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Delayed Antibiotics: for upper respiratory tract infections

Prescribing Toolkit

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Supporting primary care clinicians to reduce antibiotic prescribing for acute respiratory tract infections, by considering a delayed antibiotic prescription strategy

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Introduction

Overuse of antibiotics is an ongoing concern due to the rise in antibiotic resistance to existing antibiotics and the lack of new antibiotics in the pipeline with novel mechanisms of action. (ECDC/EMEA Technical Report The bacterial challenge: time to react) There is also evidence that antibiotic prescribing contributes to antibiotic resistance in individual patients. **A systematic review and meta-analysis found that individuals prescribed an antibiotic for a respiratory or urinary infection were around twice as likely to develop resistance to that antibiotic compared with those who hadn't taken one. This risk was greatest in the first month after taking the antibiotic, but persisted for up to a year.**

(Costelloe C, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096)

Various strategies have been proposed to reduce unnecessary antibiotic prescribing for acute respiratory infections. NICE have recommended a delayed prescription strategy, where patients are advised to wait or delay and only have their prescription dispensed if their symptoms are prolonged or become worse. National Institute for Health and Clinical Excellence. Respiratory tract infections – antibiotic prescribing. Clinical Guideline 69. July 2008.

This toolkit provides evidence that supports the use of a delayed prescription strategy in an attempt to promote prudent antibiotic prescribing in primary care.

Examples of patient decision aids are provided as a resource to engage patients and help them clarify the risks versus the benefits of an antibiotic prescription.

The recently updated MK primary care antibiotic prescribing guidelines are included. These guidelines were developed based on national HPA recommendations with local input on resistance provided by the MK microbiology team. They aim to recommend the most effective treatment for common infectious indications and minimize unnecessary side effects, for example *Clostridium difficile,* to reduce antibiotic associated morbidity and mortality.

Summary of evidence regarding antibiotic use

New evidence supports NICE guidance on antibiotics for acute otitis media in children

http://www.npc.nhs.uk/rapidreview/?p=1394

10th March 2011

Two recent RCTs showed that, when diagnosed according to stringent criteria, more children with acute otitis media recover more quickly with antibiotics than with placebo. Benefits are more likely in those who are systemically unwell or have more severe disease. However, the condition of many children taking placebo improves without antibiotics and more children taking antibiotics suffer adverse effects.

Level of evidence:
Pittsburgh study level 2 (limited quality patient-oriented evidence) and Turku study level 1 (good quality patient-oriented evidence) according to the SORT criteria.

Action
Healthcare professionals should continue to follow NICE guidance on prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. The majority of adults and children over 3 months with acute otitis media (AOM), who are otherwise well, generally do not require antibiotics because it is a self-limiting illness and complications are likely to be rare if antibiotics are withheld. NICE advises that two antibiotic management strategies should be considered: delayed antibiotic prescribing, in which an antibiotic prescription is written for use at a later date if symptoms worsen; or no antibiotic prescribing.

NICE recommend that antibiotics are prescribed immediately, and/or further appropriate investigation and/or management should be offered if the patient is systemically very unwell, or is at high risk of serious complications because of pre-existing co-morbidity, or has symptoms and signs suggestive of serious illness and/or complications. In patients with AOM this includes those who have mastoiditis.

NICE also say that, depending on clinical assessment of severity, children can also be considered for immediate antibiotics if they have bilateral AOM and are less than 2 years old, or if they have otorrhoea. However, a no antibiotic or delayed antibiotic strategy should also be considered and the decision should be made on an individual patient basis, depending on the clinical assessment of the severity of the child's illness.

For all antibiotic prescribing strategies, patients should be given advice about the usual natural history of the illness, including the average total length of the illness (four days for AOM), and advice about managing symptoms, including fever (particularly analgesics and antipyretics).

What is the background to this?
Many guidelines for the management of AOM, including the NICE guideline, recommend a watchful waiting strategy, rather than immediate antibiotics, based on the results of clinical trials that showed relatively high rates of spontaneous improvement in children with AOM. However, it is argued that such trials had limitations, for example, a lack of stringent diagnostic criteria, the inclusion of very few young children, and the use of an antibiotic with limited efficacy or that was administered in suboptimal doses. Two RCTs in Pittsburgh (US) and Turku (Finland) aimed to address these concerns by carrying out studies in the age group at greatest risk and assessing the efficacy of co-amoxiclav vs. placebo in young children diagnosed with AOM according to specified criteria.

What do these studies claim?
The Pittsburgh study found that, among children aged 6 to 23 months with AOM diagnosed according to stringent criteria, treatment with co-amoxiclav for 10 days reduced the time to resolution of symptoms and reduced the overall symptom burden and the rate of persistent signs of acute infection on otoscopic examination, compared with placebo.

Seventeen children needed to be treated with co-amoxiclav, compared with placebo for one to have sustained resolution of symptoms at day 2. This NNT was reduced to 7 for resolution of symptoms with antibiotics at day 7. Five children needed to be treated with co-amoxiclav for one fewer to suffer clinical failure (defined as the persistence of signs of acute infection on otoscopic examination) at or before the visit on day 4 to 5. This NNT was reduced to 3 at day 10 to 12. Mastoiditis developed in one child who received placebo. Diarrhoea (NNH 10) and nappy-area dermatitis (NNH 6) were more common among children who received co-amoxiclav.

The Turku study found that children aged 6 to 35 months diagnosed with AOM according to stringent criteria benefited from co-amoxiclav treatment for 7 days, compared with placebo, although they had more side effects. Four children needed to be treated with co-amoxiclav for one fewer to suffer clinical failure at day 8. However, five children needed to be treated with co-amoxiclav, compared with placebo, for one to suffer diarrhoea.

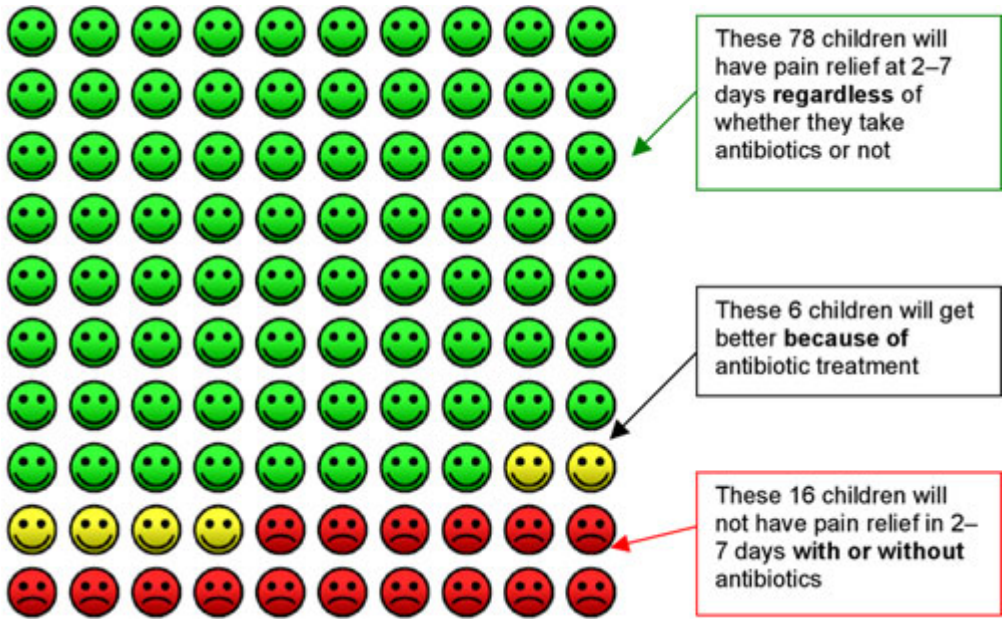
How does this relate to other studies?
The numbers needed to treat in these studies, which were undertaken in young children with AOM diagnosed according to strict criteria, appear more impressive than those seen in a Cochrane review (10 RCTs, n=2,928), which included a much broader population of children with AOM. (See **Table 1**) However, it is difficult to compare the results directly because of the different populations and antibiotic regimens, and the different outcomes considered.

The Cochrane Review found that two thirds of children had no pain 24 hours after treatment started, irrespective of whether they received antibiotics or placebo, and 78% of children receiving placebo had spontaneously recovered from pain at two to seven days. **Sixteen patients needed to be treated with antibiotics to gain pain relief in one extra patient at day 2 to 7**, but antibiotics did not reduce pain at 24 hours, or reduce tympanometry, perforation or recurrence. Few serious complications occurred in either the antibiotic or placebo group, with only one child (who was treated with penicillin) developing mastoiditis. However, **for every 23 patients treated with antibiotics, one extra will suffer harms such as diarrhoea vomiting or rash**. Putting this in the context of 100 patients taken at random, around 6 extra will gain pain relief, and around 4 extra will suffer adverse effects, as a result of treatment. This is a fine balance.

Table 1: NNTs and NNHs for selected results

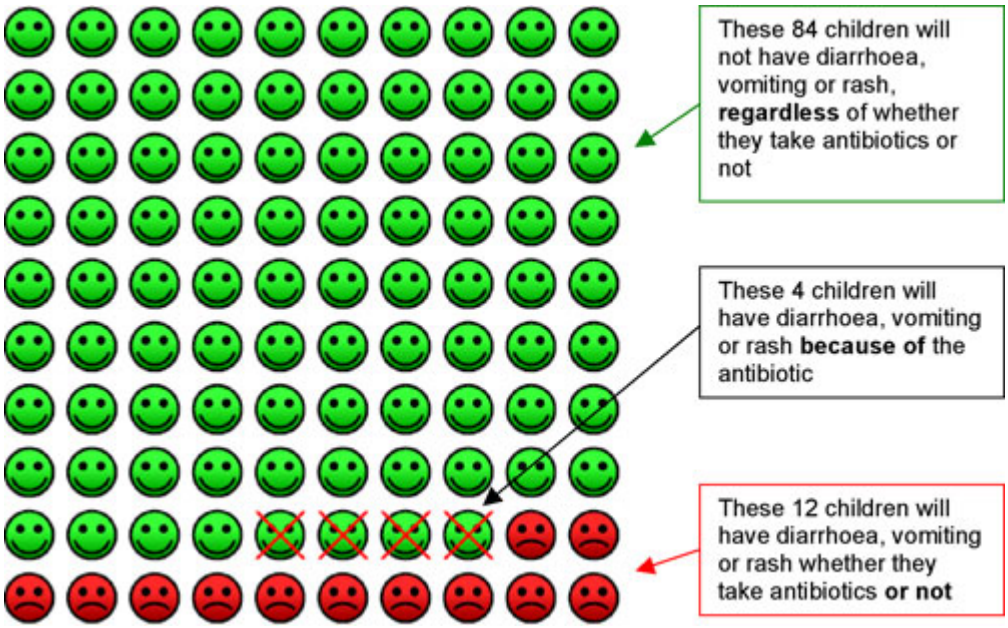
	NNT for resolution of symptoms		NNT to prevent clinical failure		NNH for adverse effects
Pittsburgh6 to 23 months	17 at day 2	7 at day 7	5 at day 4 to 5	3 at day 10 to 12	10 for diarrhoea 6 for dermatitis
Turku6 to 35 months	4 for condition improved at day 8		4 at day 8		5 for diarrhoea
Cochrane1 month to 15 years	16 for pain relief at day 2 to 7		Data unavailable		23 for diarrhoea, vomiting and rash

Figure 1: Pain at 2–7 days in children with AOM



Sometimes it is helpful to look at a pictorial representation of the benefits and risks using visual representations such as the ones shown here produced using Visual Rx, which was developed by Dr Chris Cates and can be found at http://www.nntonline.net/. **Figure 1** depicts the likely outcomes for a theoretical group of 100 patients, who are given antibiotics for AOM, and shows that around 78 children (shown by the green faces) will recover whether they take without antibiotics or not, around 6 (the yellow faces) will do better with antibiotics, but the 16 children shown by the red faces still have problems even if they have antibiotics. Of course, when prescribing we have no idea which group an individual person will fall into.

