Antibiotic prescribing for acute respiratory tract infections in Norwegian primary care out-of-hours service

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\textbf{ABSTRACT}

\textbf{Purpose:} To examine factors correlating with antibiotic prescribing for acute respiratory tract infections (ARTIs) in Norwegian primary care out-of-hours service.

\textbf{Materials and methods:} Retrospective data analysis for the year 2014 in two out-of-hours primary care units located in the towns of Hamar and Tønsberg in Norway, analysing type and frequency of different antibiotics prescribed by 117 medical doctors for ARTIs, and factors correlating with these.

\textbf{Results:} The 117 doctors in two out-of-hours units diagnosed 6757 cases of ARTIs. 2310 (34.2%) of these resulted in an antibiotic prescription, where of 1615 (69.9%) were penicillin V (PCV). Tonsillitis and sinusitis were the two ARTI diagnoses with the highest antibiotic prescription rate. The antibiotic prescription rate increased successively with increasing activity level, measured as shorter median duration of consultations per session, from 28.7% (reference) in the least busy quintile of sessions to 36.6% (OR: 1.38 (95% CI = 1.06–1.80)) in the busiest quintile of sessions. Prescribing of broad-spectrum antibiotics was not correlated with median duration of consultations per session. Female doctors had an OR of 0.61 (0.40–0.92) of a broad-spectrum antibiotic prescription compared to their male colleagues.

\textbf{Conclusions:} Antibiotic prescribing for ARTIs in the primary care out-of-hours services investigated is at the same level as in Norwegian general practice, but with a higher prescription rate of PCV. Antibiotic prescribing increases on busy sessions, measured as median duration of consultations per session. The work frame in primary care out-of-hours service might influence the quality of clinical decisions.

\textbf{Background}

Antimicrobial resistance is a serious threat to global public health [1]. The prevalence of resistant microbes in human isolates is still low in Norway and other Scandinavian countries. However, even in Norway, the development has been less favourable [2].

About 85% of all antimicrobial drugs prescribed in Norway is prescribed in primary care, and around half of the antibiotic consumption in Norway is for acute respiratory tract infections (ARTIs) in general practice [3,4]. The self-limiting course of most of these conditions make them important targets for the desired reduction of antibiotic prescribing and the desired relative decrease of broad-spectrum antibiotics [5–7].

There were 2.63 consultations per citizen in daytime general practice and 0.26 consultations per citizen in the out-of-hours service in Norway in 2015 [8]. ARTIs constitute 9% of the consultations in general practice, while the corresponding proportion in the out-of-hours service is 16.7%. Hence, this service handles a substantial part of the ARTIs, and is thereby potentially an important contributor to the overall antibiotic consumption.

The 428 municipalities in Norway (median of 4661 inhabitants (2014)) own and run the out-of-hours primary care service. Two or more municipalities often collaborate to run one unit together. Participation in the out-of-hours work is mandatory for list-holding general practitioners (GPs) in Norway. In spite of this, only 55.5% of the duties were staffed by list-holding GPs in 2015 [9]. Many of these units pay their doctors by a fee for service plan, hence making it possible to give away sessions to other GPs or to doctors in
hospital or scientific occupation with less or no experience in general practice. A high number of sessions generate higher income. In many units, a high number of consultations per session also generates more income. In most places, trained nurses decide which patients get a consultation with the doctor at the out-of-hours units, and which patients can wait to see their regular GP the next day.

In order to implement effective measures to improve the quality of the use of antibiotics in the out-of-hours setting, we need to know factors correlating with a high prescription rate. A systematic review on antibiotic prescribing for respiratory tract infections, found that acute bronchitis and features on physical exam were factors associated with antibiotic prescribing [10]. Physician’s perception of patient desire for antibiotics was a stronger prediction for prescription than patient desire for an antibiotic. Among Norwegian GPs in daytime practice, there is a correlation between a high activity level, measured as a high yearly number of consultations, and both a high prescription rate of antibiotics and the rate of broad-spectrum agents for ARTIs [11].

Former results from research on prescribing pattern in out-of-hours service have been inconsistent [12,13]. In the Norwegian city of Trondheim, there was a higher prescription rate in the out-of-hours service than in daytime practice [11,14]. The aim of our study is to explore which factors that predict antibiotic prescribing and broad-spectrum prescribing for ARTIs in an out-of-hours primary care setting. Especially we wanted to explore whether the activity level, both at each session and for each doctor, was correlated with antibiotic prescribing.

