Quality assessment of diagnosis and antibiotic treatment of infectious diseases in primary care: a systematic review of quality indicators

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ABSTRACT
Objective: To identify existing quality indicators (QIs) for diagnosis and antibiotic treatment of patients with infectious diseases in primary care.

Design: A systematic literature search was performed in PubMed and EMBASE. We included studies with a description of the development of QIs for diagnosis and antibiotic use in patients with infectious diseases in primary care. We extracted information about (1) type of infection; (2) target for quality assessment; (3) methodology used for developing the QIs; and (4) whether the QIs were developed for a national or international application. The QIs were organised into three categories: (1) QIs focusing on the diagnostic process; (2) QIs focusing on the decision to prescribe antibiotics; and (3) QIs concerning the choice of antibiotics.

Results: Eleven studies were included in this review and a total of 130 QIs were identified. The majority (72%) of the QIs were focusing on choice of antibiotics, 22% concerned the decision to prescribe antibiotics, and few (6%) concerned the diagnostic process. Most QIs were either related to respiratory tract infections or not related to any type of infection. A consensus method (mainly the Delphi technique), based on either a literature study or national guidelines, was used for the development of QIs in all of the studies.

Conclusions: The small number of existing QIs predominantly focuses on the choice of antibiotics and is often drug-specific. There is a remarkable lack of diagnostic QIs. Future development of new QIs, especially disease-specific QIs concerning the diagnostic process, is needed.

KEY POINTS
- In order to improve the use of antibiotics in primary care, measurable instruments, such as quality indicators, are needed to assess the quality of care being provided.
- A total of 11 studies were found, including 130 quality indicators for diagnosis and antibiotic treatment of infectious diseases in primary care.
- The majority of the identified quality indicators were focusing on the choice of antibiotics and only a few concerned the diagnostic process.
- All quality indicators were developed by means of a consensus method and were often based on literature studies or guidelines.

Introduction
According to WHO, antimicrobial resistance (AMR) is one of the most important public health problems in the world.[1] Several studies have shown that AMR is closely related to overuse and inappropriate choice of antibiotics.[2,3] Particularly, inappropriate use of broad-spectrum antibiotics is an important problem, because it leads to a selection of resistant strains.[4] During the last decades, the use of broad-spectrum antibiotics has increased worldwide, and in most countries, an increased prevalence of resistant strains has been observed.[1] About 25,000 persons in Europe die every year as a direct consequence of infections due to resistant bacteria.[5] A recent review on AMR reported that unless action is taken to address this huge global problem, by 2050 an additional 10 million lives a year...
worldwide will be lost, more than the number of people currently dying from cancer.[6] Consequently, it is of greatest importance to reduce the inappropriate use of antibiotics and preserve treatment only for those who will benefit the most.[1] Since the majority of antibiotic prescriptions are issued in primary care, initiatives to improve the quality of antibiotic prescribing should include general practitioners (GPs).[7]

During the past decades, there has been an extensive focus on improving the quality of care in general practice.[8,9] Most of this activity has been targeted chronic diseases, such as diabetes and cardiovascular diseases,[10] but there has only been a minor focus on quality assessment in patients with infectious diseases.

Of infectious diseases, acute respiratory tract infections (RTIs) are among the most frequent reasons for encounter in general practice,[11] and studies have shown that antibiotics are prescribed for more than 50% of patients with RTIs.[12,13] However, the majority of RTIs are caused by virus, and in most cases, antibiotics provide little, if any, benefit.[14–16]

In order to improve the use of antibiotics in primary care, valid instruments are necessary to assess the quality of care provided. Quality indicators (QIs) allow benchmarking by comparisons between practices or even between different municipalities or countries, and this has proven to be an important stimulus for quality improvement.[17] A quality indicator is defined as a specific and measurable element of practice that can be used to assess the quality of care,[18] and it is typically calculated as a ratio (e.g. number of antibiotic prescriptions related to the number of consultations). Usually, QIs are developed based on scientific evidence combined with consensus methods implemented by professionals in the field. They are often derived from retrospective reviews of medical records and can assess both appropriate and inappropriate clinical investigation or treatment. QIs are used to generate a reflection and debate about quality of care; hence, it is an indicator, rather than a definitive judgment of quality.[18,19]

In order to evaluate the quality of care in patients with infections, it is important to assess the clinical criteria that were used to establish the diagnosis, the criteria for the decision to prescribe antibiotics and the criteria for the choice of antibiotics. Hence, three different aspects of the clinical process have to be taken into account:

1. Assessment of the diagnostic process leading to the diagnosis
2. Assessment of the decision to prescribe antibiotics
3. Assessment of the choice of antibiotics

The aim of this study was to identify existing QIs for diagnosis and antibiotic treatment of patients with infectious diseases in primary care.

