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ORIGINAL ARTICLE

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Antibiotic use for airway infections in Norwegian children—A national register-based study

Eva Rydland[1,2] | Sigurd Høye[3] | Ketil Størdal[1,4,5]

[1]Department of Pediatrics, Østfold Hospital Trust, Grålum, Norway

[2]Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

[3]Antibiotic Centre for Primary Care, Department of General Practice, Faculty of Medicine, Institute of Health and Society, University of Oslo, Oslo, Norway

[4]Department of Pediatric Research, University of Oslo, Oslo, Norway

[5]Division of Pediatric and Adolescent Medicine, Oslo University Hospital, Oslo, Norway

Correspondence
Ketil Størdal, Department of Pediatric Research, University of Oslo, Pb 4956 Nydalen, NO-0424 Oslo, Norway.
Email: ketil.stordal@medisin.uio.no

Abstract

Aim: Respiratory tract infections (RTIs) are major contributors to childhood antibiotic use. We aimed to investigate geographical and temporal trends in the prescription of antibiotics and consultations for RTIs in children <18 years living in Norway from 2010 to 2017.

Methods: In a nationwide observational study, we analysed antibiotic prescriptions from the Norwegian Prescription Database and reimbursed contacts from primary care physicians. We limited the study to airway antibiotics and diagnostic codes indicating RTIs.

Results: Antibiotic prescriptions due to an RTI varied from 75 to 134 per 1000 consultation due to RTI across counties in Norway (relative risk 1.79, 95% CI 1.68–1.90 for highest compared to lowest). The use of health care varied from 414 to 585 consultations for RTI per 1000 inhabitant/year (relative risk 1.43, 95% CI 1.41–1.44 for highest compared to lowest). From 2010 to 2017, we observed a 21% reduction in antibiotic prescriptions per RTI consultation and of 6% for the number of consultations for an RTI. At the county level, the use of health care was positively associated with the proportion of RTIs that resulted in antibiotic prescription.

Conclusion: We found a reduction in doctors' antibiotic prescription and the use of health care for RTIs, and a variation across counties.

KEYWORDS
antibiotic, child, health care use, prescription, respiratory tract infection

1 | INTRODUCTION

Antimicrobial resistance is of increasing global concern. The antibiotic use in children is one of the highest of the general population.[1] Young children frequently receive antibiotics due to a high frequency of respiratory tract infections (RTIs) although mostly self-limiting and of viral origin. The use of antibiotics in Norway is lower than in most high-income countries,[2] still 32% of all children in Norway receive antibiotics before 18 months of age, and 8% have two or more prescriptions before this age.[3]

During the last decade, there has been a reduction in the total prescriptions of antibiotics in Norway. However, there is still a substantial geographical variation in prescription rates with almost 50% higher use in some areas compared to those with the lowest rates.[4] Antibiotic

Abbreviations: A&E, accident and emergency; ATC, Anatomical Therapeutic, Chemical Coding System; GP, general practitioner; ICPC-2, International Classification of Primary Care 2; NorPD, Norwegian Prescription Database; RTI, respiratory tract infection; SSB, Statistics Norway.

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overuse remains a challenge in Norway, as this variation is unlikely explained by differences in the prevalence of bacterial infections.

Previous studies on the paediatric population have investigated the total number of prescriptions regardless of the prescriber or the patients/caregivers health-seeking behaviour. Antibiotic prescription is dependent on clinicians' practices as well as on the patient/caregiver use of health care services. In Norway, 84% of antibiotics are prescribed in primary health care[5] and, therefore, it is important to examine the paediatric antibiotic prescription habits of general practitioners (GPs) and Accident and Emergency (A&E) doctors, as well as the use of healthcare services in the population.

The aim of this study is to explore geographical and temporal trends in the prescription of RTI antibiotics and RTI consultations in children. We further aim to investigate the association between antibiotic prescription habits and patients' use of healthcare.