Figure 2: Diarrhoea, vomiting and rash in AOM



In **Figure 2**, the red faces show the 12 children with AOM who will develop diarrhoea, vomiting or rash anyway, even without antibiotic treatment. The green faces which are crossed out are the extra 4 children who will develop these symptoms because of antibiotics. Again the problem is that we cannot tell in advance which of the patients prescribed antibiotics will be the ones to suffer the treatment-related harms.

NICE concluded that antibiotics for AOM are effective only in reducing duration of pain in children aged between 6 months and 15 years. The NNT in order to prevent one child from having some pain after 2 days was 15, and children who took antibiotics were more at risk of having adverse events. NICE also concluded that antibiotics may be beneficial in children younger than 2 years with bilateral AOM and children with both AOM and otorrhoea. The numbers needed to treat mean that 3 or 4 children, respectively, with those symptoms would need to be treated with antibiotics for 1 additional child to benefit. These results are similar to those seen in the studies considered in this Rapid Review. NICE do point out, however, in those children who still had pain on day 3 it was found to be generally mild. Also, most parents used suboptimal doses of analgesics. NICE stated that "It is debatable whether it is worthwhile to treat children with antibiotics, particularly when analgesic use to relieve pain has not been optimised"

So what?

In summary, these two new RCTs support NICE guidance. They show that the benefits of antibiotics may outweigh the risks for young children with AOM diagnosed according to stringent criteria. NICE advises that antibiotics are indicated in patients who are systemically very unwell or at high risk of serious complications because of pre-existing co-morbidity. Other subgroups of children who may benefit include those with symptoms suggestive of mastoiditis, or who have otorrhoea, or who are younger than 2 years with bilateral acute otitis media.

Nevertheless, for many patients with AOM the immediate prescribing of an antibiotic is almost as likely to result in side effects as it is to confer benefit. This, combined with the fact that we know that otitis media is a self limiting condition, and that antibiotics have no benefit on pain at 24

hours and other patient-orientated outcome markers, makes the routine use of antibiotics in the management of many patients with AOM questionable. In addition, antibiotic resistance increases with antibiotic exposure both in the population and in the individual patient, and inappropriate antibiotic prescribing sends out the wrong message to the patient, their family and friends, that antibiotics are necessary for self-limiting infections. The bottom line is that, in each person the benefits of antibiotic prescribing need to be balanced against the risks for that individual and for the population as a whole.

NICE found little evidence on how to identify patients who are most at risk if they don't receive an antibiotic. They stress the need for safety-netting approaches in case the patients' illness worsens or becomes prolonged, either by use of delayed antibiotic prescriptions or by offering a prompt clinical review. If a delayed prescription is given, patients should be given advice on using it if symptoms worsen or aren't resolving as expected. Similarly, if symptoms worsen despite using the delayed prescription, the patient should be advised to re-consult their doctor.

NICE advises that the patient's or parent's concerns and expectations should be addressed when agreeing which strategy should be used. It may be helpful to advise them that AOM lasts four days, on average. This means that many patients will have symptoms lasting much longer than this, whereas in others the illness will resolve quite quickly. Patients should be advised that, for the majority, antibiotics make little difference to symptoms, and they may have side effects. Advice on use of symptomatic treatments, such as analgesics and antipyretics should also be offered when appropriate.

The Pittsburgh study details
Hoberman A, et al. Treatment of acute otitis media in children under 2 years of age. N Engl J Med 2011;364:105–15

Design: RCT

Patients: 291 children aged 6 to 23 months with AOM diagnosed on the basis of three criteria: the onset, within the previous 48 hours, of symptoms that parents rated with a score of at least 3 on the AOM Severity of Symptoms scale; the presence of middle-ear effusion; and moderate or marked bulging of the tympanic membrane or slight bulging accompanied by either otalgia or marked erythema of the membrane.

Intervention and comparison: Children were randomised to receive co-amoxiclav or placebo for 10 days. The primary outcome measures were time to resolution of symptoms and symptom burden over time.

Outcomes and results: Among the children who received co-amoxiclav, 35% had initial resolution of symptoms by day 2, 61% by day 4, and 80% by day 7; among children who received placebo, 28% had initial resolution of symptoms by day 2, 54% by day 4, and 74% by day 7 (P=0.14 for the overall comparison). For sustained resolution of symptoms, the corresponding values were 20%, 41%, and 67% with co-amoxiclav, as compared with 14%, 36%, and 53% with placebo (P=0.04 for the overall comparison). Mean symptom scores over the first 7 days were lower for the children treated with co-amoxiclav than for those who received placebo (P=0.02). The rate of clinical failure (defined as the persistence of signs of acute infection on otoscopic examination) was also lower among the children treated with co-amoxiclav than among those who received placebo: 4% versus

23% at or before the visit on day 4 or 5 (P<0.001) and 16% versus 51% at or before the visit on day 10 to 12 (P<0.001). Mastoiditis developed in one child who received placebo. Diarrhoea and nappy-area dermatitis were more common among children who received co-amoxiclav.

Sponsorship: Supported by a grant from the National Institute of Allergy and Infectious Diseases.

The Turku study details
Tähtinen PA, et al. A placebo-controlled trial of antimicrobial treatment for acute otitis media. N Engl J Med 2011;364:116–26

Design: RCT

Patients: 319 children aged 6 to 35 months with AOM diagnosed according to three specific criteria: middle-ear fluid detected by means of pneumatic otoscopic examination that showed at least two tympanic-membrane findings; at least one acute inflammatory sign in the tympanic membrane; and acute symptoms, such as fever, ear pain, or respiratory symptoms.

Intervention and comparison: Children were randomised to co-amoxiclav or placebo for seven days. The primary outcome was time to treatment failure from the first dose until the end-of-treatment visit on day 8. The definition of treatment failure was based on the overall condition of the child (including adverse events) and otoscopic signs of acute otitis media.

Outcomes and results: Treatment failure occurred in 18.6% of the children who received co-amoxiclav, as compared with 44.9% of the children who received placebo (P<0.001). The difference between the groups was already apparent at the first scheduled visit (day 3), at which time 13.7% of the children who received co-amoxiclav, as compared with 25.3% of those who received placebo, had treatment failure. Overall, co-amoxiclav reduced the progression to treatment failure by 62% (hazard ratio [HR] 0.38, 95% confidence interval [CI] 0.25 to 0.59; P<0.001) and the need for rescue treatment by 81% (6.8% vs. 33.5%; HR 0.19, 95%CI, 0.10 to 0.36; P<0.001). Analgesic or antipyretic agents were given to 84.2% and 85.9% of the children in the co-amoxiclav and placebo groups, respectively. Adverse events were significantly more common in the co-amoxiclav group than in the placebo group. A total of 47.8% of the children in the co-amoxiclav group had diarrhoea, as compared with 26.6% in the placebo group (P<0.001); 8.7% and 3.2% of the children in the respective groups had eczema (P=0.04).

Sponsorship: Funded by the Foundation for Paediatric Research and others.

Treating otitis media with antibiotics makes recurrence more likely

http://www.npc.nhs.uk/rapidreview/?p=495

18th August 2009

An observational follow-up study to an RCT found that children prescribed amoxicillin for acute otitis media (AOM) were about 50% more likely to have recurrence of AOM over the following three years than those given placebo. There was no significant effect on rates of related referrals or ENT surgery.

Level of evidence:
Level 2 (limited-quality patient-oriented evidence) according to the SORT criteria.

Action
Health professionals should follow NICE guidance on management of upper respiratory tract infections. They should try to agree a no-antibiotic or delayed-antibiotic strategy for most children with AOM, and generally prescribe antibiotics **only** to children with AOM who are systemically very unwell or at high risk of serious complications because of pre-existing co-morbidity, or who appear unwell with symptoms and signs suggestive of mastoiditis. Depending on clinical assessment of severity, an immediate antibiotic antibiotic prescription could be **considered** for children with otorrhoea or children younger than two years with bilateral AOM, but it is important to weigh the likely benefits against the possible risk, including side effects. The NPC patient decision aids relating to AOM specifically and upper respiratory tract infections generally may be helpful in some consultations (please see supporting documents for link).

What is the background to this?
As discussed on the relevant section of NPC and in a MeReC bulletin in December 2006, a strategy of watchful waiting or delayed antibiotic prescribing is appropriate for most children with AOM. About two thirds of children recover within 24 hours, whether they receive antibiotics or not, and the number of children in whom antibiotics prevent pain at 2-7 days (about 7 in 100) is almost exactly the same as the number of extra children who suffer diarrhoea, vomiting or rash through antibiotic treatment (about 6 in 100). Some children are more likely to benefit from antibiotics than others (see action section above).

This study is a follow-up to an RCT which was published several years ago, in which 240 children aged 6 months to two years with a diagnosis of AOM presenting to 53 general practices in the Netherlands were randomised to receive amoxicillin or placebo, and which found results in terms of benefits and harms similar to those described above. Approximately three and half years after the start of the trial the researchers sent a questionnaire to parents of the participating children asking them about episodes of recurrent AOM, referral to secondary care (paediatrician or ENT surgeon) and ENT surgery.

What does this study claim?
Questionnaires were returned for 168 of the original 240 children (70%): this subgroup had similar baseline characteristics to the whole study population and the groups who had been given placebo or antibiotics were well matched. The authors say that 95% of parents were still unaware of the original treatment allocation.

Three years after randomisation, AOM had recurred in 47/75 (63%) children in the amoxicillin group compared with 37/86 (43%) children in the placebo group, relative risk 1.5 (95% confidence interval [CI] 1.1 to 2), odds ratio (OR) 2.22 (95%CI 1.2 to 4.2), absolute risk increase 20% (95%CI 5% to 35%), number needed to harm (NNH) 5 (95%CI 3 to 22). In other words, for every five children like those in the study given antibiotics for AOM, one developed AOM in subsequent years who would not have done had they all been given placebo.

Further analysis showed that patient sex, allergy, and history of recurrent AOM might be relevant confounding factors. Adjustment for these factors resulted in a slightly higher adjusted odds ratio of 2.5 (95%CI 1.2 to 5.0), suggesting an even greater risk of recurrence of AOM due to antibiotic treatment. There were no significant differences in the rates of referral or surgery.

So what?
This study has some limitations. In particular, the original sample size was not large, and this observational extension was smaller still. It also relies on parent-reported outcomes and is therefore at risk of recall bias, that is, inaccurate recollection of events. The authors say that this possibility should not invalidate the results (e.g. if parents of children prescribed antibiotics were more likely to recall and report later AOM infections), because most parents were still unaware of the original treatment allocation. However, it is not clear how they established this.

Despite these limitations, the findings of this study support NICE guidance that, generally speaking, antibiotics should be avoided for treatment of AOM, unless there are compelling reasons for treatment.

Study details

Bezáková N, Roger AMJ, Damoiseaux RAMJ, Hoes AW, Schilder AGM, Rovers MM. Recurrence up to 3.5 years after antibiotic treatment of acute otitis media in very young Dutch children: survey of trial participants. BMJ 2009;338:b2525

Patients: 168 of the original 240 children aged six months to two years presenting to GPs in the Netherlands with signs and symptoms of AOM.

Intervention and comparison: amoxicillin suspension 40 mg/kg/day in three divided doses for 10 days, or placebo suspension

Outcomes and results: Parents reported recurrence of AOM in 47/75 (63%) children in the amoxicillin group compared with 37/86 (43%) children in the placebo group, RR 1.5 (95%CI 1.1 to 2.0), OR 2.22 (95%CI 1.2 to 4.2), absolute risk increase 20% (95%CI 5% to 35%), NNH 5 (95%CI 3 to 22). Logistic regression analysis showed that patient sex, allergy, and history of recurrent AOM might be relevant confounding factors. Adjustment for these factors resulted in an adjusted OR of 2.5 (95%CI 1.2 to 5.0). Parents reported secondary care referral in 24/78 (31%) of children in the

amoxicillin group compared to 27/89 (30%) in the placebo group (risk difference 0%, 95%CI –14% to 14%). Parents reported ENT surgery in 16/78 (21%) of children in the amoxicillin group compared to 27/90 (30%) in the placebo group (risk difference –9%, 95%CI –23% to 4%)

Sponsorship: Netherlands Organisation for Scientific Research (grant No 90458074) funded the original trial.