Materials and methods

Literature search

A systematic search was performed to identify QIs for diagnosis and antibiotic use in patients with infectious diseases in primary care. Peer-reviewed articles published from 1974 to November 2014 in English, Danish and Swedish were identified from PubMed and EMBASE. We conducted a search based on the following keywords: “antibiotic”, “diagnosis”, and “infection”, “treatment”, and “infection”, “respiratory infection”, “general practice”, “primary care”, “outpatient care”, “quality indicator”, and the following MeSH terms: “general practice”, “general practitioners”, “primary health care”, “ambulatory care”, “outcome and process assessment”, “benchmarking”, “quality of health care”, “total quality management”, “quality improvement”, “quality indicators”, “guideline adherence” “infection/diagnosis”, “infections/diagnostic use”, “infection/drug therapy”, “infection/therapeutic use”, “infection/therapy”, and “antibacterial agents”. A complete search string is available from the authors on request.

Selection of articles

Studies including a description of the development of QIs for diagnosis and antibiotic use in patients with infectious diseases in primary care were included. A study was excluded if it only reported on (1) QIs for hospital care; (2) guidelines for the treatment of infectious diseases; (3) application of already existing quality indicators; or (4) quality indicators for gastrointestinal infections, HIV infections, tuberculosis or unspecific symptoms (e.g. fever). In addition, a Google search was performed using the following keywords: “quality indicator”, “antibiotic”, and “primary care”. This search did not retrieve any additional studies. We excluded unpublished articles and non-peer-reviewed reports (e.g. conference proceedings, technical papers, abstracts).

In order to describe and compare the identified QIs we extracted information about

(1) type of infection; (2) target for quality assessment; (3) methodology used; and (4) whether the QIs were developed for a national or international application.
The QIs were organised into three categories:

1. QIs focusing on the diagnostic process
2. QIs focusing on the decision to prescribe antibiotics
3. QIs concerning the choice of antibiotics

The review is reported according to the PRISMA statement.[20]

Results

Search results and study characteristics

The literature search identified 1787 potential studies. Another seven studies meeting the criteria for inclusion were identified after searching references of retrieved papers. After adjusting for duplicates, 1752 remained. A total of 1408 was excluded by title and 238 after reading the abstract. Fifteen were excluded based on language (Spanish, French, Hungarian, and German). A total of 91 articles were read in full text, and 80 of them were excluded because they either: did not use QIs to assess quality of care (n = 12); did not report on QIs for infectious diseases (n = 6); only had a description of methods for development of QIs (n = 5); only concerned QIs for use in hospital settings (n = 4); only dealt with quality improvement of antibiotic use in general (n = 25); were conference abstracts (n = 6); described the application of existing QIs (n = 21) or developed standards for existing QIs (n = 1). The selection process resulted in a total of 11 studies fulfilling the criteria for the synthesis of this review (Figure 1).

Quality indicators for infectious diseases

A total of 130 QIs for diagnosis and antibiotic treatment of infectious diseases were identified; seven (6%) focused on the diagnostic process, 29 (22%) on the decision to prescribe antibiotics, and 94 (72%) QIs focused on the choice of antibiotics (Table 1). Sixty-eight quality indicators concerned RTIs; 15 urogenital infections (six urinary tract infections and nine...
Table 1. Overview of quality indicators.

| Type of infection                        | Quality indicators concerning the diagnostic process (n = 7, 6%) | Quality indicators concerning the decision to prescribe antibiotics (n = 29, 22%) | Quality indicators concerning the choice of antibiotics (n = 94, 72%) | In total (n = 130, 100%) |
|-----------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------|-------------------------|
| Respiratory tract infection             |                                                                |                                                                              |                                                                     |                         |
| Urogenital infection                    |                                                                |                                                                              |                                                                     |                         |
| Skin infection                          |                                                                |                                                                              |                                                                     |                         |
| Eye infection                           |                                                                |                                                                              |                                                                     |                         |
| Unspecific                              |                                                                |                                                                              |                                                                     |                         |

Respiratory tract infection: sore throat/tonsillitis, otitis externa, acute otitis media, acute rhinosinusitis, acute cough, bronchitis, pneumonia, chronic obstructive pulmonary disease exacerbation. Urogenital infection: urinary tract infections, sexually transmitted disease.

