New tool may help cut unnecessary antibiotic prescribing for children with coughs and respiratory tract infections

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This article introduces the TARGET study algorithm paper, which reports development of a new clinical prediction algorithm designed to improve targeted antibiotic prescribing in children with respiratory tract infections.

Three PCRS-UK experts give differing opinions on the value of this new tool. This study is important because respiratory tract infections are the single most important cause of consultations in primary care[1] and this tool could provide a new layer of evidence to help healthcare professionals and parents deal with the uncertainties they face when managing these common but potentially life-threatening infections.

You can learn more about this topic at the PCRS-UK annual conference '*Beyond the respiratory consultation: inspiring lifelong change*', when Professor Andrew Bush, Professor of Paediatrics and Paediatric Respirology, Imperial College and Royal Brompton Hospital, will discuss respiratory infections in children and when to refer. The conference is being held on 29th-30th September at the Telford International Centre. For further information visit: https://pcrs-uk.org/annual-conference

The Target study

"Respiratory tract infections (RTI) with cough are the most common reason children are prescribed antibiotics by doctors in primary care, but up to a third of prescriptions may be unnecessary", say the authors of this study.

Despite national and international calls for more targeted use,[2] primary care prescription of antibiotics for coughs and colds increased by 40% in the UK between 1999 and 2011,[3] in part reflecting the uncertainties facing patients, parents and healthcare professionals when managing these common but potentially life-threatening infections.

A new study published in the *Lancet Respiratory Medicine*[4], of over 8,000 children has identified seven key predictors which could help GPs and nurses in primary care identify low risk children who are less likely to need antibiotics.

The authors estimate that, if antibiotic prescribing in this low risk group was halved, and even if it increased to 90% in high risk patients, a new algorithm they have developed, with the mnemonic STARWAVe, could reduce antibiotic prescribing to children with RTI and coughs by 10% overall, similar to other interventions used to combat antibiotic resistance.

STARWAVe, uses seven predictors of future hospitalisation that can be easily identified by doctors and nurses during a patient visit.

The seven characteristics are:

- Short illness (less than 3 days)
- Temperature (37.8°C on examination or parent reported severe fever in the previous 24 hours),
- Age under 2 years
- Respiratory distress
- Wheeze
- Asthma
- Vomiting (moderate/severe in the previous 24 hours).

To create the tool, Professor Alastair Hay from the University of Bristol and colleagues analysed data collected between July 2011 and May 2013 from almost 8,400 children aged between 3 months and 16 years with acute (less than 28 days) cough and respiratory tract infection symptoms (eg fever) who were seen at 247 GP practices across England. They used modelling to determine which of

the 50 demographic characteristics, parent-reported symptoms and physical examination signs measured might be most useful and accurate in distinguishing good from poor prognosis illnesses, defined as those resulting in hospitalisation for respiratory infection in the month following a visit to primary care.

Modelling showed that seven characteristics outlined by the STARWAVe algorithm were independently linked with hospitalisation.

Using these findings, the authors then developed a seven-item scoring system for a child's risk of future hospitalisation. For example:

- A child presenting with one or none of these characteristics would be at very low risk of hospitalisation (0.3% risk; 67% of children in the study)

- A child with 2–3 of these characteristics would be at normal risk, similar to the general population (1.5% risk; 30% of children in the study)

- A child showing 4 or more would be a high risk candidate for future hospitalisation (11.8% risk; 3% of children in the study).

The authors recommend that:

- A 'no antibiotic' prescribing strategy would be appropriate for low risk children

- A 'no antibiotic or delayed antibiotic' treatment strategy would be best for normal risk children as recommended by NICE

- Children deemed at high risk of hospitalisation should be closely monitored for signs of deterioration and followed up within 24 hours.

The accuracy of the rule was measured by a figure called the 'area under the receiver operating characteristic curve', or AUROC. An AUROC of 0.5 would mean the rule is about as good a predictor as flipping a coin. An AUROC of 1.0 is perfect. The new STARWAVe rule gave an AUROC of 0.81, which indicates it should predict the risk of hospitalisation with high accuracy.

The authors note that the results are likely to be applicable to primary care systems similar to those in the UK, but as only 78 children were hospitalised during the study, further research is needed to externally validate the tool in a randomised trial.

They argue that it could be a useful tool to improve the targeting of antibiotics to reduce the growing threat of antibiotic resistance because it is challenging for GPs and primary care nurses to easily identify serious respiratory infections.

Lead author Professor Hay, says: "Excessive antibiotic use has contributed to the development of resistance to these drugs. The aim of our study was to develop a simple, usable prediction tool based on symptoms and signs to help GPs and nurses identify children presenting in primary care at the lowest and highest risk of future complications and hospitalisation, so that antibiotics can be targeted accordingly.