Antibiotic prescribing contributes to bacterial resistance in individual patients

http://www.npc.nhs.uk/rapidreview/?p=1789

25th August 2010

A systematic review and meta-analysis found that individuals prescribed an antibiotic for a respiratory or urinary infection were around twice as likely to develop resistance to that antibiotic compared with those who hadn't taken one. This risk was greatest in the first month after taking the antibiotic, but persisted for up to a year.

Level of evidence:
Level 2 (limited quality patient-oriented evidence) according to the SORT criteria.

Action
Health professionals should ensure they prescribe antibiotics appropriately and in line with NICE or local guidance based on HPA advice. Prescribing for viral or mild, self-limiting infections such as coughs and colds is unlikely to improve the course of the illness, puts patients at risk of unnecessary adverse reactions (e.g. vomiting, diarrhoea, rash, fungal infection) and encourages further consultations. Clinicians should select the patients who are at higher risk of complications and those who are more likely to have a bacterial cause for their symptoms. In certain scenarios providing reassurance that the symptoms will resolve without antibiotic treatment and the use of watchful waiting or a delayed prescription may be preferable. The NPC Patient decision aid relating to upper respiratory tract infections (URTIs) may be helpful in some consultations. Clinicians in primary care should work with their patients to consider the implications of this study when discussing the benefits and risks of taking antibiotics.

What is the background to this?
As discussed in a MeReC Bulletin on the management of common infections in primary care, the widespread use of antibiotics is associated with the emergence of resistant bacteria, many of which are multi-drug resistant. Furthermore, as very few new antibiotics are entering practice, antibiotic resistance is now a major threat to public health.

Most antibiotic prescribing is in primary care. There are concerns that some common infections are becoming increasingly difficult to treat and that illnesses due to antibiotic resistant bacteria may take longer to resolve. The findings of this study therefore support the case for primary care clinicians and patients to see antibiotic resistance as a reason to refrain from inappropriate antibiotic use. A lack of patient awareness may be contributing to the problems caused by antibiotic resistance, and it may appear that there is a perception amongst some patients and clinicians that antibiotic resistance is only of minimal risk.

Previous studies that have examined the link between antibiotic prescribing in primary care and bacterial resistance have mostly been at *population level*. To date, only a limited number of good quality studies have reported on the relationship between prescribing and prevalence of

resistance for at *individual-patient* level. Therefore, the aim of this study was to examine the effect of antimicrobial use on the emergence of antibiotic resistance in individual patients in primary care. The authors aimed to quantify the strength and duration of any association as well as identifying which antibiotics were most and least likely to cause resistance.

What does this study claim?
This review included 24 studies; 22 involved patients with symptomatic infection and two involved healthy volunteers; 19 were observational studies (of which two were prospective) and five were RCTs. In five studies looking at the urinary tract (14,348 participants), individuals were between two and three times more likely to test positive for resistant organisms within three months of antibiotic treatment (pooled odds ratio [OR] for resistance was 2.48, 95% confidence interval [CI] 2.06 to 2.98). This was shown to reduce over time (P<0.001), although a residual association was still present at twelve months.

In seven studies of respiratory tract bacteria (2,605 participants), a non-statistically significant result was found, with a pooled OR for resistance of 1.48 (95%CI 0.95 to 2.32) within three months. However, a statistically significant association between antibiotics and resistance to respiratory tract bacteria was found within one month (pooled OR 2.10, 95%CI1.04 to 4.23), and within two months (pooled OR 2.37, 95%CI 1.42 to 3.95). No significant association between resistance of respiratory tract bacteria was seen with time (P=0.91).

Studies reporting the quantity of antibiotic prescribed found that longer duration and multiple courses were associated with higher rates of resistance. Studies comparing the potential for different antibiotics to induce resistance showed no consistent effects, possibly due to the limited number of studies available.

So what?
This study found that antibiotics prescribed to an individual in primary care were consistently found to be associated with resistance of urinary and respiratory bacteria to those antibiotics in that individual. Despite this association, the clinical significance of the findings of this study remains unclear. However, health professionals should still follow appropriate NICE guidance (for example on antibiotic prescribing for self-limiting respiratory tract infections) to ensure appropriate targeting of antibiotics to those patients most likely to benefit.

Another implication of the study was that in some instances the antibiotics prescribed in primary care may impact on bacterial resistance in individual patients for up to 12 months. Furthermore, the study's findings support the Standing Medical Advisory Committee report that recommendations that the **fewest number of antibiotic courses should be prescribed for the shortest period possible**.

Finally, this study serves to highlight the need to use first-line antibiotics whenever possible, by following appropriate NICE and local guidance based on HPA advice. This study supports the on-going need for a shift in clinicians' **and** patients' attitudes to the use of antibiotics in primary care by providing supporting evidence linking the emergence of resistance to antimicrobial use.

What are the limitations of this study?
The authors found some evidence of positive publication bias in the urinary bacteria studies investigating resistance in *E coli* but were unable to assess publication bias for the respiratory

flora, as there were too few studies. Another source of bias could include other confounding factors, such as the association between primary care prescribing and any recent hospital admissions, where antibiotics could have been used. However, the studies that attempted to adjust for potential confounders such as age, sex, comorbidities, catheter use, and smoking status rarely demonstrated substantial difference between crude and adjusted results. A further limitation was that, the existing body of evidence is mainly reliant on observational or case-controlled studies, and there is a lack of data from clinical trials. These limitations highlight that further research is needed to assess the link between antibiotics prescribed in primary care and more serious infections that require secondary care treatment, as well as to further clarify the effects of interactions between antibiotic dose, duration, and adherence on resistance.

Study details

Costelloe C, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096

Design

Systematic review and meta-analysis of 24 studies conducted in any country. The studies consisted of five RCTs and 19 observational studies, two of which were prospective, and 17 retrospective controlled observational or case control studies. The studies were included if they investigated relations between primary care prescribed antibiotics and antimicrobial resistance in bacteria sampled from any body site; analysed at the level of the individual. All studies were based in countries where antibiotics are available by prescription only

Patients

The 24 studies investigated effects in 15,505 adults and 12,103 children. Twenty-two studies sampled bacteria from patients with symptomatic infection: urinary tract infections (seven studies); respiratory tract infections (seven); otitis media (two); chronic obstructive pulmonary disease (one); methicillin resistant *Staphylococcus aureus* (MRSA) infection (four); and trachoma in children (one). Two studies examined asymptomatic healthy adult volunteers

Intervention and comparison

Studies presented a wide range of antibiotic exposure analyses including those for: macrolides (eight studies); penicillins (five); sulphonamides and trimethoprim (six); cephalosporins (six); tetracyclines (two); quinolones (two); nalidixic acid (one); metronidazole (one); nitrofurantoin (one); and “any antibiotic” (seven). The antibiotics were given between two and 104 weeks before measurement of antibiotic resistance.

Adherence to antibiotic regimen was not assessed in most of the studies as they were retrospective and researchers were only able to measure prescribing from patients’ records or questionnaires, though in one of the RCTs adherence was measured by recording medicine bottle weights at various time points throughout the study.

Outcomes and results

In five studies of urinary tract bacteria (14,348 participants), individuals were between two and three times more likely to test positive for resistant organisms within three months of antibiotic treatment (pooled odds ratio [OR] for resistance was 2.48, 95% confidence interval [CI] 2.06 to 2.98). This was shown to reduce over time ($P<0.001$), although a residual association was still present at twelve months.

A similar result was found in seven studies of respiratory tract bacteria (2605 participants), with a pooled OR for resistance of 1.48 (95%CI 0.95 to 2.32) within three months, which did not reach conventional levels of statistical significance. However, some association between antibiotics and resistance to respiratory tract bacteria was found within one month (pooled OR 2.10, 95%CI1.04 to 4.23), and within two months (pooled OR 2.37, 95%CI 1.42 to 3.95). No significant association between resistance of respiratory tract bacteria was seen with time (P=0.91).

Studies reporting the quantity of antibiotic prescribed found that longer duration and multiple courses were associated with higher rates of resistance. Studies comparing the potential for different antibiotics to induce resistance showed no consistent effects, possibly due to the limited number of studies available. The prospective Malhotra-Kumar study was the only one that reported changes in resistance over a long period; pooled ORs fell from 12.2 (95% CI 6.8 to 22.1) at 1 week to 6.1 (95% CI 2.8 to 13.4) at 1 month, 3.6 (95% CI 2.2 to 6.0) at 2 months, and 2.2 (95% CI 1.3 to 3.6) at 6 months.

Sponsorship
University of Bristol in collaboration with the University of Oxford which both received a proportion of their funding from the Department of Health's NIHR School for Primary Care Research. More information on antibiotic prescribing can be found on the common infections section of NPC.

Delayed prescribing for upper respiratory tract infections: a qualitative study of GPs' views and experiences

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Source: British Journal of General Practice, Volume 60, Number 581, December 2010 , pp. 907-912(6)

Background

Delayed prescribing has been promoted as a strategy that meets patients' expectations and helps to avoid unnecessary use of antibiotics in upper respiratory tract infections.

Aim

To explore GPs' views on and experiences with delayed prescribing in patients with acute upper respiratory tract infections.

Design of study

Qualitative study involving focus groups.

Setting

Norwegian general practice.

Method

Qualitative analysis of data collected from five focus groups comprising 33 GPs who took part in a quality-improvement programme of antibiotic prescribing.

Results

The views of GPs differed on the usefulness of delayed prescribing. GPs who endorsed the strategy emphasised shared decision making and the creation of opportunities for educating patients, whereas GPs who were negative applied the strategy mainly when being pressed to prescribe. Mild and mainly harmless conditions of a possible bacterial origin, such as acute sinusitis and acute otitis, were considered most suitable for delayed prescribing. A key argument for issuing a wait-and-see prescription was that it helped patients avoid seeking after-hours care. For issuing a wait-and-see prescription, the GPs required that the patient was `knowledgeable', able to understand the indications for antibiotics, and motivated for shared decision making. GPs emphasised that patients should be informed thoroughly when receiving a wait-and-see prescription.

Conclusion

Not all GPs endorse delayed prescribing; however, it appears to be a feasible approach for managing patients with early symptoms of mild upper respiratory tract infections of a possible bacterial origin. Informing the patients properly while issuing wait-and-see prescriptions is essential.

NeLM News

Effect of antibiotic prescribing strategies and an information leaflet on longer-term reconsultation for acute lower respiratory tract infection

Original article by: **M Moore, P Little, K Rumsby, et al.**

Reference: **British Journal of General Practice, Oct 2009, vol. 59, no. 567, p. 728-734**

Source: **British Journal of General Practice**

Keywords: **Antibiotics; Cough; Doctors-General Practice; Prescribing; Repeated Use; Respiratory Tract Infections; Patient Information Leaflets; United Kingdom;**

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Summary

by: **Pharm-line**

Study involving family practices in the Wessex region. 807 subjects (aged 3 years or older, including 136 children younger than 16 years and 133 patients older than 60 years) who had acute illness presenting with cough as the main symptom, plus at least one symptom or sign from sputum, chest pain, dyspnoea or wheeze, were included. The subjects were randomised to one of three prescribing strategies (antibiotics, delayed antibiotic, no antibiotic) and a leaflet. Prior antibiotic use and reconsultation were assessed by medical record review. Patients who had been prescribed antibiotic for cough in the previous 2 years were much more likely to reconsult (incidence rate ratio (IRR) = 2.55; 95% CI, 1.62 to 4.01) and use of a delayed prescription strategy is associated with reduced reconsultation in this group. In those with prior antibiotic exposure, there was a 34% reduction in consultation rate in the no antibiotic group (IRR = 0.66; 95% CI, 0.30 to 1.44, P = 0.295) and a 78% reduction for the delayed antibiotic group (IRR = 0.22; 95% CI, 0.10 to 0.49, P less than 0.001) when compared with those given immediate antibiotics. This effect was not observed in patients who had not been prescribed antibiotics in the previous 2 years; there was no reduction in consultations in the no antibiotic group (IRR = 1.23; 95% CI, 0.79 to 1.92, P = 0.358) or the delayed antibiotic group (1.19; 95% CI, 0.78 to 1.80, P = 0.426). There was an increase in consultation rate with an information leaflet (IRR = 1.27; 95% CI, 0.86 to 1.87, P = 0.229). Past attendance with cough, or past attendance with other respiratory illness and smoking, also predicted reconsultation with cough. Concludes that delayed antibiotic prescribing for LRTI appears effective in modifying reconsultation behaviour, particularly in those with a prior history of antibiotic prescription for LRTI.

