is related to socio-economic and racial factors; there are already a few studies in which these factors have been found to be significant in association with patients who acquire an infection after an extended stay in hospital [76,77]. In a prospective investigation, it may be useful to cross-reference data on the consumption of antibiotics, disaggregated at the municipal scale, with the highest spatial incidence of HAIs, also controlling for the origin of the patients, specifically whether they come from their own dwelling or if they are residents in nursing homes, where the level of previous infections and antibiotic use is unknown. This approach could be beneficial for understanding the pattern of clusters found for the two main identified HAIs: nosocomial infection by pneumonia and nosocomial infection of the urinary tract.

In nosocomial pneumonia, we observed the existence of high and spatially consistent values over the entire period for a wide range of municipalities located in the central region and northern Alentejo. In the extreme north of Portugal during the study period, the number of municipalities with high values decreased in the last biennium 2016–2017 (Figure S4). Something similar occurred with nosocomial urinary tract infections. During the investigation period, three clusters with high values were identified, with special emphasis on a continuous territory between the central coast and the area north of Lisboa, in the western end of the Algarve, and a set of municipalities in the interior of the Alentejo near the border. From 2016 to 2017, a cluster of high values also emerged in the northern littoral region (Figure S5).

Despite the possible clues and limitations already presented, other studies point out other reasonable justifications that may contribute to understanding some patterns, such as the total number of hospital admissions and possible variances in applying the prevention protocols applied by the hospitals [78–82]. This descriptive article sought to determine whether the clusters are randomly distributed in space over the period under consideration. The scope was not to determine which variables could explain the results. For that purpose, a multivariate regression model is currently under development, which will allow for the adjustment of variables and an understanding of causality.

4.2. Limitations

There are some limitations to this study. Specifically, due to the nature of this research, caution must be applied when analyzing data and interpreting findings from secondary sources. These results were based on information from health records summarized by medical coders, which present the possibility of bias due to possible incompleteness or inaccuracies [83]. Nevertheless, ACSS conducts regular audits on this data to ensure accuracy and quality. Another major limitation concerns the impossibility of identifying the infection cases detected after discharge within 30 days.

Even though our study methods may be applied to other countries, we cannot be certain of the replication of our results due to differences in demographics, economics, and healthcare systems.

4.3. Implications and Future Work

Despite its limitations, this study presents several strengths and implications. First, unlike most studies, this one looked at several HAI contexts, providing a full picture of the country's spatial patterns of hospitalization rates, using data from patients of all ages. This result will be valuable to adjust measures and improve the action plan for the control and surveillance of nosocomial infections. Furthermore, many of the leading causes of hospitalization in Portuguese patients (e.g., diabetes mellitus) are preventable [71], and a significant portion of the population has inefficient access to primary health care. The existence of a high-risk cluster, stable in the central region of Portugal for all HAIs investigated, may be associated with an unsuitable profile of consumption of antibiotics or with a higher prevalence of patients hospitalized in nursing houses; such an evaluation is not allowed by a descriptive ecological study. Despite the efforts of the Portuguese national health system to enhance quality, inequalities in the distribution of primary care facilities remains an important issue. Many regions have low coverage of family doctors, resulting in real barriers to access and longer wait times for assistance. Official data show that Portugal has had some difficulty allocating health providers to the most rural areas [84]. As a result, improving primary health care is likely to reduce hospital admissions. Providing the necessary assistance in the development of new public health policies may be supported by targeting specific measures for the high cluster territories. Consequently, this could lead to a reduction in the pressure on hospitals, as well as a decrease in associated costs, prolonged stays, deaths, and existing morbidity [78].

Subsequent studies are warranted to understand the reasons that could be associated with these numbers and asymmetries or to explore the possibility of a hospital-related analysis within influence areas with a higher number of cases. It can be helpful to see if they have a higher burden compared to the others. Finally, developing a platform with this information to allow consultation for the regional health delegations might also benefit the country.

5. Conclusions

This study described the incidence of HAIs in mainland Portugal for a quadrennium. A reduction in incidence was observed between 2015 and 2017, and the most representative adverse event recorded was nosocomial pneumonia, with the elderly being the most affected. Specific regions within the country recorded higher incidences, such as the center and north, and possible justifications, such as asymmetries in access to primary health care, were discussed. As an emerging issue, it is important to promote further research, including the reorganization of healthcare systems and their guidance, the improvement of diagnosis, and the effective management of procedures.

The role of the HAI control committees within the clinical context is essential for educating health care providers, and the quality of health care must be ensured by evaluating indicators and endorsing investments with cost-effective allocation of resources. As a result, these findings can help to warn analysts in surveillance systems, leading to well-informed decisions.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ijerph18094703/s1, Table S1: Description of the original database variables. Table S2. ASHR values (min, max, mean) per 100,000 inhabitants. Table S3. Moran index values. Figure S1: Spatial distribution of ASHR of HAI per 100,000 inhabitants, per municipality, for the period 2014–2017, by age group; A—Youth, B—Adults, C—Elderly; Figure S2: Spatial distribution of ASHR of HAI per 1000 admissions, per municipality, for the period 2014–2017; Figure S3: Spatial clusters of ASHR of HAI per 1000 admissions by municipalities for the period 2014–2017. Figure S4: Spatial clusters of nosocomial pneumonia for the period 2014–2017; Figure S5: Spatial clusters of nosocomial urinary tract infections for the period 2014–2017.

Author Contributions: H.T., A.F., A.S., H.G. and M.d.F.P. contributed to the study conception and design. Material preparation, data collection and analysis were performed by H.T., A.F., H.G., M.d.F.P., H.T. wrote the first draft of the manuscript and all authors commented on subsequent versions of the manuscript. H.T. and M.d.F.P. were responsible for processing the data in the SIG software for the maps. H.T., A.F. and H.G. were responsible for statistical analysis. H.T., A.S., P.N. and M.d.F.P. contributed to the discussion section (spatial patterns analysis). All authors have read and agreed to the published version of the manuscript. The authors are responsible for the correctness of the statements provided in the manuscript.

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Supplementary material

Variable	Description
ID	Episode identification number
Year	Civil Year, considering the discharge date.
SEX	User gender 1 – Male 2 - Female
Age	Age of the user, in years, at the date of entry.
District	User district of residence.
Municipality	User municipality of residence.
Parish	User parish of residence.
Date of admission	Date of admission of the user to the health institution.
Discharge date	User discharge date of from the health institution.
Length of stay	Total number of days spent in the health facility by the user, according to the statistical definition of length of stay.
Destination after discharge	Destination code of the user after discharge from a hospital service: 1 - For the home 2 - To another institution with internment 6 - Home service 7 - Exit against medical opinion 13 - Specialized aftercare (tertiary) (collected from 2011) 20 - Deceased 51 - Palliative care - medical center (collected from 2011) 61 - Post-hospital care (CMS 19-22, AP21) (collected from 2011) 63 - Long-term hospital care (CMS 19-22, AP 21) (collected from 2011)
Admission Type	Nature or method of admission of a user to a health establishment: 1 - Scheduled 2 - Urgent 3 - Others
Type of episode	Type of episode: AMB - Indicates if the episode was performed on the Ambulatory production line INT- Indicates if the episode was performed on the production line
ICD version	Coding version (ICD)
ddx1	ICD-9-CM or ICD-10 code, which identifies the Main Diagnosis of the episode - the one that is considered responsible for the patient's admission to the hospital.
ddx2...ddx30	ICD-9-CM or ICD-10 Additional Diagnostics code for the episode (up to a maximum of 30).
causad1	Code of ICD-9-CM or ICD-10 of External Cause 1 that took the user to the health institution.
causad2...causad30	Additional ICD-9-CM or ICD-10 Cause Code that took the user to the health institution.
SSI	Context of hospital infection "Surgical Site" 0 - Absent 1 - Present
Clostridium_difficile	Context of hospital infection for "clostridium difficile" 0 - Absent 1 - Present
pneumonia	Context of nosocomial infection "Pneumonia" 0 - Absent 1 - Present
trato_urinario_cateter	Context of nosocomial infection "Urinary tract infection associated with the use of a catheter."

	0 - Absent 1 - Present
corr_sang_cateter	Context of nosocomial infection "Bloodstream infections related to central venous catheter" 0 - Absent 1 - Present
Charlson_indexOri	Charlson's comorbidity index (CCI) score 0 (Min) - 33 (Max)
HospID_NUTSII	Identification of the location of the health institution (NUT II) NORTH CENTER LISBON REGION ALENTEJO ALGARVE

Table S1: Description of the original database variables.

Year	All	Youth	Adults	Elderly
2014	Min = 256.0 Max = 846.7 x = 480.5	Min = 29.4 Max = 827.2 x = 268.6	Min = 147.3 Max = 571.1 x = 229.1	Min = 1269.9 Max = 4279.9 x = 2380.4
2015	Min = 306.3 Max = 1109.2 x = 490.8	Min = 46.6 Max = 997.6 x = 262.8	Min = 123.5 Max = 539.6 x = 223.9	Min = 1281.4 Max = 4886.4 x = 2511.29
2016	Min = 280.2 Max =8 21.3 x = 483.5	Min = 70.6 Max = 795.0 x = 242.4	Min = 99.5 Max = 446.8 x = 237.2	Min = 1323.3 Max = 5159.9 x = 2449.7
2017	Min = 270.0 Max = 879.3 x = 435.5	Min=26.2 Max=495.2 x = 208.6	Min = 119.6 Max = 346.1 x = 202.3	Min = 986.4 Max = 6230.0 x = 2301.5

Table S2. ASHR values (min, max, mean) per 100,000 inhabitants.

Year	All	Youth	Adults	Elderly
2014	0.595	0.594	0.439	0.561
2015	0.522	0.648	0.351	0.561
2016	0.627	0.642	0.480	0.538
2017	0.526	0.550	0.488	0.519

Table S3. Moran index values.