Key notes

- Both parents and doctors are responsible for the overuse of antibiotics, and there are substantial geographical and temporal differences in the use of health care for respiratory tract infections.
- The proportion of antibiotic prescriptions per consultation was positively associated with the number of consultations for respiratory tract infections at a county level.
- Reduction in prescription rates and health care use during the last decade have contributed to a decrease in antibiotic prescriptions.

2 | METHODS

This is an observational register-based nationwide study. We analysed data from the Norwegian Prescription Database (NorPD) and all contacts from primary care for children and adolescents aged <18 years living in Norway from 1 January 2010 to 31 December 2017. The data available is aggregated and therefore not on an individual level, making our approach to the analysis ecological.

2.1 | Population

We included all children and adolescents <18 years of age living in Norway and categorised them into four age groups as shown in Table 1. Statistics Norway (SSB) provides population data for the 19 counties in Norway. Population per county per 1 January each year was used to estimate the number of filled prescriptions of systemic antibiotics per 1000 in the respective age groups.

Years of observation in the respective age group is the unit for the denominator. For the first year of life, we reduced the observed years by 50%, as these infants had lived on average only half their first year by the end of the calendar year.

2.2 | Antibiotic prescribing volumes

The NorPD at the Norwegian Institute of Public Health contains data on all dispensed medications in Norway. Systemic antibiotics are available by prescription only. We extracted data on all prescriptions for systemic antibiotics, including geographic location to the level of county in which the medication was dispensed. We linked prescriber data from the NorPD to the Registry of General Practitioners and were then able to distinguish doctors working in primary health care from doctors working elsewhere. For the purpose of our study, we extracted all filled prescriptions of systemic antibiotics from GPs with an active reimbursement contract at the time of prescribing.

Our focus in this study is on antibiotics for upper and lower respiratory tract infections and therefore only Anatomical Therapeutic Chemical Coding system (ATC) codes for commonly used airway antibiotics were included (Table S1).

We considered the prescription of antibiotics for prophylactic use to be outside the scope of our research and therefore individuals with >100 dispensed antibiotics during the time period were excluded. Likewise, if a prescription contained >10 batches, we considered it an indicator of prophylactic use and we excluded these from the data set.

A total of 2234341 filled antibiotic prescriptions for children <18 years during 2010–2017 were identified. These numbers include all systemic antibiotics dispensed regardless of the indication. Of all the antibiotic prescriptions, 66% were from primary health care physicians with an active contract and 76% were for antibiotics commonly prescribed for RTIs (Figure 1, flow chart).

2.3 | Diagnostic codes

In Norway, all doctor's contacts in primary health care are reimbursed and registered in the KUHR (Control and payment of health reimbursements) database. The Norwegian health care system employs The International Classification of Primary Care 2 (ICPC-2) for coding primary health care contacts, and these codes are registered by the doctor. For reimbursement, a minimum of one code in ICPC-2 for each contact is registered. GPs are contract-based, and therefore we were able to link the prescriptions to the geographical county they were prescribed.

For the purpose of the study, we have identified and grouped the ICPC-2 codes indicating airway infections as a potential contact for antibiotic prescription (Table S1). In addition to diagnostic coding, each visit includes the age of the patient and the location of the GPs office, allowing us to investigate the differences in the use of healthcare within the country. In this way, we can identify patient use of healthcare to analyse the effect this has on the volume of antibiotics.

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TABLE 1 Overview of prescription data from Norwegian Prescription Database and consultations for respiratory tract infections (RTI) during 2010–2017.

