PRImary care Streptococcal Management (PRISM) study: in vitro study, diagnostic cohorts and a pragmatic adaptive randomised controlled trial with nested qualitative study and cost-effectiveness study

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Plain English summary

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General background

The overuse of antibiotics in general practices, mostly for illnesses such as sore throat, chest infections and ear infections, is potentially a big problem for us all for several reasons. First, antibiotic overuse increases the risk of antibiotic resistance, whereby bacteria become resistant to antibiotics and are no longer killed by antibiotics. This could potentially lead to serious infections as a result of 'superbugs' becoming untreatable both now and for future generations. Antibiotics commonly cause side effects such as allergic reactions, diarrhoea and skin rashes. Using them also increases people's belief in them – because they think it is the antibiotics that helped them get better, when in fact they would have got better in the same time anyway. This leads people to think that they need to come back the next time they get an infection – so it 'medicalises' illnesses, uses NHS resources and also exposes patients to unnecessary antibiotics.

Background – the context for sore throats

Antibiotics are still prescribed for most patients with a sore throat attending their general practitioner (GP) or nurse in primary care. This is despite the best available evidence, which suggests there is a modest benefit overall from antibiotics. One approach to tackle this is to target antibiotics better, using a simple 'clinical score' – whereby doctors or nurses prescribe according to particular symptoms and examination findings. Another approach is to use rapid antigen detection tests (RADTs), which are very commonly used in many countries. To use a RADT, a swab is taken from the throat, and the RADT gives a quick answer as to whether the most important bacteria are present or not. The particular type of bacteria that RADTs pick up is a common type of streptococcus bacteria – called Lancefield group A haemolytic streptococcus (GABHS). This bacterium can cause both a sore throat and more serious illnesses.

However, there are problems with using either a clinical score or a RADT:

- There is debate about which RADT should be used and how.
- It is unclear whether other bacteria (other than GABHS) are important, particularly streptococci from other groups – Lancefield groups C and G. RADTs will not pick up these other bacteria.
- For a clinical score, it is not clear which symptoms and examination findings most clearly tell us whether bacteria are present.
- There have also been very few good studies that compare RADTs with clinical scores, or with other approaches, such as delayed antibiotic prescribing. Delayed prescribing is where the patient is advised to use an antibiotic after several days if symptoms are not starting to settle.

The PRImary care Streptococcal Management (PRISM) study was made up of several substudies that tackled these issues:

Laboratory study

If rapid antigen tests are to be used for patients in everyday practice, they have to be accurate, easy to use, inexpensive and potentially widely available. Several such tests are available, and in the first study five RADTs were tested in the laboratory with different types and concentrations of bacteria. One of the best of these was the IMI test, which was both one of the most accurate and found to be relatively easy to use.

Clinical study – developing a clinical score

Two large groups of patients (606 in the first group, 517 in the second) came to see the doctor or nurse with a sore throat and agreed to take part. Their symptoms and signs were documented and a throat swab was sent to the laboratory to see if bacteria were present. The results showed that patients who had Lancefield groups C or G bacteria had the same kind of illness as those with group A strains. It was also possible to develop a useful clinical score to help pick up the main types of bacteria (A, C or G) based on a simple count of five items. The five items make up the acronym FeverPAIN:

- **F**ever during the last 24 hours
- **P**us (white spots) on the tonsils
- coming quickly to see the doctor within 3 days (**A**ttend rapidly)
- very **I**nflamed tonsils
- and **N**o cough or runny nose.

Trial of clinical scores and rapid antigen detection tests

The trial compared three ways of managing sore throat among 1760 patients who came to see their doctor:

1. Delayed antibiotic prescribing group (the control group).
2. Clinical score group: the score was worked out and antibiotics were advised for high scores. No antibiotics were advised for low scores, and delayed antibiotics for those in the middle. The first clinical score that was developed (score 1; $n = 1129$) was replaced by a more valid score (FeverPAIN; $n = 631$) as the trial went on.
3. RADT group: the clinical score was also worked out. For low and middle scores, the plan was similar to that used in the clinical score group. A RADT was used for those with high scores, and, if the result was positive, antibiotics were advised and, if the result was negative, no antibiotics were given.

The study found that using the clinical score (FeverPAIN) improved control of symptoms, and both the clinical score and the RADT reduced antibiotic use. Moderately bad or worse symptoms resolved significantly faster (30% faster) in the clinical score group but not in the RADT group (11% faster).

Health economic analysis

If RADTs were to be used more widely, it would be important to show that using them is a cost-effective use of time and money for the health service. The study showed that using RADTs was probably more expensive and less cost-effective than using the clinical score.

Qualitative study

Face-to-face and telephone interviews were done with 51 people – GPs, nurse practitioners and patients from general practices across Hampshire, Oxfordshire and the West Midlands. Patients and nurses were very positive about using clinical scores and RADTs. Doctors had a number of concerns about both RADTs and clinical scores that would need to be addressed before widespread implementation would work – particularly related to the perceived usefulness of clinical scores in the face of clinical experience and intuition.

Conclusions

There are RADTs that are not expensive, easy to use and are potentially widely available for use in primary care. Although they will detect GABHS, RADTs are not designed to detect other strains such as Lancefield C or G strains. Lancefield C or G strains commonly cause streptococcal sore throats, and patients have a similar illness to those who have A strains. A five-item score (acronym FeverPAIN) to predict streptococcal infection is likely to be valid but further validation is preferable. When antibiotics are targeted using a clinical score (FeverPAIN), this improves control of symptoms, reduces antibiotic use and is very cost-effective. Using a RADT in addition to using the clinical score provides no clear benefits for patients over using the clinical score alone. RADT use is also more costly, probably less cost-effective and faces several barriers from clinicians. To implement the use of clinical scores more widely in everyday practice will require addressing the issues doctors have.

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