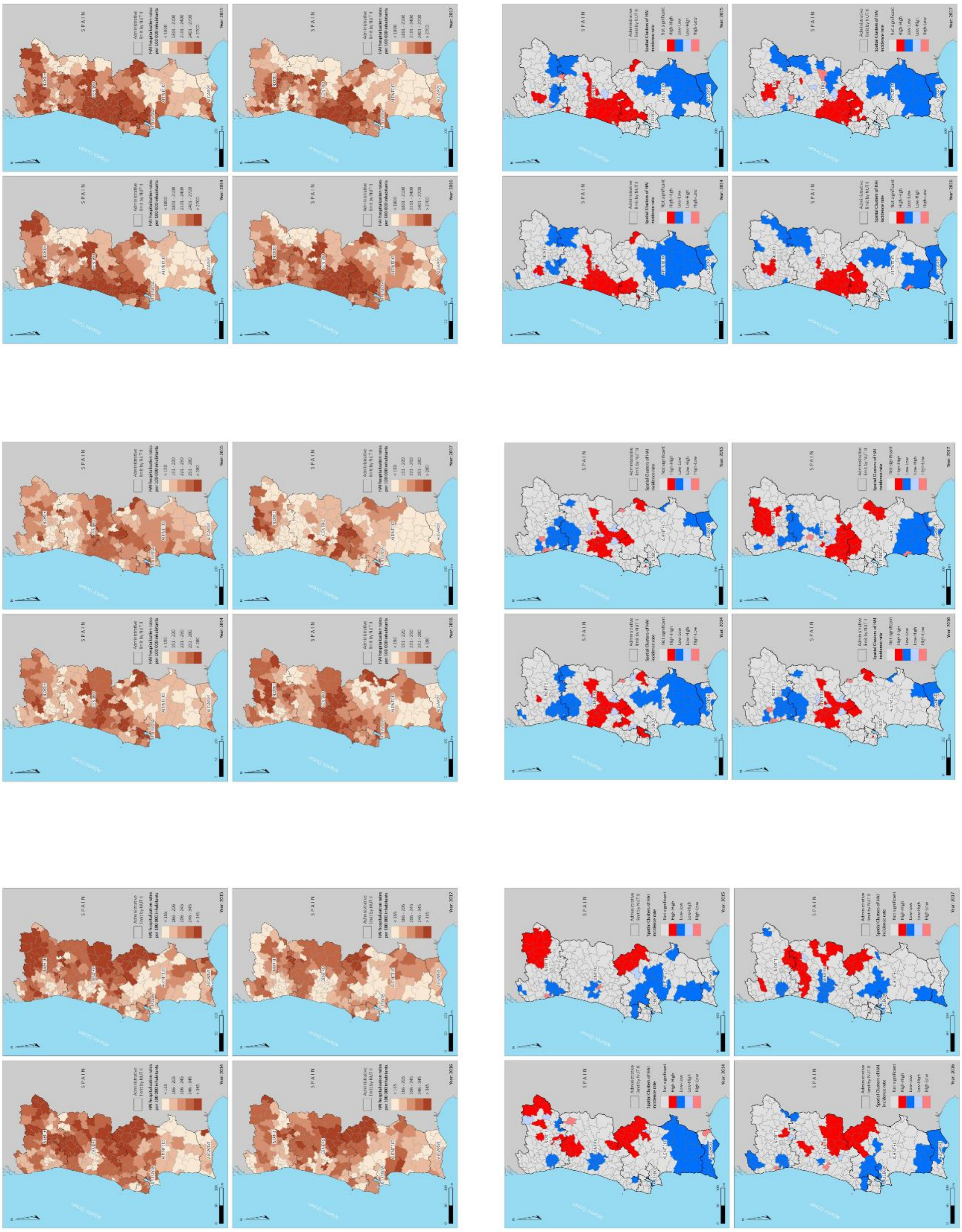

Figure S1. Spatial distribution of ASHR of HAI per 100,000 inhabitants, per municipality, for the period 2014–2017, by age group; A—Youth, B—Adults, C—Elderly.

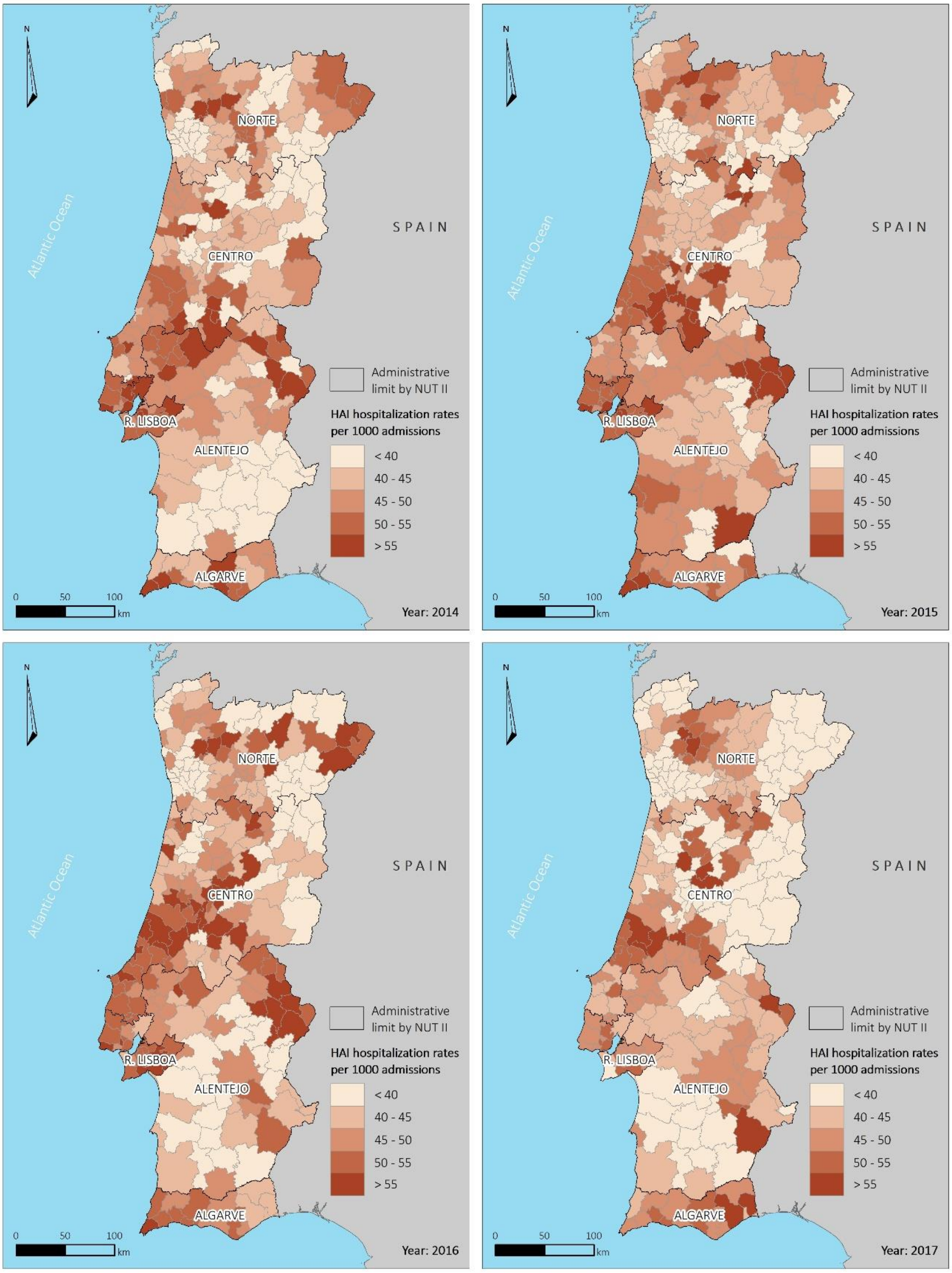

Figure S2. Spatial distribution of ASHR of HAI per 1000 admissions, per municipality, for the period 2014–2017.

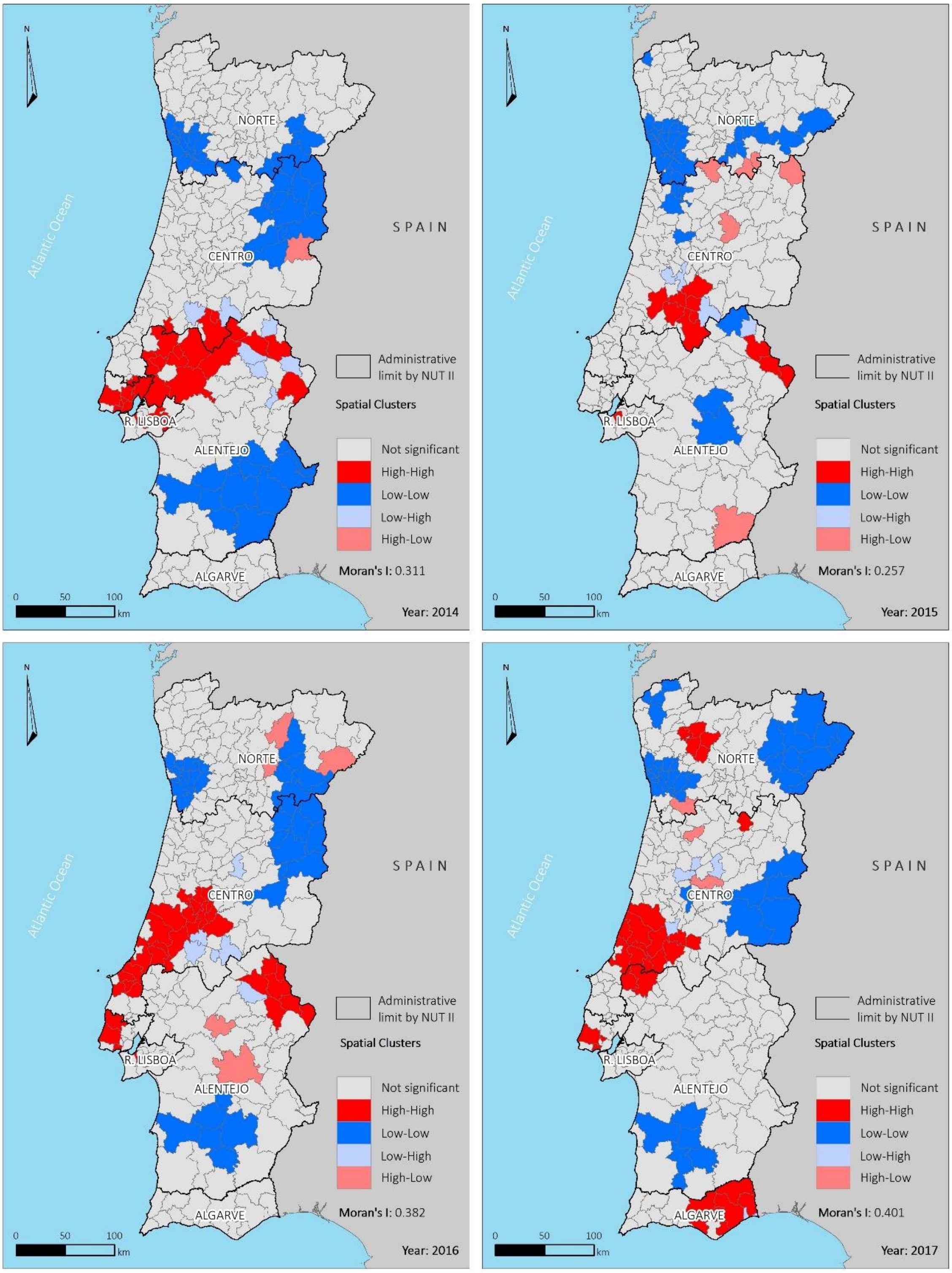

Figure S3. Spatial clusters of ASHR of HAI per 1000 admissions by municipalities for the period 2014–2017.