	Norwegian population 2014	Observed child years	Total no. of RTI prescriptions (%)	Annual RTI Prescriptions per 1000	No. of RTI consultations (%)	Annual RTI consultations per 1000
Age category						
0–2 years	153 292	1 149 690	319 642 (28)	278	1 968 470 (42)	1712
3–5 years	192 785	1 542 290	299 208 (26)	194	923 385 (20)	599
6–12 years	428 077	3 424 616	314 060 (27)	92	980 256 (21)	286
13–17 years	321 340	2 570 720	211 518 (18)	82	775 989 (17)	302
Total	1 095 494	8 687 316	1 144 428	131	4 648 100	539
Sex						
Male			586 228 (51)		2 405 274 (52)	
Female			558 200 (49)		2 242 826 (48)	
Consultation type						
General practitioner					3 679 150 (79)	
Emergency room					968 950 (21)	
Diagnosis code						
Upper RTI					2 809 176 (60)	
Lower RTI					935 095 (20)	
Ear infections					903 829 (20)	

There was a total of 15 925 370 contacts in the primary health care for children <18 years in the period 2010–2017. Infectious diseases comprised 38% of the consultations, 78% of these were due to respiratory tract infections (Figure 1, flow chart).

2.4 | Outcome

The main outcome is the number of dispensed antibiotics per 1000 children <18 years at the level of county and calendar year.

2.5 | Exposure

To model the use of health care, we used the number of RTI consultations per 1000 children as the measure of exposure. Further, as a measure of antibiotic prescription practice, we used the number of prescriptions per 1000 RTI consultation. As we aimed to determine temporal and geographical variation in antibiotic use <18 years, use of healthcare and prescriptions were estimated for each year and county.

2.6 | Statistical method

We used STATA 17 for the statistical analysis. We analysed descriptive data in percentages and calculated means and medians according to their distribution. As our data was aggregated and not on an individual level, we modelled the association between the use of health care and doctor's prescription habits for the last year with available data (2017) in a linear regression model.

2.7 | Ethics

The data sets do not include data on an individual level and consent was not required. The Regional Committee for Medical and Health Research Ethics granted a dispensation from professional secrecy requirements (2018/671 REK Sør-Øst D). Data protection was approved by the Norwegian Centre for Research Data (NSD number: 60844).

3 | RESULTS

We analysed a total of 1 144 428 antibiotic prescriptions for RTIs. The mean annual prescription rate was 131 prescriptions per 1000 person years, ranging from 278 in the youngest to 82 in the oldest age group (Table 1). There was a total of 4 686 100 consultations due to RTIs. The majority (60%) were upper RTIs, whereas lower RTIs and ear infections contributed to 20% each. The annual RTI consultations also differed by age, ranging from 1712 RTI consultations per 1000 person year for 0–2 years to the lowest number of 286 consultations for the age group 6–12 years (Table 1). This means that the youngest children are taken to the doctor approximately five times as often because of RTI symptoms. Children aged 0–5 years had the most consultations for RTIs, contributing to 62% of the RTI consultations in the whole paediatric population.

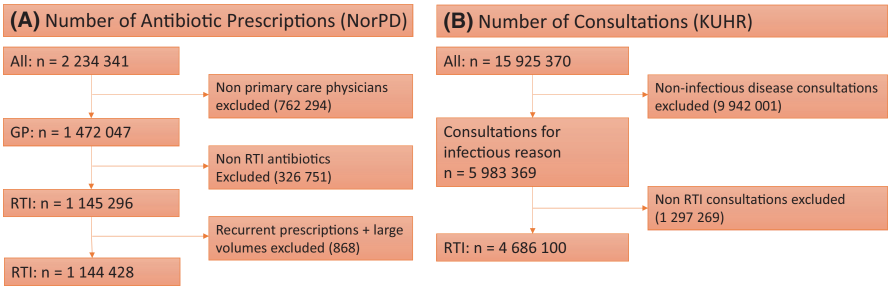

FIGURE 1 Flow chart of data management.

TABLE 2 Change in doctor's prescription practices and use of health care by county of living from 2010 to 2017.