Abstract link (IngentaConnect)

Rate of recovery similar for adults with acute cough, whether or not antibiotics are prescribed

http://www.npc.nhs.uk/rapidreview/?p=604

18 September 2009

An observational study found that adults with new or worsening cough, or symptoms suggestive of lower respiratory tract infection (LRTI) had a similar rate of recovery, whether or not antibiotics were prescribed.

Level of evidence:
Level 2 (limited-quality patient-oriented evidence) according to the SORT criteria.

Action
Health professionals should follow NICE guidance on antibiotic prescribing for self-limiting respiratory tract infections. An immediate antibiotic prescription should **only** be offered to patients who are likely to be at risk of developing complications, i.e.

- if they are systemically very unwell
- if the symptoms and signs are suggestive of serious illness and/or complications e.g. pneumonia
- if they are at high risk of serious complications because of pre-existing comorbidity
- if they are older than 65 years with acute cough and **two** or more of the following, or older than 80 years with acute cough and **one** or more of the following:
    - hospitalisation in the previous year
    - type 1 or type 2 diabetes
    - history of congestive heart failure
    - current use of oral glucocorticoids.

A no-antibiotic or delayed-antibiotic strategy should be agreed for most adults and children (≥3 months) with acute cough/acute bronchitis. Patients should also be given advice about the usual natural history of the illness, including the **average** total length of the illness (which in the case of acute cough/acute bronchitis is 3 weeks), and advice about managing symptoms, including fever. The NPC patient decision aid relating to upper respiratory tract infections (URTIs) may be helpful in some consultations.

What is the background to this?
Acute cough is given as a major reason for antibiotic prescribing in primary care. However, as discussed on the respiratory tract section of NPC and in a MeReC Bulletin, the routine use of antibiotics is unnecessary for previously well patients with acute bronchitis, regardless of the duration of cough. A Cochrane review of 5 randomised controlled trials found that antibiotics reduced the mean duration of cough by half a day over 1–2 weeks, compared with placebo (weighted mean difference 0.58 days, 95% confidence interval [CI] 0.01 to 1.16). However, this

modest benefit should be considered in the broader context of potential side-effects, medicalisation for a self-limiting condition, increased resistance to respiratory pathogens and cost of antibiotic treatment.

This cross-sectional observational study examined the variation in antibiotic prescribing for acute cough in 14 primary care networks in 13 European countries, and its impact on recovery, after controlling for clinical presentation.

What does this study claim?
This study recruited 3,402 adults with new or worsening cough, or symptoms suggestive of LRTI. Clinicians completed a case report form in 99% of cases, and 80% of patients returned a symptom diary. There were considerable differences in the decision to prescribe an antibiotic across the networks (range 21–88%, 53% overall, 63% in the English network), and wide variation in the choice of antibiotic prescribed. Overall, amoxicillin was the most common antibiotic prescribed (range 3–83%, 29% overall, 83% in the English network).

The large differences in antibiotic prescribing did not translate to clinically important differences in patient recovery. Although the rate of recovery was statistically significantly different between patients who were and were not prescribed antibiotics (once clinical presentation was taken into account), this was not considered to be clinically significant (a difference of 0.1% in the symptom severity score after 7 days). Indeed, the authors concluded that this was not clinically relevant, and entirely consistent with a placebo effect.

So what?
This large study was conducted across 13 European countries, so there may be some inconsistency between their perceptions of health, and patient-reporting of symptoms. However, the findings add further support to NICE guidance that, generally speaking, antibiotics should be avoided for the treatment of self-limiting respiratory tract infections e.g. acute cough/acute bronchitis, except in those at risk of complications. Evidence suggests that most antibiotic prescriptions do not help previously well patients recover more quickly and puts them at unnecessary risk of side effects – some with potentially serious consequences, such as *C. diff* infection. Antibiotic resistance is also a considerable problem.

Study details
Butler CC, Hood K, Verheij T, et al. Variation in antibiotic prescribing and its impact on recovery in patients with acute cough in primary care: prospective study in 13 countries. BMJ 2009;338:b2242

Design: Prospective, cross-sectional observational study.

Patients: 3,402 adults (aged ≥18 years) consulting for the first time within this illness episode with a new or worsening cough, or a clinical presentation suggestive of LRTI, with a duration of ≤28 days. Participating GPs from 14 primary care networks in 13 European countries recruited consecutive eligible patients in October and November 2006, and from late January to March 2007.

Intervention: Clinicians recorded aspects of patients' history, symptoms, comorbidities, clinical findings and management, including antibiotic prescription and other treatments/investigations, on a case report form. They also indicated the presence/absence and severity of 14 symptoms e.g.

cough, phlegm production, shortness of breath, fever. Recruited patients were given a symptom diary and asked to rate 13 symptoms each day until recovery (up to a maximum of 28 days), on a seven point scale.

Outcomes: Prescribing of antibiotics by clinicians and total symptom severity scores over time.

Results: Of the 3,402 participants, case report forms were completed for 99% and diary data were obtained from 80% of patients. Those who did not complete a diary were no more or less likely to have been prescribed an antibiotic than the other patients. Mean symptom severity scores ranged from 19 to 38 (scale range 0–100). Antibiotic prescribing by networks ranged from 20–88% (53% overall), for a median of 7 days, with wide variation in the classes of antibiotics prescribed. Overall, amoxicillin was the most common antibiotic prescribed (ranging from 3% in the Norwegian network to 83% in the English network). After adjustment for clinical presentation and demographics, considerable differences remained in antibiotic prescribing. Differences in recovery rate were small, and patients recovered at a similar rate regardless of network. Although the rate of recovery was statistically significantly different between patients who were and were not prescribed antibiotics (once clinical presentation was taken into account), this was not considered to be clinically significant.

Sponsorship: The study was funded by the 6th Framework Programme of the European Commission.

DTB: Managing acute sinusitis

Reference: **DTB 2009; 47: 26-30** Source: **Drug and Therapeutics Bulletin** Date published: **05/03/2009 14:22**

Summary

by: **Yuet Wan**

In a review in the Drug and Therapeutics Bulletin (DTB) on the management of patients with acute sinusitis, and the place of antibacterial and other treatments, the following topics are discussed:

- About acute sinusitus
- Diagnosis and treatment
- Analgesics
- Antibacterial therapy
- Steam inhalation and nasal irrigation
- Nasal decongestant
- Corticosteroids
- Patient referral
- Surgery

The authors of the review note that acute sinusitis is a common and often self-limiting condition from which most patients recover within about 10 days of seeing their GP, whether or not they receive any treatment.

In terms of antibiotics, it was noted that the current overall prescribing levels for sinusitis are not justified as they make little difference to the outcome of most patients, and NICE recommends "no antibiotic" or a " delayed" antibacterial prescribing policy for most patients. However, antibiotics are considered appropriate, though for patients who are systemically very unwell and have symptoms and signs of, or are at high risk of, serious complications. In addition, evidence suggests that there is no difference in the effectiveness of antibiotics recommended for acute sinusitis (e.g. amoxicillin, doxycycline, macrolides).

Points of note for other treatments are as follows:

- Management should include the use of paracetamol or ibuprofen taken regularly for several days, supplemented, if pain relief is inadequate, with codeine.

- There is a lack of published evidence on the efficacy of OTC nasal decongestants in acute sinusitis, and they can cause rebound congestion on withdrawal.

- Evidence on the use of intranasal corticosteroids is equivocal.

Abstract

Antibiotic strategy for preventing complications of sore throat in young people

http://www.npc.nhs.uk/rapidreview/?p=1394

A recent article highlights that *Fusobacterium necrophorum* is the cause of around 10% of acute pharyngitis cases in adolescents and young adults. One of the supparative complications of this infection is Lemierre's syndrome, which can be potentially life-threatening. Empirical, immediate antibiotic prescribing (penicillin or cephalosporin, but not a macrolide) is recommended when three or more Centor criteria* are present.

Action

Healthcare professionals in primary care should continue to follow NICE clinical guideline 69 for antibiotic prescribing in respiratory tract infections for adults and children presenting with acute sore throat/pharyngitis/tonsillitis.

For most patients (adults and children) a no antibiotic or delayed antibiotic prescribing strategy is appropriate. Depending on clinical assessment of severity, immediate antibiotic prescribing **should be considered** for patients when three or more Centor criteria are present. These are:

- presence of tonsillar exudate
- presence of fever
- presence of cervical lymphadenopathy
- absence of cough.

Immediate antibiotic and/or further appropriate investigation and management is appropriate for those likely to be at risk of complications (see NICE guideline for details). Penicillins and cephalosporins **(but not macrolides)** are suitable first-line antibiotics when empirical prescribing is appropriate.

What is the background to this?

Most sore throats are largely viral in nature and self limiting, and antibiotic treatment is unnecessary. Most patients who consult their GP with acute sore throat are not at major risk of serious complications, and a no antibiotic or delayed antibiotic strategy is appropriate, in accordance with the NICE clinical guideline on the prescribing of antibiotics for self-limiting respiratory tract infections.

The difficulty prescribers face lies in identifying the small number of patients who will suffer severe and prolonged illness, or more rarely, go on to develop complications. The NICE clinical guideline provides a safety net whereby patients who are at risk of developing complications are prescribed antibiotics immediately. Those who are offered a no antibiotic or a delayed antibiotic strategy are advised on managing symptoms, and to use their delayed prescription and/or reconsult as appropriate.

What does the article claim?

This Perspectives article in the Annals of Internal Medicine considers the causative organisms and

antibiotic treatments to avoid potential complications in adolescents and young adults who present with sore throats. Most antimicrobial therapy for bacterial pharyngitis has focussed on a group A beta-haemolytic streptococcus (GABHS) as the causative agent and the avoidance of the associated complication of acute rheumatic fever. However, this article, citing several studies, points out that another organism, *Fusobacterium necrophorum* (FN), a gram-negative anaerobe, occurs at a similar frequency to that of GAS **in young adults and adolescents** with acute pharaygitis (about 10%). FN can cause suppurative complications including Lemierre's syndrome, which can be life-threatening. Lemierre's syndrome is considered to be a more dangerous and probable complication of pharyngitis than rheumatic fever in young adults and adolescents. In the absence of clinical data, and no simple means of identifying FN, the author recommends that the 30% of patients who present with at least three of the Centor Criteria* be prescribed an antibiotic strategy that would be sufficient to treat both GAS and FN. Penicillins and cephalosporins are considered appropriate antibiotics for this; macrolide antibiotics, to which FN is not sensitive, is not recommended.

So what?

The recommendation to prescribe antibiotics immediately for young adults and adolescents with at least three Centor criteria* is consistent with NICE guideline 69, although the guideline only suggests 'considering' antibiotics under such circumstances depending on a clinical assessment of severity. As a rapid response to the article indicates, it is not certain that the isolation of FN from a throat swab of a sore throat patient equates to causation. Empirical treatment of all patients with three or more Centor criteria* could lead to considerable unnecessary therapy for viral pharyngitis in young people. No recommendations for *which* antibiotic to prescribe empirically is given in the NICE guideline, although the recommendation in this article to avoid macrolide antibiotics in young adults and adolescents would seem reasonable, given the frequency of FN in acute pharyngitis and its lack of sensitivity of FN to macrolides.

