University of Southampton

FACULTY OF MEDICINE, HEALTH & LIFE SCIENCES

School of Medicine

The Management of Acute Infective Conjunctivitis in General Practice

by

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Thesis for the degree of Doctor of Philosophy

July 2006

UNIVERSITY OF SOUTHAMPTON

ABSTRACT

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THE MANAGEMENT OF ACUTE INFECTIVE CONJUNCTIVITIS IN GENERAL PRACTICE

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Acute infective conjunctivitis (AIC) is a common self-limiting condition presenting to general practice. However, evidence is limited on GPs current management of AIC, patients' understanding of conjunctivitis or the most appropriate management strategy for AIC in general practice.

The aims of this thesis where to: 1) To determine GPs' current management strategies for AIC. 2) To gain an understanding of patients concerns and beliefs about AIC and develop a patient information leaflet (PIL). 3) To assess the effect of common management strategies for AIC on symptom resolution and patients belief in antibiotics.

Three complementary studies were used: 1) A postal survey of 300 GPs regarding their diagnosis and management of AIC. 2) A qualitative study involving interviews with 25 patients to explore conjunctivitis from the patients' perspective. 3) An open randomised controlled trial, with 307 recruits, to assess the effect of different management strategies (immediate, delayed or no offer of antibiotics; a patient information leaflet and an eye swab) for AIC in general practice.

The results were: 1) Survey: 95% of responding GPs usually prescribe topical antibiotics for AIC despite 58% stating that they thought at least half of the cases they see are viral in origin. Only 36% of GPs believed they could discriminate between viral and bacterial infection. 2) Qualitative study: patients regarded conjunctivitis as a minor illness although some considered it might become more serious if not treated. They stated a preference not to take medication but believed that conjunctivitis would not clear without treatment. However, they were open to alternative management approaches (e.g. delayed prescription approach) because they trusted their GPs judgement. Once aware of the self-limiting nature of conjunctivitis, patients felt they would prefer to wait a few days to see if it improved before seeking medical advice even if this resulted in a few more days of symptoms. 3) Randomised trial: different prescribing strategies did not affect symptom severity in the first 3 days, but duration of moderately bad symptoms was less with antibiotics (control 4.83 days, immediate 3.26 days (p=0.001), delayed 3.86 days (p=0.002)). Compared with no initial offer of antibiotics, antibiotic use was higher in the immediate group (control 30%, immediate 99% (p=0.001), delayed 53% (p=0.004)) as was belief in the effectiveness of antibiotics (control 47%, immediate 67% (p=0.03); delayed 55% (p=0.35)) and intention to re-consult (control 40%, immediate 68% (p=0.001), delayed 41% (p=0.98)). A patient information leaflet or an eye swab had no affect on the main outcomes, but an eye swab seemed to increase patient worry about AIC and a PIL seemed to increase satisfaction with the consultation and the amount of information received. Re-attendance in the next two weeks was less in the delayed group (delayed OR 0.33 (0.11;0.98); immediate OR 0.65 (0.26; 1.63)).

In conclusion: Most general practitioners prescribe topical antibiotics for most cases of acute infective conjunctivitis –a self-limiting condition. Most patients are unaware of the self-limiting nature of AIC. A delayed prescribing approach is probably the most appropriate strategy to use for the management of acute conjunctivitis in primary care – it reduces antibiotic use by nearly 50%, shows no evidence of 'medicalisation', provides similar symptom duration and severity to immediate prescribing and reduces re-attendance in the short term compared with no offer of antibiotics.

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Acknowledgements

This research was funded by the Medical Research Council as part of a Research Clinical Training Fellowship based at the Department of Primary Medical Care, Southampton University.

Thanks go to:

- My supervisors, Professor Paul Little and Dr Satinder Kumar.
- Professor Peter Smith for statistical support for the RCT.
- The MRC Trial steering committee (Prof C. Butler (chair), Dr A. Hay (independent committee member).) and Miss R. Cannings (statistician)) for their advice and support with the RCT.
- The GPs that participated in the survey and recruited patients for the qualitative study and the RCT.
- Sandy King who transcribed the qualitative interviews.
- The patients who gave their time to participate.

Chapter 1: Introduction

Patients with acute infective conjunctivitis commonly present to general practice[1-5]. On average, a full-time general practitioner sees a patient with infective conjunctivitis every week. However, there is little information available on how GPs currently manage this condition or on patients concerns and beliefs and what they expect when they present to primary care. Evidence is also lacking on the most appropriate management strategy for acute infective conjunctivitis in general practice.

This thesis presents a body of work that was undertaken to help clarify these issues.

1.1: Research Aims

- To determine GPs current management strategies for acute infective conjunctivitis.
- To gain an understanding of patients concerns and beliefs about acute infective conjunctivitis and develop a patient information leaflet (PIL) for acute infective conjunctivitis.
- To assess the effect of common management strategies for acute infective conjunctivitis on symptom resolution and patients belief in antibiotics.

1.2: Research methods

Three complementary studies were used to address the research aims. The studies employed different research methodologies to address the different research aims.

- A postal survey of general practitioners regarding their current practice for diagnosis and management of acute infective conjunctivitis.
- A qualitative study involving face to face interviews with patients to explore conjunctivitis from the patients' perspective. Information from the interviews was used to aid the development of a patient information leaflet and to inform the development of the randomised controlled trial.
- An open randomised controlled trial to assess the effect of different management strategies for acute infective conjunctivitis in general practice. Information from the GP survey and patient interviews were used to inform the development of the trial.

Chapter 2: Literature Review

2.1: Search strategy

I undertook a literature review to ascertain the current state of knowledge on the management of acute infective conjunctivitis. I was particularly interested in work in a general practice setting but there were few papers specifically related to general practice so my search included papers on acute infective conjunctivitis in all settings.

MEDLINE and EMBASE databases were searched with the MeSH terms/keywords: Conjunctivitis, Infective, Acute, Bacterial, Viral, Eye, General Practice, Primary Care, Patient information, Leaflet, Qualitative, Medicalisation, Self-care, Swab. Searches were restricted to the English language and to studies in Humans. The Cochrane Library and the Cochrane Controlled Trials Register were also searched. Information was also sought from the Royal College of General Practitioners and the Royal College of Ophthalmologists about the frequency of GP consultations for eye related conditions and any guidelines on the management of conjunctivitis.

Abstracts of papers which appeared relevant were downloaded from the searches and where appropriate, the full paper was obtained for reading in detail. Reference lists of all papers identified were searched for additional papers that may have been missed in the electronic searches. I also contacted a researcher in the field (Dr Aziz Sheikh) who had just completed a Cochrane Systematic Review of Antibiotics for Acute Bacterial Conjunctivitis[6] for any further papers.

2.2: Acute infective conjunctivitis

2.2.1: Incidence

Acute infective conjunctivitis is a common presentation in general practice in the UK[5]. Two to five percent of general practice consultations are related to eye conditions and approximately 40 percent of these are concerned with conjunctivitis[1-4]. Thus, on average a full-time general practitioner sees a patient with conjunctivitis every week[1-5]. Acute infective conjunctivitis is most common in preschool children but may present at any age[5]. It affects both sexes and all races. The Morbidity Statistics for General Practice: Fourth National Study 1991-1992[7] gave a prevalence for conjunctivitis (infective and allergic) (ICD codes 372.0 to 372.3) of 396 per 10,000 person years at risk. This is a 39% increase on the level of 284 per 10,000 found in the 1981-1982 Study.

2.2.2: Aetiology

The conjunctiva is a thin flexible epithelial layer that covers the inner surface of the eye lids and anterior sclera. It contributes to the tear film with the production of mucus and acts together with its secretions to form a barrier to foreign matter and infection. It is sterile at birth but is rapidly colonised by bacteria. Staphylococcus epidermidis and diphtheroids predominate among the flora isolated from healthy eyes but more virulent organisms such as Staphylococcus aureus, Streptococcus Pneumoniae and Pseudomonas aeruginosa are also found[8;9]. This 'normal flora' usually helps to provide protection against colonisation of the conjunctiva by organisms of greater virulence and pathogenic potential[8].

The tear film constantly dilutes and flushes free floating organisms from the surface of the eye. Lactoferrin, antibodies, lysozyme, betalysins, ceruloplasmin, orosomucoid and components of the complement system in the tear film aid the control and elimination of bacteria from the ocular surface[8]. Bacterial adhesion to the corneal surface is inhibited by epithelial glycocalyx. This increases the effectiveness of the flushing action of tears.