	Doctor's prescription practices: No. of antibiotic prescriptions per 1000 RTI consultations			Use of health care: No. of RTI consultations per 1000		
County in Norway	**Year 2010**	**Year 2017**	**% change**	**Year 2010**	**Year 2017**	**% change**
Sogn og Fjordane	123	80	−35		455	−14
Nordland	104	75	−28	456	414	−9.2
Oppland	135	99	−27	538	475	−12
Oslo	159	117	−26	705	585	−17
Østfold	174	132	−24	578	521	−10
Sør-Trøndelag	134	103	−23	491	492	+0.2
Vestfold	171	132	−23	583	534	−8.4
Nord-Trøndelag	150	117	−22	584	521	−11
Møre og Romsdal	137	107	−22	576	521	−10
Aust-Agder	134	106	−21	503	514	+2.2
Hordaland	154	123	−20	496	538	+8.5
Troms	103	83	−19	461	461	0
Akershus	141	114	−19	575	534	−7.1
Rogaland	154	125	−19	545	538	−1.3
Hedmark	161	134	−17	593	567	−4.4
Buskerud	138	115	−17	564	529	−6.2
Telemark	112	95	−15	488	458	−6.1
Vest-Agder	143	126	−12	547	526	−3.8
Finnmark	77	81	+5.2	471	492	+4.5
	Mean reduction		−21%	Mean reduction		−5.9%

Correspondingly their share of antibiotic prescription was 54% of the total RTI prescriptions.

The doctors' prescription habits varied from 75 to 134 RTI antibiotic prescriptions per 1000 inhabitants in the year 2017 (relative risk 1.79, 95% CI 1.68–1.90 for highest compared to lowest, Table 2). In the same year, patients' use of healthcare varied from 414 to 585 consultations for airway infections per 1000 person year across regions (relative risk 1.43, 95% CI 1.41–1.44 for highest compared to lowest, Table 2).

Figure 2 displays the patients' use of health care by doctors' prescription habits for 2017. Use of health care was positively associated with the proportion of RTIs that resulted in antibiotic prescription. In a linear regression model, the coefficient was 1.88 (95% CI 1.28–2.49, $p < 0.0001$) and the degree of explained variation (R^2) was 0.71.

Our data shows that from 2010 to 2017 the national reduction in antibiotic prescriptions for RTIs was 21%. The reduction in use of healthcare for RTIs overall was 5.9%, with a reduction notably for lower RTIs and ear infections (Figure 3). There were considerable differences within the 19 counties in Norway regarding these reductions, with the highest reduction at 35% regarding antibiotic prescriptions and 17% reduction in patients' use of healthcare, while some counties, although few, had an increase in both doctors' prescriptions and increase in use of healthcare during the time period (Table 2).

4 | DISCUSSION

The main finding of our study is a variation across geography and over time in doctors' prescription habits and patient use of health

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care RTIs in children. The use of health care for RTIs was strongly associated with the prescription habits for RTIs at a county level. Furthermore, we have registered a reduction in both use of health-care and prescription rates from doctors, the most marked change was in doctors' prescription habits.

A previous study from Norway concluded that the doctors' prescribing and patients' consulting had an equal impact on the antibiotic burden.[6] This study used data from the NorPD and KUHR in similar ways as in this study, but the data was captured for only 1 year. Furthermore, the previous study was not specific for the paediatric population.

Our population-level descriptive data regarding antibiotics and RTIs are in line with findings from other studies. Young children are at the highest risk of antibiotic prescription, and antibiotics for RTI are the most commonly prescribed, being the main target group for potential intervention and further investigation.[7]

There has been a clear reduction in antibiotic use in Norway in the paediatric and the adult population since 2012. This is probably due to campaigns increasing both patient and prescriber awareness, but also contributing and specific for the paediatric population is the introduction of the pneumococcal conjugate vaccine since 2005, with an upgrade from a 7-valent to a 13-valent pneumococcal vaccine in 2011, which has reduced the incidence of common RTIs.[8] Other vaccines for RTIs have not changed during the period. Our data is specific for the paediatric population, which are high consumers of both health care services (with a higher annual consultation rate the younger the child) and antibiotic prescriptions.