Reference

Centor RM. Expand the pharyngitis paradigm for adolescents and young adults. Ann Intern Med 2009;151:812–5More information on the management of common respiratory tract infections including sore throat can be found on the respiratory tract section of NPC *Centor criteria are:

- presence of tonsillar exudate
- presence of fever
- presence of cervical lymphadenopathy
- absence of cough.

NICE issues guidance on the prescribing of antibiotics for self-limiting respiratory tract infections http://www.npc.nhs.uk/rapidreview/?p=175

National Institute for Health and Clinical Excellence. Respiratory tract infections – antibiotic prescribing. Clinical Guideline 69. July 2008.

Implementing NICE guidance should reduce inappropriate prescribing of antibiotics in primary care

Action – Clinicians should seek to reach agreement with patients to defer from prescribing antibiotics immediately for most people who present with ear infections, sore throats, sinusitis, coughs and colds.

Immediate prescribing of antibiotics and/or further appropriate investigation and management should **only** be offered to patients (both adults and children) if the patient is systemically very unwell, if the patient has symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital and intracranial complications), if the patient is at high risk of serious complications because of pre-existing comorbidity, and if the patient is older than 65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following: hospitalisation in the previous year, type 1 or type 2 diabetes; a history of congestive heart failure; current use of corticosteroids.

All patients should be offered advice about the natural history of the disease, how long it is likely to last, and how to manage symptoms.

Prescribers should familiarise themselves with and follow the NICE guidance.

What is the background to this? – After a fall in antibiotic use in the late 1990s, antibiotic prescribing in primary care in England is now increasing and population usage is considerably higher than other northern European countries. Most people presenting in primary care with an acute uncomplicated respiratory tract infection will still receive an antibiotic prescription – with many doctors and patients believing that this is the right thing to do. In most cases, antibiotics are unnecessary as the conditions are self limiting, yet they expose the patient to undesirable side effects. Symptom resolution may be falsely attributed to the taking of antibiotics, and lead to expectation of further antibiotic prescribing for similar situations in the future. Antibiotic resistance rates are a major public concern, and strongly related to antibiotic use in primary care. Therefore, it is important that we are more judicious in the use of antibiotics and only use them where there is clear evidence of benefit [NICE guideline].

What does the guideline recommend?

- The guideline applies to adults and children (older than three months)

- Following clinical assessment, a **no antibiotic prescribing strategy or a delayed antibiotic prescribing strategy** should be agreed for patients with acute otitis media; acute sore throat/acute pharyngitis/acute tonsillitis; common cold; acute rhinosinusitis or acute cough/acute bronchitis.
- All patients, regardless of the antibiotic prescribing strategy, should be given advice about the usual natural history of the illness, including the average total length of the illness (before and after seeing the doctor),
    - acute otitis media : 4 days;
    - acute sore throat/acute pharyngitis/acute tonsillitis: 1 week;
    - common cold: 1½ weeks;
    - acute rhinosinusitis: 2½ weeks;
    - acute cough/acute bronchitis: 3 weeks

and advice about managing symptoms, including fever (particularly analgesics and antipyretics).

- When the no antibiotic prescribing strategy is adopted, patients should be offered reassurance that antibiotics are not needed immediately, because they are likely to make little difference to symptoms and may have side effects (e.g. diarrhoea, vomiting and rash), and a clinical review if the condition worsens or becomes prolonged.
- When the delayed antibiotic prescribing strategy is adopted, patients should be offered reassurance that antibiotics are not needed immediately because they are likely to make little difference to symptoms and may have side effects, and advice about using the delayed prescription if symptoms are not starting to settle in accordance with the expected course of the illness or if a significant worsening of symptoms occurs. Advice should also be given about re-consulting if there is a significant worsening of symptoms despite using the delayed prescription.
- **Immediate prescribing of antibiotics** and/or further appropriate investigation and management should **only** be offered to patients (both adults and children) in the following situations:
    - if the patient is systemically very unwell
    - if the patient has symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital and intracranial complications)
    - if the patient is at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely
    - if the patient is older than 65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following: hospitalisation in the previous year, type 1 or type 2 diabetes; a history of congestive heart failure; current use of corticosteroids.
- Depending on clinical assessment of severity, also **consider an immediate prescribing strategy** for:
    - children younger than 2 years with bilateral acute otitis media;
    - children with otorrhoea who have acute otitis media;
    - patients with acute sore throat/acute pharyngitis/acute tonsillitis when three or more Centor criteria (tonsillar exudate, tender anterior cervical lymphadenopathy or lymphadenitis, history of fever and an absence of cough) are present.

Antibiotics are not needed for most patients with acute rhinosinusitis

MeReC Rapid Review of Lancet 2008;371:908-914

http://www.npci.org.uk/blog/?p=82 Tuesday, March 25th, 2008

Young J, Sutter A, Merenstein D, et al. Antibiotics for adults with clinically diagnosed acute rhinosinusitis: a meta-analysis of individual patient data. Lancet 2008;371:908-914

What is the background to this?

Careful prescribing of antibiotics may help to delay the development and spread of antibiotic resistance. It is important to reserve the use of antibiotics to those at higher risk of complications and in those where a bacterial cause is likely. Although antibiotics confer little average benefit to patients with sinusitis, there may be subgroups that may benefit. A recent meta-analysis attempted to identify whether common signs, symptoms, or specific characteristics of patients with acute rhinosinusitis can be used to identify a subgroup that would be benefit from antibiotic treatment.

What does this study claim?

The study found that, on average about 15 adult patients with rhinosinusitis-like complaints would need to be treated with antibiotics for one extra patient to be cured (i.e. being free of symptoms). However, taking into account the wide confidence intervals (CIs) around the mean estimate of their effect, the number of patients that would need to be treated to gain benefit could be as low as seven, but it is also possible that no patients benefit and one in every 190 would suffer harm.

Common clinical signs were unable to identify a subgroup of patients for whom treatment was justified. Only purulent discharge in the pharynx had some prognostic value, although eight patients with this sign still needed to be treated for one patient to benefit. The authors suggest that antibiotics are not warranted, even when symptoms are present for longer than seven to ten days, which is commonly recommended as a period of watchful waiting before use of antibiotics. They go on to suggest that treatment with antibiotics is only essential if symptoms are suggestive of serious complications (e.g. high fever, periorbital swelling, erythema or intense facial pain). The authors point out that their **results do not apply to children or patients with suppressed immune systems.**

How does this relate to other studies?

Previous reviews of the use of antibiotics have suggested that about 15% of patients may gain benefit from the use of antibiotics (e.g. Hickner et al 2001); a number needed to treat (NNT) of about seven. The present study suggest a higher NNT (fewer patients gaining benefit), but is likely

to be more representative of the situation in primary care in the UK, as it excluded patients who were diagnosed on the basis of imaging, laboratory tests or bacterial culture.

A MeReC bulletin in 2006 reviewed the use of antibiotics in acute sinusitis and pointed out the need to restrict their use to patients with systemic illness, or several severe signs and symptoms which have lasted longer than seven to 10 days, or worsened after five to seven days. It advocated the use of watchful waiting or delayed prescription for most patients, recognising that two-thirds of patients experience resolution of symptoms without antibiotic treatment.

So what?

The present meta-analysis provides good-quality evidence confirming the limited benefits to be obtained from antibiotics for the treatment of **adult** rhinosinusitis in primary care. Routine use is clearly inappropriate, with, on average, about 93% of patients gaining no benefit. Even in patients with purulent discharge, antibiotics appear to have no effect in about 88% of cases. The study gives reassurance that a policy of symptomatic treatment and watchful waiting (or delayed prescription) of antibiotics is appropriate for most patients with acute rhinosinusitis. Only symptoms suggestive of serious complications would seem to justify immediate antibiotic treatment.

Action

Prescribers should continue to use antibiotics sparingly for the treatment of sinusitis. For most patients providing reassurance that the symptoms will resolve without antibiotic treatment and the use of watchful waiting will be all that is necessary. Only where symptoms are suggestive of serious complications (e.g. high fever, periorbital swelling, erythema or intense facial pain) should they be prescribed immediately. Prescribers should be aware a NICE guideline for respiratory tract infections is under development and is anticipated to be published in July this year.

Study details

Individual patients' data from 2547 adults in nine double-blind randomised trials were checked and re-analysed for consistency. Analysis was by intention to treat. The outcome of interest was the proportion of patients cured at the time the primary outcome of the trial was assessed. 'Cure' was most often defined as being free of symptoms but this outcome did vary between studies. The overall effect of antibiotic treatment and the prognostic value of common signs and symptoms were assessed by calculating the NNT with antibiotics to cure one additional patient. In a meta-analysis of aggregated data, the estimated odds ratio (OR) for the overall treatment effect of antibiotics relative to placebo was 1.35 (95%CI 1.15 to 1.59). In an analysis of individual patients' data, the estimated OR for the overall treatment effect was 1.37 (95% CI 1.13 to 1.66). The mean NNT for 10,000 simulated new patients was 15 (95%CI NNT [benefit] 7 to NNT [harm] 190), which implied that 15 patients had to be given antibiotics before one additional patient was cured. Patients who were older, reported symptoms for longer, or reported more severe symptoms also took longer to cure but were no more likely to benefit from antibiotics than other patients.

Routine use of antibiotics to prevent serious complications of URTIs is not justified

MeReC Rapid Review of BMJ, doi: 10.1136/bmj.39345.405243.BE, (Published 18 October 2007)

Friday, November 9th, 2007

Petersen I et al. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. *BMJ* published online 18th October 2007 doi:10.1136/bmj.39345.405243.BE

What is the background to this? – Most antibiotic prescribing is in primary care, and most of it is for respiratory tract infections. Evidence-based clinical guidelines such as CKS (formerly Prodigy) advise against routine use of antibiotics in upper respiratory tract infections (URTIs) including coughs, colds, sore throat and otitis media. Although rates of prescribing for acute respiratory tract infections in UK general practice fell by 45% between 1994 and 2000, this seems to be more because patients are less likely to present with URTIs than because GPs (and now nurse prescribers) are less likely prescribe when patients present. More information about this and other aspects of antibiotic prescribing can be found on the common infections floors of NPCi. The authors of this study looked at the risk of serious complications among people with respiratory tract infections given antibiotics and those not given antibiotics, in a large UK general practice sample.

What does this study claim? – Primary care prescribers should not base their prescribing for sore throats, otitis media or other URTIs on a fear of serious complications: more than 4000 people would have to be treated to prevent one case of quinsy, mastoiditis or pneumonia respectively. However, in patients with chest infections, especially older people, antibiotics may be useful in preventing pneumonia: the number needed to treat (NNT) to prevent one case of pneumonia in people 65 years and older = 39 (95%Confidence interval [CI] 36 to 42). NNT (95%CI) in people aged 16-64 years = 119 (105 to 136)

How does this relate to other studies? - Clinical guidelines (such as CKS (formerly Prodigy) advise against routine use of antibiotics in upper respiratory tract infections (URTIs) including sore throat and otitis media. However, the advice for lower respiratory tract infections (chest infections, LRTIs) is more complex. Antibiotics are essential in pneumonia. CKS (formerly Prodigy) advises that in other types of chest infection in adults, antibiotics are not indicated in people who are otherwise well. However, health professionals should carefully assess the symptoms and signs of people presenting with acute cough in people with characteristics and / or pre-existing conditions that increases the probability of pneumonia. More information and advice on determining who is likely to benefit from antibiotics is given in the CKS (Prodigy) guidance and on the common infections - respiratory tract floor of NPCi.