Overgrowth of the normal flora or infection by another organism (viral or bacterial) can result in conjunctival inflammation, ie conjunctivitis. Damage to the conjunctiva, eg abrasion, dry eye conditions, eyelid disease and extended contact lens wear can predispose to infective conjunctivitis. Conditions of increased bacterial inoculation such as poorly cleaned contact lenses, neighbouring dacryocystitis and use of contaminated eye makeup or ocular preparations also increase the likelihood of bacterial conjunctivitis[8].

Conjunctivitis may also be caused by allergy[10] or chemical irritation[11-13]. Allergic conjunctivitis is mediated primarily by type 1 hypersensitivity reactions and may be seasonal, perennial or atopic[10]. Many substances can cause chemical irritation to the eye eg household cleaning products, alkalis, contact lens solutions[12].

It is likely that at least 50% of acute infective conjunctivitis presenting to general practice is viral in origin[14]. Viral conjunctivitis is most commonly caused by an adenovirus infection. It often presents concurrently with upper respiratory tract symptoms but may also cause epidemics of conjunctivitis especially in school-aged children[15].

Bacterial conjunctivitis is most often caused by Streptococcus pneumoniae, Haemophilus influenzae or Staphylococcus aureus[8;9;15;16]. Haemophilus influenza is the most common organism in children[17].

Ophthalmia neonatorum is a bacterial eye infection seen in neonates, usually within a few days of birth. It may be caused by Escherichia coli, Staphylococcus aureus and Haemophilus influenzae but the most virulent form is caused but Neisseria gonorrhoeae[8]. It can cause

extensive infection and damage to the eye with the potential for secondary meningitis, cellulitis and septicaemia.

Chronic infective conjunctivitis (ongoing infection for greater than four weeks) is most commonly caused by Staphylococcus aureus because of its ability to establish and maintain growth on the eyelid and in the associated glands. Long term infection can result in eyelid disorders such as trichiasis, hordeola and chalazia[8].

This research focused on acute infective conjunctivitis: viral and bacterial conjunctivitis in adults and children, excluding ophthalmia neonatorum. Chronic infective conjunctivitis was not addressed.

2.2.3: Diagnosis

Clinicians use the history of the eye complaint and the presenting symptoms and signs to diagnose conjunctivitis, distinguish it from more serious eye complaints and try to determine its cause so that an appropriate management strategy can be implemented. However, there is a lack of evidence on which features of the history, signs and symptoms and clinical examination GPs find most useful when assessing patients presenting with suspected conjunctivitis[1;2]. Most eye disease presents to and is managed solely by general practitioners (GPs)[2]. However, GPs have been found to be generally under-confident in diagnosing eye conditions[3] although they make up a significant part of a GPs workload[18]. The GP survey[19] chapter of this research explores GPs diagnosis and management of acute infective conjunctivitis.

Acute infective conjunctivitis needs to be distinguished from the other forms of conjunctivitis and from other eye conditions. Acute conjunctivitis involves inflammation of the conjunctiva which may lead to symptoms such as red eyes, discomfort and discharge[15]. It may be caused by bacterial or viral infection, allergy or chemical irritation. Similar symptoms may also be caused by a foreign body in the eye. The presence of 'alarm symptoms' (eg eye pain, reduced visual acuity, photophobia, restricted eye movements) may mean that more serious eye conditions (such as keratitis, iritis, orbital cellulitis) are present and that specialist referral is required.

Allergic conjunctivitis is usually distinguished by severe itching, allergen exposure (eg pollen) and a marked seasonal variation[10]. Conjunctivitis caused by chemical irritation usually has a history of exposure to a noxious substance[12]. Foreign body in the eye is commonly unilateral and often has a clear history, although this may not be the case in young children.

Acute infective conjunctivitis usually presents with acute onset of a vague foreign body sensation or a surface irritation in the eye/eyes accompanied by tear production. There is no severe or deep pain in the eye. There may be itching. Conjunctival injection causes the appearance of a red eye and conjunctival oedema and mild eye lid swelling may occur[8]. Mucopurulent discharge may accumulate in the nasal palpebral fissure and on the eye lid margins. The discharge can accumulate whilst sleeping and the eye lids be stuck together upon awakening[8]. There should be no significant photophobia and visual acuity should be normal once any discharge has been wiped away.

2.2.3.1: Discriminating between bacterial and viral conjunctivitis

Discriminating between viral and bacterial conjunctivitis clinically, is not straightforward[14]. In practice, clinicians' ability to discriminate is poor and only 50% of cases clinically diagnosed as bacterial conjunctivitis in research trials are shown to have positive bacterial cultures[20-23].

In everyday practice conjunctival culture by eye swab is rarely performed due to cost and delay (the result takes several days). Eye swabs are not, in any case, a completely reliable method for determining the presence of infection. In some circumstances, swab technique and transport and culture methods can lead to bacteria not being identified[24]. Alternatively, the presence of bacteria does not necessarily indicate a bacterial cause of the conjunctival symptoms as pathogenic organisms are cultured from a significant number of healthy eyes[8;9]. At present, however, there is no more reliable method for determining the presence of bacterial conjunctivitis than performing an eye swab.

If a validated reliable method for predicting a bacterial cause for a case of acute infective conjunctivitis could be found, that was quick and easy to undertake in the GP surgery, it could enable better targeting of antibiotic treatment to those most likely to benefit and reduce unnecessary prescribing.

In textbooks, a variety of signs and symptoms are proposed as potential discriminators between viral and bacterial conjunctivitis but their usefulness is uncertain[14]. For instance, it has been suggested that unilateral infection followed a few days later by involvement of the other eye, watery eye discharge and/or the presence of a periauricular lymph node may indicate a viral cause[15]; whereas involvement of the second eye within 24 to 48 hours, purulent eye discharge and/or a papillary or pseudomembraneous conjunctivitis may be suggestive of a bacterial infection. However there has been little scientific evidence behind these assertions. A recent systematic literature search[14] found no methodologically sound studies (critically appraised using the QUADAS instrument[25]) on the diagnostic usefulness of clinical signs or

symptoms in distinguishing bacterial conjunctivitis from viral conjunctivitis[14] Thus there is a need for further research into this area. (The QUADAS instrument includes 14 items which are scored to give an indication of quality in studies of diagnostic accuracy. The items include patient spectrum, reference standard, disease progression bias, verification bias, review bias, clinical review bias, incorporation bias, test execution, study withdrawls, and indeterminate results.)

A recent cohort study in general practice in Holland[26] in 177 adult patients (published after the GP survey[19] from this work) investigated the usefulness of potential discriminators. They identified three potential features for predicting bacterial conjunctivitis, all of which could be ascertained from clinical history taking. Optimal diagnostic discrimination occurred for a combination of early morning glued eyes, itch and a history of conjunctivitis, with the first of these indicators increasing the likelihood of a bacterial cause and the other two decreasing it. They found a 32% prevalence of positive bacterial culture. Using their scoring system, they concluded that antibiotic prescription could be reduced from 80% (current prescribing in the study population) to 40%, with 67% sensitivity (correctly treated patients) and 73% specificity (correctly untreated patients). However, this would still mean 33% of patients would not receive antibiotics where there is a bacterial cause and 27% of those with negative bacterial aetiology would be treated unnecessarily. Furthermore, these findings need replication in a separate sample as developing and testing a score in the same population will overestimate the predictive value of the score. Studies are also needed in children.

There is no data in the research literature regarding GPs beliefs about their ability to discriminate between viral and bacterial conjunctivitis and what features they use to do this - an area I aim to address in the GP survey.

2.2.4: Natural history

Acute bacterial conjunctivitis is commonly a self-limiting condition[6;27]. A Cochrane systemic review of the literature[6] on topical antibiotics for acute bacterial conjunctivitis showed that clinical remission occurs in 64% (99% CI 54% to 73%) of microbiologically confirmed cases of bacterial conjunctivitis treated with placebo by days 2-5.

Viral conjunctivitis is also self-limiting[15] but has a more uncertain course. It may be transitory with an upper respiratory tract infection or last several weeks.

There is no evidence about the time course of the severity of symptoms, nor of the predictors of prolonged or severe symptoms.

2.2.5: Complications of acute infective conjunctivitis

Orbital cellulitis, keratitis and panophthalmitis have been suggested as potential complications of acute bacterial conjunctivitis. However they appear to be rare. For instance, in the Cochrane systematic review[6], no serious outcomes were reported in either the active or the placebo arms in any of the trials. Thus they concluded that sight-threatening complications are an infrequent occurrence. However the numbers in the trials were small, so rare complications may not have been assessed adequately due to low power.

Evidence for a potential protective effect of prescribing topical antibiotics on the development of complications was not found when reviewing the literature, but no studies have been sufficiently large to assess this. This is an important consideration when considering reducing antibiotic prescription for minor illnesses.