Table 2. Quality indicators focusing on the decision to prescribe antibiotics.

| Type of infection                        | Target for quality assessment: decision to prescribe antibiotics |
|-----------------------------------------|-----------------------------------------------------------------|
| Acute tonsillitis/pharyngitis           | Proportion treated with antibiotics [36]                       |
|                                         | Proportion with a positive Strep A test treated with antibiotics [36] |
| Acute otitis media                      | Proportion treated with antibiotics [36]                       |
|                                         | Proportion <2 years treated with antibiotics [36]              |
| Acute chronic rhinosinusitis            | Proportion treated with antibiotics [36]                       |
|                                         | Proportion >2 years treated with antibiotics [35]              |
|                                         | Proportion >2 years with less than three days of symptoms treated with antibiotics [36] |
| Acute bronchitis/bronchiolitis          | Proportion treated with antibiotics [36]                       |
| Pneumonia                               | Proportion aged between 18–75 years treated with antibiotics [35] |
| Acute exacerbation of COPD              | Proportion treated with antibiotics [36]                       |
|                                         | Proportion not fulfilling all the Anthonisen criteria treated with antibiotics [36] |
| Acute respiratory tract infection       | Proportion treated with antibiotics [36]                       |
| Acute upper respiratory tract infection | Proportion >1 year treated with antibiotics [35]                |
| Acute lower respiratory tract infection | Proportion treated with antibiotics [36]                       |
|                                         | Proportion with a C-reactive protein <20 mg/l treated with antibiotics [36] |
| Acute urinary tract infection           | Proportion of female patients >18 years treated with antibiotics [35] |
|                                         | Consumption of antibiotics expressed in DID [23]               |
|                                         | Seasonal variation of the total antibiotic consumption [23]    |

Anthonisen criteria: increased dyspnoea, increased and purulent expectorate.
COPD: chronic obstructive pulmonary disease; Strep A: streptococcus A antigen; DID: defined daily doses (DDD) per 1000 inhabitants per day. Seasonal variation: consumption in the winter quarters (October, December, January, March) compared with the summer quarters (July, September, April, June) of a 1-year period starting in July and ending the next calendar year in June, expressed as percentage: [DDD (winter quarters)/DDD (summer quarters) – 1] × 100.

sexually transmitted diseases); three skin infections, two eye infections, and finally, 42 QIs were not related to a specific type of infection. Seven QIs focused on the quality of the diagnostic process by measuring the proportion of patients having a specific clinical investigation before establishing the diagnosis. All seven indicators concerned sexually transmitted diseases and were derived from one study.[21]

QIs focusing on the decision to prescribe antibiotics are presented in Table 2. The majority of these QIs concerned RTIs and, in general, they assessed the proportion of patients with a specific infection that were treated with antibiotics. Some QIs measured the proportion of antibiotic use in subgroups specified by age (e.g. children <2 years with acute otitis media), specific symptoms (e.g. patients with COPD not fulfilling all the Anthonisen criteria), duration of symptoms (e.g. patients with less than three days of symptoms of acute otitis media), or the result of point-of-care tests (patients with tonsillitis and a positive Strep A test or patients with lower RTIs and a C-reactive protein (CRP) < 20 mg/l). One indicator measured seasonal variation in antibiotic use by calculating the consumption in winter quarters compared with summer quarters. The majority of QIs focusing on the decision to prescribe antibiotics were primarily designed to assess overuse of antibiotics; hence, a low value (e.g. a low percentage of patients treated with antibiotics) was associated with a high quality of antibiotic prescribing. An example of such a quality indicator is the proportion of patients >2 years old with acute otitis media with less than three days of symptoms treated with antibiotics (Table 2). A small group of QIs were designed to assess if patients with infectious disease were sufficiently treated with antibiotics. An example of such an indicator is the proportion of patients with acute tonsillitis and a positive Strep A test treated with antibiotics (Table 2). For this group of QIs, a high value is associated with a high quality of antibiotic prescribing.
Table 3. Quality indicators focusing on the choice of antibiotics.