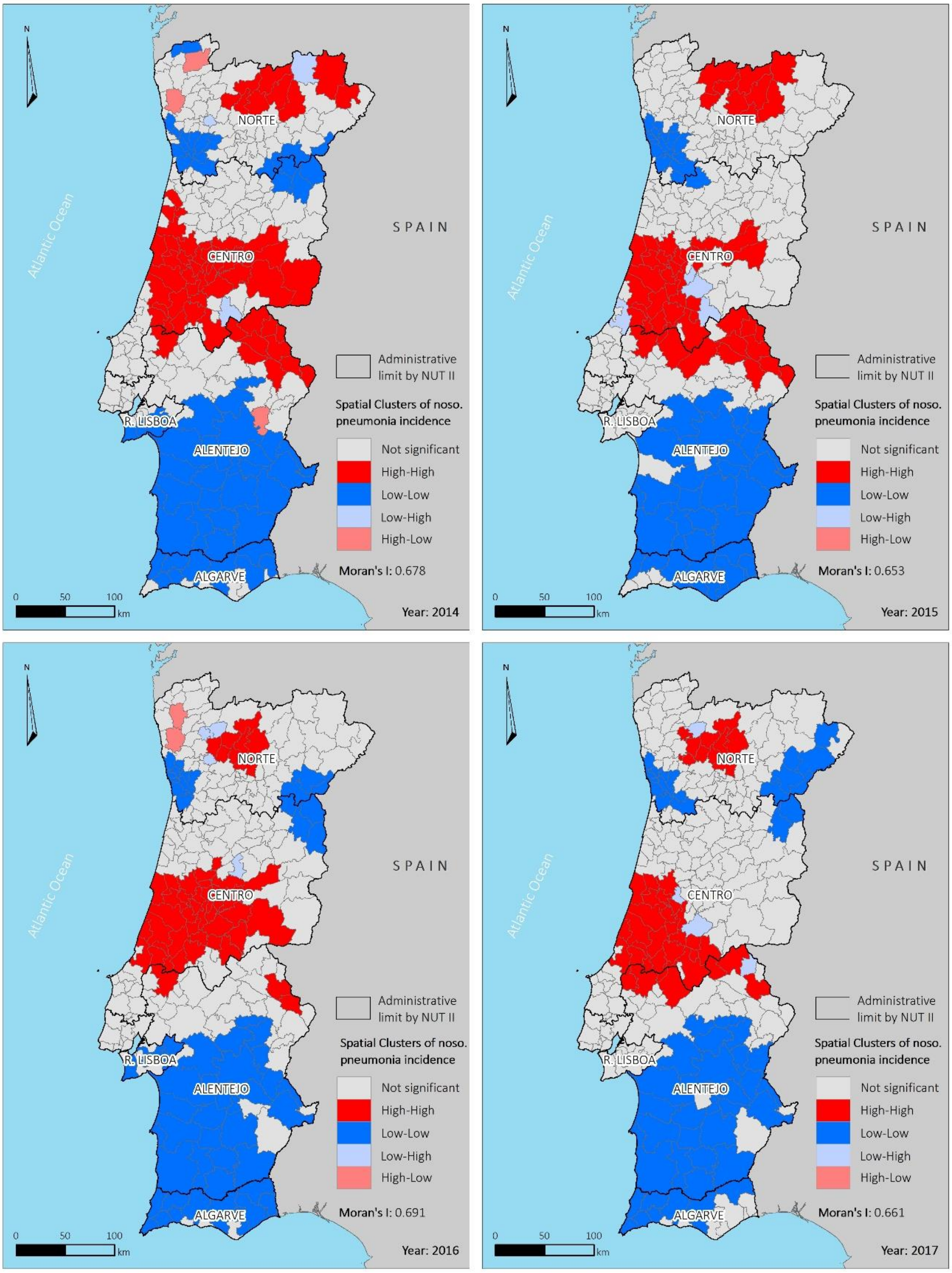

Figure S4. Spatial clusters of nosocomial pneumonia for the period 2014–2017.

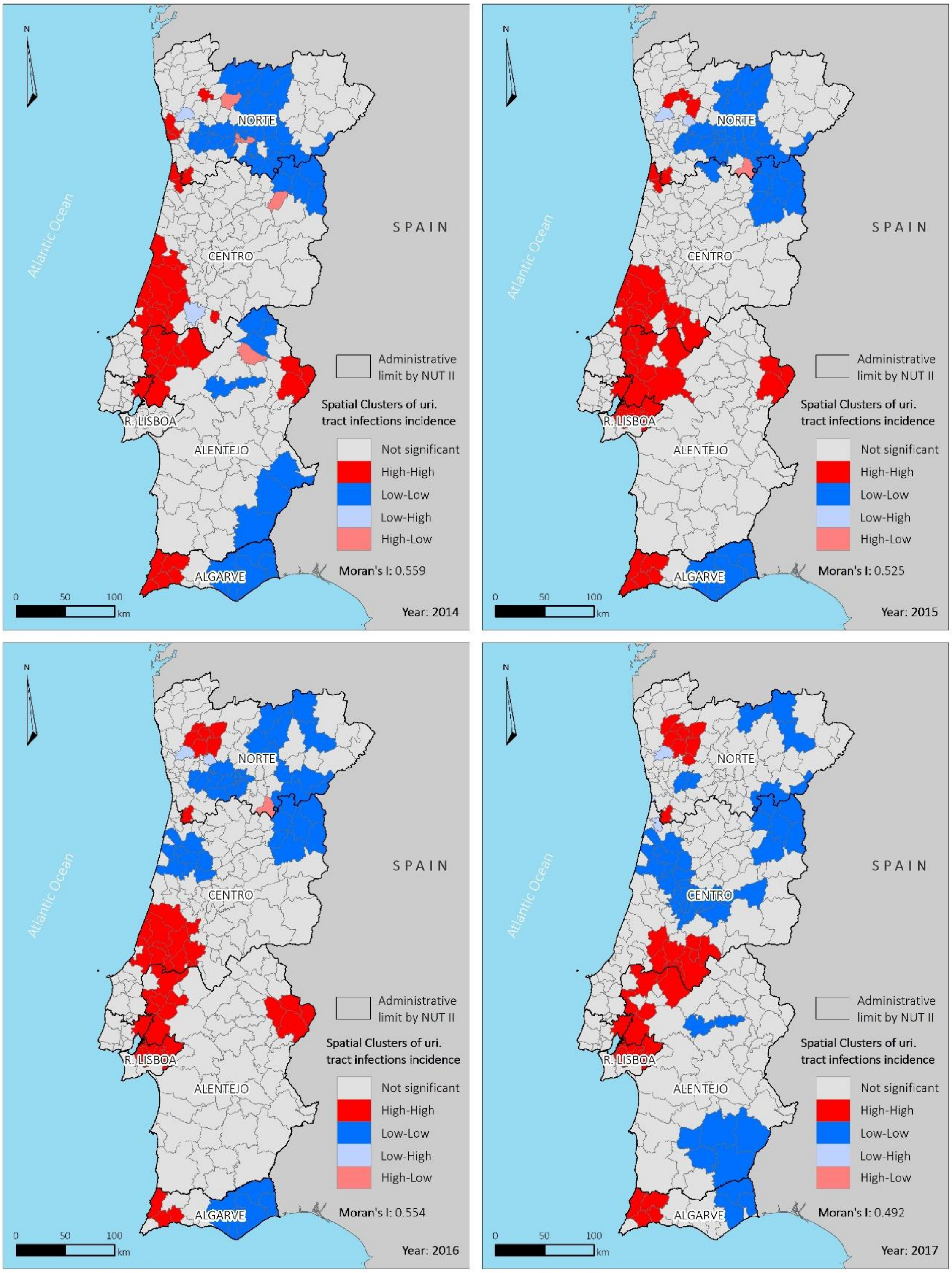

Figure S5. Spatial clusters of nosocomial urinary tract infections for the period 2014–2017.

4. Development of a 3D GIS-based model of a hospital indoor space

Teixeira, H.; Norton, P.; Gonçalves, H.; Pina, M.d.F.; to support spatiotemporal analysis of events: application to COVID-19 cases among healthcare workers (submitted).

Development of an indoor Geographical Information System for space-time analysis of COVID-19 among hospital workers

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Abstract:

Since the start of the coronavirus 2019 pandemic, healthcare workers have been the most exposed group, and their safety and health are vital for controlling any outbreak and providing continuous safe patient care. New applications of GIS in health science have emerged, presenting the opportunity to explore dynamics or patterns that occur within a building. The aim of this study was to develop a spatial model in GIS for the indoor spaces of the largest hospital in the northern region of Portugal, and to illustrate its applicability to analyzing COVID-19 cases among healthcare workers. The model implementation comprised the digital computer-aided design (CAD) floor maps that generate topological maps. A field survey was carried out to categorize and validate each hospital space. A geodatabase was constructed, defining the structure and relations of different tables, avoiding redundancy and inconsistency. COVID-19 cases among health practitioners were provided by the occupational health department of the hospital and georeferenced using the model as a base map. The GIS model was built and implemented, with a total of 12 floors and 4613 areas mapped. The pedestrian access was modelled, taking into consideration essential elements such as the corridors, doors, lifts, and stairs. A total of 871 cases among the health workers with positive COVID-19 were registered. Spatiotemporal analysis has identified several clusters among the different hospital services. This approach can uncover previously hidden factors, enabling policymakers and health practitioners to have more information to support decisions. Besides, it demonstrates general trends and raises awareness of the need to produce scientific knowledge, which can contribute to developing a wide-ranging plan to assess resource allocation or monitoring and planning interventional measures.

Keywords: Indoor GIS, Three-dimension model, Hospital, Covid-19, Spatiotemporal analysis

1. Introduction:

Since March 2020, when the World Health Organization (WHO) declared the pandemic of the COVID-19 disease, caused by the novel coronavirus SARS-COV-2 [1], which has afflicted the world for more than two years, has posed unprecedented challenges to healthcare systems [2]. The first confirmed case of COVID-19 in Portugal was reported on March 2, 2020, in a 60-year-old man who was admitted to the São João University Hospital on February 26, the date on which the patient reported the first symptoms [3].

The increased risk of infection to frontline healthcare workers when compared to other infectious diseases is of particular concern [4]. Despite that fact, healthcare professionals have always demonstrated an extraordinary dedication to patients, even though the apprehension related to the possibility of infection [5,6]. However, this places extra demands on healthcare systems for personal protective equipment and infection prevention and control measures, some of which are already overburdened dealing with such settings [7]. The spread of SARS-CoV-2 infections among healthcare workers is critical issue since they lead to shortages of human resources due to isolation and treatment periods, quarantining of contacts, hospitalization, mortality, and the prolonged period of COVID-19 [8]. Combining the established measures to protect workers (such as the wearing of masks), together with the possibility of understanding how the disease behaves in space, could make it more effective to prevent an increase in COVID-19 cases since preventing new cases of hospital-based infection is a critical part of the healthcare system's work.

Understanding the spatial dynamics of COVID-19 spread among hospital workers, by location of work, may provide useful insights for the occupational health department and trigger a package of more-targeted infection control measures [9]. Several studies have also been conducted to investigate the surveillance of infectious diseases or to predict new hypotheses related to the spatiotemporal distribution of infection vectors [10,11].

The influence of information technology (IT) has touched almost all aspects of our lives, and the health care sector has been no exception [12]. When shared with scientific knowledge, Geographical Information Systems (GIS) can be used as a supportive answer to this issue, in the decision-making process [13,14], in the reduction of operational costs and in the improvement of efficiency [15]. Geographical Information Systems have been widely used in health-related sciences over the last few decades [16], to map diseases and analyze their relationships with environmental and socioeconomic factors [17-19], to conduct infectious disease surveillance studies [20], and to predict new hypotheses related to the spatiotemporal distribution of infection vectors using cluster analysis [21], among other studies. Defined as a decision support system, GIS is designed to integrate and manipulate a widespread variety of data (spatial and alphanumeric) and consequently its visualization and analysis in a multi-scale perspective [22-24]. Its role in health-related sciences is growing since it joins sophisticated procedures and the use of geoinformation to provide different techniques of spatial analysis [25-27]. Most of GIS applications in health studies have been used to assess external geographic spaces, such as neighborhoods, cities, or regions [28] to understand how people interact with their environment, or to create health prevention measures and policies [29-31]. Undeniably, the concept of space and its characterization is gaining interest, with several studies endorsing and focusing the exploration of dynamics or phenomena that occur in the indoor environments [32-34]. Therefore, using GIS technologies to indoor spaces might be a challenging and exciting task, due the existence of a wide variety of complex infrastructures such as hospitals or health units, for example, with a high circulation of persons per day [35]. However, few studies considering the use of GIS to georeference and study health events within buildings have been carried out [36-39].

This study aims to develop and implement a GIS to map the indoor spaces of the largest hospital in the north region of Portugal (São João University Hospital), and georeference the COVID-19 cases among the healthcare workers to identify spatial clusters of the disease, in the hospital environment. As a secondary goal, the developed model can be the starting point for other epidemiological studies.

2. Methods

This section discusses the study area description, the construction and implementation of the indoor space model, the circulation network, and the covid-19 data that was used.

Study area

Inaugurated on June, 24th of 1959, the São João University Hospital is placed on the northwest of mainland Portugal (Fig. 1), in the Porto city, being the second largest hospital in the country. This hospital provides direct assistance to the population of Porto, and surround municipalities (around 450 000 inhabitants) and it works as a reference for the entire north region.