2.3: Treatment of acute infective conjunctivitis

2.3.1: Background

Despite acute infective conjunctivitis being considered a self-limiting condition, it has traditionally been treated with topical antibiotic preparations (eg chloramphenicol or fusidic acid (fucithalmic) eye drops or ointment)[2;3]. Antibiotics have been used in an attempt to reduce the duration and severity of symptoms and possibly reduce transmission and complications from conjunctivitis (eg orbital cellulitis). However there is little research evidence on their role in affecting these outcomes (see discussion above (2.2.5) and below).

In the U.K. general practitioners most commonly prescribe topical chloramphenicol for acute infective conjunctivitis[19] (approximately 80% of GPs use chloramphenicol first-line) with fusidic acid as the next most common prescription. However in other countries (eg The Netherlands and the U.S.A.) fusidic acid[28], bacitracin, polymyxin B, ciprofloxacin, ofloxacin and gentamicin are more commonly used. The different topical antibiotics have different spectrums of antibacterial activity, with chloramphenicol, ciprofloxacin, gentamicin and ofloxacin having a broad spectrum and fusidic acid selective for gram positive bacteria and polymyxin B selective for gram negative bacteria[29]. However, comparative studies show the different topical antibiotics to have similar effectiveness in acute infective conjunctivitis[20;21;29-34].

Resistance to chloramphenicol among bacteria isolated from the conjunctiva of patients presenting with acute infective conjunctivitis is low[29;35], though evidence is limited and from hospital clinic studies rather than the general practice population. More resistance is reported for fusidic acid and quinolones[29]. Rietveld el al[28] reported 66% of the cultured species in their

general practice based trial of fusidic acid versus placebo for acute infective conjunctivitis were resistant to fusidic acid.

Topical antibiotics are unlikely to have any effect on viral conjunctivitis and there are no other recognised treatments to shorten viral conjunctivitis[15;36]. Evidence is lacking for the use of topical antibiotics in viral conjunctivitis as prophylaxis against superimposed bacterial infection[15].

The difficulty distinguishing bacterial from viral conjunctivitis has meant that most (over 90%) of patients presenting with acute infective conjunctivitis have been treated with antibiotics empirically[1-3]. This means a significant number of patients who present to general practice (50% or more) are likely to be given antibiotics unnecessarily. These patients are exposed to potential side effects of antibiotics (eg allergic reactions (see 2.3.3.2: Side effects)) and the potential medicalising effect of prescribing[37] (see 2.3.3.3: Medicalisation) without the potential benefits.

Even in confirmed bacterial conjunctivitis there is some uncertainty regarding the role of antibiotics. The evidence for a beneficial effect from antibiotics is fairly weak, as few randomised controlled trials have been published comparing the effect of antibiotics with placebo. At the time of initiating this research, most of the trials had taken place in the USA in secondary care, none in general practice[6;38]. The research evidence was summarised by a Cochrane systematic review[6] undertaken in April 1999 (published at the time of the development of this research). This revealed 3 published trials that fulfilled the criteria for inclusion in the review; Gigliotti et al 1984[27] with 66 subjects; Leibowitz 1991[39] with 177 subjects and Miller et al 1992[40] with 284 subjects. They were all undertaken in selected specialist care populations and were heterogeneous in terms of their inclusion and exclusion criteria, the nature of the intervention and the outcome measures assessed (described below in the Table 2.3.1.1). None of the trials recorded an a priori sample size, described methods of randomisation or indicated if researchers were blinded to treatment allocation[6].

Meta-analysis of the three studies in the Cochrane review[6] indicated that acute bacterial conjunctivitis is frequently a self-limiting condition with clinical cure/significant improvement occurring by day 2 to 5 in 64% (99% CI 54 to 73) of those treated with placebo. Treatment with antibiotics was associated with significantly better rates of clinical remission: Days 2 to 5 RR 1.31 (99% CI 1.11 to 1.55 NNT = 5); Days 6 to 10 RR1.27, (99% CI 1.00 to 1.61, NNT=5).

Thus, at the time of initiating this research, there was some evidence that antibiotics improved clinical remission in the secondary care population but caution was required if one attempted

to extrapolate these finding to primary care as the case mix was likely to be different[6]. There was a clear need for further research on the effect of antibiotics in a general practice population.

2.3.1.1: Table 1: Studies included in the Cochrane systematic review 2000

(Table adapted from the study table in the Cochrane systematic review[6])

Study	Participants	Intervention	Outcomes
Gigliotti[27]	66 children one month to 18 years (gender and ethnicity not specified) from paediatric clinics in the U.S.A. with swab proven Haemophilus influenzae or Streptococcus pneumoniae and conjunctival inflammation or exudate. Excluded those with history suggestive of allergy, history of trauma or foreign body in the eye or use antibiotics previous week. 34 in active arm and 32 in placebo	Ophthalmic ointment: 10,000 U/g polymixin and 500U/g bacitracin or placebo. Given four times a day for 7 days.	Early (day 3 to 5) and late (day 8 to 10) clinical cure and microbiological eradication. Symptoms reported by parents. Day 3-5: 21/34 (62%) of topical antibiotic group clinically cured and 71% bacterial eradication, placebo 9/32 (28%) cured (p=0.02) and 19% eradication (p=0.001) Days 8-10: 31/34 (91%) antibiotic group cured, 79% eradication, placebo 23/32 (72%) cured (p=ns), 31% eradication (p=0.001).
Leibowitz[39]	177 patients (age, gender and ethnicity not specified) from a hospital clinic in U.S.A. with swab proven conjunctivitis. Excluded those with antibiotics or anti-inflammatory medication in the preceding 48 hours; 140 in active arm and 37 in placebo	Ophthalmic eye drops Ciprofloxacin 0.3% or placebo, one to two drops 2hrly for two days then 4hrly for one day	Early (day 3) microbiological outcome: pathogen eradication/ reduction/ persistence/ proliferation. Eradication/reduction bacteria at day 3 = 93.6% (131/140) in antibiotic group, 59.5% (22/37) for placebo (p=0.001)
Miller[40]	284 patients over 18yrs old (mean age 38yr) from hospital centres in U.S.A., Mali and Morocco (75% participants Caucasian and 56% female) with a clinical diagnosis of acute bacterial conjunctivitis or blepharo-conjunctivitis. Excluded those with Neiserria gonorrhoea, sensitive to quinolones or benzalkonium or who had received topical antibacterials in the preceding 48hrs. 143 in active arm and 141 in placebo arm.	Ophthalmic eye drops 0.3% Norfloxacin and 0.0025% benzalkonium chloride preservative or placebo. Given one drop 2hrly on day 1 and then four times a day up to 7 days	Outcomes at day 2/3 and 5/7. Clinical (cure, improved, no change, worsened) and microbiological (pathogen eradication, suppression/ persistence. Day 5: 88.1% (126/143) clinically improved in antibiotic group, 71.6% (101/141) in placebo group (p=0.01). Eradication day 2/3 = 52.7% (40/76) in antibiotic group 23.9% (16/67) in placebo (p=0.01), 64.7% and 26.3% (p=0.01) if coagulase-negative staphylococci excluded. Adverse events (none serious) = 4.2% with antibiotic 7.1% in placebo.

In the last year, two new trials[28;41] and an update of the Cochrane systematic review[42] have been published regarding treatment for acute infective conjunctivitis in general practice. Rose et al[41] published the results of a randomised double blind placebo controlled trial of chloramphenicol treatment for acute infective conjunctivitis in children in primary care in the U.K. in the Lancet in July 2005. Rietveld et al[28] published a double blind placebo controlled trial of fusidic acid for acute infectious conjunctivitis in adults in primary care in Holland in the British Journal of General Practice in December 2005. The details of these trials are summarised in table 2.3.1.2 below.

The Rose et al[41] trial appears to be a rigorously conducted trial with a low drop out rate: only nine children were lost to follow up - one in the chloramphenicol group and 8 in the placebo group. It was undertaken in Oxfordshire, an area of relatively less deprivation than the general population of the UK, but there is no reason to believe that this should have a significant impact on the results. The level of pathogen identification was higher (80%) than previous studies where levels of 36%[26] and 50%[21;22;33] have been found. The authors attribute this to the training given in the sampling technique and the diagnostic ability of the referring physicians. The conclusion from the Rose et al trial[41] was that most children presenting with acute infective conjunctivitis in primary care will get better by themselves and do not need treatment with an antibiotic. They suggest that the health economic argument against prescribing for acute infective conjunctivitis is compelling, as every year one million children present to UK general practitioners with conjunctivitis. However they highlight that parental concern and the current exclusion policy of many schools and nurseries could make implementation of change in prescription policy difficult.