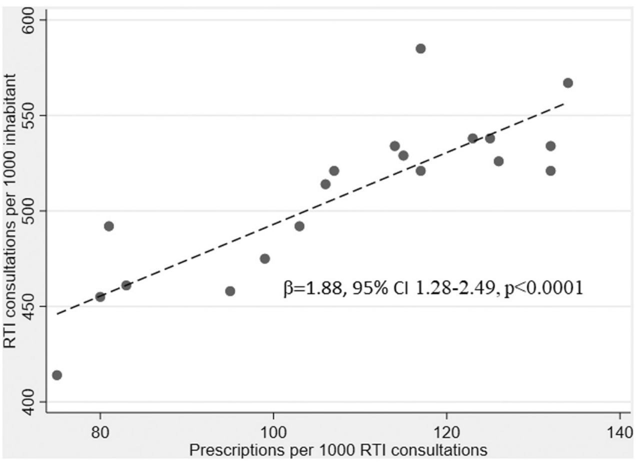

FIGURE 2 Scatter plot with a fitted line of number of RTI consultations per 1000 inhabitant by doctor's prescription of antibiotics per 1000 RTI consultations (data per county for 2017).

Primary care consultations for RTIs in the Norwegian paediatric population have previously not been studied. Our study shows that corresponding to the decrease in antibiotic prescriptions there is a similar trend for RTI consultations with a clear reduction from 2012. The trend is most apparent for consultations related to lower RTIs and ear infections, whereas the trend for upper respiratory tract infections is less evident. Diagnostic codes for sinusitis, acute tonsillitis and streptococcal pharyngitis belong to the latter group of RTIs and are potential sources of many antibiotic prescriptions. A decrease in the lower RTI consultations could partly be a result of doctors improved ICPC-2 coding, but more so, it may be a result of increased patient education and awareness.

High consultation rates give a higher rate of antibiotic use. A study in England found that the decrease in RTI antibiotics prescribed was mainly due to the publics' reduction in doctor consultations.[9] They found that the largest reduction in consultation rates was for the upper RTIs, like common cold, laryngitis and sore throat. In contrast to this study, our data suggests that the RTI antibiotic decrease is linked to both the patient and doctor, but the doctor's prescription habits changed more markedly over time. Furthermore, the findings from these two studies differ in regard to the type of consultations that have decreased, with our study finding the largest decrease for consultations of lower RTIs and ear infections.

The number of consultations at the GPs office not linked to infection is subtly increasing during the 8-year observation time (data not shown). This indicates that the GPs are working more, giving them less time per patient. Previous studies have shown

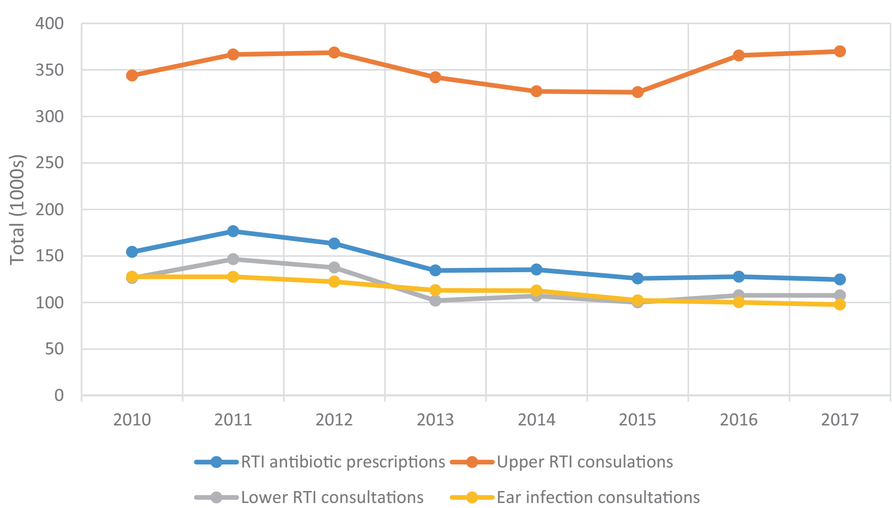

FIGURE 3 Trends of respiratory tract consultations and respiratory tract antibiotics over time.