So what? - This study reassures us that, although antibiotics have a statistically significant effect in reducing the rate of complications of URTIs, these are now so rare that many thousands of

patients would need to be treated – and exposed to side effects – to prevent one case. Widespread prescribing of antibiotics is a major contribution to the rate of development of antibiotic resistance. For people presenting with LRTIs it is important to assess their baseline risk of pneumonia, assess the signs and symptoms and their severity and then consider, on the basis of all this, whether an immediate prescription, a delayed prescription, or no prescription (with watchful waiting) is most appropriate.

Action – Primary care prescribers should not base their prescribing for sore throats, otitis media or other URTIs on a fear of serious complications. Prescribers should think carefully about the best strategies for individual patients who have LRTIs.

Study details

- **Design** – retrospective cohort study using the records of the 162 UK general practices contributing to the UK GPRD database, 1st July 1991 to 30th June 2001.
- **Patients** – patients presenting with common respiratory tract infections: upper respiratory tract infection (1,081,000 episodes), sore throat (1,065,088 episodes), otitis media (459,876 episodes) and chest infection (749,389 episodes).
- **Outcomes** – risk of developing serious complications (pneumonia, quinsy, mastoiditis and pneumonia, respectively) in the month after consultation and the odds ratio for the development of complications (antibiotics prescribed on the day of consultation vs. no antibiotics

Results :

Infection/adverse outcome	Adjusted odds ratio (95%CI)	NNT (95%CI)	P value
Otitis media/ mastoiditis (all ages)	0.56 (0.37 to 0.86)	4,064 (2,393 to 13,456)	0.008
Sore throat/ quinsy (all ages)	0.84 (0.73 to 0.97)	4,300 (2,522 to 14,586)	0.021
Other URTI/ pneumonia (all ages)	0.68 (0.58 to 0.79)	4,407 (2,905 to 9,126)	<0.001
Chest infection/ pneumonia	-	-	-
0-4 years	0.22 (0.17 to 0.27)	101 (85 to 125)	<0.001
5 -15 years	0.18 (0.13 to 0.24)	96 (73 to 137)	<0.001
16 -64 years	0.27 (0.23 to 0.32)	119 (105 to 136)	<0.001
65 years and older	0.35 (0.33 to 0.38)	39 (36 to 42)	<0.001

- **Sponsorship** – UK Department of Health

Summary of evidence regarding delayed strategies

(Adapted from Geoffrey Spurling- personal communication)

Best Strategies for reducing antibiotic use

1. No antibiotics
2. Leave script at reception
3. Give patient a delayed script

The strategy which resulted in least antibiotic use was "no antibiotics".

Delayed antibiotics: leave delayed script at reception vs give patient delayed script vs no antibiotics

Studies testing effect of delay on clinical outcomes, patient satisfaction and antibiotic use

Studies where script was left at reception		**Antibiotic use**
Little 1997	pick up script at the surgery 3 days later	55/176
Little 2001	pick up script at the surgery 3 days later	36/150
Little 2005	pick up script at the surgery	39/197
Dowell 2001	pick up script at reception after 1 week	43/95
Total :		173/ 618 = 28.0% of scripts dispensed where script left at reception

Studies where script was given to patient		**Antibiotic use**
Arroll 2002	given the script and instructed to fill it 3 days later	32/67
Spiro 2006	given the script (which was to expire after 3 days) and instructed to fill it within 3 days	50/132
Chao 2008	given script and instructed to fill it in 2-3 days	40/106
Total:		122/ 305 = 40% of scripts dispensed where script given to patient

Comparing delayed script left at reception with delayed script given to patient

OR 0.58 (95% CI: 0.44 to 0.78) p<0.01 (chi squared)

i.e. 42% less likely to get script dispensed if left at reception compared with giving to patient

Studies with a 'no antibiotic' arm

No Antibiotics were given at first consultation (Little 1997, Little 2005a, Little 2005b, Chao 2008) = 65/466

i.e. 13.9% scripts dispensed where an antibiotic was received at a subsequent consultation

Comparing delayed script left at reception with no antibiotics

OR 0.24 (95% CI: 0.17 to 0.34) p<0.01 (chi squared)
i.e. 76% less likely to have a script dispensed using 'No antibiotic' strategy than to leave prescription at reception

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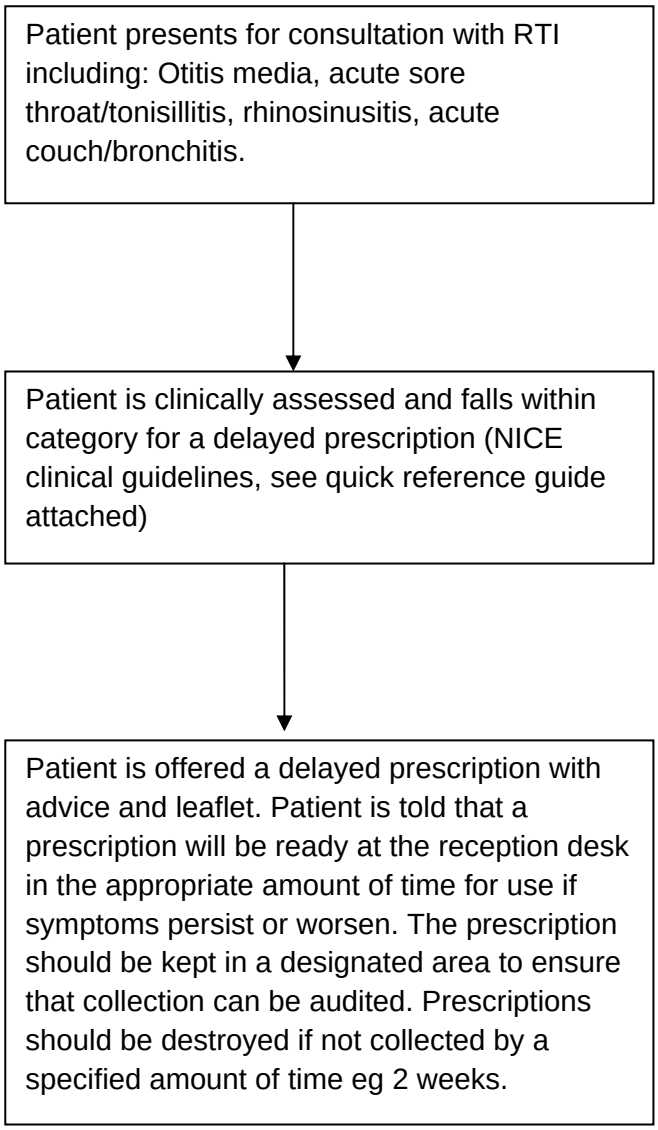
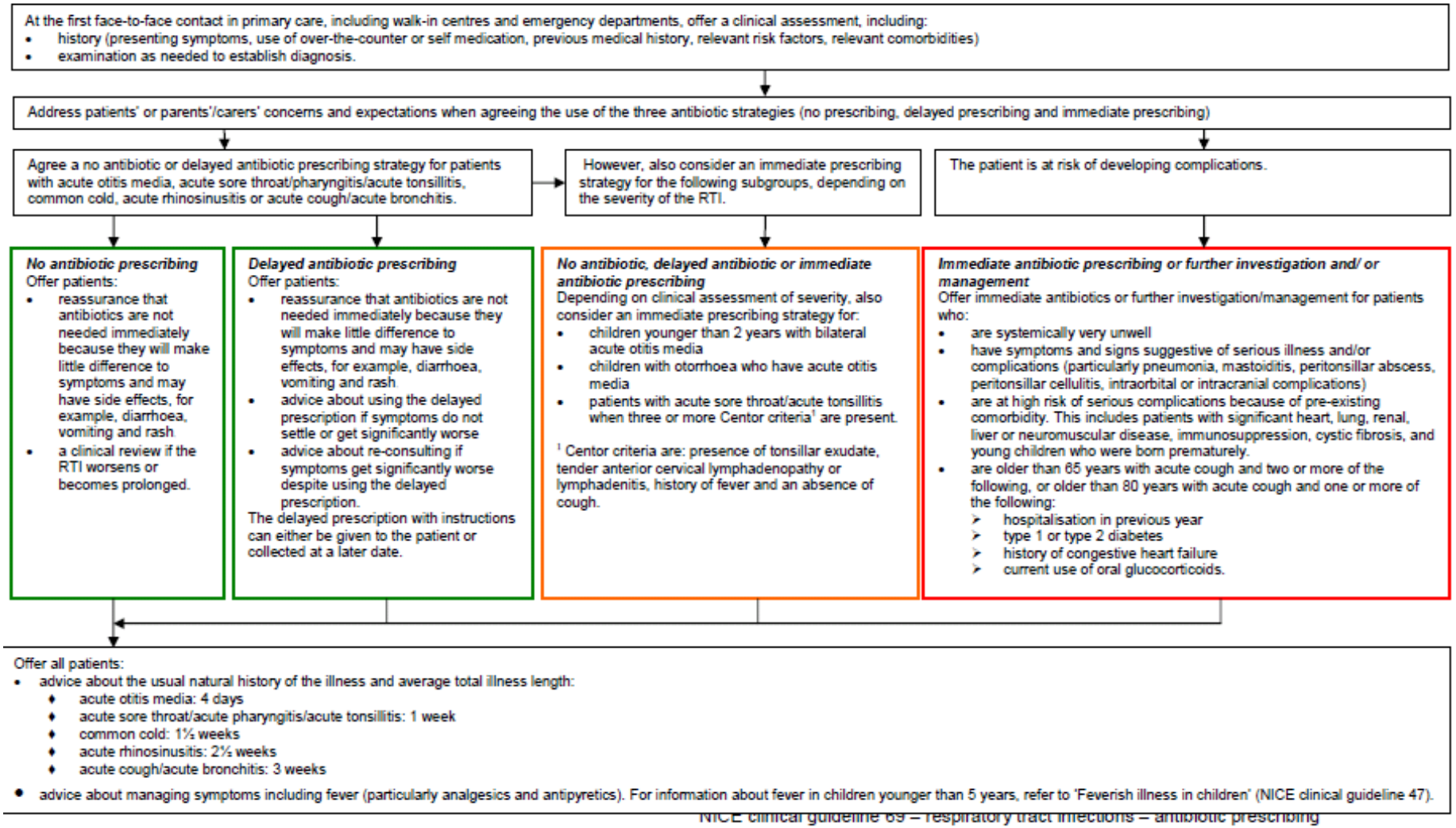
Delayed Prescribing Protocol

As a result of the above evidence we recommend an auditable delayed prescription protocol based on the flow chart below:

Delayed Prescribing Protocol:



1.2 Care pathway for respiratory tract infections



Other Strategies to Reduce Antibiotic Use in Primary Care:

NeLM news service

NHS eyes on evidence expert commentary on behavioural strategies to influence antibiotic prescribing

Source: **NHS Evidence** Date published: **15/03/2012 17:12**

Summary

by: **Hina Radia**

The March edition of 'Eyes on Evidence', the free monthly e-bulletin from NHS Evidence covering major new evidence with an explanation about what it means for current practice, includes an expert commentary on new evidence from two systematic reviews of both qualitative and quantitative evidence, assessing the effectiveness of antimicrobial prescribing interventions that aim to influence behaviours in acute care.

The systematic reviews showed that qualitative evidence highlights the influence of social norms, attitudes and beliefs on antimicrobial prescribing behaviour. However, these influences on prescribing are generally not considered when designing and evaluating interventions, and the researchers suggest that the lack of this approach may be a contributing factor to the challenges that beset interventions aiming to influence prescribing behaviour and optimise antimicrobial prescribing.

According to an expert commentary by Dr Kieran Hand (Consultant Pharmacist Anti-Infectives at University Hospital Southampton NHS Foundation Trust) "this research suggests that multi-faceted, multi-disciplinary interventions incorporating lessons learned from behavioural science and social marketing are most likely to be effective in optimising antimicrobial prescribing. However, these interventions can be relatively resource-intensive to deliver and further research into cost-effectiveness and sustainability is of paramount importance."