The Rietveld et al[28] trial had uneven randomisation groups, with 81 in fusidic acid and 100 in placebo group because of an unrestricted randomisation procedure. This may have affected the study's precision. 18 patients were lost to follow up (8 in the fusidic acid and 10 in the placebo group), thus analysis occurred on 163 patients. They had calculated a required sample size of 88 patients per group and ended up with 73 in the fusidic acid group and 90 in the placebo group and thus were under-powered to detect the difference they set out to detect. The baseline characteristics of the randomisation groups were different for sex, age, history of conjunctivitis, foreign body sensation in the eye and bilateral involvement which is unfortunate in a randomised trial. This may be due to chance or to some problem with the randomisation procedure. However, the ability of the study to assess a treatment effect may be compromised if the two groups are different at baseline. This trial had a 32% (58/181)

66% of the cultured species in the trial were resistant to fusidic acid, limiting the chances of the trial finding a treatment difference between fusidic acid and placebo. Adverse events (most commonly a burning sensation after instilling the medication) were noted in 10/73 (14%) of the fusidic acid group and 3/90 (3%) of the placebo group (risk difference 10.4%, 95% CI 1.6 to 19.1). Rietveld et al's main conclusion was that recovery rates after seven days were essentially the same in the fusidic acid and placebo groups but that their trial was too small to exclude clinically relevant treatment differences. However, they felt their findings did not support the current prescription practices of fusidic acid by GPs.

The newly published trials[28;41] add valuable information regarding the management of acute infective conjunctivitis in general practice but have some limitations. The Rose et al[41] trial provides data on the use of chloramphenicol drops in children in a general practice setting, but does not include adults. The Rietveld et al[28] trial provides evidence for fusidic acid in adults but not children. Neither trial allows assessment of the overall benefit of using drops since both randomisation groups received drops (there may be some effect of regular use of drops in helping flush out pathogens).

In light of the new trials[28;41] Sheikh and Hurwitz have updated their Cochrane systematic review of topical antibiotics for acute bacterial conjunctivitis[38] and published the updated meta-analysis in the BJGP in December 2005 [42]. The new meta-analysis includes 5 double blind randomised controlled trials[27;28;39-41] (summarised in Tables 1 and 2) with a combined total of 1034 patients. Their results show that topical antibiotics are of benefit in improving early (days 2 to 5) clinical (RR=1.24, 95% CI 1.05 to 1.45) and microbiological (RR 1.77, 95% CI 1.23 to 2.54) remission with these benefits being reduced, but persisting for late (days 7 to 10) clinical (RR 1.11, 95% CI 1.02 to 1.21) and microbiological (RR 1.56, 95% CI 1.17 to 2.09) remission. Sheikh and Hurwitz conclusions are that acute bacterial conjunctivitis is frequently a self-limiting condition and that topical antibiotic use offers only marginal benefit in improving clinical outcomes. They also state that the risk of adverse events with placebo eye drops appears to be low.

2.3.1.2: Table 2: Summary of recently published acute infective conjunctivitis trials

Study	Participants	Intervention	Outcomes
Rose[41]	326 children 6 mths to 12 yrs (gender and ethnicity not specified) from 12 General practices in Oxford, UK, with a clinical diagnosis of acute infective conjunctivitis. Recruited – October to April 2001-02, 2002-03 and 2003-04. Exclusions: those known to be allergic to chloramphenicol, taking any antibiotic currently or within the last 48 hours, the immunocompromised and those with evidence of severe infection (eg periorbital cellulitis). 163 children received chloramphenicol eye drops and 163 placebo.	Chloramphen-icol 0.5% eye drops or placebo given 2 hourly for 24 hours (when child awake) and then four times a day until 48 hours after infection resolved.	Bacterial and viral swabs at presentation and day 7. 1° outcome measure: clinical cure day 7, assessed by parent completed diaries. Follow up at 6 wks. Clinical cure by day 7 = 83% (128/155) for placebo, 86% (140/162) for chloramphenicol (risk difference 3.8%, (- 4.1%; 11.8%). Mean difference in time to cure = 0.3 days (logrank test p=0.025). NNT for one more clinical cure by day 7 =14 to 25. 4% (7/162) with chloramphenicol and 3% (5/155) with placebo had further conjunctivitis episodes within 6 wks (difference1.2%, (- 2.9%; 5.3%). Pathogen identified in 261 (80%) children, 217 (67%) grew ≥1 bacterial pathogens, 9 (3%) a virus alone, 34 (10%) both a virus and bacteria. Microbiological cure by day 7 = 40% 50/125 chloramphenicol group, 23% 29/125 with placebo.
Rietveld [28]	181 patients from 25 primary care centres in the Netherlands, recruited Oct 1999 to Dec 2002. 59% female, mean age = 46yrs fusidic acid group, 41yrs placebo group, ethnicity not specified. Inclusion criteria: presentation with red eye and either (muco) purulent discharge or glued eye lids. Exclusion criteria: age < 18 years, pre-existing symptoms > 7 days, acute loss of vision, wearing contact lenses, antibiotic use within the previous 2 wks, ciliary redness, eye trauma and a history of eye operation	Fusidic acid eye ointment or placebo one drop four times a day until one day after signs and symptoms recovered.	Swabs taken for bacterial culture at presentation and day 7. Patients completed a symptom diary. GP evaluation of recovery at day 7. Main outcome measure: difference in recovery rates at day 7, 2° outcomes: difference in bacteria eradication rates, duration of symptoms, difference in recovery rates of culture positive and negative patients. 163 patients analysed, 45/73 (62%) in treatment and 53/90 (59%) in placebo recovered by day 7 (risk difference 5.3% (-11; 18). No difference in mean duration of symptoms. Baseline bacterial culture rate 32% (58/181), eradication rate 76% in treatment and 41% in placebo (risk difference 35% (9.3; 60.4)

2.3.2: Scale and cost of treatment

The 2004 'Prescription Cost Analysis for England' document published by the Department of Health[43] reveals that, in the community, more than 3.2 million prescription items for anti-bacterial eye preparations (BNF group 11.3.1) were dispensed in England in 2004 with an net ingredient cost of more than £5.2 million. The treatment of infective eye conditions imposes a significant financial burden on general practice budgets.

2.3.3: Complications of prescribing

2.3.3.1: Antibiotic resistance

In the past, antibiotics were prescribed routinely for minor self-limiting conditions such as sore throat[44] (pharyngitis/tonsillitis), otitis media[45] and cough[46]. However, the emergence of increasing resistance in common bacteria[47], the acknowledgement of the potential harmful effects of antibiotics and systematic reviews casting doubt on the effectiveness and cost-effectiveness of antibiotics for these conditions[48;49], have focused attention on reducing antibiotic prescribing wherever possible[50]. Antibiotic resistance has been a particular concern for oral antibiotics but can also occur to topical preparations[18;29]. It is now recognised that use of antibiotics should be restricted as far as possible to cases of proven need and benefit[51] and that in many situations infections will be self-limiting and no antibiotic therapy is appropriate[52].

2.3.3.2: Side effects

A significant proportion (5 to 14%) of patients experience side effects from topical antibiotics including stinging and local discomfort[21;30]. Local allergic reactions[29] can occur causing uncomfortable red itchy eyes – symptoms that are very similar to conjunctivitis itself.

The use of topical chloramphenicol (the most common treatment for conjunctivitis in the U.K.) and the rare possibility that it may cause aplastic anaemia was raised as a concern in recent years.[53;54] However, the risk was subsequently deemed to be very small. A population based prospective case control surveillance study of aplastic anaemia with a study population of 67.2 million person years indicated that although an association between ocular chloramphenicol and aplastic anaemia could not be excluded, the risk was less than one per million treatment courses[55]. Most UK GPs continue to prescribe chloramphenicol for infective conjunctivitis. The aplastic anaemia concern did however lead to a marked reduction in the use of chloramphenicol in the U.S.A..

2.3.3.3: Medicalisation

The possible medicalising effect of prescribing antibiotics[37;56-58] has been raised in recent years. This is the idea that prescribing antibiotics for minor self-limiting illness may reinforce patients' belief in antibiotics and the intention to seek medical help, when self-care may be more appropriate. The use of GP services for conditions which are amenable to self care can reduce patient empowerment, increase inappropriate use of antibiotics and increase NHS costs[37] – potential opportunity costs in a resource limited service. Prescribing leading to increased belief in the effectiveness of antibiotics and to increased re-attendance for subsequent episodes (i.e.medicalisation) has been demonstrated for sore throat[37]. There is no evidence about whether prescribing topical antibiotics medicalises conjunctivitis.