Methods

We have made a retrospective data analysis for the year 2014 at two out-of-hours primary care units, located in the towns of Hamar and Tønsberg, covering respectively, four and six municipalities, with a total of 170,000 inhabitants. All the 128 doctors scheduled with at least one session in one of these units during 2014 were invited to participate. Fifty-nine doctors in Tønsberg (93%) and 63 in Hamar (97%) agreed to participate. Four doctors were not included due to lack of conducted sessions. We excluded one doctor as we were not able to extract the prescription data.

Data were retrieved from the two units’ electronic patient record systems (Winmed 2), using software designed by one of the authors (SG) for this particular study. The following data were used in the analysis: GP identity (anonymised), gender and specialty status, number of sessions during 2014, date, duration and type of consultations, the total number of consultations on each session, prescribed antibiotics and patients’ sex and age. For all consultations with R-diagnoses, except R06 and R84-R99 and all H-diagnoses indicating otitis media (H01, H70-72 and H74) from the 2nd International Classification of Primary Care (ICPC-2), the diagnose was retrieved.

Antibiotics were divided into groups based on similar antimicrobial effects or clinical indications. In some of the analyses, we dichotomised antibiotics into either penicillin V (PcV) or others. Some diagnoses were also grouped together based on their clinical similarities and in line with former publications; upper ARTIs and respiratory symptoms (R01–05, 07–29, 74 and 80), ear infections (H01, 71, 72 and 74), acute tonsillitis (R72 and 76) and ‘other RTIs’ (R71, 77, 82 and 83) [11,15]. Acute sinusitis (R75), acute bronchitis (R78) and pneumonia (R81) were analysed as single diagnoses.

As we did not have access to the work schedule, we defined one session as the time between the opening of the first journal and the closing of the last journal. When the time interval between two open journals exceeded eight hours, we defined it as a new session. Each consultation’s duration was found in the electronic patient record software.

As a measure of each session’s busyness, we built the variable median duration of consultations per session, based on the duration of and number of consultations. All sessions were divided in quintiles, based on their consultations’ median duration, with the sessions with the longest duration of consultations as the reference quintile. As a measure of each doctor’s session rate, we examined a variable called median days between sessions, divided in quintiles, with the longest time between sessions as the reference quintile. We performed two multilevel binary logistic regression analyses. The dependent variables were (a) antibiotics prescribed, yes or no and (b) broad-spectrum antibiotics versus PcV. The independent variables were the two out-of-hours primary care units, the patients’ sex and age group, the groups of diagnoses, the doctor’s age, gender and specialty status (family medicine), median duration of consultations per session and median days between sessions, with the individual GPs as clusters.

STATA 14 (College Station, TX) was used for the multilevel binary logistic regression and IBM SPSS Statistics Data Editor Version 22 (Armonk, NY) for the descriptive statistics.

The study was presented to and approved by The Regional Committee for Research Ethics (2015/398/REK...
ser-oest) and by The Norwegian Social Science Data Services (42185/3/LMR).

Results

The material consists of data from 40,197 consultations (34,874 patients, 117 doctors), either in the out-of-hours office (39,796, 99%) or in the patient’s home (34,874 patients, 117 doctors), either in the out-of-hours care units.

Our study is a retrospective data analysis. The results reflect the present reality as registered in the electronic patient records. The doctors involved were not

### Table 1. Antibiotic prescription practice of 117 doctors in 6757 ARTI consultations in two Norwegian out-of-hours units during the year 2014 by the antibacterial agents issued for the various ARTI diagnoses.