Eyes on Evidence March 2012

Multifaceted educational programme reduces antibiotic dispensing in primary care http://www.npc.nhs.uk/rapidreview/?p=4948

21st March 2012

A practice based randomised controlled trial in Wales found that use of a multifaceted educational programme (STAR) resulted in a statistically significant 4.2% reduction in antibiotic dispensing compared with control practices who did not receive the programme. The clinical significance of this finding is uncertain.

Level of evidence:
Level 3 (other evidence) according to the SORT criteria.

Action
Antibiotic prescribing remains at a high level with wide variation between general practices. Changing prescribing behaviour is a complex problem (see MeReC Bulletin 22 No.2 December 2011). Although guidance, such as that from NICE on respiratory tract infections and the Health Protection Agency (HPA), are important, their ability to change prescribing behaviour is limited without additional support. An educational programme, such as the Stemming the Tide of Antibiotic Resistance (**STAR**) programme, might be used to encourage more appropriate prescribing of antibiotics for self-limiting infections in the community. The clinical and cost-effectiveness of this programme have yet to be established. This approach should be of interest to those concerned with antimicrobial stewardship and those involved in improving the quality of prescribing by changing clinician behaviours.

What is the background to this?
Antibiotic resistance poses a significant threat to public health. Emerging resistance against antimicrobials that are currently used, and the upsurge in a number of infections, some of which had previously been well-controlled, are two factors that contribute to this threat. Much of the prescribing of antibiotics in primary care is for self-limiting respiratory tract infections; this is of questionable value, puts patients at risk from side-effects and increases the risk of antibiotic resistance.

Changing prescribing behaviour is a complex problem. Guidelines by themselves such as the NICE guidance on antibiotic prescribing for self-limiting respiratory tract infections have an important role, but may not be sufficient to change practice by themselves. Public awareness campaigns have not been associated in the past with reductions in all cause antibiotic prescribing and there is unexplained wide variation between individual practices.

Recognising these issues, the authors developed the multifaceted STAR educational programme, using a variety of learning methods and topics, based on social learning theory. It attempts to develop clinicians' sense of importance of change (the 'why') and their confidence in their ability to achieve change (the 'how'). General practices in Wales were randomly assigned to receive the educational programme. The volume of oral antibiotics dispensed from prescriptions arising from these practices was compared with those of practices not provided with the programme. Dispensing, rather than prescribing volume, was chosen as a better proxy for antibiotics actually consumed to take account for the use of 'delayed' prescriptions (as per NICE guidance on respiratory tract infections). Re-consultations, hospital admissions for selected causes, and costs were measured as secondary outcomes.

What does this study claim?

In this study, practices exposed to the education programme reduced antibiotic dispensing on average by 14 items per 1000 registered patients, while control practices increased antibiotic dispensing by 12 items per 1000 registered patients (difference 26.1 items per 1000 registered patients). Taking into account baseline dispensing rates, this equated to a reduction of 4.2% (95% confidence interval [CI] 0.6 to 7.7%; p = 0.02) for all age groups in the year after the intervention.

There were no significant differences in re-consultations, admissions to hospital, or costs between the groups. The reduction in antibiotic dispensing was achieved at an average cost of £2893 per practice. Although the costs of dispensing were not significantly reduced, the authors speculate that the cost of the programme might be recouped within 3.5 years from reduced dispensing costs.

So what?

The authors point out that most of the studies that have looked at interventions to reduce unnecessary antibiotic prescribing have only looked at one or two approaches. In contrast to these, and recognising the complex nature of the issue, the authors, explored both the 'how' and 'why' of change in a flexible learning format , using practice-specific prescribing and resistance data, information about guidelines, reflections in practice based experience, academic outreach, and a web forum. They claim to have included all elements showing promise or effective previously. As pointed out in the MeReC Bulletin: 'Rather than a 'scattergun' approach of employing multiple approaches in an unsystematic way, recent research advocates a consideration of the full range of options and using a rational system for selecting from among them.'

These data add some knowledge about the role of educational programmes for reducing inappropriate antibiotic prescribing. However, we do not know if this multifaceted approach represents a good use of money and other resources compared to other, simpler interventions. The editorial accompanying the article states: 'The results are similar to (although at the lower end of) reductions seen with other such programmes.' Although the 4.2% reduction in prescribing is within the range of other studies, meaningful comparisons with other studies is difficult in view of the heterogeneous nature of the study designs, interventions, and outcome measures. The study looked at dispensing across practices, and in many cases not all GPs within the practices receiving the educational intervention participated in the programme, so the reduction found may underestimate the effect of the benefit. Indeed, the benefit was only seen in practices where more than 67% of GPs participated; in those practices with fewer participants the dispensing actually increased.

Few, if any, other studies have gathered information on complications, repeat consultations or costs. The cost of providing the intervention (at about £3000 per practice) may be partly offset by reductions in dispensing costs (on average £830 per practice), but this reduction in dispensing costs was not statistically significant. Although the study showed a difference in antibiotic dispensing between groups, the clinical significance in terms of clinical outcomes is uncertain. The study was not powered to identify small differences in re-consultations or hospital admissions, although no significant increase between groups was identified. The lack of diagnostic data meant that the study was only able to identify the proportion of prescriptions for antibiotics that were clinically inappropriate. The effect on antibiotic resistance was not evaluated, although the accompanying editorial to the article suggests that 'the small reduction seen in the STAR study is unlikely to lead to a clinically important change in resistance patterns.'

A rapid response to this study, whilst recognising that it is difficult to identify an effective strategy to change behaviour, points out some important further limitations:

'Firstly, a multifaceted intervention might be a way forward, but "bundling" them into one is difficult to demonstrate which component is the most effective: the audit and feedback, educational activity, printed educational materials, educational outreach visits, or having an opinion leader to spread the gospel; each of these approaches have been assessed by EPOC with modest outcomes at best. Having at least another group with any of the above might improve the evidence base; however, this would have been at the expense of reduced number of practices in each arm and therefore the power of the study. Even then, a much larger trial and length of follow up would be required to answer the question relating to the "dose" and effect of interventions.

Secondly, the online training might be time consuming (average of 238 minutes or nearly four hours) and some GPs and nurse practitioners might not be able to find the time to do this. In the related qualitative study, most of the sample of 31 practitioners found the educational programme useful, but a small number considered it "a waste of time and money" and found it difficult to engage in online learning.

Thirdly, with an overall mean cost of nearly £3000 per practice and annual saving of £830 per year for an average intervention practice, it might take 3.5 years to recoup the cost. In an era of austerity and efficiency savings, this poses a huge financial barrier.' [Note: cited references to supporting information have been removed from this quote]

Study details
Butler CC, et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. BMJ 2012;344:d8173

Design
Practice based randomised control trial of multifaceted educational programme (STAR) compared with usual care. Clinicians and observers were blinded to group allocation until after randomisation.

Practices
68 general practices in Wales with about 480,000 patients.

Outcomes and results

The rate of oral antibiotic dispensing (items per 1000 registered patients; in the year after the intervention adjusted for the previous year's dispensing) decreased by 14.1 in the intervention group but increased by 12.1 in the control group, a net difference of 26.1. After adjustment for baseline dispensing rate, this amounted to a 4.2% (95% CI 0.6% to 7.7%) reduction in total oral antibiotic dispensing for the year in the intervention group relative to the control group (p = 0.02). Reductions in dispensing of individual classes of antibiotics were only statistically reduced for phenoxymethylpenicillins (penicillin V) (7.3%, 95%CI 0.4% to 13.7%) and macrolides (7.7%, 95%CI 1.1% to 13.8%), although CIs were wide for all classes.

There were no significant differences between intervention and control practices in the number of admissions to hospital or in re-consultations for a respiratory tract infection within seven days of an index consultation. The difference in the rate of hospital episodes for possible respiratory tract infection and complications between groups (on average increased in the intervention group) was 1.9% (95% –8.2% to 13.2%, p = 0.72). The difference in the rates of re-consultations between groups (per 1000 registered patients) for respiratory tract infections within 7, 14 and 31 days after the original consultations (on average decreased in the intervention group) were –0.65 (–1.69 to 0.55), –1.33 (–2.12 to 0.74) and –2.32 (–4.76 to 1.95) respectively (all p >0.4).

The mean cost of the programme was £2923 per practice (standard deviation £1187). There was a 5.5% reduction in the cost of dispensed antibiotics in the intervention group compared with the control group (−0.4% to 11.4%), equivalent to a reduction of about £830 a year for an average intervention practice.

Study sponsorship

The study was funded by the UK Medical Research Council.

Further information on common infections can be found on NHS Evidence and in the common infections e-learning section of the NPC website. The NPC e-learning resources include two patient decision aids, which may be helpful when discussing the benefits and risks of using antibiotics with patients, (please see supplementary materials section for link).

Let's be responsible with antibiotics – European Antibiotics Awareness Day 2011

http://www.npc.nhs.uk/rapidreview/?p=4628

7 November 2011

The Department of Health (DH) has published information to support European Antibiotics Awareness Day, which is on the 18th of November 2011. The aim of this annual event is to tackle the rise in antibiotic resistance and encourage responsible use of antibiotics. Support materials have been produced for both hospital and primary care settings and can be downloaded from the DH website.

Action

Prescribers and prescribing managers should consider using the support materials to promote the appropriate use of antibiotics. Healthcare professionals should follow NICE guidance on respiratory tract infections and/or local guidance based on advice from the Health Protection Agency (HPA).

The HPA advises that an antibiotic should be used only when there is likely to be a clear clinical benefit and, broad spectrum antibiotics (which include quinolones and cephalosporins) should be avoided where a narrow spectrum agent is indicated. Generally, prescribing for viral or mild, self-limiting infections such as coughs and colds is unlikely to improve the course of the illness, puts patients at risk of unnecessary adverse reactions (e.g. vomiting, diarrhoea, rash, fungal infection) and encourages further consultations.

NICE recommends that antibiotics should be offered immediately, with or without further appropriate investigation or management, in certain cases. For example, if the patient is likely to have a serious bacterial infection, or is at risk of suffering a prolonged or severe illness or complications, if he/she is systemically unwell or has pre-existing co-morbidities such as heart or lung disease. However, for many patients providing reassurance that the symptoms will resolve without antibiotic treatment and the use of watchful waiting or a delayed prescription may be more appropriate.

The NPC has produced resources to support the QIPP initiative, based on the document, Key therapeutic topics – medicines management options for local consideration. These include a set of slides with supporting notes and a recorded commentary to help clarify the key issues around antibiotic prescribing, especially quinolones and cephalosporins.

Why is the responsible use of antibiotics important?

As the DH letter says, the number of infections due to antibiotic-resistant bacteria is growing globally and is related to the overuse of antibiotics and inappropriate prescribing. Recently there have been decreases in MRSA and *Clostridium difficile*.However, infections are still a major threat to public health with many examples of recent media attention to this subject. While resistance to antibiotics is inevitable, prudent prescribing can help slow the development of resistance.

What support materials are available?

The support materials include factsheets aimed at prescribers and prescribing managers detailing the main issues surrounding antibiotic resistance, and a slide presentation which can be used for staff and medical students in hospital training. Resources for patients include leaflets, posters and non-prescription pads, which can be printed and given to patients as a aide memoire as to why antibiotics have not been prescribed at a consultation. In addition the Royal College of General Practitioners has produced a booklet 'When should I worry' for use in primary care consultations with parents about the management of respiratory tract infections in children. There are also short videos for use in patient waiting areas to remind patients to 'Take care, not antibiotics'.

Improving communication skills and measuring CRP may facilitate appropriate antibiotic prescribing http://www.npc.nhs.uk/rapidreview/?p=344

20th May 2009

A randomised controlled trial has shown that communication skills training and the use of near-patient C reactive protein (CRP) testing can reduce antibiotic prescribing for patients with lower respiratory tract infection in primary care.