2.4 Acute infective conjunctivitis: the patients' perspective

Consideration of the patients' perspective is especially important when undertaking research into acute minor illnesses in general practice. The patients' perception of the condition directly affects whether they present to the medical profession. Seeking medical advice for minor illness depends on many factors including: the severity of the symptoms[59], the perceived seriousness of the condition[59-61], the illnesses impact on the patient's life[59], the potential treatments available[62], patients' expectations and the patient's perception of their ability to self-care for the condition[60;61]. Qualitative research to look at the patients' perspective of acute self-limiting illness has been undertaken into a number of acute respiratory conditions (e.g. acute sore throat[60], acute otitis media[63] and acute cough[59;62 61;64]) but has not investigated the specific area of conjunctivitis. Whilst many of the concepts relevant to the other minor illnesses will have a role in conjunctivitis, there may be additional specific concerns regarding an illness affecting the eyes that are relevant in conjunctivitis (eg concerns about a potential threat to sight). Understanding patients' beliefs, concerns and attitudes regarding conjunctivitis will help GPs provide the most appropriate management for the condition. For instance, how important would the potential of a few extra days of conjunctivitis symptoms be to the patient, compared to the inconvenience of making and attending for a GP appointment and applying topical antibiotics four times a day if the condition were known to be minor and self-limiting?

Qualitative research can also provide valuable information for the development of quantitative research[65]. This is especially the case in poorly researched areas where preliminary qualitative work can inform the development of questionnaires and ensure that measurement tools incorporate items relevant to patients. For instance, understanding the patients' perspective can help to ensure that a patient information leaflet is responsive to patients' needs, ideas and

concerns and is context sensitive. (See below, 2.5.3, for a discussion on patient information leaflets and 'Development of the patient information leaflet' Chapter 4.5). Awareness of the patients' perspective can also ensure that symptoms that patients find worrying or troublesome are included in outcome measures such as symptom diaries (see 'Trial Documentation and Procedure' 5.8.3).

Thus there is a clear need to undertake a qualitative study to explore the patients' perspective regarding acute infective conjunctivitis. (Chapter 4).

2.5: Potential Management Strategies for acute infective conjunctivitis

2.5.1: Background

My research explores GPs' current management and patients' perceptions of acute infective conjunctivitis and then trials the most common management strategies in general practice to assess the most appropriate way to mange this condition. The following paragraphs discuss the research evidence behind the alternative management strategies (prescribing alternatives, use of a patient information leaflet and use of eye swabs) that were considered when designing the study.

2.5.2: Prescribing alternatives

Immediate prescribing of a topical antibiotic is the norm for acute infective conjunctivitis[3]. However, as discussed above, the evidence for this being the most appropriate strategy is limited. Any trial in general practice will need to compare alternative management strategies to this current norm.

One alternative is not to prescribe antibiotics at all and to examine the speed and level of recovery. Those who do not recover within a defined time frame or who deteriorate could be reviewed, reassessed and then prescribed antibiotics at a later stage if this were deemed appropriate. The strategy of not prescribing antibiotic drops would be likely to reduce medicalisation[37] of the condition and is already known that many patients will recover quickly without treatment[6]. It would reduce inappropriate use of antibiotics by those with viral conjunctivitis. It is also likely to reduce the incidence of side effects and may have an impact on bacterial resistance to the antibiotics. However, it has the disadvantage of potentially longer and more severe symptoms in those presenting with bacterial conjunctivitis[6]. The effect on complication rates is unknown but likely to be small as complications are probably rare (see Section 2.2.5) and no serious side effects have been recorded in placebo controlled trials for bacterial conjunctivitis[6]. Thus, not prescribing appears to be a reasonable alternative strategy

in this self-limiting minor illness. This strategy would need to incorporate review procedures to ensure that patients with deteriorating or prolonged symptoms were reassessed but this is the case with all treatments.

Another potential strategy is delayed antibiotic prescribing[44;66;67]. This is when the GP (or other clinician) does not prescribe antibiotics immediately but advises the patient to wait and see if the condition resolves without antibiotics. The patient is advised that if the condition is not starting to resolve within a specified time frame (eg three days) that they should then start the antibiotics without the need for a further medical consultation. This strategy allows a limited time frame for spontaneous resolution to occur and thus reduces the use of antibiotics in those where resolution is imminent. It can potentially also avoid medicalisation[37] of the condition, as patients may feel safe to wait a few more days before seeking medical help in future episodes of the condition. Additionally, there is the advantage of reducing the need for re-attendance for the acquisition of antibiotics in those whose condition continues. As with the non-prescribing alternative any deterioration in symptoms would require further medical advice. Delayed prescribing has been used in other trials on self limiting illnesses (eg sore throat[44] and otitis media[45]) and has been shown to be acceptable to patients, to reduce antibiotic use and to reduce re-attendance rates.

I will compare these three prescribing strategies (immediate, delayed or no antibiotics) in the randomised control trial component of this research (Chapter 5).

2.5.3: Patient Information Leaflets

The research literature indicates that a significant problem for parents managing acute illnesses in their children is lack of information and poor information exchange between clinicians and parents[61;64]. Research into the use of written information for the treatment of minor illnesses has had variable results[68]. Some studies have shown patient information leaflets (PILs) to be a helpful way of providing information to patients[69-71] and suggested that PILs can modify help-seeking behaviours by informing patients of the natural history of the illness, safe methods of symptom relief and when to seek medical advice. For instance, it has been shown that a patient information leaflet for acute lower respiratory tract infection can change objective measures of service utilisation eg reduce re-attendance at surgery by 7%[70]. Other studies[46;72;73] have shown little effect from leaflets.

The information has been provided in different circumstances in the studies. In some studies[70] [46]disease specific leaflets have been provided at the presentation of a particular condition and in others[72;73] general leaflets on minor illness have been posted to patients. It appears that

providing relevant disease specific information at the time of presentation with a illness is most likely to have an effect[68].

Currently, it is likely that most patients expect antibiotics when presenting to the GP with acute infective conjunctivitis (I explore this in the qualitative work – Chapter 4). If antibiotics are not to be prescribed immediately, then a PIL could be helpful in providing additional information to the patient regarding management of the condition and reassurance that not prescribing or a delayed prescription is a valid approach. Thus a PIL may be a useful component of a successful management strategy for acute infective conjunctivitis.

There are a number of patient leaflets on minor illness that include a small paragraph on conjunctivitis but searching the literature revealed no separate leaflets on acute infective conjunctivitis that had been subject to research study.

In order to develop a PIL for acute infective conjunctivitis it is helpful to have an understanding of patients' concerns and beliefs about conjunctivitis, hence the need for qualitative research.

2.5.4: Eye Swabs

Microbiological culture by performing a eye swab is not routinely undertaken in patients who present to general practice with acute infective conjunctivitis[1;26]. This is partly due to cost and also to the time taken for results to become available (several days).

However I decided to undertake eye swabs to look for bacterial infection as part of the randomised controlled trial for a number of reasons. Firstly, it provides valuable microbiological data about the cohort. It would be of interest to see the proportion of patients presenting in a U.K. general practice setting with a bacterial aetiology as this subset of patients has the greatest potential to benefit from the prescription of topical antibiotics. Two recent studies[26;41] in general practice have shown a wide range in the proportion presenting with a bacterial aetiology from 32%[26] in a Dutch adult general practice population to 77% in a UK child general practice population[41].

Additionally, I wished to look for a potential medicalising[57] effect of performing an intervention on participants in the trial, the theory being that performing a procedure (eye swab) may increase the patients' belief in the need to attend medical services for acute infective conjunctivitis. Thus, I determined to undertake eye swabs in half the participants in the trial so that the beliefs of those having and not having an eye swab could be compared (see Chapter 5 for further discussion on the trial method).

2.6: Summary

The literature review revealed that the management of acute infective conjunctivitis was a poorly researched area. The available evidence suggested that it is commonly a self-limiting illness[6;42], that half of the patients presenting to general practice are likely to have a viral aetiology[26] and that those with a bacterial cause are likely to resolve without treatment within a week[6].

There was limited evidence on the benefits of topical antibiotics in shortening symptom duration and/or severity, particularly in the general practice population. It appeared that topical antibiotics may reduce symptoms duration by a few days in bacterial cases[6]. No evidence was available on the effect of antibiotics on the transmission of conjunctivitis. Complications from conjunctivitis are probably rare and there was a lack of evidence as to whether antibiotics affect complication rates.

Meanwhile the current high level of prescribing may be 'medicalising' conjunctivitis – and thus increase the general practice workload, induce side effects and increase costs with uncertain benefit to the patient. There was no research evidence on the patients' perspective of acute infective conjunctivitis, and no recent evidence, since the fall in antibiotic prescribing in the mid 1990s, about current management strategies by GPs.