"This is the first study of its kind, based on a large representative sample of children who visit the doctor with respiratory illness. We hope that our proposed clinical tool might eventually enable doctors to quickly and easily identify their lowest and highest risk patients, although more research will be needed to determine just how effective it is in clinical practice. The rule should supplement not replace clinical judgement, and doctors and nurses should still advise parents about the symptoms and signs they should look out for, and when to seek medical help."

In a linked comment in the *Lancet Respiratory Medicine*,[5] Professor David Price, Chair of Primary Care Respiratory Medicine at the University of Aberdeen and colleagues discuss the need to test the tool in whole study populations and not just those recruiting and consenting to enter a study.

They write: "Notwithstanding the inclusion of patients prescribed an antibiotic and the absence of an independent validation cohort, STARWAVe promises to achieve better targeting of antibiotics in primary care. There are few efficacious interventions for respiratory tract infection available to primary care clinicians beyond offering reassurance and self-management advice, so the modest benefit offered by antibiotics can persuade general practitioners to prescribe them.

They add: "STARWAVe offers primary care clinicians an evidence-based practical tool to help guide antibiotic prescription decisions and, through shared decision-making, has the potential to reduce antibiotic prescription based on prognostic uncertainty or on non-medical grounds.[6] Combining this tool with point-of-care C-reactive protein (CRP) testing, or to triage for CRP testing[7] might help to target antibiotic use further."

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What the experts say:

Dr Noel Baxter
PCRS-UK Chair, GP South London, Co-Lead NHS London Respiratory Network, Primary Care Lead National COPD Audit

"My reflections on this paper come from the position of an experienced GP who still dreads those difficult decisions I need to make in tandem with anxious parents and guardians about young children day in day out during the winter respiratory infection season when certainty can't be provided. I was also the research lead for the Target study at Surrey Docks health centre during the recruitment and the notes review period so can also reflect how the experience resulted in a change in my own practice from simply taking part.

"It is important to say that the study does not yet provide us with a validated tool for this coming winter, but future work will hopefully move us towards that point. I'm sure I am not alone in finding Wells, Centor, CRB65 and other scoring systems useful as an objective check against what my gut instinct tells me – something that was noted as a statistically significant predictor for admission. It would therefore be useful to have a validated tool too for this scenario.

"The key characteristics identified from their statistical modelling do seem plausible to me and they fit with the features that I tend to look for as a GP. What I will do differently now is ensure that I have considered these and begin to get used to noting and, indeed, coding them where possible. Developing a template with these codes and making recording these items of health status an easy thing to do might be an opportunity within a practice or cluster or federation.

"An element from the paper that I think we can communicate to parents and that may help assess risk or provide assurance is that, in this study, out of 8,394 children presenting unwell to their GP surgery with similar symptoms to their child, only 78 were subsequently admitted.

"The practice-changing experience for me from being the lead in a study centre was that I had to grade the carer's score out of 10 for how ill they thought their child was. The paper does in fact show it to be a marker statistically significant for risk of admission and it did help change the feel of the consultation. It allowed me to use a tool to ensure that I was taking their concerns seriously and including them in my assessment. Hearing the concern of the child's carer is of course a basic lesson for a medical student studying paediatric care, but the process of recording it as part of the assessment was a new process for me and one that I think is helpful."

Dr Katherine Hickman
GP, Leeds, PCRS-UK Regional Lead, York and Humber, CCG Respiratory Lead for Leeds and Bradford

"Clinicians and patients are aware of the growing problem of antibiotic resistance but we still have a long way to go. By discussing the Centor Score with every patient who presents with a sore throat, I have rarely had to enter into a disagreement over antibiotics. This is reflected in not only in my day-to-day practice, but also when working at out-of-hours service. So often patients just want reassurance, backed up by good evidence and appropriate safety netting. My experience has been overwhelmingly positive. Problems occur when patients feel they are not being listened to or their concerns are ignored.

"The STARWAVe algorithm, therefore, is a welcome adjunct to daily practice. It allows a logical conversation to occur, backed up by emerging evidence and can be reassuring for both parties. There will always be certain patients who are adamant they want antibiotics and if they don't get them from their GP, they will get them from elsewhere. These patients should be the exception not the rule.

"For this tool to be truly effective, ideally it should be adopted by the practice as a collective as well as by out-of-hour providers. Patients shouldn't be deciding which clinician to see based on whether or not they are more likely to get antibiotics. We all have a responsibility to send out a clear message to our patients that so often antibiotics simply aren't the answer."

