










# Hospital Contacts for Infectious Diseases Among Children in Denmark, Finland, Norway, and Sweden, 2008–2017

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**Purpose:** Comparing rates of childhood infectious disease hospitalisations across countries may uncover areas for improvement in the prevention of severe childhood infections. We compared rates of childhood infectious disease hospital contacts across Denmark, Finland, Norway, and Sweden with the overall objective to elucidate potential differences in burden of disease and in organisational and registration practices.

**Methods:** Using national registries, we estimated incidence rates for infectious disease hospital contacts between 2008 and 2017 among children aged 0–14 years. We investigated the rates for different types of contacts (inpatient or outpatient including emergency room), duration of admission, and by sex.

**Results:** During the study period, the rate of all hospital contacts per 1000 person-years was highest in Sweden (125.2) followed by Finland (87.1), Denmark (79.0), and Norway (62.1). The rates aligned for inpatient contacts with overnight stays; 19.3 (Denmark), 16.6 (Finland), 16.3 (Norway), and 13.0 (Sweden); these were highest in early infancy in all countries. A peak around 1 year of age was seen in all countries except in Sweden. The rates were higher among boys compared with girls in early childhood, after 13 years of age the rates among girls surpassed the boys.

**Conclusion:** Large cross-country differences were observed for outpatient and short-term hospital contacts for infectious diseases, affected by differences in organisational structures and coding practices across and within countries over time. Inpatient contacts requiring overnight stays reflected more comparable levels of severe infections across countries. Childhood infectious disease morbidity was greatest among boys and before 2 years of age.

**Keywords:** infectious disease hospitalisations, paediatric, patient registry, multinational study, Nordic countries

## Introduction

Infectious diseases are common in childhood.<sup>1,2</sup> Minimizing the burden of paediatric infectious diseases is of public health interest<sup>3</sup> with national preventive strategies, eg, vaccination programs in place to fulfil this aim.<sup>4</sup> In high-income countries, measures of hospital care utilisation for infections are often used to ascertain the burden of paediatric infectious diseases. Cross-country comparisons of burden of childhood infectious diseases are important to understand and inform health-care policy. However, differences in the organisation of health care, definitions of hospital contacts, and registration practices that can influence hospitalisation rates need to be considered when making cross-country comparisons.<sup>5</sup>

The Nordic countries Denmark, Finland, Norway, and Sweden have many similarities, including the welfare state model promoting universal tax-funded healthcare for all.<sup>5,6</sup> Previous Nordic studies describing paediatric hospitalisations for

infections are limited to single country investigations,<sup>1,7–16</sup> and are often restricted to specific types of infections,<sup>7–11,13,14,16</sup> hampering cross country comparison.

In the present study, we aimed to compare the rates of childhood infectious disease hospital contacts by type of contact (all contacts or inpatients only) and duration of inpatient admission across the Nordic countries according to time, age, sex, and group of infection. Our overall objective was to investigate differences between countries and to elucidate whether differences might be related to differences in health-care organisations and registration practices or differences in burden of disease. We thus aim to identify metrics of infectious disease hospitalisations that may increase consistency in measures of infectious disease hospital contacts across countries and through comparison of these measures, identify potential areas for improvement in the handling and prevention of paediatric infections.

## Materials and Methods

We conducted an observational study using nationwide register data from Denmark, Finland, Norway, and Sweden for infectious disease hospital contacts in children aged 0–14 years from 2008 to 2017. This age interval was chosen based on availability of data. Our primary aim was to compare the rates by type of contact and duration of admission over time and according to age. Secondary aims included comparisons by group of infection and sex.

### Setting

The Nordic countries are characterized by the Nordic welfare state model.<sup>6</sup> In Denmark and Norway, all hospital care is free of charge.<sup>17,18</sup> In Finland and some regions in Sweden, a small patient fee up to an annual maximum may be charged for inpatient contacts.<sup>19,20</sup> A more detailed comparison of the Nordic countries and health-care systems is described elsewhere.<sup>3</sup>

### Data Sources

Individual-level information on hospital contacts, including type of contacts, diagnoses (international classification of disease version 10 (ICD-10)) and dates of admission and discharge, was obtained from the Danish National Patient Registry, Finnish Care Register for Health Care, Norwegian Patient registry, and the National Patient register in Sweden.<sup>3</sup> Date of birth and sex were obtained from the Civil Registration System in Denmark,<sup>21</sup> Statistics Norway (only year and month of birth), and Statistics Sweden.<sup>22</sup> In Finland, this information was obtained from the patient register.

Information on the underlying population at risk was obtained from publicly available population statistics.<sup>23–26</sup>

### Defining Infectious Disease Hospitalisation Contacts

ICD-10 codes related to infections were selected based on an evaluation of codes used in previous studies ([Appendix 1](#)). The infectious disease codes were grouped as upper respiratory tract infections (URTI), lower respiratory tract infections (LRTI), gastrointestinal infections (GI), and other infections (OI), and further into subgroups ([Appendix 1](#)).

We identified infectious disease hospital contacts (including inpatient, outpatient, and emergency room contacts) and included both primary and secondary diagnoses, as coding practices may differ across countries and time. Infectious disease hospital contacts occurring within 14 days after discharge from a previous infectious disease hospital contact were regarded as the same infectious disease episode and counted as a single hospital contact.

We defined four different types of contacts: 1) all hospital contacts (inpatient, outpatient, emergency room); 2) all inpatient hospital contacts (including those with no overnight stays); 3) inpatient hospital contacts with overnight stays; 4) inpatient hospital contacts lasting at least two nights.