Thus, there was a good case for assessing the current status quo of prescribing, exploring patients' perspectives, and developing and testing alternate management strategies.

Chapter 3: Survey of GPs regarding the Diagnosis and Management of Acute Infective Conjunctivitis in General Practice

3.1: Introduction

Little is known about how GPs currently diagnose and manage acute infective conjunctivitis (see Literature review Chapter 2). It is important to gain this baseline information regarding the current state of clinical practice so the results from the randomised controlled trial can be placed in a clinical context.

Previous research indicates that GPs used to prescribe for nearly all cases of acute infective conjunctivitis[1-4]. However this may have changed in recent years because of the publicity regarding over-prescription of antibiotics for minor illnesses[47]. GPs have been encouraged to reduce prescribing for sore throat, cough and otitis media[51;52;74]. Following these recommendations, they may have also changed their prescribing behaviour for other self-limiting minor illnesses such as acute infective conjunctivitis.

The data from this survey will help to clarify the current position in the use of antibiotics for acute infective conjunctivitis in general practice.

3.2: Method

3.2.1: Rationale for using a Survey approach and its limitations

Information on how GPs diagnose and mange acute infective conjunctivitis could be collected in a number of ways. The most robust method would be a prospective observational study to document the actual treatment received by patients presenting to general practice. This method has been used in past studies[1;4]. However it is expensive and time consuming, so surveys of GPs have also been undertaken[2;3;75]. A survey can be used to canvas the views of a large number of GPs, can provide information about commonly used management strategies and is relatively rapid and cost efficient. Thus it was a suitable method for gaining the data I wished to collect.

However, surveys have some limitations that must be considered in the planning, data collection and interpretation of results stages of the research. A significant limitation of surveys is that they give information on reported rather than actual behaviour. Reported and actual behaviour may differ due to a variety of biases. For instance GPs' perceptions of their behaviour may be inaccurate. If these inaccuracies are random then a large enough sample should reduce this source of bias. However if there is some systematic inaccuracy in reporting

(ie consistently under or over-reporting an aspect of behaviour) then the survey results would be biased – a fact that must be considered when interpreting the results of surveys. Another potential source of bias is expectation bias. This is when the person filling in the questionnaire gives responses that reflect what they think the researchers want to hear rather than actual behaviour (eg GPs may report what they believe is best practice rather than what they actually do). Ensuring that the respondents know that their responses are confidential may help to reduce this source of bias.

Another source of bias in surveys is response bias. This occurs when not all respondents complete the survey and when those that respond differ systematically from those that do not respond. This can be reduced by achieving a high response rate. Potential response bias can be assessed by comparing the characteristics of the responders to the non-responders.

Care must also be taken when constructing questionnaires for surveys to ensure that they are collecting the correct information and that the questions are understandable and not open to differences in interpretation. This is achieved by paying attention to reliability and validity[76] (see below).

Streiner and Norman[76]describe reliability as 'a fundamental way to reflect the amount of error, both random and systematic, inherent in any measurement'.

Reliability is a measure of the ratio of the variability between patients to the total variability (the sum of the patient variability and measurement error). Thus zero indicates no reliability and one indicates no measurement error and perfect reliability[76].

Streiner and Normans definition, that includes random error, means that reliability is specific to the population in which the test is performed. They see this as 'a realistic view of the act of measurement and not a limitation on reliability'. However, others hold conflicting views, Bland and Altman[77] see the link of the measure to the population in which the test is performed as a failure of conventional methods in assessing reliability. They have proposed an alternative method for examining agreement between different methods of clinical measurement which attempts to separate the bias of the instrument from random error.

Inter- and intra–observer reliability can both be assessed. However, inter-observer reliability was not relevant to this survey (since I was attempting to find out what GPs did, not whether they were right in doing so). However, intra-observer (test-retest) reliability (assessing whether responses change if the questionnaire is re-administered to the same participant within a short time frame) was a potentially important issue and was assessed (see 3.2.5: Test/retest reliability). Internal reliability was not assessed for this study. It was less important to assess the correlation of items on the questionnaire with each other, than to try and achieve a high

level of content validity for the questionnaire; furthermore the aim was not to generate scales using a variety of questions to get at one underlying concept, but to provide simple data about a range of issues, in a relatively brief format that GPs would answer.

Validity is often divided into three components[76]: content, criterion and construct validity. Content validity involves ensuring the questionnaire asks appropriate questions so that appropriate inferences can be drawn from the results. This was achieved by undertaking a literature review to assess the important issues in GP diagnosis and management of acute infective conjunctivitis and by interviewing five GPs on what they thought were the important issues (see below Section 3.2.2). These GPs were 'experts' in that they were all practicing GPs who saw patients and thus had a first hand knowledge of the day to day issues of diagnosing and managing conjunctivitis in general practice. They also all had an interest in minor illness research and had participated in research studies and thus were aware of questionnaire development and design. GPs and not ophthalmologists were used as the 'experts' because this was a general practice based study and the vast majority of acute infective conjunctivitis is managed in general practice.

Criterion validity is the correlation of the scale with another measure – ideally a 'gold standard' that has been used and accepted within the field[76]. Unfortunately, there are no validated measures for measuring GP management of minor illness – so no 'gold standard' to test this questionnaire against. Potentially the results from the questionnaire could be compared to direct observation of management behaviour or information gathered by reviewing patients' records but this was beyond the scope of thus study.

Construct validity is the third aspect of validity that is most commonly assessed[76]. Constructs are theories that explain the relationships between behaviours and attitudes or attributes. In this study there were no prior constructs to test that may predict prescribing behaviour, for instance that attributes such as sex, GP experience, ophthalmology experience or achievement of the MRCGP should predict prescribing behaviour.

3.2.2: Questionnaire Development

To inform the development of the questionnaire and ensure content validity, a literature review was undertaken, five GPs were interviewed about their diagnosis and management of conjunctivitis and GPs within Primary Medical Care at Southampton University were asked to comment on the content validity of the questionnaire and its ease of completion.

The literature review was undertaken using Medline and the Cochrane library – see literature review chapter (Chapter 2).

GP interviews. GPs in the Southampton and Salisbury areas, who had shown an interest in minor illness research in the past, were contacted by letter to ask if they would like to participate in the research. The letter explained the nature of the research project and their participation. All the GPs (four males (three full-time and one part-time) and one female (part-time)) chose to be interviewed in their surgeries. The interviews were semi-structured qualitative interviews on the area of diagnosis and management of acute infective conjunctivitis. All information gathered during the interviews was confidential. The interviews were tape-recorded and then transcribed verbatim. The interviews lasted between twenty and forty minutes. The rationale for the interviews was to give some idea of the common range of management for acute infective conjunctivitis and thus there was no attempt to build theoretical constructs from the data. Nevertheless, reviewing these interviews gave useful input into development of the questionnaire. For instance it highlighted the most common signs and symptoms and aspects from the history that the GPs used to diagnose infective conjunctivitis and their most common management strategies.

Below are some examples from the interviews:

HE: Do you have thoughts you would like to start with about acute infective conjunctivitis?

Dr1: Well I mean it's a very common condition and I I doubt if it's, if it's possible or easy to differentiate between viral and bacterial conjunctivitis. Although I know that sort of traditionally there are pointers I mean a watery discharge is supposed to indicate a viral and a very purulent discharge is supposed to indicate a bacterial conjunctivitis but I I suspect that the, the distinction is probably much less clear and most of them are probably secondary to viral infections '(Dr1 p1)

HE: What signs do you look for to diagnose infective conjunctivitis?

Dr2: I would look for – infection in both eyes, uh stickiness in the mornings, um redness, grittiness um – sometimes a swollen lid with it.(Dr2 p1)

HE: What do you actually do when you see someone with conjunctivitis?

Dr3: 'I think... I take a history, now look at the eyes, unless they are having terrible pains, and problems, I don't normally go for more. I look at the eyes... evert the lower eyelid if I think it's allergic. I might possible evert the upper eye, only because I am worried about foreign bodies or anything else, or if it just doesn't feel right, I'll put some fluorescein in it, and um I'll look at it carefully with my opthalmoscope.' (Dr 3 p 4)

HE: When you are examining an eye, what features make you pretty confident that you've got an infective conjunctivitis?

Dr1: 'Um well an acute history, - and particularly the presence of pus, the lids being stuck down, this is really from the history, um – uh – and – and obviously any associated features of an upper respiratory tract infection. Coryza, you know,..other things, Um sore throat, and then on examination, um generally speaking there should be a a fairly global, inflammation of the whole conjunctiva. Which means the, the orbital conjunctiva and the tarsal conjunctiva and so – um that's what I'm looking for and I mean if you've got that then there's no real question about it.(Dr1 p3)

HE: What sort of examination do you do when somebody comes in with an eye problem?