| Diagnoses group          | Total number of consultations | Total number of consultations with antibiotic prescriptions (%) | J01CE penicillin V (%) | J01CA + J01CF, penicillins with extended spectrum (%) | J01FA + J01FF, macrolides/lincosamides (%) | J01AA, tetracyclines (%) | Other J01 (%) |
|--------------------------|-------------------------------|---------------------------------------------------------------|-----------------------|------------------------------------------------------|-------------------------------------------|-------------------------|---------------|
| URTIs and respiratory tract symptoms\(^a\) | 3543                          | 670 (18.9)                                                    | 501 (74.8)            | 27 (4.0)                                             | 101 (15.1)                                | 30 (4.5)                | 11 (1.6)      |
| Acute tonsillitis        | 538                           | 432 (80.3)                                                    | 368 (85.2)            | 10 (2.3)                                             | 52 (12.0)                                 | 1 (0.2)                 | 1 (0.2)       |
| Acute sinusitis          | 315                           | 239 (75.9)                                                    | 161 (67.4)            | 8 (3.3)                                              | 45 (18.8)                                 | 21 (8.8)                | 4 (1.7)       |
| Acute bronchitis         | 340                           | 136 (40.0)                                                    | 57 (41.9)             | 14 (10.3)                                            | 24 (17.6)                                 | 36 (26.5)               | 5 (3.7)       |
| Pneumonia                | 598                           | 300 (50.2)                                                    | 145 (48.3)            | 39 (13.0)                                            | 56 (18.7)                                 | 52 (17.3)               | 8 (2.7)       |
| Ear infections           | 654                           | 375 (57.3)                                                    | 300 (80.0)            | 46 (12.3)                                            | 19 (5.1)                                  | 2 (0.5)                 | 8 (2.1)       |
| Other ARTIs              | 769                           | 158 (20.5)                                                    | 83 (52.5)             | 12 (7.6)                                             | 35 (22.2)                                 | 23 (14.6)               | 5 (3.2)       |
| Total                    | 6757                          | 2310 (34.2)                                                   | 1615 (69.9)           | 156 (6.8)                                            | 332 (14.4)                                | 165 (7.1)               | 42 (1.8)      |

\(^a\)Macrolides form 92.8% (erythromycin 78.6%, azithromycin 12.0%, clarithromycin 1.8% and lincosamides form 7.2%).

Discussion

34.2% of children diagnosed with an ARTI received an antibiotic prescription, and three out of four of these were PcV. Acute tonsillitis and sinusitis were the two diagnoses with the most frequent prescribing. Antibiotic prescription rate increased with shorter median duration of consultations per session.

### Strengths and limitations

Our study is a retrospective data analysis. The results reflect the present reality as registered in the electronic patient records. The doctors involved were not
aware of the plans of a research project at the time of the consultations, and there may be a lack of accuracy in the giving of diagnosis. An unknown but probably small number of children received an antibiotic mixture at the unit in Tønsberg. These are recorded in the same way as paper prescriptions and are therefore not detected by the data retrieval. We have no possibility to distinguish the patients who were at the out-of-hours units due to antibiotic treatment failure or follow-up due to former started treatment. We assume that the number of such patients is few, but it may influence our findings. The rate of doctors agreeing to participate was high. Hence, we believe that the results are valid and reflect the clinical reality.

The group of diagnoses called upper respiratory tract infections and respiratory symptoms include most respiratory tract symptoms, also diagnoses less likely to be associated with respiratory tract infections. The grouping is concordant with former research from Norwegian general practice, enabling a comparison with this research [11]. However, this way of grouping diagnoses may have led to an underestimation of the antibiotic prescription rate of upper respiratory tract infections. The variable Median duration of consultations per session includes consultations for all possible diagnoses and not just ARTIs. By using median rather than mean duration of consultations, the variable also reflects that night sessions may be busy until

| ARTI                                      | Number of ARTI episodes | Number of ARTI episodes with antibiotic prescriptions (%) | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|----------------------------------------------------------|--------------------|
| URTIs and respiratory tract symptoms      | 3543                    | 670 (18.9)                                               | 1 (reference)      |
| Acute tonsillitis                         | 538                     | 432 (80.3)                                               | 24.11 (18.66–31.14)|
| Acute sinusitis                           | 315                     | 239 (75.9)                                               | 12.39 (9.22–16.60) |
| Acute bronchitis                          | 340                     | 136 (40.0)                                               | 2.74 (2.12–3.54)   |
| Pneumonia                                 | 598                     | 300 (50.2)                                               | 4.79 (3.85–5.95)   |
| Ear infections                            | 654                     | 375 (57.3)                                               | 7.63 (6.26–9.29)   |
| Other ARTIs                               | 769                     | 158 (20.5)                                               | 1.30 (1.04–1.61)   |

| Patient's gender                          | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|--------------------|
| Male                                      | 2964                    | 1 (reference)      |
| Female                                    | 3793                    | 1.07 (0.95–1.21)   |