| Type of infection                      | Target for quality assessment: the choice of antibiotics |
|----------------------------------------|----------------------------------------------------------|
| Acute tonsillitis/pharyngitis          | Proportion treated with a specific antibiotic (narrow-spectrum penicillin, macrolides, cephalosporins, broad-spectrum penicillin± clavulanic acid) [36]  |
| Acute otitis media                     | Proportion >1 year treated with a specific antibiotic (beta-lactamase sensitive penicillins, quinolones) [35]  |
| Acute/chronic rhinosinusitis           | Proportion treated with a specific antibiotic (narrow-spectrum penicillin, broad-spectrum penicillin± clavulanic acid, macrolides, cephalosporins, quinolones) [36]  |
| Acute bronchitis/bronchiolitis         | Proportion aged between 18–75 years treated with a specific antibiotic (penicillins with extended spectrum, tetracyclines, quinolones) [35]  |
| Pneumonia                              | Proportion treated with a specific antibiotic (narrow-spectrum penicillin, broad-spectrum penicillin± clavulanic acid, macrolides, cephalosporins, quinolones) [36]  |
| Acute exacerbation of COPD             | Proportion treated with a specific antibiotic (broad-spectrum penicillin± clavulanic acid, macrolides, cephalosporins) [36]  |
| Acute RTI                              | Proportion with no history of penicillin allergy treated with a specific antibiotic (macrolides) [36]  |
| Acute upper RTI                        | Proportion >1 year treated with a specific antibiotic (beta-lactamase sensitive penicillins, quinolones) [35]  |
| Acute lower RTI                        | Proportion treated with a specific antibiotic (narrow-spectrum penicillin, broad-spectrum penicillin± clavulanic acid, macrolides, cephalosporins, quinolones) [36]  |
| Urinary tract infection                | Proportion of female patients >18 years treated with a specific antibiotic (nitrofuran derivatives, trimethoprim and derivatives, quinolones, other antibiotics) [35]  |
| Unspecific                             | Consumption of a specific antibiotic (macrolides, lincosamides, streptogramins, penicillins, cephalosporins, quinolones) expressed in DID [23]  |

DID: defined daily doses (DDD) per 1000 inhabitants per day.

Table 3 shows QIs focusing on the choice of antibiotics. The majority of these QIs concerned RTIs (n = 45) or were not related to a specific infection, so-called drug-specific QIs (n = 39). In general, they assessed the proportion of patients exposed to a specific subgroup of antibiotics as a proportion of all patients treated with antibiotics. Nearly, half of the QIs assessed the proportion of patients treated with critically important antibiotics of highest priority (CIA), as defined by WHO.[22] The QIs focusing on the use of CIA included quinolones (n = 22), cephalosporins (n = 10), and macrolides (n = 8). Some QIs focused on the use of broad- and narrow-spectrum penicillin, and one quality indicator measured the seasonal variation for a specific class of antibiotics (quinolones).[23] The majority of QIs focusing on the choice of antibiotics were primarily designed to assess overuse of antibiotics (i.e. high use associated with a low quality) and only few were designed to assess whether patients were sufficiently treated with the drug of choice.

A full tabular summary of all QIs is available in the online Supplementary Appendix 1.

Methods for development

A consensus method was used for the development of all QIs included in this review. A consensus method is a structured technique that seeks consensus among a group of experts by synthesising opinions.[24] Five studies developed QIs by means of a modified Delphi technique involving repetitive administration of anonymous questionnaires [25] (Table 4). Three studies did not use the Delphi method but developed QIs by means of other consensus methods with a detailed description of how consensus was obtained, typically involving one or more meetings among the experts. Three studies did not specify the consensus method used for the development of QIs. Most expert panels consisted of GPs and often also involved other specialists, such as clinical microbiologists, clinical pharmacologists and researchers in the area being investigated. The number of experts participating in the Delphi studies ranged from nine to 305 and was generally higher than the number of experts involved in the studies not using the Delphi technique (range three to eight). Nine studies based the development of QIs on a literature study and/or guidelines. Two studies used neither a literature study nor guidelines. Drug-specific QIs for national application were mainly developed by means of a non-Delphi technique, whereas studies using the Delphi technique predominantly developed disease-specific QIs for international application. Five studies, all developing QIs for national application, [26–30] were designed in a way that the QIs could be applied to data from specific databases.
Discussion