Dr2: Uh well I'd take a history first of all, find out what their symptoms are, and then I'd look at their eye to see whether or not it is red, see what the type of redness is, whether it seems to be around the iris or whether it is a general redness. Uh look for evidence of crustiness, look for evidence of of um blepharitis, um and then depending really on what their symptoms are... I don't do a full visual check for somebody who has got straightforward conjunctivitis. If they, if they've complaining of photophobia, then I would um want to look more closely to make sure, to try and distinguish between conjunctivitis and iritis or uveitis. Um if they- um – you read that people should all have their visual acuity check every time they come in with a with a red eye. Um I don't do that, but I do ask them about their vision, um to make sure that.. you know.. they can see, um and um I would check, it if it seemed to be indicated, there isn't any question about that. Um and fundoscopy um – I don't think I normally do fundoscopy um would more commonly if they are presenting early, they may only have one eye affected, and then I might stain the eye, and look with my, with my um light, my blue light and see whether or not there is any uptake on the cornea.(Dr2 p2)

HE: And coming onto try and discriminate bacterial from viral, do you feel that you can do that?

Dr5: I think so, and I think um (coughs) there is potential for the GP's to do so, but the tendency is to just give chloramphenicol to everything, and the reason is because it's safer in some ways, or may be safer, you can argue the toss on that about chloramphenicol side effects. But basically a viral infection will tend to present with a a pinkish eye rather than a dark red eye, it will tend to present bilaterally, and it will tend to present with a history of going round the family. Um and it would be with surface irritation rather than with some deep discomfort, um and sometimes you may look in the eye and you see sort of cobblestone appearance on the eyelid and um a folliculitis. um bacterial infections tend to be more unilateral they tend to be more severe with lid swelling and um redness of the eye, tend to be with more pus and muck um and there may be some other factors linked in such as new born baby um and ophthalmia neonatorum is obviously a serious problem not to miss, um uh or the persons got some previous cataracts or some previous surgery not cataracts but other surgery or underlying chronic eye problem which makes it more likely to get it.(Dr5 p1)

HE: What proportion of patients who come in with conjunctivitis would you give treatment (topical antibiotics) to?

Dr4: 70%

HE: And how would you decide which ones to treat and which ones not to treat?

Dr: Treat the moderate to severe ones and not the mild ones but again I'd often give them a delayed, give them a prescription and say If it's not better in 48 hours then try this(Dr4 p2)

HE: Thinking of infective conjunctivitis, do you ever take eye swabs?
Dr2: - Only... only in somebody who would have to have recurrent episodes or in babies.(dr2 p2)

I kept the questionnaire short (one side of A4), with an easy to complete format in an attempt to maximise the response rate. The questions asked included: the signs and symptoms used in the diagnosis of acute infective conjunctivitis (AIC); examination and investigations undertaken; confidence with diagnosis; discrimination of bacterial from viral conjunctivitis; the proportion of AIC considered to have a bacterial aetiology and usual management strategies including prescription, use of a delayed prescription strategy and patient information leaflets (see Appendix 1). The questions were mostly closed in nature but the GPs were also encouraged to provide further information or comments.
The GPs were also asked to provide information on their gender, number of years as a GP principal, practice list size, number of sessions, attainment of the MRCGP and any specialist ophthalmology experience so as to be able to define the characteristics of the study group and compare it to national data sets.

3.2.3: Sample size

The NQuery computer package was used to estimate the required sample size. To estimate a proportion prescribing antibiotics of 90% (as found in previous research[1]) with a 95% confidence interval (CI), range of 10% required 150 respondents. 150 would also be sufficient to estimate a proportion prescribing antibiotics of 70% with 95% CI range of 15%. Thus, assuming a minimum response rate of 50% the survey would need to be sent to 300 GPs.

3.2:4: Method

In January 2001 I posted the questionnaire to 303 general practitioners in the Southampton and South West Hampshire and Portsmouth and South East Hampshire Health Authorities areas. The list of GPs was complied from the health authority lists on the internet. All the GPs were principals on the Health Authority list. The questionnaire was sent to all the GPs on the Southampton and South West Hampshire Health Authority list and the most westerly practices on the Portsmouth and SE Hampshire list to reach the required sample size. A freepost return envelope was provided. Two follow up mailings were sent to non-responders.

3.2.5: Test Retest Reliability of the questionnaire

The reliability of the data collected on the questionnaire was assessed by asking 50 GPs to complete a second identical questionnaire two weeks after returning the first (test-retest reliability).

3.3: Results

3.3.1: Response rate

Of the 303 GPs approached, 3 had either left the practice or were on long-term sick leave, giving a study group of 300 GPs. 234 questionnaires were returned, a response rate of 78%.

3.3.2: Study population

The study respondents did not differ significantly from the non–respondents in sex or in the index of multiple deprivation (IMD) of their GP practice area.

The index of multiple deprivation score (2004) (IMD) is a measure of deprivation published by the Office of the Deputy Prime Minister. Seven indicators of deprivation (income, employment, health and disability, education, skills and training, barriers to housing and services and crime and living environment) are combined to calculate a score for small areas of England called super output areas which each include approximately 120 houses. The index of multiple deprivation score for the super output area containing a GP practice could be found on the neighbourhood statistics website[78] by entering the postcode of the practice. This enabled comparison of the level of deprivation of the areas in which the study GPs worked.

Sixty four percent of the GPs approached were male, 63% of the respondents were male and 69.7% of non-respondents were male (difference = -5.1%, 95% (CI -14.7% to 4.4%) p=0.3)

The index of multiple deprivation score for the practice areas of the GPs approached ranged from 1.97 to 48.56, median 13.35 IQR 2.08 to 43.76. The median IMD for respondents practice areas was 12.69 IQR 2.2 to 43.76, median IMD for non-responders was slightly higher at 15.48, but with a similar IQR 2.08 to 42.98.

The characteristics of the respondents were also compared to all registered GP principals in the UK[79] and were similar in gender, number of GP sessions worked and experience (years as a GP). 63% of respondents were male, 84% worked 6 or more sessions a week in general practice and 63% had been a GP for 11 or more years.

64% had attained MRCGP and 11% had received any specialist experience or training in ophthalmology.

3.3.3: Test Retest Reliability of the questionnaire

34 (68%) of the 50 retest questionnaires were returned. SPSS was used to determine the agreement between the two questionnaires. The median percentage agreement was 84.6% (Interquartile range 69.9 to 96.9%). Additionally, Kappa was used as a measure of agreement for the dichotomous variables and Kendalls-tau B for the ordered scales. The median Kappa was 0.63 (Interquartile range 0.39 to 0.84). The median Kendalls-tau B was 0.49 (0.28 to 0.77). This shows the questionnaire to have moderately good reliability[80].

3.3.4: Diagnosis of acute infective conjunctivitis

The questionnaire responses indicated that the main features that GPs use to diagnose conjunctivitis were eye discharge (99% of respondents) and conjunctival injection (94% of respondents) (see Table 3). However there was considerable variability in other features used. 32% of GPs said that they use presence of a swollen eyelid in diagnosis and 31% used conjunctival oedema.

All GPs said they performed a visual inspection of the eye when presented with a presumed case of acute infective conjunctivitis, 26% said they usually perform ophthalmoscopy (although exactly what is examined is unclear, for example it is unlikely that fundoscopy is performed in 26%); 17% said that they usually stain the cornea (see Table 3).

92% (215/233) of GPs were confident or very confident in their ability to diagnose conjunctivitis. The other 8% gave a neutral response, with no GPs indicating that they were not confident. However, despite this high level of confidence with diagnosis only 36% felt that they could discriminate bacterial from viral infection. Of those that felt they could discriminate, again there was variability in the features used: 85% believed a history of a cold could be used to discriminate, 87% the nature of the discharge and 47% the amount of discharge.

There was also considerable variability in the proportion of cases of acute infective conjunctivitis that the GPs believe are caused by a bacterial infection (ranging from less than 10% to greater than 90% of cases). Most of the GPs (58%) thought that less than half of cases of acute infective conjunctivitis that they see are caused by a bacterial infection.