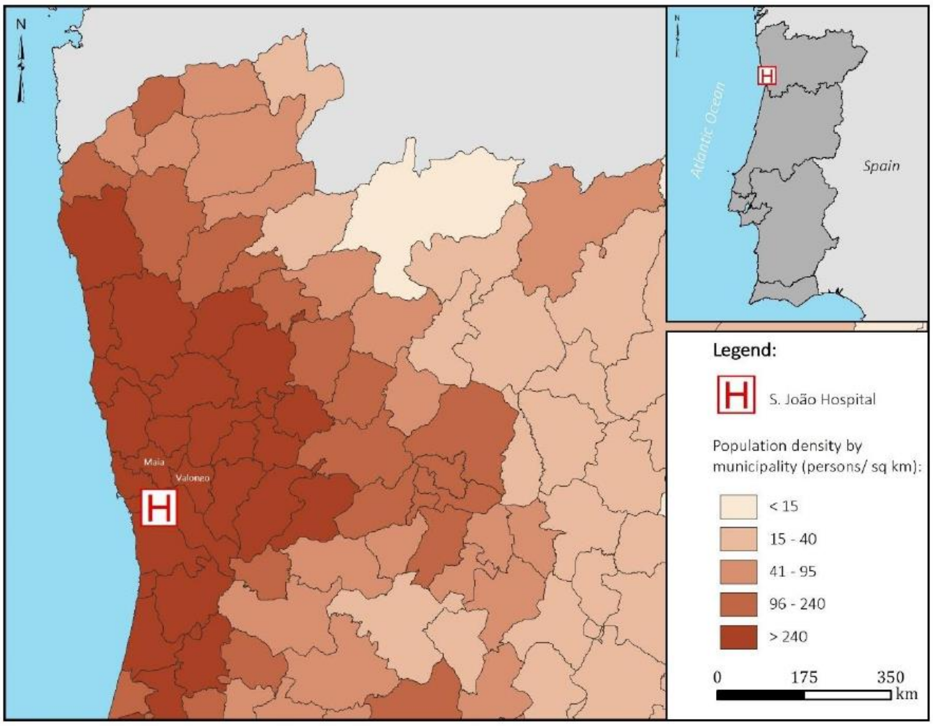


Fig. 1 Hospital location in mainland Portugal. The map was created using ArcGIS 10.5.1 software. The cartographic data was retrieved from Direção-Geral do Território (DGT), and the population density data was obtained from National Statistical Institute of Portugal (INE).

According to Meyers [40] definition, we can consider this hospital as a complex building, given the high number of people that work there (around 7000), and with an official capacity of 1200 beds and 45 cots, with a total area of 126 842 m2 divided into 4 613 spaces, and a total of 59 services (medical and non-medical), which are then distributed over a total of 12 floors. In addition, on average, 15 000 people circulate per day within the hospital, including health professionals, technicians, suppliers, patients, or visitors. This type of complexity represents a considerable management challenge for researchers, as, in such a confined space, more people and goods interact than in some cities in the country. The optimal management of such structures is a critical aspect of dealing with dynamic settings, contributing to proper surveillance.

Data and Materials

Base Maps: Digital computer-aided design (CAD) drawings by floor, provided by the engineering department of the hospital, were used as base to generate topological vector maps for each floor, to be used in the GIS. The *topology* describes how the geographical features are spatially related to each other through a set of relational tables stored in a geodatabase [41], allowing the development of spatial analysis. For being frequently the first step in the spatial data analysis process, the database georeferencing procedure (converting a location description – for instance, an address – to a position on the earth's surface [42]) was made based on a topographic survey from the year of 2013, using a specific projected coordinate system (Datum 73, Lisbon).

Health data: From the occupational health department database, we selected the positive cases of COVID-19 among healthcare practitioners between March 1st, 2020, and February 28th, 2021. We georeferenced each case in the services where the workers are located. Figure 2 depicts the cumulative COVID-19 case counts by month over the course of a one-year pandemic. As a result, 874 cases of COVID-19 were detected among healthcare practitioners, with November recording the highest number, coinciding with the second wave of infection.

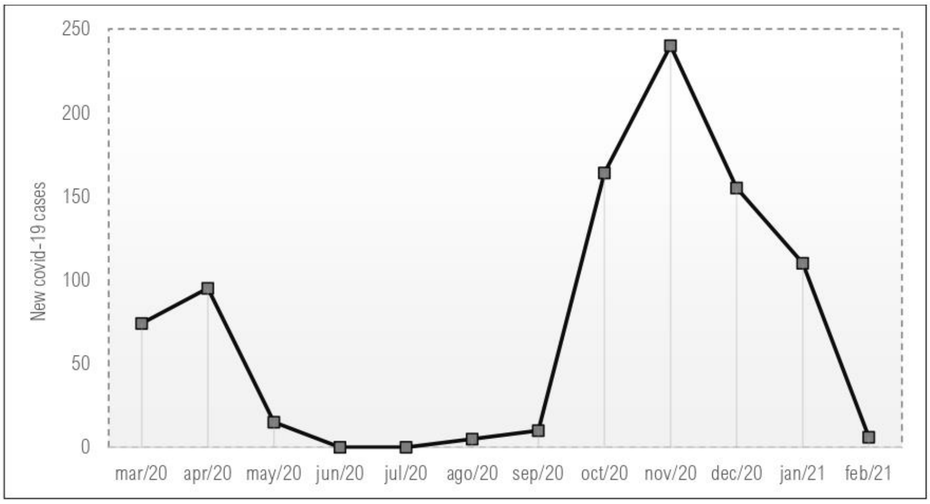


Fig. 2 Monthly number of COVID-19 cases among health professionals of São João University Hospital between March 2020 and February 2021.

Conceptual modeling of the hospital infrastructure

To model the internal structure of the buildings in a geodatabase, we represented the relationships between the several entities in an entity relationship diagram (ERD) [43]. The ERD diagram (Fig. 3) was essential to understanding how the hospital is managed, organized, and structured. It was developed after meetings with the hospital staff.

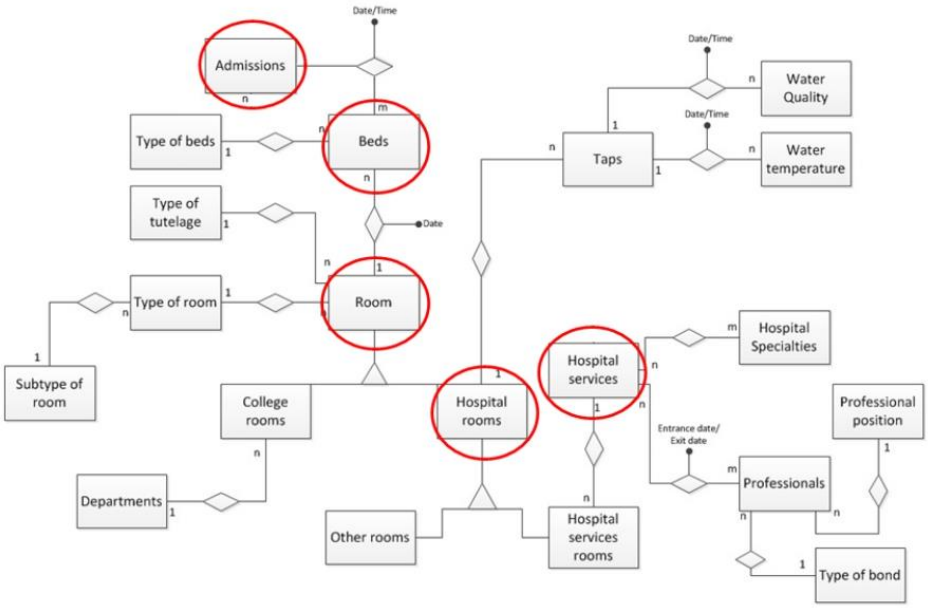


Fig. 3 Conceptual model of the hospital spatial database.

Figure 4 shows all the steps in the process of the development of the hospital geodatabase. A field survey was conducted by one of the authors (HT) together with the team from the occupational health department to identify and categorize all spaces represented in the CAD draws on each floor of the hospital, including wards, rooms, bathrooms, corridors, lunchrooms, technical areas, lifts, doors, and beds (Fig. 4 A). Paper plants were also consulted whenever necessary to complement all the procedures.

Selected features from CAD files were loaded into the GIS database, converted to GIS format, and edited to remove geometric errors (such as undershoot or overshoot and open polygons) to generate the topology (Fig. 4 B). After that, we assigned geocodes for each space and alphanumeric information such as: name and typology of the space, medical service, department, etc., to each room (Fig. 4 C). The location of beds, doors, corridors, and lifts were collected in the field survey and, georeferenced in the spatial database (Fig. 4 D).

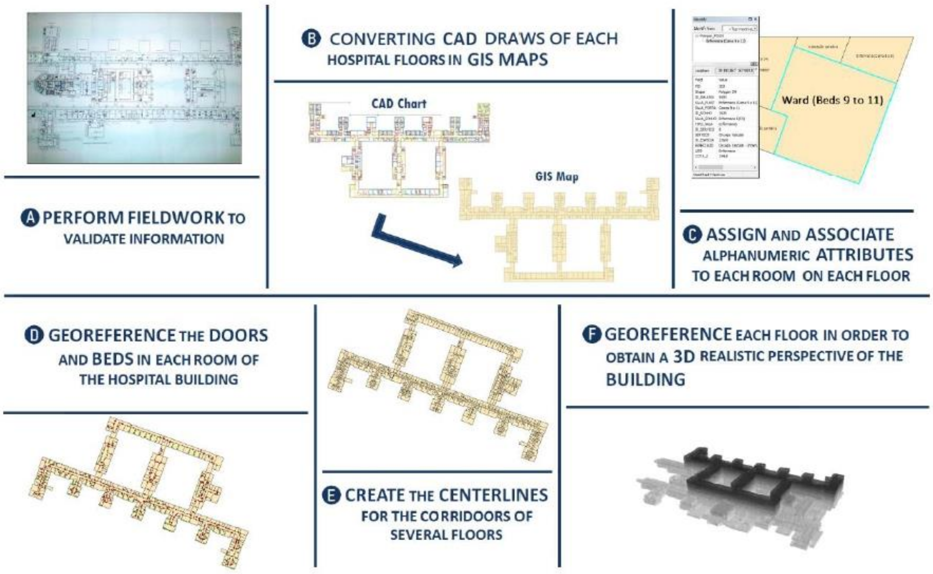


Fig. 4 The schematic process adopted in the construction of the spatial database model.

The circulation network was created by connecting the centerlines of the corridors with doors, stairs, and lifts (Fig. 4 E). This process includes functionalities such as geo-coding or route optimization [44,45]. Route optimization is a technique in which the most economical (fastest, shortest, or another) route is determined according to the chosen impedance. If the impedance is time, the best route is the fastest route. However, if the impedance is another attribute, such as the lowest cost, the best route will be determined accordingly [46]. Any cost attribute can be used as an impedance when determining the best route.

Lastly, we georeferenced the map of floor 1 using an existing topographic survey from 2013, with the geodesic system composed by cartographic projection Gauss-Kruger, Datum 73/Lisbon, and the International Ellipsoid of Hayford (1924). All the other floors maps were georeferenced in relation to the floor 1. The height information of each floor was included to build the three-dimensional representation of the building (Fig. 4 F).

In the end, the floor maps (e.g., walls and columns) were extruded according to their height values to obtain the model, where the z-axis is normally used to portray the temporal aspect [47]. These structures were added in the 3D view for geometric representation, but not for path calculation.

Statistical analysis

To calculate the incidence rate by hospital department, we selected the number of positive SARS-CoV-2 cases and divided them by the total number of people who worked there during the studied period.

To identify space-time clusters that occurred between the medical services areas during the study period (1st March 2020 to 28th February 2021), we utilized the retrospective version of the Poisson space-time scan statistic [48] and implemented it in SaTScan™ [49]. In other words, we identified COVID-19 space-time clusters and "disregard" clusters during the study period that do not have a statistically significant ($p < 0.05$) excess relative risk (RR). Table 1 shows the input parameters used in our analysis, with the assumption that the COVID-19 cases follow a Poisson distribution according to the at-risk population.