### Statistical Analyses

We estimated the incidence rate (IR) as the number of infectious disease hospital contacts per 1000 children in the population, corresponding to approximately 1000 person-years (PY). Since common infectious diseases are linked to seasonal incidence patterns,<sup>2</sup> we defined an epidemiological year as running from July 1 to June 30 the following year. Our study period was July 1, 2008 to June 30, 2017.

We estimated age-standardized rates among all children aged 0–14 years according to epidemiological year using the average population of each 1-year age group across countries and epidemiological years as the standard. Rates according to epidemiological years were calculated for each type of contact and by group of infection.

We also estimated the age-specific rates in 1-month intervals among children aged 0–35 months and 1-year intervals among children aged 3–14 years for each type of contact. For inpatient contacts with overnight stays, we further estimated the age-specific rates according to group of infection and sex.

To assess potential differences in coding practices, we calculated the frequency (%) of the most common subgroups of infection registered within each main group of infection ([Appendix 1](#)). Most GI infections cannot be discerned based on symptoms only. Thus, we grouped all GI together, which precluded an analysis by subgroup of infections.

We used Stata version 16.0 (StataCorp, College Station, Texas, USA) to conduct the analyses and R version 3.3.3 to visualize data.

## Ethics

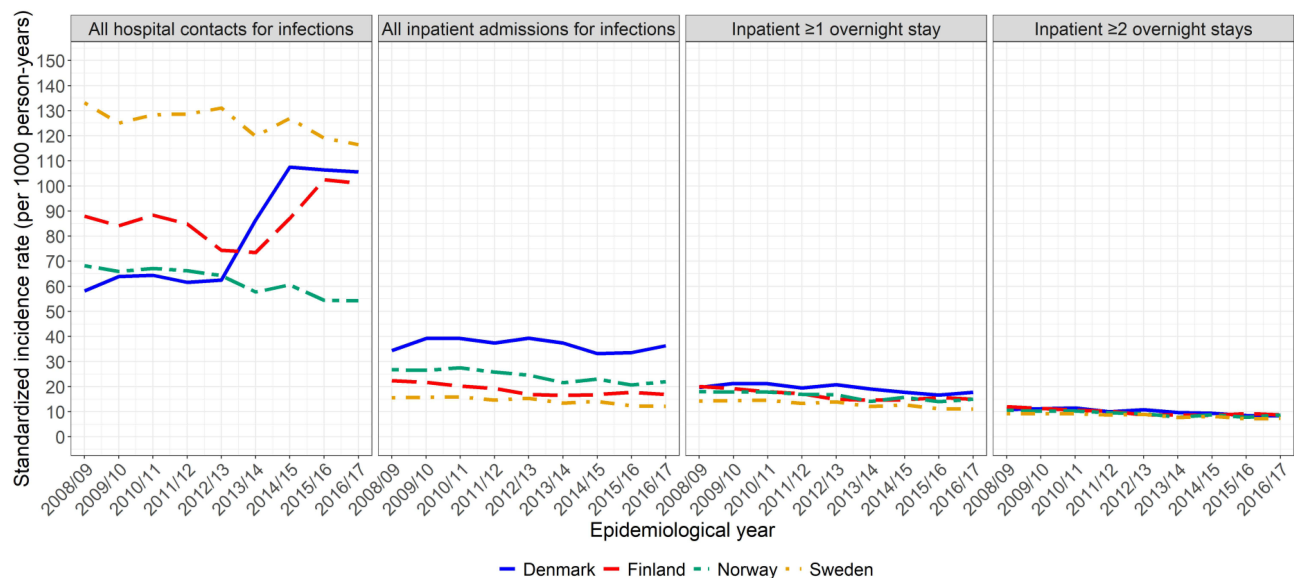
Ethical approval is not required for registry-based studies in Denmark and Finland. However, the study was approved by the Danish Data Protection Agency and by the Institutional Review Board of the Finnish Institute for Health and Welfare. In Norway, study approval was obtained from the Regional Ethics Committee, South-East. In Sweden, study approval was obtained from the Regional Ethical Review Board, Stockholm, Sweden.

## Results

### Rates Across Time by Type of Contact

The age-standardized incidence rates of all infectious disease hospital contacts (including inpatient, outpatient, and emergency room contacts) for children aged 0–14 years in the study period varied across countries: the rates per 1000 PY ranged from 62.1 in Norway to 125.2 in Sweden ([sTable 1](#)). The rates were higher in Sweden compared with the other countries in all epidemiological years ([Figure 1](#), panel 1). Until year 2012/13 the rates were also higher in Finland compared with Denmark and Norway, whereafter a steep increase was observed in Denmark from 62.5 in 2012/2013 to 107.5 in 2014/2015. The Finnish rates increased from 73.4 in 2013/2014 to 102.5 in 2015/16.