Main findings

This review identified 130 QIs for diagnosis and antibiotic treatment of infectious diseases in primary care. Most of the indicators concerned RTIs, or were not related to a specific diagnosis. The majority (72%) of the identified QIs focused on the choice of antibiotics, 22% on the decision regarding antibiotic prescription and only 6% focused on the quality of the diagnostic process. None of the diagnostic indicators focused on RTIs or urinary tract infections, which are the most frequent types of infections in primary care. Some indicators were restricted to subgroups of patients specified by age, specific symptoms, duration of symptoms and the result of a point-of-care test. Other QIs focused on the use of CIA such as quinolones, cephalosporins and macrolides. All QIs were developed by means of a consensus method, five of the eleven studies using the Delphi technique.

Strengths and limitations

To our knowledge, this is the first systematic review identifying QIs for diagnosis and antibiotic treatment of infectious diseases in primary care. The number of relevant studies was surprisingly low, considering the large number of patients with various infections attending primary care. Our review may have failed to include some potentially relevant studies due to language restrictions, and one also needs to acknowledge the risk of publication bias. During the study period, we became aware of a number of unpublished or non-peer-reviewed QIs. We chose not to include these indicators, since their development was not well described. Several of these indicators concerned the diagnostic process. This might indicate that the need for this type of indicator exists, but may be more difficult to develop, probably because of different settings and recommendations that all need to be taken into account when designing this type of indicators.
The purpose of developing and using QIs varies, depending on the audience. A clinician is interested in the QIs that can easily measure the quality of his own work. Contrary, a researcher (or perhaps a politician) are possibly more interested in how the QIs were developed and how they can be applied to various sorts of data. However, the aim of this review was to identify the existing QIs for diagnosis and antibiotic treatment of infectious diseases and to inform the readers about the various methods used for development of QIs.

Comparison with relevant literature

Concerning patients with infectious diseases, one of the most important decisions for the GPs to take is whether to prescribe antibiotics or not. However, a rational decision concerning prescribing depends on a proper diagnosis. Thus, it seems particularly important that the quality assurance includes the diagnostic process.

The diagnostic process in primary care settings can be challenging. It is often based on symptoms and signs that have a low predictive value.[31] Studies have shown that only about half of patients with typical symptoms of urinary tract infections have significant bacteriuria,[32] and in patients with symptoms of pneumonia, only the minority can be confirmed by radiography.[33] Therefore, supplementary investigations or tests may be helpful to ensure a correct diagnosis.

In several countries, point-of-care tests are recommended in primary care in order to guide the GPs to take a rational decision about antibiotic prescribing. In the Nordic countries, for example, Strep A test and CRP test are widely used for testing patients with suspected RTIs. A newly published Cochrane review found that the use of CRP tests can reduce antibiotic use in patients with RTIs without harming the patients.[34] Interestingly, we identified only very few QIs that focused on the use of point-of-care tests.

Several studies aimed to develop QIs for international use.[23,35,36] However, these QIs can be difficult to apply to a national setting, as GPs may prefer QIs that fit into their local setting. Thus, Hansen et al. found that a set of internationally developed QIs were not rated suitable as an assessment tool by a group of Danish GPs.[37] Recommendations for diagnosis and antibiotic treatment of infectious diseases vary considerably between countries, and sometimes even within the same country. The lack of similarity between recommendations challenges the development of QIs in this area. However, initiatives have been taken to standardise recommendations for the diagnosis and treatment of a few infectious diseases on a European level, for example the European Position Paper on Rhinosinusitis and Nasal Polyps.[38]

Several indicators concerning choice of antibiotics focused on the use of CIA such as quinolones, cephalosporins, and macrolides. These antibiotics are especially important in the treatment of serious infections and are known to select for resistant bacteria.[22] The use of specific types of antibiotics differs substantially between countries.[39] Consequently, not all indicators are relevant for evaluating the quality of antibiotic use in all countries.[37]