| Patient's age                             | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|--------------------|
| <6                                        | 2148                    | 1 (reference)      |
| 6–12                                      | 502                     | 1.38 (1.08–1.77)   |
| 13–18                                     | 502                     | 1.35 (1.05–1.75)   |
| 19–44                                     | 1850                    | 2.25 (1.90–2.65)   |
| 45–64                                     | 919                     | 2.11 (1.72–2.58)   |
| 65–79                                     | 499                     | 1.60 (1.25–2.06)   |
| >80                                       | 337                     | 1.03 (0.76–1.40)   |

| Doctor's gender                           | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|--------------------|
| Male                                      | 4825                    | 1 (reference)      |
| Female                                    | 1932                    | 0.91 (0.65–1.27)   |

| Doctor's age                              | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|--------------------|
| 26–29                                     | 946                     | 1 (reference)      |
| 30–33                                     | 1408                    | 1.17 (0.69–2.00)   |
| 34–39                                     | 848                     | 1.20 (0.71–2.02)   |
| 40–44                                     | 1347                    | 1.54 (0.90–2.62)   |
| 45–68                                     | 2208                    | 1.02 (0.58–1.98)   |

| Specialty family medicine                 | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------------------------------|-------------------------|--------------------|
| No                                        | 4142                    | 1 (reference)      |
| Yes                                       | 2615                    | 1.04 (0.68–1.60)   |

| Median days between duties, in quintiles (number of GPs) | Number of ARTI episodes | Odds ratio (95% CI) |
|----------------------------------------------------------|-------------------------|--------------------|
| >32.5 (25)                                               | 311                     | 1 (reference)      |
| 15.5–32.0 (20)                                          | 796                     | 1.16 (0.68–1.97)   |
| 9.0–15.0 (20)                                           | 1021                    | 1.19 (0.70–2.03)   |
| 4.5–8.5 (24)                                            | 1088                    | 0.94 (0.54–1.64)   |
| 1.0–4.0 (23)                                            | 3541                    | 1.41 (0.83–2.41)   |

| Median duration of consultations per session in quintiles (number of sessions) | Number of ARTI episodes | Odds ratio (95% CI) |
|--------------------------------------------------------------------------------|-------------------------|--------------------|
| >14.77 (425)                                                               | 958                     | 1 (reference)      |
| 11.63–14.75 (429)                                                        | 1280                    | 1.15 (0.91–1.45)   |
| 9.42–11.63 (424)                                                         | 1423                    | 1.24 (0.97–1.57)   |
| 7.28–9.48 (425)                                                          | 1658                    | 1.16 (0.91–1.48)   |
| 0–7.27 (425)                                                              | 1438                    | 1.38 (1.06–1.80)   |

| Out-of-hours unit | Number of ARTI episodes | Odds ratio (95% CI) |
|-------------------|-------------------------|--------------------|
| Hamar             | 4216                    | 1 (reference)      |
| Tønsberg          | 2541                    | 1.17 (0.87–1.59)   |
midnight, when most of the consultations occur, and then more quiet until early morning. Hence, we find that the variable is a valid proxy for the doctors’ perceived time pressure, or busyness, in the actual session.

Results discussion

Prescription rate

We found an overall antibiotic prescription rate of 14.7%. A similar study from Danish out-of-hours primary care found a much higher prescription rate of 26.1% [16]. Still, the antibiotic consumption in the two countries are quite similar [17]. Hence, the overall antibiotic prescription rate in the out-of-hours service may reflect how the service is organized and used by the population, rather than the overall antibiotic consumption.

Patients in Norway will normally see their GP during daytime, both for acute and non-acute conditions. The out-of-hours services are supposed to handle conditions that cannot wait until the GPs open the next day or after the weekend. Although some people find it convenient to seek the out-of-hours units to avoid abstaining from work, there is reason to believe that the out-of-hours patient population is more acutely ill than the population in regular GP practice [18].
The patients are also unknown to the GP, and the possibility to follow-up is limited. The antibiotic prescription rate of 34.2% for ARTIs in our material is quite similar to the 33.5% found in daytime general practice [11]. This finding is therefore somewhat surprising, but in line with a former Norwegian study on tonsillitis and otitis in the out-of-hours care, and also in line with results from Flemish primary care [12,19]. A Dutch study on febrile children, however, suggests that GPs prescribe more antimicrobial drugs in the out-of-hours service than in regular GP practice [13].