Including only inpatient contacts resulted in lower and more comparable rates across the four countries: the IR across the study period ranged from 14.3 in Sweden to 36.7/1000 PY in Denmark ([sTable 1](#)). The rates were stable with a minor

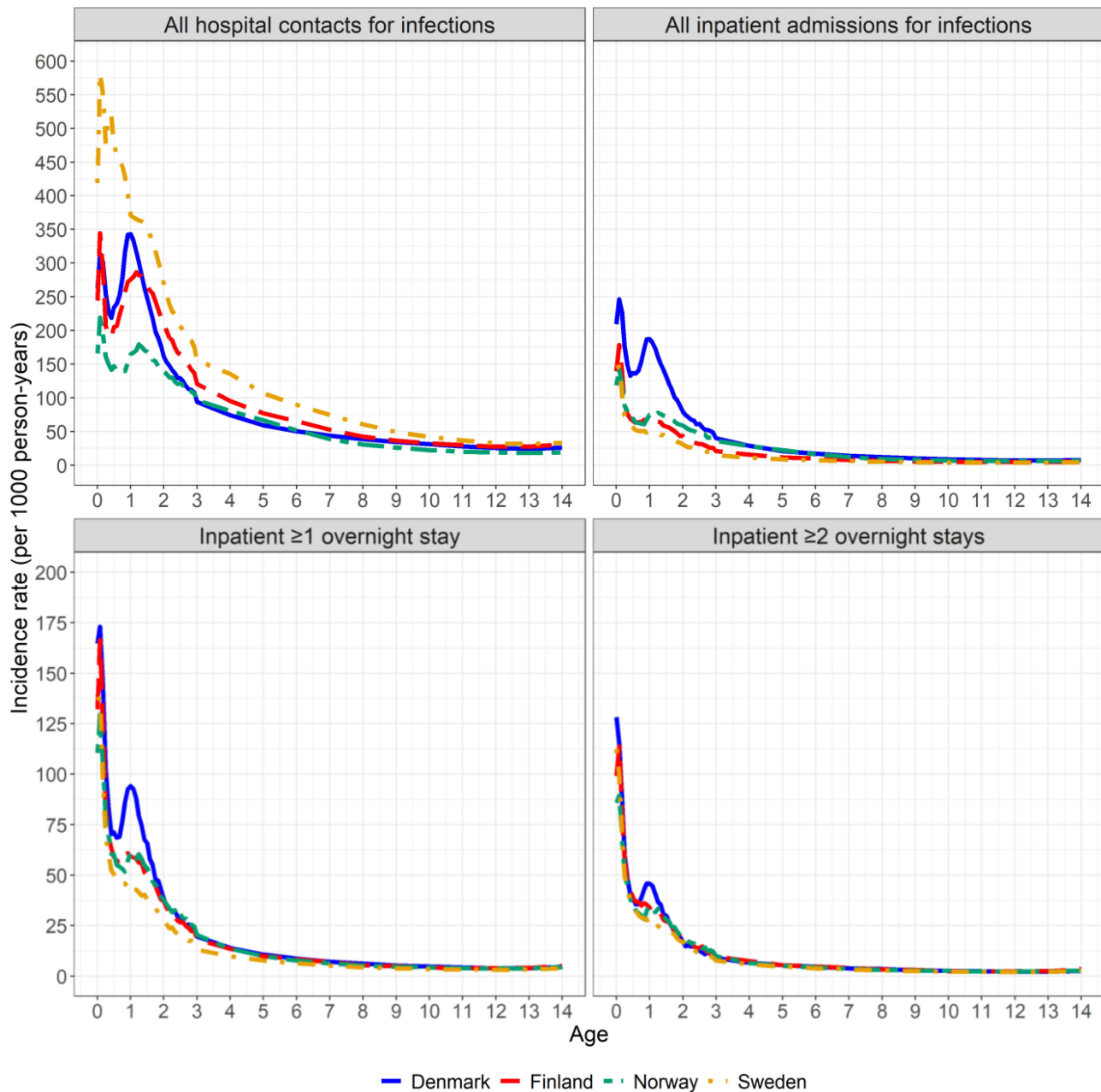


**Figure 1** Age-standardized incidence rate (per 1000 person-years) of infectious disease episodes<sup>a</sup> with hospital contacts among children aged 0–14 years by epidemiological year (2008/2009–2016/2017), country and type of hospital contact. <sup>a</sup>Hospital contacts with infections, which occur less than 14 days after discharge/visit date of a previous contact with infection are defined as the same infectious disease episode.

decreasing trend across the epidemiological years with consistently higher rates in Denmark (Figure 1, panel 2). Cross-country differences diminished with longer duration of admission (Figure 1, panel 3+4 and sTable 1).

## Rates by Age

The rates including all hospital contacts were highest in the first two years of life in all countries (Figure 2, top left panel and sTable 2). The rates were highest in Sweden at all ages. Including only inpatient contacts, the rates were highest in the first year of life with peak incidence before 3 months of age in all countries followed by a smaller peak around 1 year of age in Denmark, Norway, and Finland (Figure 2 and sTable 2). The rates were higher in Denmark across all age groups, but cross-country differences gradually decreased with longer duration of admission and older age of the children.