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that when GPs have less time per patient, there is a higher risk of antibiotics being prescribed,[10] also seen in the out-of-office (A&E) services.[11] Despite the increase in total use of health care, antibiotic prescriptions are decreasing. Lack of time, due to many patients, is a negative factor in this setting and these data could therefore support political incentives to decrease the shortage of doctors in primary health care. With the inherent limitations of the study design, we speculate that restrictive antibiotic prescription for RTIs may impact on health-seeking for self-limiting infections.

Strengths of this study is that the registries used are robust and complete. Nation-wide data based on health care registries avoids any selection bias and provides large-scale data which allows for precise estimates. NorPD data contains all dispensed prescriptions, as opposed to all prescribed medications, this means that the data is complete with all antibiotics that are actually acquired by the patient.

Limitations of our study is that our data is not on an individual level, precluding any multilevel analysis. Completeness is slightly lower in areas where private companies provide health care to the population. These do not report their data to KUHR and therefore these contacts are not included. The dispensed antibiotics for these providers are also not part of our study, and unless they have a valid contract as a GP they are not included. It must also be acknowledged that there could be differences in the age distribution of children cared for by the GP, and this may again impact the antibiotic prescription rate. Regarding the A&E, the shifts are mainly covered by GPs, but also doctors working elsewhere cover some shifts and these prescriptions are not included in our data. In some rural areas, some antibiotics are dispensed outside the pharmacies, directly from the GPs office or the A&E and will therefore not be included in our data set. This will inevitably lead to falsely low estimates for antibiotic use, but likely accounts for a small amount of antibiotics. Prophylactic use was not measured but estimated based on a high number of filled prescriptions and excluded. This may introduce some imprecision in the estimates but is unlikely to differ over time and regions.

The classification of antibiotics as RTI antibiotics introduces some uncertainty because the diagnosis prompting a prescription of an antibiotic is not registered in the NorPD. This would however be a non-differential bias, which is unlikely to affect prescription data differentially by geography and time.

The geographic density of GPs specialists and areas where private companies or out-patient contract specialist (i.e paediatricians, ENT specialist) are potential confounders as high density of specialist would probably be consistent with lower antibiotic prescriptions, we have not been able to adjust for this, as these data was not available.

Lastly, overuse of antibiotics should be balanced against the risk of underuse. Future studies should address whether downward regional or temporal trends in antibiotic use are associated with complications like the need of hospital care as a balancing measure. If such complications are not observed, this would ensure the safety of lowering the use of antibiotics in primary care.

5 | CONCLUSION

Our study shows that there is a substantial geographical difference in an antibiotic prescription for airway infections, which is likely due to both the patients' use of health care and doctor's prescription habits. There has been a greater reduction in doctor's prescription rates than in the use of healthcare for RTIs, and during the study period, the antibiotic rates have decreased substantially.

AUTHOR CONTRIBUTIONS

Eva Rydland: Writing – original draft; formal analysis; visualization; investigation. **Sigurd Høye**: Funding acquisition; conceptualization; writing – review and editing; methodology; data curation; supervision; resources; formal analysis; validation; investigation; software. **Ketil Størdal**: Conceptualization; funding acquisition; writing – review and editing; methodology; formal analysis; project administration; supervision; resources.

FUNDING INFORMATION

No funding received.

CONFLICT OF INTEREST STATEMENT

None.

ETHICS STATEMENT

The data sets do not include data on individual level and consent was not required. The Regional Committee for Medical and Health Research Ethics granted a dispensation from professional secrecy requirements (2018/671 REK Sør-øst D). Data protection was approved by the Norwegian Centre for Research Data (NSD number: 60844).

ORCID

Ketil Størdal https://orcid.org/0000-0002-2620-7646

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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