An important finding in our study is the high proportion of PcV prescribing of 69.9%, close to the national goal of a 80% proportion of PcV for ARTIs [20]. This is about the same level found in the out-of-hours unit in Trondheim, but it is clearly higher compared to the findings of 41.2% in regular GP practice [11,14]. In both Trondheim and the two units in Hamar and Tønsberg, a report about diagnosis and treatment is sent to the family physician after the consultation at the out-of-hours units. An explanation may be that doctors working in transparent out-of-hours units are more adherent to guidelines than doctors working in regular general practice. This explanation is consistent with the findings from the RxPAD study, where audit and feedback among Norwegian GPs in peer continuing medical education groups, i.e. increasing the transparency of each GP’s prescribing, led to a significant decrease in broad-spectrum antibiotic prescribing [11,15]. The lack of transparency in general practice may be seen as a challenge when it comes to antibiotic stewardship [21].

Factors associated with antibiotic prescribing

In a recent review, factors associated with antibiotic prescribing for respiratory tract infections were examined. More than 80 factors were found, and the article highlights doctors’ perception of patient desire for antibiotics, the diagnosis acute bronchitis, as well as certain clinical findings such as fever, purulent sputum, abnormal respiratory exam and tonsillar exudate as the most important [10]. Our material does neither describe clinical findings nor doctors’ perceptions. Also in our study, acute bronchitis is a predictor of antibiotic prescribing. However, as possibly bacterial infections are included, it is not surprising that these infections (sinusitis, tonsillitis) are stronger predictors of antibiotic prescribing than acute bronchitis. Working in the out-of-hours service is recognised as professionally demanding, and many GPs want to avoid working in the out-of-hours service, thereby giving away their duties to other doctors [18]. A majority of out-of-hours practices have a fee for service plan [9]. This may trigger an economic incentive both for some doctors to take many duties and, if possible, to increase the consultation rate. A Canadian study found that high-volume practice was associated with inappropriate antibiotic prescribing and GPs’ consultation rates has been identified as a predictor of antibiotic prescribing for ARTIs in a Norwegian study [11,22]. The variable median duration of consultations per session in our study is a measure of how busy each session is for the doctor. This is a factor with little doctor’s influence, as the triage is done by nurses. The doctors’ job is to keep up with the pace decided by the triage. At busy sessions, ARTIs may be ‘easy’ consultations and an opportunity to reduce any delay. Even though duration of consultations is not, or only weakly, associated with antibiotic prescribing, doctors may consider to prescribe antibiotics partly to shorten consultations [23,24]. Hence, it is not unexpected that we found an increase in the prescription rate of antibiotics in sessions with shorter median duration of consultations.

The variable median days between duties is a variable highly influenced by the individual doctor, as each doctor can choose to take extra sessions to earn more money. We found no correlation between this variable and prescription rate.

Factors associated with broad-spectrum antibiotics

A Swedish study showed that older GPs chose broad-spectrum antibiotics to a higher degree than younger GPs and interns [25]. Female doctors had a higher overall prescription rate than their male colleagues, but there was no difference concerning the rate of broad-spectrum antibiotics. We could not confirm these findings. In contrary, our study showed that female doctors prescribe less broad-spectrum antibiotics than male doctors. Other factors that have been shown to be associated with broad-spectrum antibiotics are lower respiratory tract infections, patients’ age (higher for older patients), long patient list, doctors being high prescribers and doctors with a high practice volume [11,22,26]. We also found a high broad-spectrum prescription rate in the elderly and for acute bronchitis and pneumonia. We found no association neither between median duration of consultations per session nor median days between duties and broad-spectrum antibiotics. Like an American study, we also found a geographical difference between the two units [27]. The distance between our two units is too small to expect any difference in microbial flora. It is
more likely that the observed difference is explained by local factors, such as a variation in the treatment culture of the involved doctors.

Conclusion/implications
We found an antibiotic prescribing for ARTIs similar to earlier results from studies on Norwegian general practice, but with a higher prescription rate of PcV. This may be due to the higher degree of transparency in the out-of-hours units, and whether the routine to send a report to the patient's GP should be implemented in all out-of-hours units needs to be investigated further. Antibiotic prescribing increased on busy sessions, measured as shorter median duration of consultations per session. As the workload in the out-of-hours units is highly determined by the number of patients getting an appointment, the question of how the triage influences work frame and thereby clinical decisions, needs further attention.

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