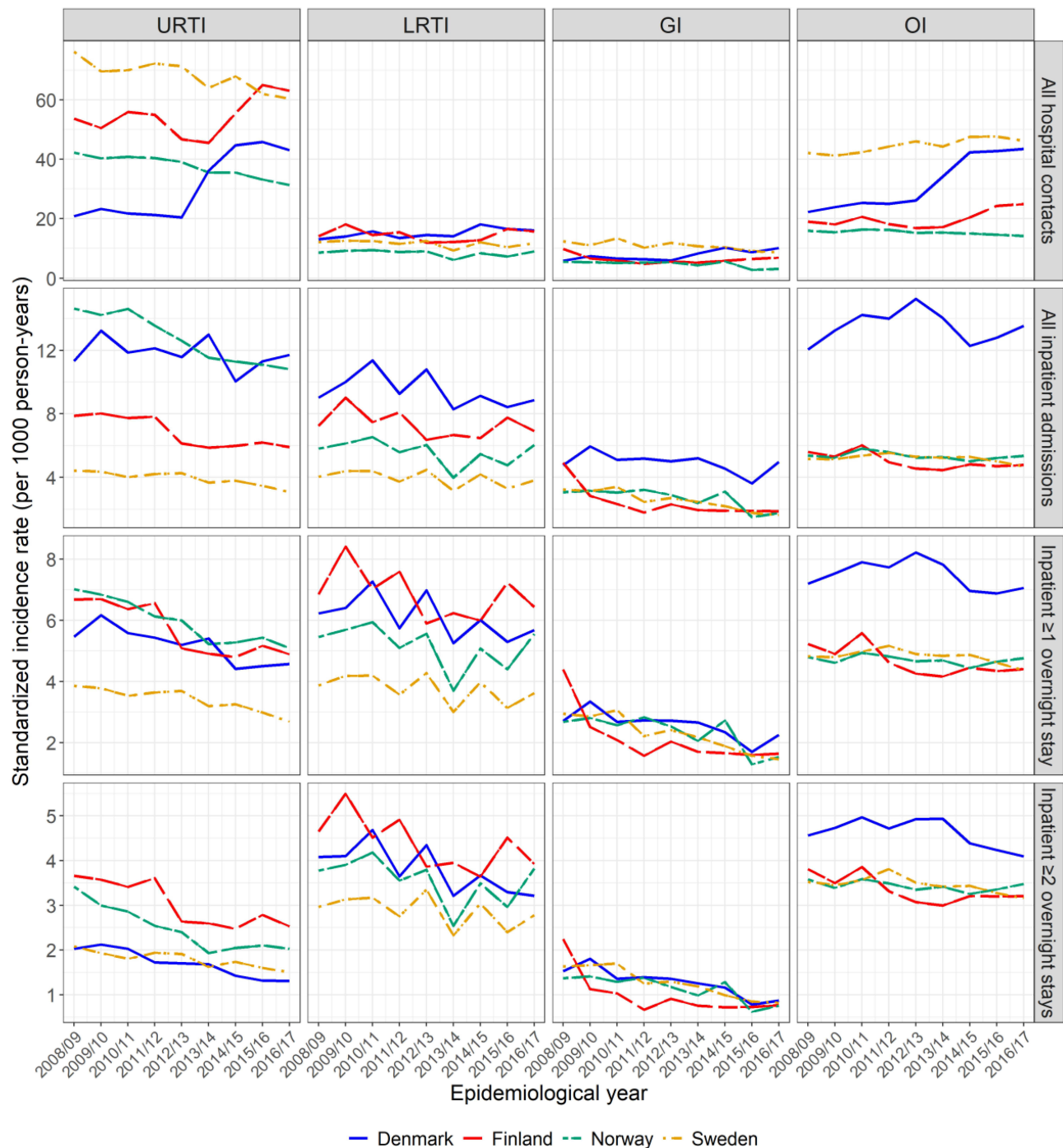


**Figure 2** Incidence rate (per 1000 person-years) of infectious disease hospital episodes<sup>a</sup> for epidemiological years 2008/2009–2016/2017, by age, country, and type of hospital contact. <sup>a</sup>Hospital contacts with infections, which occur less than 14 days after discharge/visit date of a previous contact with infection are defined as the same infectious disease episode.

**Note:** The scale of y-axis is different in the upper and lower panels.

### Rates by Group of Infection

Including all contacts, higher rates of URTI were observed in Sweden and Finland across all epidemiological years (Figure 3, first row). Sweden experienced the highest rates of OI across the study period. From year 2012/13 in Denmark and 2013/14 in Finland, the rate of URTI and OI increased. Looking only at inpatient contacts, Denmark and Norway had the highest rates of URTI, followed by Finland and Sweden, whereas Denmark had higher rates of LRTI, GI and OI than the other countries



**Figure 3** Age-standardized incidence rate (per 1000 person-years) of infectious disease hospital contacts<sup>a</sup> among children aged 0–14 years by group of infection<sup>b</sup>, epidemiological year (2008/2009–2016/2017), country and type of hospital contact. <sup>a</sup>Hospital contacts with infections, which occur less than 14 days after discharge/visit date of a previous contact with infection are defined as the same infectious disease episode. <sup>b</sup>Different types of infections within an infectious disease hospital episode are counted, thus summing the rates over types of infections will give greater rate, than the rates presented in Figure 1.

**Note:** The scale of the y-axes is different in each row.

**Abbreviations:** URTI, upper respiratory tract infections; LRTI, lower respiratory tract infections; GI, gastrointestinal infections; OI, other infections.

(Figure 3, second row). For inpatient contacts with overnight stays, the rates were relatively similar across countries (Figure 3, third row). A general downward-going trend was observed for URTI in all countries. However, higher rates of GI in 2008/09 in Finland and OI across all years in Denmark were observed. The rates of URTI and LRTI were lower in Sweden than in the other countries across the study period. Similar patterns were observed for inpatient hospital contacts lasting at least two nights, but with smaller differences between the countries (Figure 3, fourth row).

## Age-Specific Rates of Inpatient Hospital Contacts with Overnight Stays by Group of Infection and Sex

In all countries, LRTI and OI were the most frequently registered infections within inpatient contacts with overnight stays in early infancy (before 3 months of age) followed by admissions with URTI (Figure 4). A second peak was registered around 1 year of age for LRTI and URTI in Denmark, Finland, and Norway, with the highest rates in Denmark. The Swedish rates levelled off at this age and at lower rates compared with the other countries.