Parameters used in the retrospective analysis	
Probability model	Discrete Poisson
Scan for areas	High or Low rates
Type of analysis	Purely spatial
Spatial window shape	Circular
Maximum temporal cluster size	50% of the study period
Minimum temporal cluster size	2 units
Study period	1 March 2020 to 28 February 2021

Table 1. Parameter setup for the retrospective Poisson space-time scan statistic.

The null hypothesis H_0 asserts that the model represents a constant risk with a proportional intensity to the at-risk population. The alternative hypothesis H_A indicates that the number of COVID-19 instances observed is more than the expected number of cases based on the null model (elevated risk within a cylinder). The expected number of COVID-19 cases (μ) under the null hypothesis H_0 is obtained as respects in Equation (1):

$$\mu = p^* \frac{C}{P} \tag{1}$$

with p the population in i; C the total COVID-19 cases among the health staff; and P the total estimated population that is working at the hospital. It's worth noting that the model assumes that the population of each hospital service remains constant over time, which is reasonable given the study period of one year.

Regarding the value of RR for each location service, it is obtained from the following equation (2):

$$RR = \frac{c/e}{(C-c)/(C-e)} \tag{2}$$

where c is the total number of COVID-19 cases in a service, and e is the total number of expected cases in a service, and C is the total number of observed cases in the entire hospital. RR is thus calculated by dividing the predicted risk within a location by the risk outside of the location. If a cluster has an RR of 2.5, for example, the workers inside the cluster are 2.5 times more likely to have COVID-19 than the workers outside the cluster.

3. Results

The three-dimensional GIS database of hospital building

The three-dimensional representation of the building (Fig. 5) is an expression regularly used to define the capability of making a virtual world, thus presenting people a sensation of reality in the imaginary world [50], where the temporal (variation in time), thematic (characteristics variation) and spatial (place alterations) elements can be included.

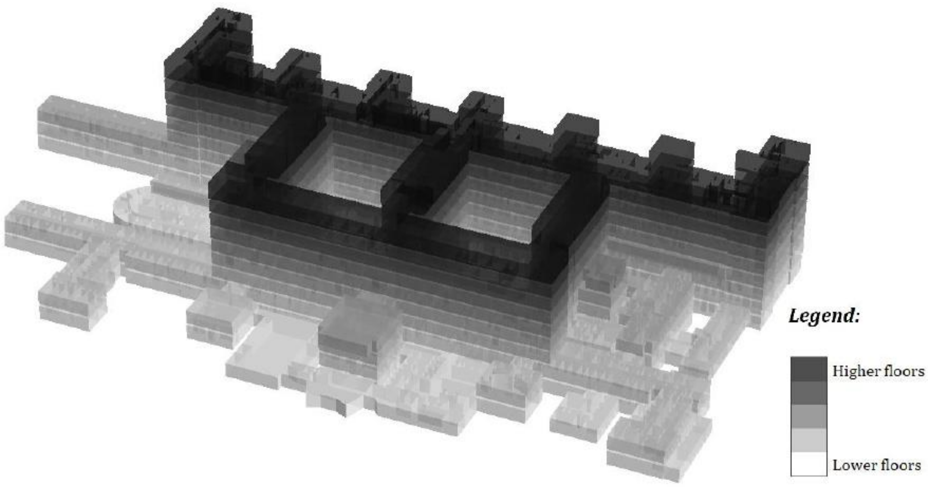


Fig. 5 The three-dimensional perspective of the São João University Hospital building.

The main building of São João University hospital has a total area of 126 842 m2 divided into 4 613 spaces, and a total of 59 services (medical and non-medical), which are then distributed for a total of 12 floors. The building presents a circulation network with an approximate length of 10 617m (Appendix 1). The structure also includes 4 805 georeferenced doors, 1 193 beds and 211 lift accesses. The hospital spaces were classified according to their uses (Table 2) and assigned to specific departments or services. Despite a hospital being a place of health, not all areas are clinical-related. Clinical areas are those that involve direct observation and treatment to the patient, such as, wards, medical offices, exam rooms, emergency rooms, surgical wards, post-surgery rooms and intensive care units.

Space typology	n	Space typology	n
Wards	344	Storage rooms and pharmacies	270
Medical offices	208	Eating areas	124
Surgery wards	42	Dirty/ Clean and waste rooms	194
Work and exams rooms	298	Non-clinical areas	913
Labs	63	Technical areas	245
Bathroom and locker rooms	757	Others	803
Faculty areas	352	TOTAL	4613

Table 2. Number of hospital spaces by typology.

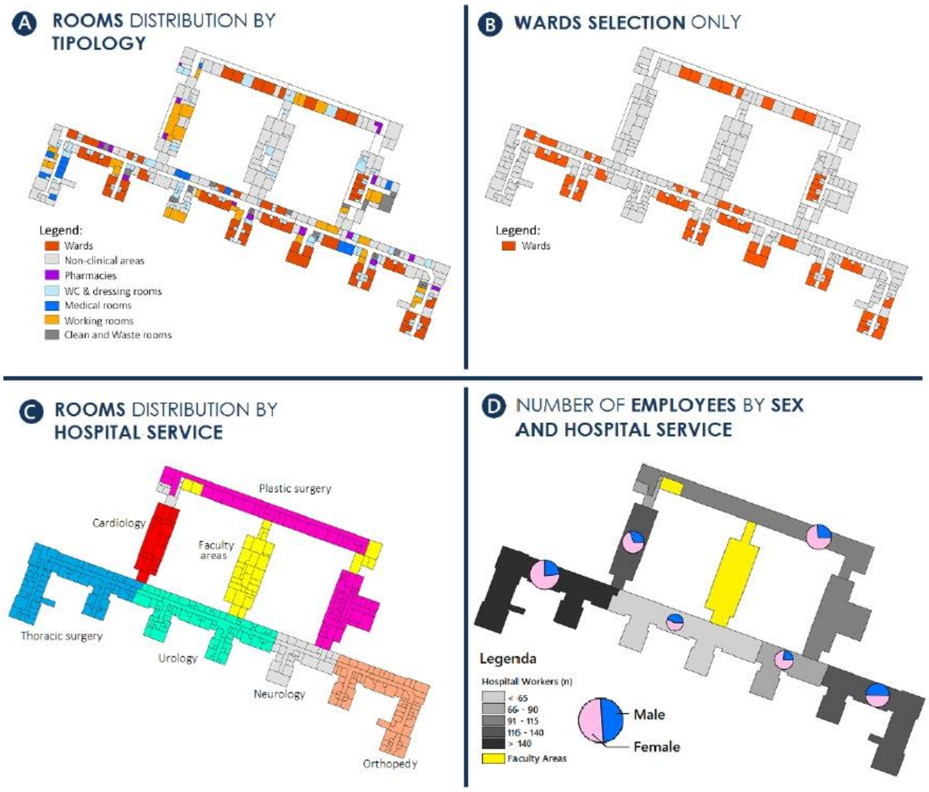


Fig. 6 Selected information for each floor.

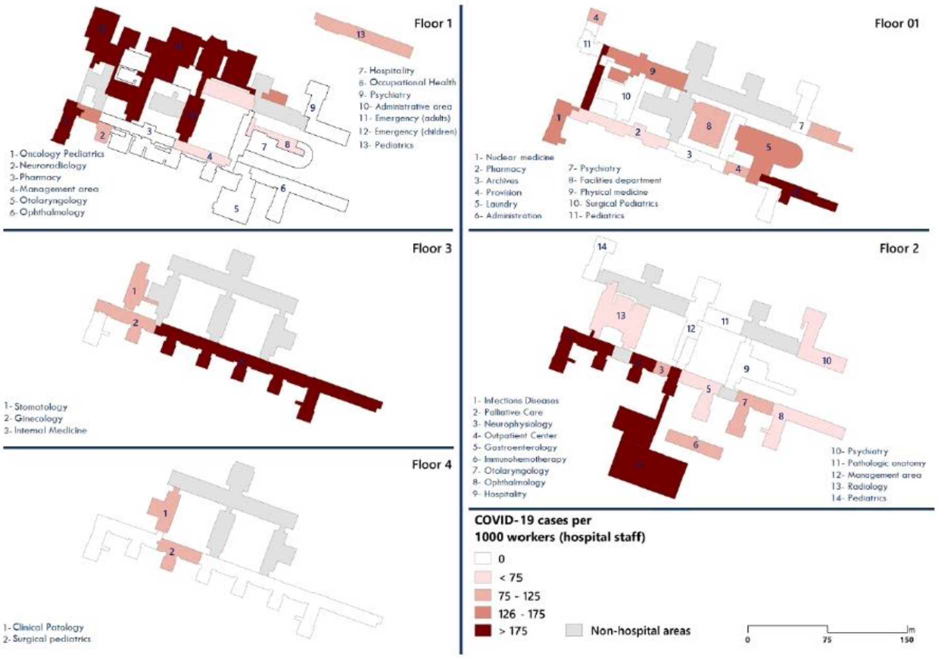
According to Table 2, it is possible to observe that there are a higher number of non-clinical areas when compared with clinical-related areas.

Figure 6 represents floor 7 and describes the type of information mapped for each floor, such as space typology, hospital services, and the distribution of the number of employees by service and per sex. In this way, the information provided by these functions might be maximized by eliminating overlapped data and leaving major indices for a detailed analysis.

Statistical Analyses of the COVID-19 cases

During the study period (between March 1st, 2020, and February 28th, 2021), a total of 874 hospital workers tested positive for COVID-19. This incidence study was performed on a group comprising a total of 6582 workers. Of the total, approximately 13.3% acquired COVID-19, presenting an overall incidence of 132.8 cases per 1000 employees.

Figure 7 depicts the spatial distribution of COVID-19 incidence among hospital staff by department and floor. Substantial spatial disparities were verified, with several departments and floors presenting incidence values between 31.7 (floor 1) and 300.0 (Vascular Surgery, floor 9) per 1000 employees.



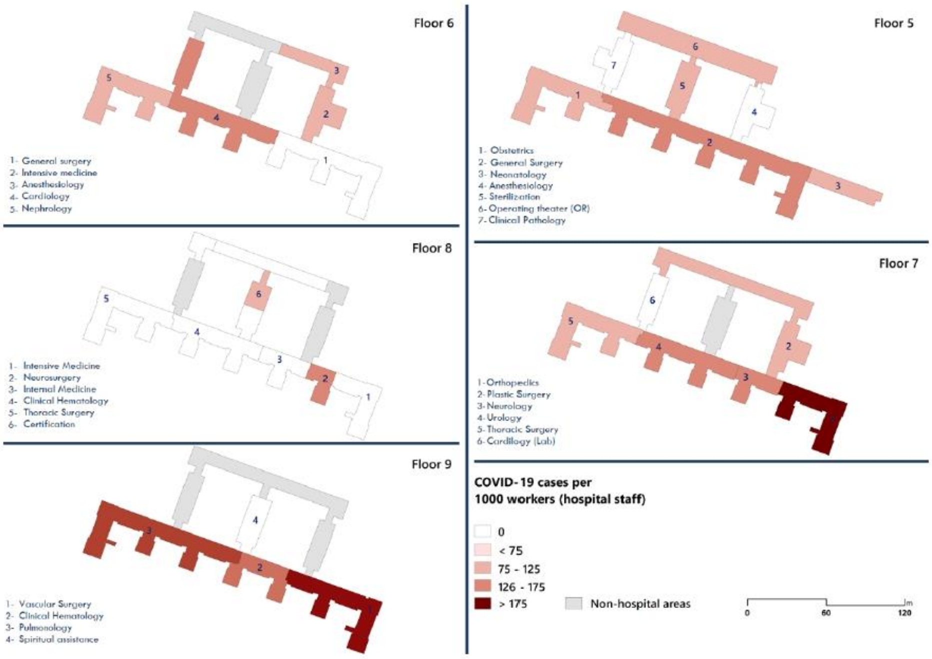


Fig. 7 Incidence rates of COVID-19 among health practitioners of São João University Hospital by floor and hospital department.