We identified 42 QIs not related to a specific diagnosis. Politicians and health economists often use these drug-specific QIs as an instrument to survey antibiotic use and compare antibiotic use on a general level between regions and even countries. In most countries, prescribing information is obtained from health insurance and prescription databases containing data with no information on the indication for the prescription. Disease-specific QIs cannot be applied to this type of data, and therefore, drug-specific QIs are more frequently used.[23,27–30,40]

However, drug-specific QIs provide us with a black-and-white simplification of the quality of prescribing and may not be useful for the individual prescriber.[23] The benefit of QIs comes from the debate associated with the results and, hopefully, the debate can help GPs optimise their antibiotic treatment of patients with various infectious diseases. Most of the drug-specific QIs were designed as they could be applied to data from specific databases. This is probably a result of the limited data availability in many countries. However, by prioritising feasibility, the QIs have a narrow focus, allowing only limited assessment and the validity of the indicator might become more questionable.[29] In countries with no diagnose-based databases, the use of audit interventions in general practice makes it possible to apply QIs on data with information on the indication for the prescription.[41]

Several of the studies included in this review used the Delphi technique to develop QIs. This method is widely used in the prescribing research, and it is effective since the group of experts can be consulted from geographically dispersed areas, although different viewpoints cannot be debated face to face. Another consensus method, The RAND method, has been described as the only systematic method of combining expert opinion and evidence. In the RAND appropriateness method, experts are asked to rate predetermined statements, meet for discussion, and then re-rate
statements. None of the studies included in this review used the RAND method.

The diversity of the number of experts in the panel was large. Using many experts could indicate a very careful approach, but when face-to-face meetings are incorporated in the method, the sample should not exceed 12 in order to facilitate group discussion and prevent the group becoming too unwieldy. [25] Achieving consensus by means of postal questionnaires allow participation of a large group of experts, which most likely explains the generally higher number of experts in the studies using the Delphi technique. Scientific evidence for developing QIs is often limited. Instead consensus techniques are used, which systematically combine evidence and expert opinion allowing a broader range of aspects of health care to be assessed. [18, 24] If possible, experts will be provided with the most updated evidence for the specific topic (e.g. national guidelines) and are encouraged to relate this information to their opinions. The majority of the studies included in this review used guidelines and/or literature review as a scientific base for the development of the QIs. Only two studies based the development of QIs solely on expert opinion and experience.

Conclusion

Despite infections being a frequent reason for encounter in primary care, only few QIs for infectious diseases were identified by this review. The remarkably small amount of existing QIs in this area should encourage future development of new QIs. We believe that it is a drawback that the QIs almost only assess easily measurable aspects of care and fail to encompass the more subjective aspects within the diagnostic process. In order to include the diagnostic process in quality assessment, national disease-specific QIs taking specific local conditions into account are needed.