In all countries, the rates of inpatient hospital contacts with overnight stays were higher among boys compared with girls until 5–7 years of age (Figure 5). Thereafter, the rates were similar until 13 years of age when the rates for girls surpassed that of boys.

## Analysis of Subgroups of Infections

The proportion of registrations of specific subgroups of infections within each group of infections during inpatient hospitalisations with at least one overnight stay varied across countries (Table 1), eg, pneumonia diagnoses ranged from 32% to 33% in Finland and Norway to 52% in Denmark, and pyelonephritis ranged from 13% to 14% in Denmark, Norway, and Sweden to 23% in Finland.

## Discussion

We observed large differences in the rates of infectious disease hospital contacts both across the Nordic countries and within countries over time when including both inpatient, outpatient, and emergency room contacts. The rates gradually aligned as we restricted the analyses to inpatient contacts and longer duration of admission. The rates of inpatient contacts with overnight stays were highest in early infancy in all countries, mostly driven by LRTI and OI. The rates of inpatient contacts with overnight stays were higher among boys compared with girls until about 5 years of age, whereas they were higher among girls compared with boys after the age of 13 years.

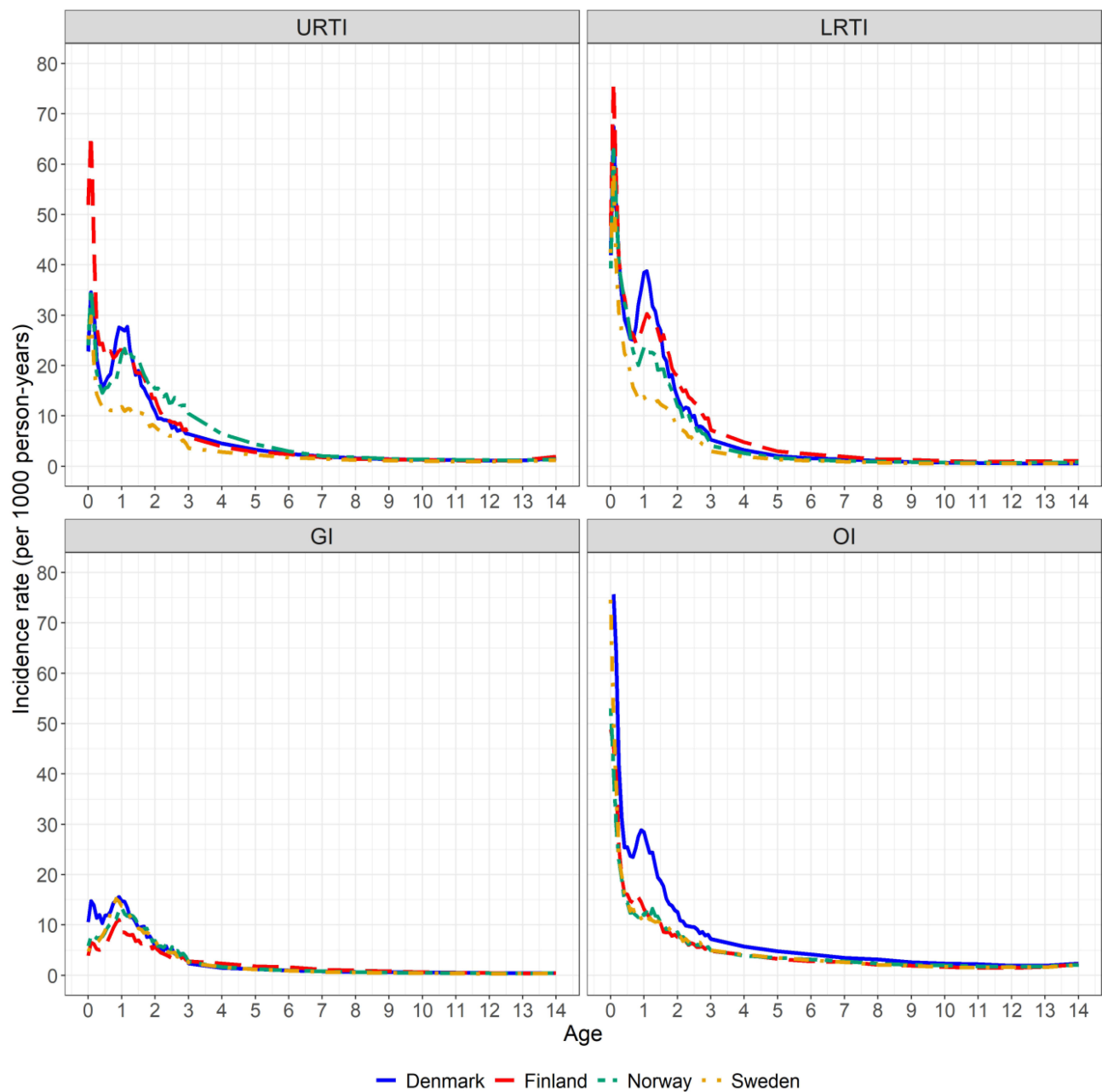
## Strengths and Limitations

In the Nordic countries, reporting to the patient registries is mandatory. The registries contain both inpatient, outpatient, and emergency room contacts and diagnoses are coded according to ICD-10 in all countries.<sup>3,5</sup> This facilitated the cross-country comparison in the present study.