Looking at the overall picture of the several classes of incidence, there seems to be a large variation, with no particular pattern detected. Despite this fact, there were hospital services presenting higher incidence rates when compared to others. However, it was expected that those cases would be directly linked to the treatment of patients with COVID-19 (e.g., Emergency - Adults, Infectious diseases, Internal medicine, and the area dedicated to Outpatient Consultations and triage).

Table 3 and Figure 8 provide the characteristics of the statistically significant space-time clusters of COVID-19 at the service and floor level from March 10th, 2020, and February 12th, 2021. Cluster 1 was found on floor 01 and includes 9 services with a RR below 1, and the same was observed in cluster 3, which includes five services, meaning that these services have a lower risk of COVID-19 infection. On the other hand, cluster 2 contains two services located on floor 1 with a RR of 2.3, which means that these services have a higher risk of COVID-19. Being located on floor 2 of the hospital, the clusters 4-8 comprise a total of 14 services with RR registering values between 0.4 (8 services) and 3.1 (4 services).

Cluster	Floor	Observed	Expected	RR	p-value
1	0	5	14.1	0.3	0.027
2	1	103	73.8	2.3	< 0.001
3	1	3	12.7	0.2	0.011
4	2	108	69.5	3.1	< 0.001
5	2	38	14.8	3.1	< 0.001
6	2	15	35.9	0.4	< 0.001
7	2	56	32.9	2.1	0.001
8	2	13	30.2	0.4	0.004
9	3	23	38.4	0.5	0.003
10	7	50	33.5	2.1	0.003
11	7	17	30.2	0.5	0.021
12	9	24	11.6	3.3	< 0.001
13	9	8	18.4	0.3	0.001

Table 3. Space-time clusters of COVID-19 among health practitioners of São João University Hospital. RR stands for Relative Risk and was computed according to equation (2).

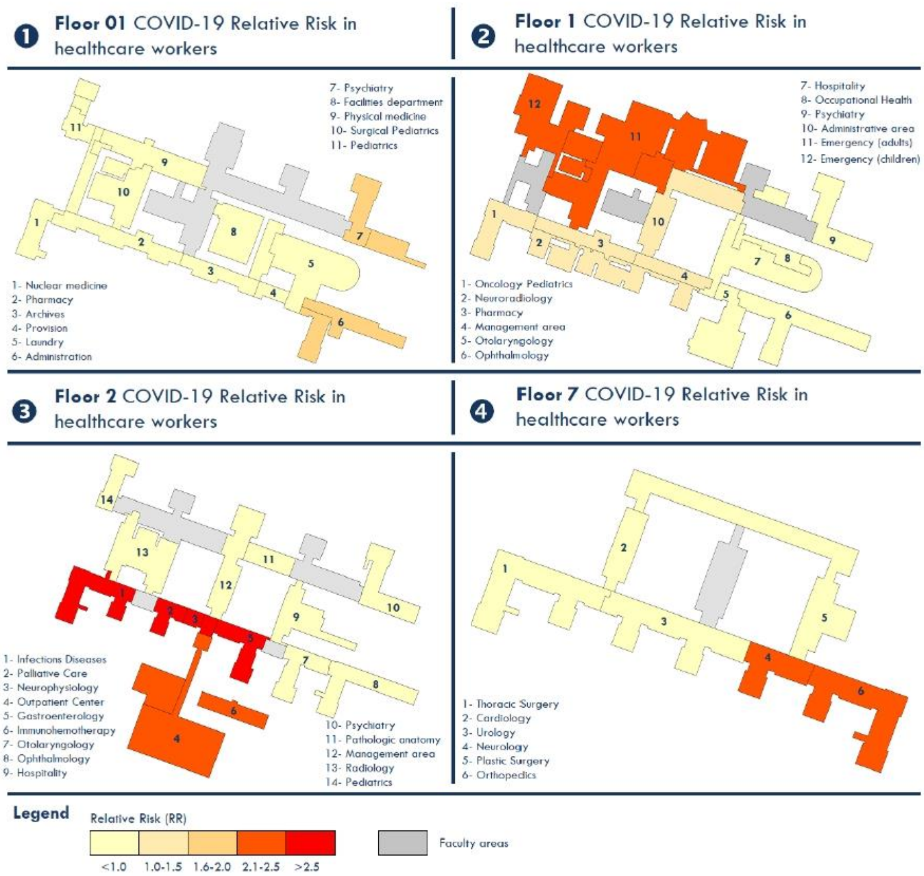


Fig. 8 Spatial distribution of clusters of COVID-19 among health practitioners of São João University Hospital with the value of RR, for the floors 01, 1, 2 and 7.

Cluster 9 is located on the 3rd floor with 3 services indicating a RR of 0.5. Clusters 10 and 11 are located on the 7th floor and contain all six services, with a RR varying from 0.5 (4 services) to 2.1 (2 services). Finally, clusters 12 (RR=3.3) and 13 (RR=0.3), both located on floor 9, cover the four services there.

Figure 8 shows the locations and spatial patterns of 10 space-time clusters of COVID-19 at the service level, that emerged during the study period. It is possible to analyze that the clusters with higher values of RR are those located on floors 1, 2 and 7, including services such as General Emergency, Pediatric Emergency, Intensive Medicine, Infection Diseases, Palliative Care, Neurophysiology, Gastroenterology, Day Hospital and Outpatient Center, Immunochemotherapy, Neurology, and Orthopedics.

On the other hand, almost all services (Nuclear Medicine, Pharmacy, Clinical Archives, Provision, Laundry, Facilities Department, Physical Medicine and Surgical Pediatrics) located on floor 01 presented a RR of below 1. It is equally important to highlight the low RR clusters located on floors 2 and 7, since there is an evident contrast between the north and south wings. Overall, the reported space-time clusters in Table 3 and Fig. 9 tell a story of the rapid COVID-19 dispersal and transmission across the several workers belonging to the services of the hospital.

4. Discussion

COVID-19 as an object of study is an important and a challenging task, where the geographical variables are present in numerous aspects [14]. Some authors suggested that to face COVID-19, it is necessary to use interdisciplinary approaches, with solid measures and global and local perspectives [51-53]. Therefore, we used the COVID-19 positive counts among healthcare workers within the study period, as a case study and the developed spatial database as a base map. We also employed a retrospective space-time scan statistical analysis to detect emerging clusters at the service level, providing interesting results and replications. Our study demonstrated that there was a significant space-time clustering in the distribution of COVID-19 cases among the healthcare professionals from the São João University Hospital. Multiple testing problems are taken into consideration in retrospective scan statistics, which is known as the most powerful method for evaluating geographical and temporal distribution utilizing routinely obtained data [48,54]. We assume that the main strength of this approach is the ability to input updated COVID-19 data and evaluate the statistics again to make it possible to identify new emerging clusters [55,56].

Recent studies also analyzed reported data on the incidence of COVID-19 infection in healthcare workers [57-59] but did not use this spatial component to understand the dynamics, as it was only possible to obtain this type of visual information once a spatial database was mapped, allowing the spatial analysis.

Nevertheless, producing a spatial database model for a complex building, such as a hospital, highlights some challenges. According to Mennis and Yoo [32], a big challenge is associated with the scale of analysis, since a correct illustration of time and space is crucial for data collection and analysis, as it affects findings and interpretations. Another key issue is the lack of data availability and the researchers' insufficient training in geospatial studies that analyze events that occur in indoor spaces [60,61]. The final concerns are related to the quality of raw data (engineering plants), to model the interiors, and ethical and legal issues that may arise; especially if people's privacy is put at risk, leading to social questions such as reactions ranging from uneasiness to a direct refusal to adopt the technology [62].

In this paper, we provided a detailed process to develop a spatial database to represent the indoor space of a hospital building. Its main goal was to offer health researchers, managers, and policymakers the opportunity to measure, analyze, and understand indoor events such as the spread of diseases, which can be an essential addition for decision support. The scale and location at which geostatistical analyses and mapping are carried out are significant if GIS is to be used as a useful tool for health science [16]. At this moment, it is pointless to constrain the term “place” to an external territory since 80% of people’s daily lives are being spent within indoor spaces [63]. Indeed, complex buildings (such as hospitals) present a high variability and heterogeneity of dynamics, movements, behaviors, and interactions of people, which can be the object of studies and analyses [32,34,64]. Consequently, adapting the utilization of conventional disease mapping methods in the external geographical context to analyze the occurrence of diseases and areas at risk within a building presents an immense potential [39,65,66]. Taking advantage of the existing integration between CAD data and GIS tools, empowering the representation of the entire infrastructure in map-based views, and by exploiting tools to evaluate the spatial relationships [26,67], it was conceivable to develop a coherent computational model of the hospital building. Research on this topic can be leveraged by having as its focus this perspective on place representation and its associated characteristics, data, and relations [37,68], such as the possibility of studying hospital epidemiology (with the control of outbreaks), producing knowledge (statistical indicators), and helping decision makers. By combining this statistical methodology with the spatial database model from the hospital, we are in front of a surveillance tool, capable of identifying locations that are currently hot spots or might be soon. This could represent a huge leap for occupational health departments or infection control committees, allowing them to implement targeted measures and guidelines to prevent the spread of COVID-19 or other diseases within hospitals [69,70].

Despite this, an opportunity is presented, once there are very few studies about epidemiological analysis within a hospital building. Nevertheless, one of the few was developed by Kho, Johnston, Wilson and Wilson [37] which focused on the implementation of a GIS-based software for infection control within hospital wards, describing the value of data visualization in maps as a support for decision making [23,64]. There is an opening opportunity to contribute to a more comprehensive building view and more efficient analyses [71] leading to the development of solutions which are essential for the existing problems.

Limitations

Not all aspects of the spatial database model could be assessed in this work. Some of its aspects need additional assessment, including more data collection (such as air and water pipelines) and the production of more formal statistical reports. Data related to positive cases of COVID-19 among hospital employees was obtained from the date on which the PCR test was positive. We cannot say with 100% certainty that employees acquired the virus within the hospital. For analysis purposes, since many of the health professionals circulate through the various areas and floors of the services, only the one where the head is located was considered.

5. Future directions and conclusions

Thus far, we have presented a methodological article, highlighting the development and implementation of a spatial database for the largest hospital in the north region of Portugal (São João University Hospital), using the GIS technologies. To the best of our knowledge, this is one of the initial studies, describing the different approaches, strengths, challenges, and limitations about this topic. This methodology is clearly in its first steps, and still incipient and considerably less developed, when compared with the utilization of GIS to study health events in external spaces [39].

As an emerging GIS theme, it is more oriented for problem-solving, that benefit the most thoughtful possibilities for analysis, highlighting a more narrative and storytelling perspective. However, the future directions of this type of research area, may not be entirely evident, since we realized there is a lack of complex building maps to replicate this technique to other hospitals, and an absence of a standard methodology to obtain this type of data.

As a main result of this work, the methodology already allowed us to perform a scan statistic to detect COVID-19 emerging clusters across the hospital services. The widespread distribution of this applied method presents an unprecedented opportunity, raising the awareness of researchers to the potential of GIS for the analysis of indoor spaces of health spaces, providing literature support for further work to evaluate visual models in real-world environments for decision support. Future work will take into consideration the development of a user-friendly interface, to allow non-expert end-users to manipulate the system.