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References

[1] Leung E, Weil DE, Raviglione M, et al. The WHO policy package to combat antimicrobial resistance. Bull World Health Organ. 2011;89:390–392.
[2] Costelloe C, Metcalfe C, Lovering A, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010;340:c1–11.
[3] Goossens H, Ferech M, Vanderstichele R, et al. For the ESAC project group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005;365:579–587.
[4] Gopal Rao G. Risk factors for the spread of antibiotic-resistant bacteria. Drugs. 1998;55:323–330.
[5] Norrby R, Powell M, Aronsson B, et al. The bacterial challenge: time to react. Eur Cent Dis Prev Control. 2009 [cited 2016 Jul 12]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2009/11/news_detail_000044.jsp.
[6] O’Neill J. Tackling a global health crisis: initial steps. The Review on Antimicrobial Resistance; 2015 [cited 2016 Jul 16]. Available from: http://amr-review.org/Publications.
[7] Agersø Y, Bager F, Boel J, et al. DANMAP. 2013. [cited 2016 Jul 16]. Available from: http://orbit.dtu.dk/en/publications/danmap-2013(551c507b-7bbf-4d99-b3b8-704bc509db5).html.
[8] Mainz J, Johnsen S, Bartels P. På vej mod evidensbaseret kvalitetsudvikling [Towards evidence-based quality improvement]. Ugeskr Laeger. 2010;172:790–794.
[9] Grol R. Improving the quality of medical care: building bridges among professional pride, payer profit, and patient satisfaction. JAMA. 2001;286:2578–2585.
[10] DAK-e – De praktiserende lægers og regionernes fælles enhed for kvalitetsudvikling [Internet]; [cited 2015 Feb 2]. Available from: http://www.dak-e.dk/.
[11] Bjerrum L, Gahm-Hansen B, Hansen MP, et al. Luftvejsinfektioner – diagnose og behandling. Klinisk vejledning for almen praksis [Respiratory tract infections - diagnosis and treatment. Clinical guidelines for general practice]. Dansk Selsk Almen Med. 2014; [cited 2016 Jul 12]. Available from: http://vejledninger.dsam.dk/luftvejsinfektioner/.
[12] van den Broek d’Obrenan J, Verheij TJM, Numans ME, et al. Antibiotic use in Dutch primary care: relation between diagnosis, consultation and treatment. J Antimicrob Chemother. 2014;69:1701–1707.
[13] Petersen I, Hayward AC. Antibacterial prescribing in primary care. J Antimicrob Chemother. 2007;60: i43–i47.
[14] Fahey T, Stocks N, Thomas T. Systematic review of the treatment of upper respiratory tract infection. Arch Dis Child. 1998;79:225–230.
[15] Arroll B, Kenealy T. Are antibiotics effective for acute purulent rhinitis? Systematic review and meta-analysis of placebo controlled randomised trials. BMJ. 2006; 333:2–4.
[16] Lindbaek M. Antibiotics for acute bronchitis. J Fam Pract. 1998;47:421–422.
[17] Adriaenssens N, Coenen S, Versporten A, et al. European surveillance of antimicrobial consumption...
Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA. 1997;278:1440–1445.

Bent S, Simel DL, Fihn SD. Does this woman have an acute uncomplicated urinary tract infection? JAMA. 2002;287:2701–2710.

Holm A, Nexoe J, Bistrup LA, et al. Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. Br J Gen Pract. 2007;57:547–554.

Aabenhus R, Jensen-Jens US, Jørgensen KJ, et al. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Database Syst Rev. 2014;(11):CD010130. doi: 10.1002/14651858.CD010130.pub2.

Adriaenssens N, Coenen S, Tonkin-Crine S, et al. European Surveillance of Antimicrobial Consumption (ESAC): disease-specific quality indicators for outpatient antibiotic prescribing. BMJ Qual Saf. 2011;20:764–772.

Hansen MP, Bjerrum L, Gahrn-Hansen B, et al. Quality indicators for diagnosis and treatment of respiratory tract infections in general practice: a modified Delphi study. Scand J Prim Health Care. 2010;28:4–11.

Hansen MP, Bjerrum L, Gahrn-Hansen B, et al. Quality indicators for treatment of respiratory tract infections? An assessment by Danish general practitioners. Eur J Gen Pract. 2013;19:85–91.

Lund V, Fokkens W, Mullol J, et al. European position paper on rhinosinusitis and nasal polyposis. 2012;50(Suppl. 298):1–298.

European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2012. 2014; [cited 2016 Jul 12]. Available at: http://ecdc.europa.eu/en/activities/surveillance/ESAC-Net/Pages/index.aspx.

Pulcini C, Lions C, Ventelou B, et al. Drug-specific quality indicators assessing outpatient antibiotic use among French general practitioners. Eur J Public Health. 2013;23:262–264.

Bjerrum L, Munck A, Gahrn-Hansen B, et al. Health alliance for prudent antibiotic prescribing in patients with respiratory tract infections (HAPPY AUDIT) - impact of a non-randomised multifaceted intervention programme. BMC Fam Pract. 2011;12:1–8.

Giesen P, Willekens M, Mokkink H, et al. Out-of-hours primary care: development of indicators for prescribing and referring. Int J Qual Health Care. 2007;19:289–295.

van Roosmalen MS, Braspennin JCC, De Smet P, a GM, et al. Antibiotic prescribing in primary care: first choice and restrictive prescribing are two different traits. Qual Saf Health Care. 2007;16:105–109.