Including both primary and secondary diagnoses increased the likelihood of capturing all infectious disease contacts<sup>27</sup> regardless of coding practices over time and across countries. However, it also entailed a risk of including infections from admissions with non-infectious primary causes and thus overestimating the rates.

Due to a lack of documentation and registration, it was not clear which services that constitute an outpatient contact. As such, it was not possible to separate, eg, phone consultations from in-person outpatient contacts, nor was it clear to which extent such contacts contributed to the registered rates. This may in part explain the cross-country differences in outpatient contacts seen in this study.

Furthermore, outpatient contacts cannot be separated from emergency room contacts in Sweden, thus limiting the possibility to examine these two types of contacts separately. Furthermore, we did not include information from primary care. Therefore, it was not possible from this study to identify the overall burden of infectious diseases leading to medical contacts.

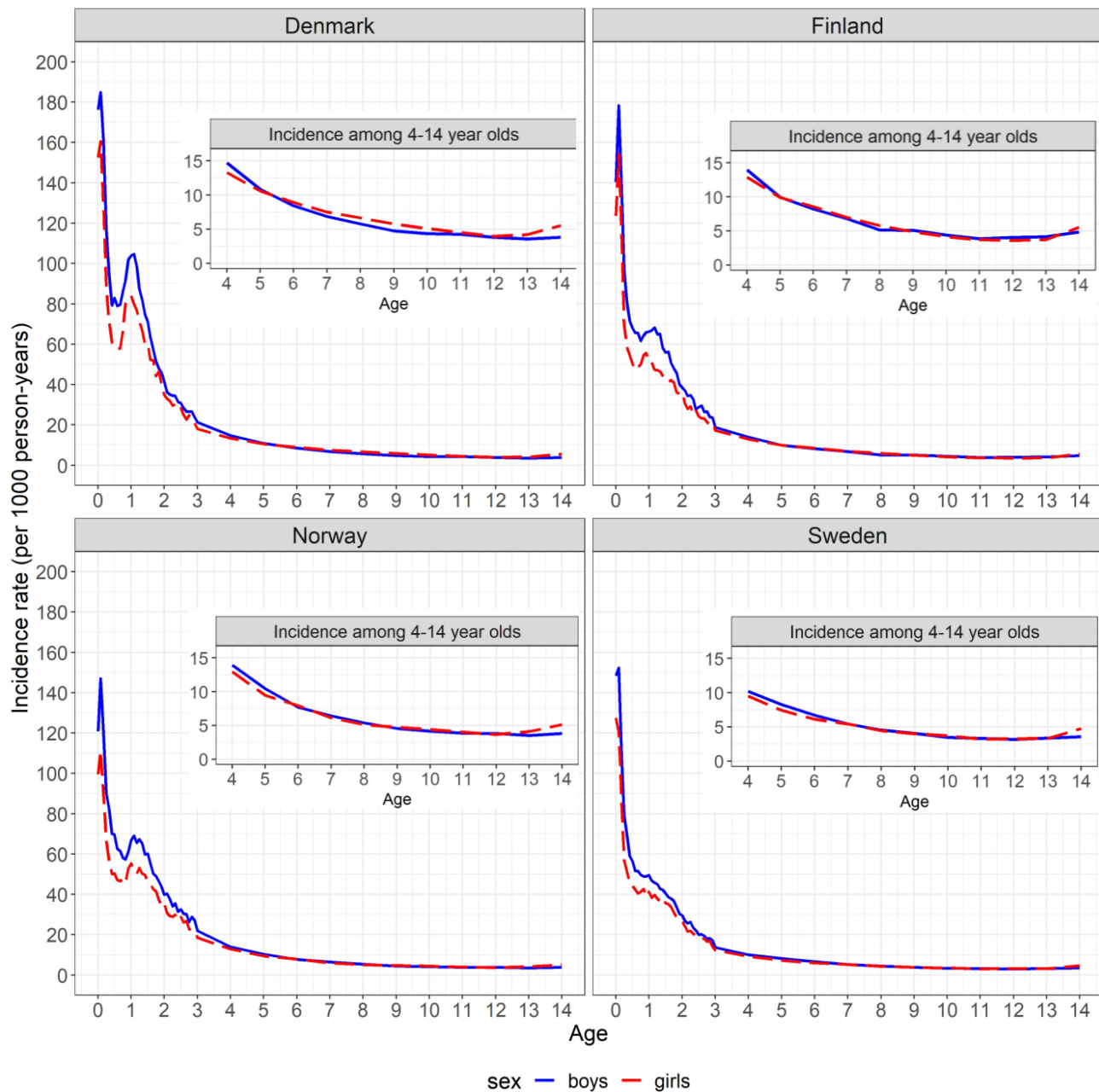


**Figure 4** Incidence rate (per 1000 person-years) of inpatient contacts with minimum 1 overnight stay for epidemiological years 2008/2009–2016/2017 by group of infection<sup>a</sup>, age, and country. <sup>a</sup>Different types of infections within an infectious disease hospital episode are all counted toward that type of infections (eg if both ICD-10 codes for GI and LRTI is registered during an infectious disease hospital episode the contact is counted both as GI and LRTI), thus summing the rates over types of infections will give greater rates, than the rates presented in [Figure 1](#).

**Abbreviations:** URTI, upper respiratory tract infections; LRTI, lower respiratory tract infections; GI, gastrointestinal infections; OI, other infections.