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Authors contributions

The contributions to this manuscript can be divided in the following ways: (1) Conceptualization: HT, PN and FP; (2) Methodology: HT and FP; (3) Software: HT; (4) Validation: PN; (5) Formal Analysis: HT; (6) Writing-original Draft Preparation: HT; (7) Writing-Review & Editing: HT, PN, HG and FP; (8) Visualization: FP; (9) Supervision: FP and HG; (10) Funding Acquisition: HT. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials

The including data in the health information system is not available. The figures in better resolution are available upon reasonable request only.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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5. Using GIS to analyze spatial patterns of nosocomial pneumonia

Teixeira, H.; Sarmento, A.; Pina, M.d.F.; Gonçalves, H. Using GIS to analyze spatial patterns of nosocomial pneumonia in São João University Hospital (Portugal) (under revision).

Using GIS to identify spatial patterns of hospital-acquired pneumonia in São João University Hospital (Portugal)

Hugo Teixeira; António Sarmento; Maria de Fátima Pina; Hernâni Gonçalves

Abstract

Each year, nearly 80,000 patients acquire an infection related to healthcare in public Portuguese hospitals, resulting in an estimated 5000 deaths, on average. Our goal was to describe our experience using a Geographic Information System to investigate the distribution of the most common healthcare-related infection episodes, specifically nosocomial pneumonia, at São João University Hospital. We selected all hospitalizations with the diagnosis of hospital-acquired pneumonia on the medical specialties located on the 7th floor of the building, between the years of 2014 and 2017. The kernel approach was used to estimate the density of cases across the study period. The study results revealed that the incidence of cases is not randomly distributed in space. In particular, some differences were found in specific medical services, such as thoracic surgery and neurology. This method has the potential to be a useful complement in the prevention of nosocomial infection transmission.

Keywords: GIS, nosocomial pneumonia, spatial patterns, Portugal.

Introduction

In hospitals, patient safety is a critical issue. In clinical settings, a variety of risk factors for patients can be found, including hospital-acquired infections (HAIs) [1]. Approximately 80,000 patients acquire infections related to healthcare in public Portuguese hospitals each year, resulting, on average, in an estimated 5000 deaths [2]. Current methods for detecting HAIs are typically delayed by medical evaluation of microbiological data, and they rely on infection control practitioners' ability to discern complex temporal and geographic patterns of nosocomial transmission in the end [3]. Furthermore, infection control specialists lack the necessary resources to undertake hospital-wide audits and observations [4]. The utilization of different approaches, such as the integration of Geographic Information Systems (GIS), could potentially help the understanding related to the spread of HAIs and be of great value in this regard [5]. In fact, this technology allows for an efficient spatial analysis of daily generated data within the hospital through the georeferencing method. When this is combined with scientific knowledge, it can become a helpful tool to tackle the problem of HAI, as well as in the decision-making process [6], reduction of operational costs, and improvement of efficiency [7]. Despite GIS technology having become increasingly important in public health and spatial epidemiology, few studies have investigated its use in nosocomial infection detection and analysis within hospital buildings [8]. We hypothesized that using a spatial GIS-based model of the indoor spaces of a hospital - the São João University Hospital as a study case - to georeference and visualize patterns of HAIs could be used to provide a better understanding and analysis.

In this paper, we describe the used method, the obtained results, and their presentation in a different visual format, in a way to highlight distinctly the issues that might contribute to the understanding of the HAIs phenomena.

Methods

Study Design

We carried out a retrospective and observational population-based ecological study using data from the Integrated Hospital Information System (SONHO). The respective geographic and temporal units of analysis were the hospital building and the calendar year for the period of 1 January 2014 to 31 December 2017.

Study area

The São João University Hospital, first opened on June 24th, 1959, is in the Porto municipality and is the country's second largest hospital. This hospital provides direct help to the residents of Porto, Maia, and Valongo municipalities (about 450 000 people) and serves as a reference for the entire northern region in specific cutting-edge areas.

Data Source

We obtained hospitalization data from the SONHO database system, which is managed by the Data Intelligence Service of the hospital. This system was developed in the 1990s to support the administrative services of hospitals, including the control of production and billing, and to allow the export of information for statistical indicators. This system is being gradually replaced by the SONHO V2, which is technologically and functionally better suited to current needs. It is a comprehensive electronic medical record that includes information on patient demographics, diagnoses, laboratory tests, prescriptions, imaging investigations, and pathology reports. These data refer to hospital admissions and are provided for research upon request. We used a 3D GIS-based model to represent the geometry of the internal structure of the hospital building (Figure 1). The model includes all the complex indoor space structures and properties in terms of geometry, network connectivity, and alphanumeric information.

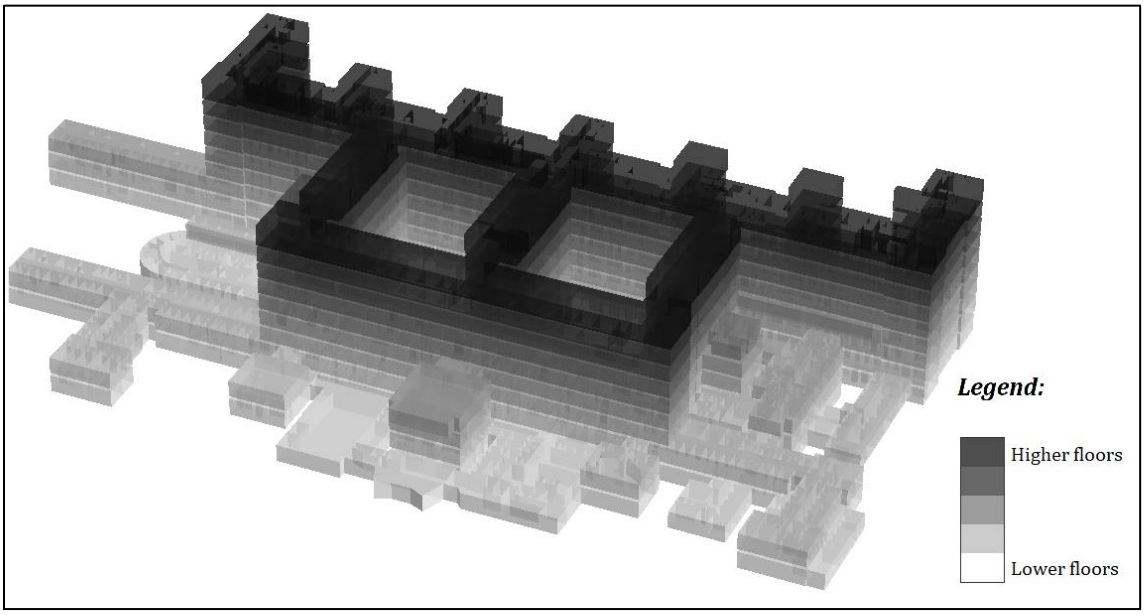

Figure 1. The three-dimensional GIS-based model perspective of the São João University hospital building.

Study case area

Figure 2 illustrates the study area, which includes 54 wards that belong to the several hospital services (Thoracic Surgery, Urology, Neurology, Orthopedics, and Plastic Surgery) located on floor 7.

Figure 2. Wards from the services located on floor 7 of the São João University hospital building.

Data Selection

Given the nature of the studied condition, we decided to select only those cases that suggested nosocomial pneumonia since, according to a recent study [2], it was the most representative adverse event recorded in mainland public hospitals. Through evidence research [9-12], we identified the most common pathogens and then obtained a list of all inpatient episodes with positive culture results for *escherichia coli, haemophilus influenzae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, and streptococcus pneumoniae*. Finally, we defined as nosocomial pneumonia any positive culture result 48 hours after hospitalization and with a pneumonia diagnosis. Infectiology professionals, helped to determine whether these episodes represented or not a nosocomial infection, helping with a cross-validation process.

Data Analysis

The data was analyzed using two related approaches: GIS to georeference the cases of nosocomial pneumonia through the several wards; and spatial statistics throughout the kernel density method [13] for pattern analysis. The kernel approach evaluates the density of cases in the vicinity of certain elements. We used first-order neighborhoods, calculated using the "densities" and "planar" options, which consider the planar distances between the different cases besides the spatially adaptive smoothers. This method was used to estimate the densities to predict a "relative risk" area, based on the asymptotic theory.

For compatibility with ArcGIS 10.5.1 software (ESRI, Redlands, CA, USA) equipped with the Spatial Analyst extension, data related to positive culture results were stored in Microsoft Access (Microsoft Corp, Redmond, WA, USA) table format.

Ethics Statement

The used data was acquired following the current Portuguese legislation. The ethical committee from the São João University Hospital approved this study since it did not include samples or experiments on humans or their personal information.

Results

According to data from the Portuguese Hospital Discharge Register, during the study period, there were a total of 174,745 admissions to the São João University Hospital. The yearly average number of hospitalizations was 43,686, corresponding to approximately 840 admissions per week. Every year, approximately 6,600 patients are admitted to the medical services of the 7th floor. Approximately 8.4% of these people had acquired nosocomial pneumonia while being hospitalized, since there were a total of 2233 cases of nosocomial pneumonia (Table 1 and Figure 3).

Medical Services	**Total**	**2014**	**2015**	**2016**	**2017**
Total cases, n (%)	2233	568	535	576	554
Plastic Surgery, n (%)	396 (17.7)	104 (18.3)	79 (14.8)	109 (18.9)	104 (18.8)
Thoracic Surgery, n (%)	549 (24.6)	121 (21.3)	134 (25.0)	159 (27.6)	135 (24.4)
Neurology, n (%)	376 (16.8)	107 (18.8)	96 (17.9)	96 (16.5)	78 (14.1)
Orthopedics, n (%)	241 (10.8)	59 (10.4)	65 (12.1)	58 (10.1)	59 (10.6)
Urology, n (%)	671 (30.0)	177 (31.2)	161 (30.1)	155 (26.9)	178 (32.1)

Table 1. Overall frequencies of nosocomial pneumonia cases by medical services between 2014 and 2017.

Figure 3. Spatial distribution of nosocomial pneumonia cases throughout the medical services located on floor 7 of the São João University hospital building, for the period 2014-2017.

The total number of cases declined between 2014 and 2015, whereas the number of episodes increased slightly between 2015 and 2016. Even though the year 2015 had the lowest number of cases, the year 2017 had the smallest number of minimum and maximum values. The urology service consistently presented the highest number of cases over the 4-year period, except for 2016, where thoracic surgery presented a higher number (27.6%). On the other hand, the orthopedics service constantly had the lowest value. Moreover, the neurology service presented a significant number of cases, despite having only four wards.

Spatial patterns

The spatial distribution of the level of risk is shown in Figure 4. A few spatial disparities were verified across the study period, with the surgical and neurology specialties presenting more vulnerable areas.

The average values related to the kernel density decreased between the years of 2014 and 2015. However, from 2015 to 2017, we observed a global increase throughout the several hospital areas. Despite the year 2014 presenting some sections with darker black (meaning a higher concentration of cases), the year 2016 was presented as globally the worst.

