

Trial Scenarios: Monitoring

2. Trial of prescribing strategies in managing sore throat¹

Background:	The management of sore throats in primary care is controversial and use of antibiotics varies.
Design:	Open randomised trial of 3 prescribing strategies
Setting:	11 general practices in one regional primary care research network in the UK
Study population:	Patients aged 4 years or more presenting with sore throat to their GP
Eligibility criteria:	≥4 yrs old; sore throat + local sign of infection (inflamed tonsils or pharynx, exudate, or cervical adenopathy).
Intervention:	Group 1 - immediate prescription for 10 day course of standard antibiotics - penicillin V (or erythromycin if allergic) Group 2 - no antibiotic prescription Group 3 – prescription (as in Grp 1) to be collected if symptoms are not starting to settle in 3 days
Randomisation:	Sealed envelopes in GP surgery containing advice sheet for the assigned treatment strategy
Trial supplies:	Prescriptions dispensed by high street chemist
Outcomes:	Patient assessed: duration of symptoms recorded by patient diary; duration of time off work/school; patient satisfaction
Data management:	Paper CRF. Data entry at coordinating centre.
Experience:	Coordinating centre and network practices have undertaken a number of similar trials previously

What are the particular hazards of the trial?

This is a very low-risk trial – a comparison of commonly-used treatment strategies in a patient population that is not seriously ill undertaken by an experienced group of investigators.

The particular concerns are:

- 1 Randomisation process – use of sealed envelopes in an open trial makes the study vulnerable to the random allocation of treatment being compromised – either through ignorance or intentionally. Centralised process should be used if at all possible.

¹ This scenario was based in part on a trial report by Little P, Williamson I, Warner G, Gould C, Gantley M, Kinmonth AL Open randomised trial of prescribing strategies in managing sore throat. (*BMJ*, 1977; 314:722), but some of the details have been altered or invented.

- 2 Although not a vulnerable population, the inclusion of children introduces the issue of providing information about the trial for different levels of capacity to understand.
- 3 An open trial with patient-assessed outcomes introduces the hazard of differential and biased outcome assessment. Complete follow-up and a robust data collection instrument for the primary outcome are important.

Suggested Approaches to Monitoring

Trial Oversight:

- A trial management group that includes the collaborators. An independent DMC is unnecessary

Before the start of recruitment:

- Investigators' meeting that includes all those who will be involved in obtaining patient consent, the randomisation procedure, and follow-up for discussion/training plus written assurance from each investigator that the practice is prepared and setup complete;
- or**
- visit to each practice to undertake same

During the trial

Because the trial is being conducted in a small network of practices in the same region, site visiting may pose few logistical or financial difficulties, and in view of the concern over the randomisation process may be the best way to monitor the conduct of the trial. Depending on whether or not site visiting is undertaken, one of the following plans is suggested:

	Without site visiting	With site visiting
Understanding of and adherence to protocol and trial procedures	Annual investigator meetings	Annual site visits, including check of randomisation envelopes
Verification of participant existence	Collect signed consent form at coordinating centre (with patient consent) Alternatively, ONS flagging would be possible but generally considered unnecessary	Check practice database or clinic notes
Consent	Collect signed consent form at coordinating centre (with patient consent)	Check consent forms in patient's clinical records

Centralised classification of outcomes blind to treatment group is recommended.

At the end of the trial

Local PCT arrangements for archiving of documents should be followed.