Dr Steve Holmes
PCRS-UK Education Lead, GP trainer, Associate Postgraduate Dean Health Education England (South West), Clinical Respiratory Lead Somerset CCG, Trustee of Education for Health

"This paper is interesting and well worth a read. It highlights that a frightening 37% of presentations for cough/URTI result in antibiotic prescriptions. It does indeed identify the factors that appeared commoner in children more likely to be admitted with respiratory problems (wheeze, asthma, age under 2 years, fever, etc.) in the 78 admissions out of 8,394 children studied.

"However, fundamentally the paper is trying to recommend when to use or not to use antibiotics based on whether the patient is admitted to hospital, and the identifiable factors around that. The problem is that, of the 78 admissions, only 21 had a potential bacterial respiratory infection (26.9%) on the hospital discharge letter (and we know how reliable these can be).

"Many of the factors (asthma, wheeze in younger people) suggest more viral origin and, indeed, need for asthma-like treatment rather than antibiotics. It is also worth noting that the severity of illness in those being admitted was relatively low with only 28% having a raised respiratory rate and 26% a raised temperature when assessed.

"The paper did not look at the impact that the antibiotic had in preventing the admission in the first place (or potentially preventing) although with the method used this would not have been feasible.

"There are many validated tools in clinical practice and although this study is exploring an interesting area of current practice, we are probably better using our Centor Score for sore throat, BTS/SIGN guideline on the management of asthma,[1] NICE guidance on fever in children[2] and sepsis[3] at the current time. More research is needed, as ever, as we discover the best way to treat our patients."

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2. Fever in under 5s: assessment and initial management. NICE, May 2013. https://www.nice.org.uk/guidance/cg160

3. Sepsis: recognition, diagnosis and early management. NICE, July 2016. https://www.nice.org.uk/guidance/ng51

The Centor criteria

Centor criteria to aid diagnosis of group A beta-haemolytic streptococcus (GABHS) as a cause of presentation with a sore throat:

- o tonsillar exudate
- o tender anterior cervical lymph nodes
- o absence of cough
- o history of fever

- Presence of three or four of these clinical signs suggests that the chance of the patient having GABHS is between 40% and 60% so the patient may benefit from antibiotic treatment

- Absence of three or four of the signs suggests that there is an 80% chance that the patient doesn't have the infection and antibiotics are unlikely to be necessary

- In patients with tonsillitis who are unwell and have three out of four of these criteria, the risk of quinsy is 1:60 compared with 1:400 in those who are not unwell

- Centor criteria are not ideal and will lead to some patients with bacterial pharyngitis not being treated and result in unnecessary antibiotic treatment

MeReC Bulletin 2006;**17**(3):12-14

Streptococcal score card

The streptococcal score card gives an indication of the likelihood of a sore throat being due to infection with group A beta-haemolytic streptococci GABHS. The criteria are:

- Age 5–15 years

- Season (late autumn, winter, early spring)

- Fever (≥38.3°C [≥101°F])

- Cervical lymphadenopathy

- Pharyngeal erythema, oedema or exudate

- No symptoms of a viral upper respiratory infection (conjunctivitis, rhinorrhoea or cough).

If five of the criteria are met, a positive culture for GABHS is predicted in 59% of children; if six of the criteria are met, a positive culture is predicted in 75% of children.

NICE guidance

A no-antibiotic prescribing strategy or a delayed antibiotic prescribing strategy should be agreed for patients with the following conditions:

- acute otitis media

- acute sore throat/acute pharyngitis/acute tonsillitis

- common cold

- acute rhinosinusitis

- acute cough/acute bronchitis

Depending on clinical assessment of severity, patients in the following subgroups can also be considered for an immediate antibiotic prescribing strategy (in addition to a no-antibiotic or a delayed antibiotic prescribing strategy):

- bilateral acute otitis media in children younger than 2 years

- acute otitis media in children with otorrhoea

- acute sore throat/acute pharyngitis/acute tonsillitis when three or more Centor criteria are present

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 (before and after seeing the doctor):

- acute otitis media: 4 days

- acute sore throat/acute pharyngitis/acute tonsillitis: 1 week

- common cold: 1.5 weeks

- acute rhinosinusitis: 2.5 weeks

- acute cough/acute bronchitis: 3 weeks

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, for example, diarrhoea, vomiting and rash

- 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, for example, diarrhoea, vomiting and rash

- 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 about re-consulting if there is a significant worsening of symptoms despite using the delayed prescription. A delayed prescription with instructions can either be given to the patient or left at an agreed location to be collected at a later date
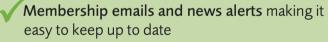
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