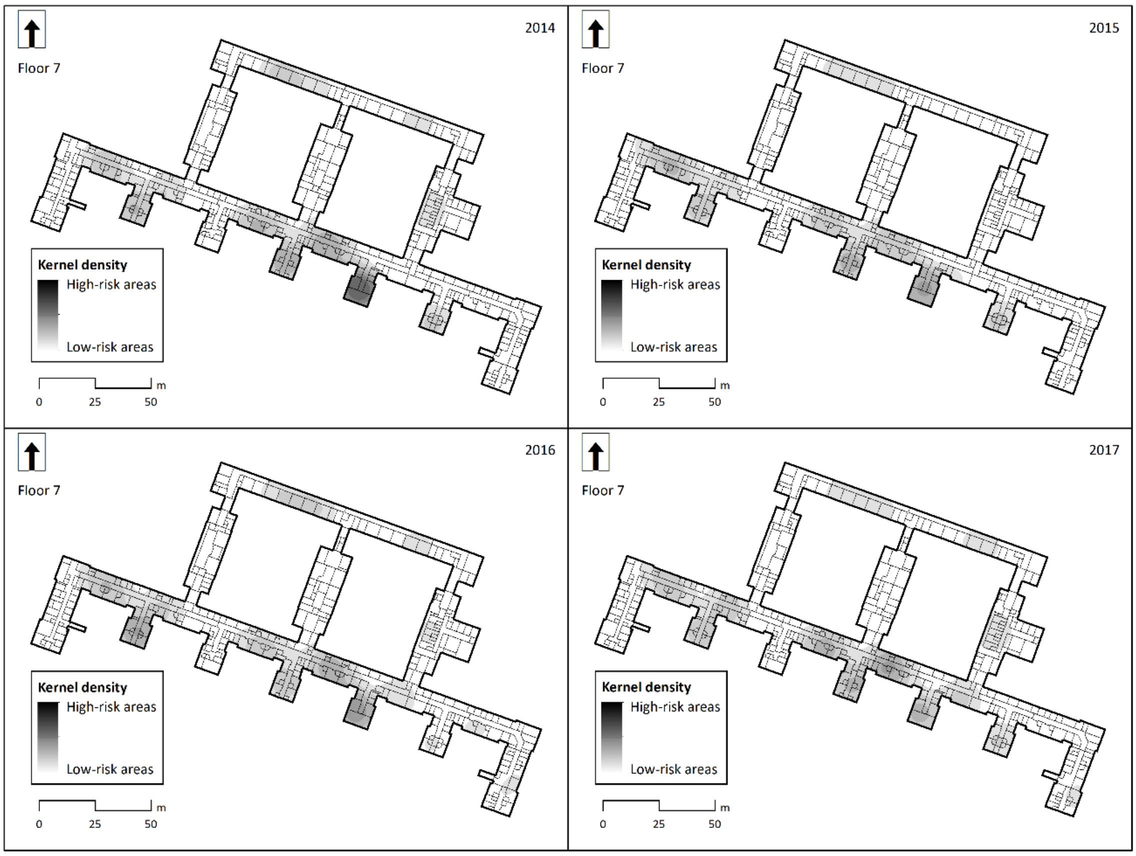

Figure 4 Spatial patterns of nosocomial pneumonia risk throughout the medical services located on floor 7 of the São João University hospital building, for the period 2014-2017.

Discussion

To the best of our knowledge, this is the first study using GIS to analyze the cases of nosocomial pneumonia within a Portuguese hospital. This retrospective four-year study analyzes the hospitalizations of patients who acquired nosocomial pneumonia based on data collected from the SONHO platform and from the national hospital discharge register, which collects information from public hospitals. Our findings reveal that the incidence of cases is not randomly distributed in space; there are a few differences, with some specific medical services presenting a higher number of cases.

It is generally assumed that provider-to-patient transmission is the most common source of hospital infections [14]. Even though infection control practitioners monitor patients with cultures positive for the specified pathogens daily, assessing health care provider movements and patterns of nosocomial transmission is a challenging task when only paper records are accessible [15]. According to a scientific review [16], a greater integration of spatiotemporal approaches into HAIs research could be extremely beneficial since it could highlight previously undiscovered patterns of infection and maximize understanding of disease dynamics. Therefore, it makes it possible to comprehend if that specific space within walls is risky or safer, according to the loaded information [17]. Our goal was not to identify individual signs, but rather to discover general patterns of behavior related to the infection spread, and for that reason, we are confident that this study, associated with a more-oriented educational campaign in medical wards, will improve the efficiency and accuracy of the HAIs surveillance process [18].

Limitations

There are some limitations to this study. Due to the nature of this research, caution must be applied since it is essential to point out that this perspective of analysis does not mean that the infection occurred in that ward, but it was the ward where the patient was diagnosed with the infection. Another limitation is related to the anonymous process, since it is impossible for the authors to identify the infection cases detected after discharge within 30 days. Another limitation is that lower frequencies of nosocomial pneumonia cases throughout the different medical services, do not necessarily or even often mean lower true prevalence rates.

Opportunities

An opportunity is presented here, since it is known that standardized surveillance systems, infection control programs, and the instigation of antibiotic stewardship programs may be effective strategies to minimize the future risk of HAIs. The possibility of combining these with the employed method approach will lead to the development of outcome measures for hospital epidemiology and will provide investigators and health managers with a strong instrument to manage the execution of different research projects, which will be linked to the improvement of HAI prospective surveillance.

The wider availability of such techniques is a once-in-a-lifetime opportunity, enhancing researchers' awareness of the GIS potential for the analysis of health spaces and giving the literature support for evaluating visual models in real-world contexts to help with decision-support. The creation of a user-friendly interface for non-expert end-users will be considered for future work, as well as the possibility of almost real-time analysis of phenomena.

Conclusions

In fact, there are several obstacles to the practical application of HAI prevention programs. These can include resource constraints, institutional culture (example: "we've always done it this way"), and, in some cases, a lack of support from the mentorship [19].

However, we truthfully believe and recommend that, even in its early stages of development, this technology could and should become widely used in nosocomial infection surveillance, providing more informed judgments and decisions, given that in a small and contained area, such as a hospital, there is a higher potential for infection misclassification.

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6. General Discussion and Conclusions

This section summarizes the findings from the four chapters that make up this thesis and provides an overview of the current state of the art. In addition, some relevant recommendations and insights for future research are given based on the experience and views gained throughout this effort.

The first chapter addressed our first published article, to fulfill the first objective of this thesis, since it was vital to explore the scientific evidence, through a systematic review, related to GIS utilization to model the indoor space or to analyze and comprehend the spatial phenomena that are occurring in this type of environment. For many years, these techniques were linked with sciences such as geography or cartography, but with the widespread utilization of GIS since the late 1980s, supported by increased data availability, they have proven to have no limits [59]. The word "place" is no longer constrained to an external territory since 80% of people's daily lives are spent within indoor spaces [60], and for that reason, several authors [50,61-63] have started to give more attention to space characterization, and specifically to indoor space, which is typically defined as bounded and constrained by an architectural structure [64]. Our findings identified 50 studies covering multiple techniques and procedures for representing and modeling indoor spaces, which present a wide range of analysis opportunities, such as facility management, spatial pattern analysis, emergency simulation, route navigation, indoor modeling, or optimal resource allocation. Our paper, intended to characterize and understand the spatial patterns of HAIs in Portugal, obtaining a valid portrait [65] with data from all age groups of patients. Additionally, this paper discusses nosocomial pneumonia as the most frequently reported HAI, with the elderly being the most vulnerable age group. Besides, it helped to consolidate perceptions and irreversibly recognize health-acquired infections as a significant and actual problem in the Portuguese hospital wards. To reduce the prevalence of HAIs, it is consequently important to reduce the number of hospital admissions, specifically those that should be preventable [66]. Despite the efforts of the Portuguese national health system to improve quality, disparities in the availability of primary care facilities continue to be an important challenge. There are still many regions with low coverage of medical family doctors [67], resulting in physical difficulties accessing healthcare and lengthier wait times for assistance. Furthermore, scientific evidence shows that inefficient access to primary health care is directly related to higher hospitalization rates [68]. As a result, our findings may be extremely valuable in adjusting local measures and improving action plans because improving primary health care is likely to lead to a decrease in the total number of hospital admissions [69,70]. The task of hospital infection control committees, on the other hand, is critical for educating health providers and resulting in a better surveillance protocol.

To truly understand and systematize the growing problem of HAIs, we realized that a multi-disciplinary approach is absolutely required since some studies have pointed to the utility of using a hospital-wide GIS application to act as a central base map for spatial and temporal data of healthcare-associated infections [71,72]. Even though research on GIS utilization in indoor spaces is still emerging, we decided to develop a space data model for the largest hospital in the north region of Portugal, challenging the healthcare environment's complexity [73]. This methodological work was described in the third paper of this thesis and highlights the various approaches, assets, and weaknesses regarding it. Besides, and looking at the actual reality, we decided to perform a scan statistic to detect COVID-19 cases among healthcare professionals to understand the emerging clusters across the hospital services.

Finally, in chapter 4, we performed a spatial analysis of the HAI patterns within the São João University Hospital. First, we selected and georeferenced the episodes of nosocomial pneumonia diagnosed between 2014 and 2017, and after employed the Kernel density approach, we obtained as a result, the areas with higher concentration of cases. Despite the fact that GIS can provide the necessary complement to act as a support spatial decision-making tool, caution must be exercised because the success of its use is strongly dependent on the user's expertise and on the quality and availability of data [74].

Future work

Subsequent studies should be conducted to understand the reasons that could be associated with these different results, such as the incidence of HAIs not being randomly distributed in the space. Besides, it could be helpful to develop a platform with this HAI information, allowing consultation for the regional health delegations, which might benefit the country. The evidence shows a lack of spatial database models made for hospital buildings, and it should be important to replicate these techniques in other hospitals.

Some interesting ongoing studies can be suggested among the various possibilities of using georeferencing technologies in hospital environments. Unfortunately, these studies were not performed in this thesis for the mere matter of time and the absence of essential data and should be collected prospectively in the future.

Hospital Epidemiology

An exciting step towards advancing the control and prevention of infections acquired within hospitals is creating a computerized system capable of triggering health teams within hospitals for the risks of infection in an automated and early manner. The same infection can occur in different spaces within the hospital in different ways, with a higher occurrence in each site considering historical trends based on secondary data. Prospectively, the system could alert, based on the profile of patients admitted to the areas, the degree of risk that a given patient has of developing a given infection if prevention and control measures are not taken in time. This system should help hospital infection control committees act early and ensure patient safety within the inpatient environment. Some artificial intelligence systems are currently used for this purpose, but not at the patient level, nor do they interface with geographic information systems in indoor spaces, which would be considered innovative [75-78].

Transition of Care

As the scientific community knows and is well supported by evidence, prolonged hospital stays increase costs, delay rehabilitation, and expose patients to hospital-acquired infections. Therefore, the transition of care and hospital discharge at the right time is a crucial factor for preventing these infections and improving clinical outcomes for patients in the home and outpatient setting [23,79,80]. Currently, hospitals face a significant challenge in reorganizing their services and reassessing practices related to discharges and the transition of care. The overall goal is to reduce readmission rates within 30 days, prevent adverse events within the hospital environment (such as hospital-acquired infections), and, above all, ensure a safe transition of patients to their homes and for outpatient follow-up. This need is becoming more important, but few published studies have demonstrated a significant reduction in hospital readmission rates [81-84]. Therefore, modern hospitals must implement an effective transitional care program to improve patient safety during their stay in the hospital environment and after discharge. GIS can be a valuable tool in identifying patients at higher risk within the hospital environment. In addition, it highlights the need for pre-and post-discharge assessment and interventions related to nosocomial infections, thus avoiding the occurrence of events, very early discharges, excessive length of stays, or readmissions. It can also help assess the risk of readmission by sector where the patient was previously hospitalized, translating important information for actions to control these infections and better plan the transition of care.

Conclusions

When combined with statistical analysis and databases, the GIS broadens the possibility of understanding the dynamics of pathogen circulation in space and time and could be extremely valuable in helping the identification of relationships between the different factors (e.g., etiological agents, vectors, and hosts) [71,85]. In fact, statistical analysis has proved to be of great value in the epidemiological surveillance of infectious diseases [86], since it is an important method adopted by medical geography, as it allows, for planning health strategies and optimizing local prevention and control measures.

In summary, due to the large amount and variety of existing microbiological data, we strongly recommend the utilization of automated methods using spatial statistics and GIS for cluster detection of such cases.

Finally, the purpose of this thesis was to bring to the table the discussion about the use of these types of approaches to increase the understanding of researchers, managers, but also internal and external customers, about the dynamics of agent circulation in hospitals and the infectious process, thereby contributing to prevention and control policies that can be better developed, targeted, and effective. Furthermore, it can also contribute by bringing new and diverse perspectives to this system utilization, with the purpose of enhancing the processes and related outcomes.

7. References

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