## Differences in Organisation and Access to Care

Sweden followed by Finland had higher rates of all types of hospital contacts for infections than Denmark and Norway, dominated by higher rates of URTI. All specialized outpatient clinics operated by doctors report to the patient registries in Sweden. In Finland, also day-surgery at private ear-, nose-, and throat-clinics is registered at the patient register. These may explain the higher rates of URTI. Reporting from specialized outpatient clinics outside hospital settings is incomplete in Norway and thus not included in the data for the present study, and only services from public hospitals are included in the Danish Patient Registry.



**Figure 5** Incidence rate (per 1000 person-years) of infectious disease inpatient hospital episodes<sup>3</sup> with minimum 1 overnight stay for epidemiological years 2008/2009–2016/2017 by age, sex, and country. <sup>3</sup>Hospital contacts with infections, which occur less than 14 days after discharge/visit date of a previous contact with infection are defined as the same infectious disease episode.

In Sweden, paediatric outpatient clinics, which manage common and mild conditions in early childhood<sup>28,29</sup> further contribute to the observed higher rates, including higher rates of OI. In the other countries, such conditions are usually handled in primary care and thereby not included in the patient registries.

The steep increase in rates, including all contacts in Denmark around year 2014 coincides with the introduction of a new out-of-hours primary care medical service organised within the emergency room department in the capital region of Denmark.<sup>30</sup> This organisational change resulted in registration of contacts in the patient registry, which previously would have been recorded in primary care. Similar organisational changes in emergency care and registration in the patient registry were developed from 2009 in Finland<sup>31</sup> and further implemented during 2013 and 2014,<sup>32</sup> which coincides with the increase in the Finnish rates in 2013/14. Different rates of infectious hospital contacts that include



**Table 1** Distribution of the Most Common Subgroups of Infections for Inpatient Hospital Episodes with at Least One Overnight Stay, by Group of Infection and Country

Denmark	Finland	Norway	Sweden
<b>Upper respiratory tract infections</b>			
Infections of the ear N=16,834 (25.9%)	Infections of the ear N=23,586 (48.3%)	Other URTI N=17,721 (33.3%)	Infections of the ear N=17,156 (31.9%)
Tonsillitis N=15,376 (23.7%)	Other URTI N=12,353 (25.3%)	Tonsillitis N=14,609 (27.4%)	Other URTI N=16,581 (30.8%)
Laryngitis N=12,287 (18.9%)	Laryngitis N=4872 (10.0%)	Infections of the ear N=12,303 (23.1%)	Tonsillitis N=9882 (18.4%)
Other URTI N=8655 (13.3%)	Tonsillitis N=4704 (9.6%)	Laryngitis N=4283 (8.0%)	Laryngitis N=5111 (9.5%)
Nasopharyngitis N=8243 (12.7%)	Abscessus peritonsillaris N=1308 (2.7%)	Nasopharyngitis N=1731 (3.2%)	Nasopharyngitis N=1459 (2.7%)
<b>Lower respiratory tract infections</b>			
Pneumonia N=39,151 (52.3%)	Other LRTI N=36,632 (63.1%)	Other LRTI N=27,587 (61.4%)	Other LRTI N=33,040 (54.5%)
Other LRTI N=33,948 (45.3%)	Pneumonia N=18,810 (32.4%)	Pneumonia N=14,804 (33.0%)	Pneumonia N=24,942 (41.2%)
Influenza N=1795 (2.4%)	Influenza N=2568 (4.4%)	Influenza N=2517 (5.6%)	Influenza N=2625 (4.3%)
<b>Other infections</b>			
Viral infections N=28,197 (30.6%)	Pyelonephritis N=9259 (23.3%)	Viral infections N=8172 (17.7%)	Viral infections N=27,282 (33.0%)
Fever NOS <sup>a</sup> N=15,803 (17.2%)	Viral infections N=8366 (21.1%)	Pyelonephritis N=5923 (12.8%)	Pyelonephritis N=11,732 (14.2%)
Pyelonephritis N=11,615 (12.6%)	Sepsis N=5049 (12.7%)	Infectious agents <sup>b</sup> N=5286 (11.4%)	Fever NOS <sup>a</sup> N=9693 (11.7%)
Sepsis N=5417 (5.9%)	Fever NOS <sup>a</sup> N=4485 (11.3%)	Fever NOS <sup>a</sup> N=3690 (8.0%)	Infectious agents <sup>b</sup> N=6270 (7.6%)
Cellulitis and abscess N=4699 (5.1%)	Cellulitis an abscess N=2604 (6.6%)	Sepsis N=3141 (6.8%)	Sepsis N=4019 (4.9%)

**Note:** <sup>b</sup>Bacterial, viral, and other infectious agents as the cause of diseases classified to other chapters.

**Abbreviation:** <sup>a</sup>NOS, not otherwise specified.

outpatient and emergency room contacts are thus unlikely to reflect different levels of infectious disease morbidity but are instead heavily affected by different organisation of care and coding practices within and across countries. This points to the potential for reducing hospital contacts and cost of care, to the extent that children are allocated to specialist care with diseases that could have been dealt with in general practice.

Across the study period, Denmark had notably higher rates of inpatient contacts including contacts without overnight stays, mainly for the youngest children, compared with the other countries. Norway also experienced slightly higher rates

compared with Finland and Sweden. The difference was dominated by higher rates of URTI and OI and may be an artefact of different registration practices given that admissions without overnight stays are commonly registered as outpatient contacts in Finland and Sweden.