Action
The aim when assessing patients with an acute respiratory tract infection with cough as the predominant symptom is to select out the minority of patients who already have or who may be at higher risk of developing a more serious illness (including pneumonia) from the majority of patients who have a less serious and self-limiting illness.

NICE Guidance on respiratory tract infections advises that antibiotics are prescribed immediately, and/or further appropriate investigation and/or management should be offered, if a patient has signs and symptoms suggestive of pneumonia or is at risk of suffering a prolonged or severe illness or complications. For example, if he/she is systemically unwell or has pre-existing co-morbidities, or is older than 65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following criteria: hospitalisation in previous year, type 1 or type 2 diabetes, history of congestive heart failure, or current use of oral glucocorticoids.

If the criteria for serious illness or the risk of serious illness are not met, NICE recommends prescribing either a delayed antibiotic or no antibiotic. The patient's concerns and expectations should be addressed when agreeing which strategy should be used. Enhanced communication skills and shared decision-making, as used in this study, are key to improving patients' participation in discussions about their care and achieving evidence-based decisions on prescribing. Near patient tests, including CRP, should not be introduced without a national policy decision involving evaluation of all data on clinical and cost effectiveness.

What does this study claim?
This randomised controlled trial evaluated the effect of GPs using a near-patient test for CRP and being trained in enhanced communication skills, separately and combined, on antibiotic prescribing for lower respiratory tract infection (RTI) and on patient recovery.

The use of near-patient CRP testing and training in enhanced communication skills both significantly reduced antibiotic prescribing at the index consultation for lower RTI (the primary outcome) and antibiotic prescribing during the 28 days' follow-up period, without affecting clinical recovery, patients' satisfaction or reconsultations. GPs prescribed antibiotics for 31% of patients in the CRP test group, compared with 53% in the no test group (P=0.02). GPs trained in enhanced communication skills prescribed antibiotics for 27% of patients, compared with 54% in the no

training group (P<0.01). Both interventions together produced no statistically significant additional effect to either of the interventions alone (P=0.78).

So what?

The study authors state that CRP testing may contribute to safely withholding antibiotics from most people with low CRP values who probably would not benefit from antibiotic treatment. However, CRP near-patient tests are not widely used in the UK and GPs may be inexperienced in interpreting results and using them to guide treatment. In countries where these near-patient tests are available, excessive testing has been reported and could limit the cost-effectiveness of this intervention. A cost-effectiveness analysis of this study is being undertaken. An editorial accompanying the study discusses some other limitations of using CRP testing and points out that a recent systematic review concluded that a CRP test could help rule out community-acquired pneumonia only if the probability of the patient having this condition is more than 10%, and this is more likely after initial selection of patients, for example in emergency departments. The editorial also questions whether CRP testing may increase the long-term likelihood of patients consulting for similar illnesses in the future.

However, this paper supports the NICE approach to managing patients with a delayed or no prescription where this is appropriate. Good communication skills can increase patients' understanding of prescribing decisions without the feeling of being dismissed. It is important that patients' concerns and expectations are addressed and they understand that symptoms following a respiratory infection with acute cough as the predominant symptom may last for a number of weeks. Patients should be advised that, for the majority, antibiotics make little difference to symptoms, and may have side effects.

Antibiotics are always indicated for adults and children with suspected pneumonia. They lead to a clinical cure or improvement in 80% or more of people treated in the community or in hospital. But when NICE looked at the evidence for antibiotics to treat acute cough/bronchitis, they found that, although antibiotics had a significant effect on the duration of cough and productive cough, and on feeling ill, the benefits were small – a fraction of a day in an illness lasting several weeks. They concluded that a delayed or no prescribing strategy should be offered to patients with acute cough who are not at an increased risk of suffering a prolonged or serious illness or developing complications.

NICE stress the need for safety-netting approaches in case the patients' illness worsens or becomes prolonged, either by use of delayed antibiotic prescriptions or by offering a prompt clinical review. If a delayed prescription is given, patients should be given advice on using it if symptoms worsen or aren't resolving as expected. Similarly, if symptoms worsen despite using the delayed prescription, the patient should be advised to re-consult.

The usual approach to the prescribing of antibiotics for an acute respiratory tract infection with cough as the predominant symptom would require modification in the circumstances of an influenza epidemic or pandemic.

Study details

Cals JWL, Butler CC, Hopstaken RM, et al. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. BMJ 2009;338:b1374, doi: 10.1136/bmj.b1374 (Published 5 May 2009)

Design: Cluster randomised, factorial, controlled trial.
Patients: Forty GPs from 20 practices recruited 431 sequential eligible adults within regular consultation hours during the winters of 2005–6 and 2006–7. Patients were eligible if they had a suspected lower RTI with a cough lasting less than four weeks together with one chest and one systemic symptom.
Intervention: GPs were trained to provide finger prick near-patient CRP tests and/or a communication skills intervention built around 11 key tasks (e.g. exploring patients' fears and expectations, asking patients' opinion on antibiotics, and outlining the natural duration of cough in lower RTI) with information exchange throughout based on the elicit-provide-elicit framework from counselling in behaviour change.
Comparison: Patients were randomised to four groups: GP use of CRP testing, training in enhanced communication skills, both, or usual care.
Outcomes: The primary outcome was antibiotic prescribing in the index consultation. Secondary outcomes were antibiotic prescribing during 28 days' follow-up, reconsultation, clinical recovery, and patients' satisfaction and enablement. Cost effectiveness is to be reported separately. Patients rated symptoms (cough, phlegm, shortness of breath, disturbance of daily activities, sleeping problems, and generally feeling unwell) on a 7 point scale in a daily diary for 28 days. Antibiotic prescribing and reconsultation data for the 28 days of follow-up were obtained from the participants' medical records.
Results: GPs in the CRP test group prescribed significantly fewer antibiotics than those in the no test group (31% v 53%, P=0.02). Similarly, those in the communication skills training group prescribed significantly fewer antibiotics than those in the no training group (27% v 54%, P<0.01). The two interventions showed no statistically significant interaction effect (P=0.78). There was no statistically significant difference in reconsultations. Antibiotic prescribing at any point during the 28 days' follow-up (prescribing rates at the index consultation combined with prescribing rates at reconsultations) remained significantly lower in patients in the CRP test group compared with those in the no test group (45% v 58%, P<0.01) as well as for patients in the communication skills training group compared with patients in the no training group (38% v 63%, P<0.001). Comparable median daily symptom scores were seen for all four groups of patients suggesting that the interventions had no effect on recovery. Overall, satisfaction with the index consultation was high, with no statistically significant differences between treatment groups.
Sponsorship: Netherlands Organisation for Health Research and Development.

Effect of interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing

Reference: **BMJ 2009; 339: b2885**

Summary

by: **Yuet Wan**

In this pragmatic cluster randomised controlled trial, researchers set out to establish whether training clinicians in the use of an interactive booklet on respiratory tract infections in children, designed to enhance communication within the consultation, and act as a take home resource for parents, would have an effect on rates of reconsultation and antibiotic prescribing.

The study conducted at 61 general practices in England and Wales involved 558 children (aged 6 months to 14 years) presenting to primary care with an acute respiratory tract infection (7 days or less). The study excluded children with suspected pneumonia, asthma or a serious concomitant illness, or needing immediate hospital admission.

Clinicians in the intervention group were trained in the use of the interactive booklet and asked to use it during consultations with recruited patients, and provide it as a take home resource. Clinicians in the control group conducted their consultations as usual. The main outcome measure was the proportion of children who attended a face-to-face consultation about the same illness during the two week follow-up period. Secondary outcomes included antibiotic prescribing, antibiotic consumption, future consulting intentions, and parental satisfaction, reassurance, and enablement.

Main outcome data were available for 528 (94.6%) children as follows:

• Reconsultation occurred in 12.9% of children in the intervention group and 16.2% in the control group (absolute risk reduction 3.3%, 95% CI, –2.7% to 9.3%, p = 0.29).

• Using multilevel modelling (at the practice and individual level) to account for clustering, no significant difference in reconsulting was noted (odds ratio 0.75; 0.41 to 1.38).

• Antibiotics were prescribed at the index consultation to 19.5% of children in the intervention group and 40.8% of children in the control group (absolute risk reduction 21.3%, 95% CI, 13.7 to 28.9), p < 0.001). A statistically significant difference was still present after adjusting for clustering (odds ratio 0.29; 0.14 to 0.60).

• There was a statistically significant difference in the proportion of parents who said they would consult in the future if their child developed a similar illness (odds ratio 0.34; 0.20 to 0.57).

• 7 patients (3 intervention group and 4 in control group) were subsequently admitted to hospital or observed in a paediatric assessment unit.

• Satisfaction, reassurance, and parental enablement scores were not significantly different between the two groups.

The researchers conclude that use of this booklet in primary care consultations led to important reductions in antibiotic prescribing and reduced intention to consult without reducing satisfaction with care. They suggest that "the routine use of this intervention in primary care should now be considered along with other effective interventions such as delayed prescribing" adding that "the magnitude of the reduction in antibiotic prescribing achieved suggests that its use could have important implications for patients, and, as a result of the threat posed by increasing antimicrobial resistance, for public health."

Abstract

The public's attitudes to and compliance with antibiotics

Original article by: **CAM McNulty, P Boyle, T Nichols, P Clappison, P Davey**

Reference: **Journal of Antimicrobial Chemotherapy, Aug 2007, vol. 60, no. Suppl. i, p. i63-i68**

Keywords: **Antibiotics; Drug Storage; General Public; Health Education; Patient Compliance; Patient Counselling; Patient Information; Prescriptions-Drug; Self Medication; Medicines-unused;**

Summary

by: **Pharm-line**

Although a third of the public still believe that antibiotics work against coughs and colds, simply getting the public to believe otherwise may not be enough to reduce the level of prescribing. The large Dept of Health sponsored household survey demonstrated that those with a greater knowledge about antibiotics were no less likely to be prescribed an antibiotic, and although those with increased knowledge about antibiotics were more likely to complete a course they were also more likely to self-medicate and to keep left-over antibiotics. Future campaigns that are aimed at reducing the level of prescribing should be focused towards those more likely to be prescribed antibiotics at present: younger women and those with a lower level of education. They should also examine and consider modifying consultation behaviour and other behavioural components involved in patient' expectations for antibiotics. This should include delayed antibiotic prescriptions. The easiest way to reduce the use of leftovers may be to shorten the course of antibiotics prescribed to 3 or 5 days. We should also promote a 'Do not recycle antibiotics' message towards the more highly educated, young women who are more likely to store, take and share antibiotics without advice. (13 refs.)

Supporting Materials

- http://elearning.rcgp.org.uk/login/index.php to register for free access to RCGP training including two modules on Managing Acute Respiratory Tract Infection (MARTI) training

- www.npc.nhs.uk/therapeutics/common_infections/respiratory/elearning.php

- NICE Guidance CG 69 July 2008: Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care http://www.nice.org.uk/Guidance/CG69

- Spurling GKP, Del Mar C, Dooley L, Foxlee R. Delayed antibiotics for respiratory infections (review). Cochrane Database of Systematic Reviews 2007, Issue 3 http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004417/frame.html

Patient Decision Aids:

During a consultation with a healthcare professional, the decision aids below can be used to visually clarify for patients, the risks vs benefits of treatment with an antibiotic.

Otitis media: risks and benefits of antibiotics
http://www.npc.nhs.uk/therapeutics/common_infections/respiratory/resources/pda_rti_aom.pdf

Common infections: respiratory tract infection
http://www.npc.nhs.uk/therapeutics/common_infections/respiratory/resources/pda_rti_general.pdf

Milton Keynes PCT Antibiotic Guidelines

See attachment - Antibiotic in the community 2011

Useful resources

A number of useful leaflets / posters have been attached.

Antibiotic leaflets

Bacterial infections PIL . - also available in some foreign languages

Coughs and colds PIL - can be downloaded and printed locally

Antibiotic Posters-to view:

Germs PILs

You can also contact Naomi Fleming for up to date versions of these resources
naomi.fleming@mkchs.nhs.uk