## Inpatient Contacts with Overnight Stays

The greater similarity between countries in rates of inpatient hospital contacts with overnight stays likely reflects that more severe infections requiring hospitalisation overnight are less likely to be influenced by health-care organisation and coding practices. In all countries, the highest rates were observed among young infants (up to three months of age). This may be a result of neonatal complications and hospitalisation of children born preterm with a higher risk of infections<sup>33</sup> but may also reflect secondary diagnoses among otherwise healthy new-borns (ie, eye infections)<sup>1</sup> as well as low thresholds for admitting the youngest children with otherwise uncomplicated infections overnight.

Despite the similarity, the rates remained higher in Denmark across all epidemiological years, dominated by higher rates of OI and LRTI among 1-year-olds. It is not possible, based on the available data, to determine whether these excess hospitalisations are due to increased burden of disease or lower threshold for admitting young children for infectious diseases in Denmark. Finland and Norway also experienced higher rates among 1-year-olds compared with Sweden, which coincides with the common age for entry into day care. The lower rates across epidemiological years in Sweden were explained by lower rates of LRTI and URTI among 1-year-olds. Swedish parents may extend their parental leave up to 68 weeks after birth,<sup>34</sup> which might explain the lower incidence in Sweden.

Patient fees may affect health care seeking behaviour and thus influence the rates of infectious disease hospitalization. Reassuringly, the rates in Finland, where patients must pay a minor fee for inpatient care, were similar to the rates in Norway, where no fee is charged. Thus, this study does not provide indication that low-level patient fees withhold parents from seeking care for their children for infections leading to hospitalisation.

## Sex Differences

The age-specific patterns of sex differences were similar across countries, indicating sex-differential susceptibility to infections requiring hospitalisation according to age. Sex differences in infectious diseases are well established, but not fully understood.<sup>35</sup> Girls have been found to mount stronger immunological responses which may reduce susceptibility towards some infections and explain the lower rates in this study.<sup>35</sup> In addition, sex hormones affect the immune system differently at different ages,<sup>35</sup> which has been proposed to contribute to the divergent sex differences in infections according to age.<sup>1</sup> This aligns with our observation that boys had higher rates of inpatient contacts with overnight stays until approximately 5 years of age and lower rates after 13 years of age compared with girls.

## Rates by Group of Infections and Correlation with Health Interventions

The rates of GI dropped in Finland from 2009, and in Norway from 2014 which coincides with the national introduction of rotavirus vaccination<sup>36,37</sup> (sFigure 1). However, the incidence of inpatient contacts with overnight stays for GI also decreased across years in Denmark, where rotavirus vaccination was not offered, and in Sweden, where rotavirus vaccine was only implemented in some regions in 2014.<sup>38</sup> The rates of URTI decreased over time in all countries, which may partly be attributable to reductions in otitis media following introduction of pneumococcal conjugate vaccines in all countries<sup>39,40</sup> (sFigure 1). All vaccines within the national immunisation programmes are administered free of charge. Furthermore, the proportion of adult smokers has also decreased across the study period in all countries,<sup>41</sup> which may contribute to the downward going trend for respiratory tract infections as a result of decreased passive smoking exposure.<sup>42</sup>

The proportions of specific subgroups of infections varied greatly across the countries, which is unlikely to be explained solely by differences in burden of disease. Instead, reporting of specific subgroups of infections depends on the diagnostic accuracy for that infection and registration practices. A previous Danish validation study found that the positive predictive value was 72% for all medical contacts when identification was made on a 5-digit ICD-10 level, but increased to 81% on the 3-digit-level.<sup>27</sup> These previous findings coincide with the findings from the present study, as the combined rates by the broader groups of infections (LRTI, URTI, GI, and OI) were similar across countries, while the distribution of the more specific subgroups differed.

## Comparison to Other Studies

Few studies have reported on the overall rates of childhood infectious disease hospitalisations. In the United States, the incidence of infectious inpatient hospitalisations was estimated at 70.1/1000 children below 1 year of age in 2003,<sup>2</sup> which is considerably lower than in Denmark, but comparable to the other Nordic countries. Many paediatric infections are first cared for in emergency room departments in the United States, whereof only 5% resulted in hospitalisation.<sup>43</sup>

## Conclusion

Differences across countries and over time to a large extent reflect differences in health-care organisation and registration practices for outpatient contacts and inpatient contacts without overnight stays. When focusing on the comparable outcome, rates of inpatient contacts with overnight stays, we found that these differed similarly across countries with regard to age and sex of the child, with the anticipated highest rates in the youngest males. Some of the between-country and within-country differences observed coincide with introduction of vaccines, decreased prevalence of smoking, and entrance into day-care and point towards areas for improvement of prevention of childhood infectious disease.

Register data offer an excellent opportunity to study large, comprehensive, and representative cohorts under routine care for long periods of time with relatively low resources. The present study displays that valid cross-country comparison is enhanced with increasing duration of admission as a measure of infectious disease severity. Meanwhile, differences in diagnostic accuracy and reimbursement incentives may hamper cross-country comparison for some subgroups of infections.

## Data Sharing Statement

Data on hospital contacts used in this study arises from nationwide registers. Due to data protection rules, we are not allowed to share the individual-level data, but other researchers fulfilling the requirements from the data providers could obtain similar data.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

AAP and HN are investigators in vaccine-related studies for which THL has received funding from GSK, Pfizer and Sanofi Pasteur. Dr Signe Sørup reports grants from NordForsk, during the conduct of the study. The remaining authors report no relation that could be construed as a conflict of interest.

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