3.3.5: Table 3: Diagnosis of Acute Infective Conjunctivitis

Diagnosis of Acute Infective Conjunctivitis	
Features used in diagnosis	
Feature	*GPs using feature (%; 95%CI)*
Eye discharge	231/232 (99%; 98 to 100)
Conjunctival injection	217/232 (94%; 89 to 96)
Red eye	211/232 (91%; 87 to 94)
Eyelashes stuck together in the morning	190/231 (82%; 77 to 87)
Irritation or grittiness of the eye	184/229 (80%; 75 to 86)
History of contact with conjunctivitis	134/229 (59%; 52 to 65)
Swollen eye lid	74/229 (32%; 26 to 38)
Conjunctival oedema	72/229 (31%; 25 to 38)
Features believed to distinguish bacterial from viral infection	
Feature	*GPs using feature (%; 95%CI)*
History of a cold	75/88 (85%; 76 to 92)
Type of discharge	82/94 (87%; 79 to 93)
Amount of discharge	43/92 (47%; 36 to 57)
Bilateral vs unilateral infection	49/92 (53%; 43 to 64)
Examination normally performed	
Examination	*GPs using examination (%; 95%CI)*
Visual inspection	233/233(100%; 98 to 100)
Ophthalmoscopy	61/232 (26%; 21 to 32)
Corneal staining	39/231 (17%; 12 to 22)

3.3.6: Management of Acute Infective Conjunctivitis

In this survey, most GPs (95%) indicated that they prescribe topical antibiotics for acute infective conjunctivitis. Most do not use a delayed prescription strategy, a patient information leaflet (PIL) or take an eye swab (see Table 4).

21% of GPs said that they prescribed topical antibiotics for every case of acute infective conjunctivitis. The remaining 79% of GPs said that they were happy not to prescribe for acute infective conjunctivitis in certain cases (eg for mild infection or in babies with sticky eyes) but they still prescribed for the vast majority of patients.

Neither GP experience (number of years as a GP) or having had specialist ophthalmology training were related to prescribing for acute infective conjunctivitis or using a delayed prescribing approach.

Amongst the 67% of GPs that ever take eye swabs in cases of acute infective conjunctivitis, most (84%) do so in a small minority of cases (<10%).

3.3.7: Table 4: Management of Acute infective Conjunctivitis

Management of Acute infective Conjunctivitis	
Use of antibiotics	***GPs using this* strategy (%; 95%CI)**
Prescription of topical antibiotics	217/229 (95%; 91 to 97) usually use this strategy
Which antibiotic prescribed:	
Chloramphenicol first line	186/213 (87%; 83 to 92)
Fucithalmic first line	27/213 (13%; 8 to 17)
Delayed prescription strategy*	106/232 (46%; 39 to 52) ever use this strategy
Other management strategies	**GPs using this strategy (%; 95%CI)**
Eye swabs	155/232 (67%; 61 to 73) ever use this strategy
Patient information leaflet	35/232 (15%; 11 to 20) ever use this strategy

*advise to patient not to use the topical antibiotics immediately but give the patient a prescription to use if the condition does not settle within a set time frame.

3.4: Discussion

3.4.1: Background

To my knowledge this is the first study to explore GPs diagnosis and management of acute infective conjunctivitis in detail.

The good response rate (78%) for the survey, the fact that the characteristics of the responders were similar to national data sets[79] and that I have shown the questionnaire to have moderately good levels of reliability[80], mean that the results should be reasonably reliable and generalisable.

3.4.2: Limitations of survey data

Inevitably the results from a survey are of reported rather than actual behaviour, thus there is the possibility of bias due to over or under-reporting. However, this does not appear to have had a great influence on this data. For instance, a significant finding of this survey is the high level of prescribing for acute infective conjunctivitis (95%). This is unlikely to be due to biased reporting as current trends are to discourage prescribing for minor self-limiting conditions. Additionally, there is no reason why the responses to diagnostic questions should be biased in any particular direction.

3.4.3: Discussion of Main Results

Previous GP surveys on eye related conditions have shown a general lack of confidence in Ophthalmology amongst general practitioners[2;75]. In contrast, this survey shows GPs to have a high level of confidence in diagnosing acute infective conjunctivitis. This is encouraging as it is probably the most commonly seen eye condition in general practice[1-4].

However, the results show considerable variability in the features that GPs use to diagnose acute infective conjunctivitis and in the features they believe discriminate between viral and bacterial infection. Additionally, most GPs (64%) did not feel that they were able to discriminate between bacterial and viral conjunctivitis. This diagnostic uncertainty may partly explain why GPs are prescribing topical antibiotics for most cases of acute infective conjunctivitis despite believing that a significant proportion of the cases are not bacterial in origin.

Clinical scoring systems have been developed for a number of minor illnesses (including sore throat and otitis media)[68;81] but there is only a preliminary report among adults for acute infective conjunctivitis[26]. Further research is needed to determine whether a clinical scoring

system could be developed to enable GPs to better target antibiotic prescriptions for acute infective conjunctivitis.

3.4.4: Discussion of Management Issues

The results show that GPs prescribe topical antibiotics for most cases of acute infective conjunctivitis. This is consistent with past research - Sheldricks' study[1] undertaken in 1990 showed GPs prescribed topical antibiotics for 92% of cases of infective conjunctivitis. This continued high level of prescribing is surprising given the current pressure to reduce antibiotic prescription for minor self-limiting infections.

A delayed prescription strategy (giving the patient a prescription to use after a few days if there is no improvement in symptoms) could be a useful management strategy for acute infective conjunctivitis as a significant number of patients are likely to improve without treatment within a few days[6]. However, only a minority of GPs ever used the delayed prescription strategy in this survey.

Also highlighted by this survey is GPs use of patient information leaflets (PIL). The results show that only 15% of the GPs said that they had access to a PIL on conjunctivitis and even then they were rarely used. Studies have shown that patient information leaflets given within the GP consultation can reduce re-consultation rates for certain self-limiting illnesses[68] (eg cough[70]). It is possible that a concise clear leaflet on conjunctivitis, that addressed patients' fears and expectations for recovery, could improve patients' confidence and their ability to manage acute infective conjunctivitis without the need for a prescription. More research is needed to clarify the advantages and disadvantages of prescribing topical antibiotics for acute infective conjunctivitis and the potential role of a delayed prescribing strategy and a patient information leaflet.

4: Qualitative Study of Patients' Perceptions of Acute Infective Conjunctivitis.

4.1: Introduction

The literature review (Chapter 2.4) highlighted the lack of information regarding the patients' perspective on acute infective conjunctivitis. Gaining an understanding of patients' ideas, concerns and beliefs about acute infective conjunctivitis, and why they attend, could help health professionals provide more effective management strategies for the condition.

4.2: Aims of the qualitative research

- To gain an understanding of patients' ideas concerns and beliefs about acute infective conjunctivitis.
- To inform the development of a patient information leaflet (PIL) for acute infective conjunctivitis.
- To inform the development of the randomised controlled trial of management strategies for acute infective conjunctivitis (including gaining an understanding of outcome measures relevant to patients and informing the development of trial materials).

This research was undertaken in a health care setting with the intention of providing information to health care professionals to inform management decisions regarding acute infective conjunctivitis. The aim was not to undertake a detailed interpretive approach with in-depth theory development but to provide some insight into the most important issues for patients so that health professionals could be more informed of the patients' perspective.

4.3: Rationale for using a qualitative research approach

4.3.1: Background

Surveys and qualitative research are the main methods used for collecting data regarding participants' opinions. Qualitative research methods allow exploration of a research area when there is little prior knowledge of the main issues[82]. Constructing a survey with appropriate questions is very difficult in these circumstances. Additionally, surveys cannot provide a detailed exploration of patients' understanding or of important contextual factors. The literature review has revealed a paucity of information regarding patients' views of acute infective conjunctivitis thus a qualitative approach is the most appropriate way to explore this area. Qualitative research is often more time consuming than collecting survey data and thus

far fewer participants are normally involved. The results of qualitative research attempt to capture the range of opinions and beliefs that exist in a sample and to provide conceptual explanations of the participants' views in contrast to surveys which use statistical methods to represent the data.

4.3.2: Choice of qualitative approach: a constant comparison approach informed by the principles of Grounded theory

There is a choice of possible qualitative methodologies[65;83;84]. Defining the research aims above, undertaking reading about qualitative methodologies, attending a qualitative research methods course and discussions with my supervisor (an experienced qualitative researcher) helped me to decide the most suitable qualitative methodology to use. I determined undertake face to face semi-structured interviews and use content analysis with a constant comparison approach informed by the principles of Grounded theory[85;86] for a number of reasons:

- Methods taken from Grounded theory have been used successfully in previous acute illness research in general practice and thus are likely to be accessible and acceptable to general practitioners[60;87]
- It has a systematically explicit method of collecting and analysing the data [86].
- The emphasis on iterative data collection and analysis, with repeated testing of developing concepts and themes, gives opportunities to test the integrity of the data and its analysis which maximises the internal and external validity of the findings.

I was keen not to restrict the information collected by imposing a tight framework to the interviews, particularly as this area had not been researched before but I needed to ensure that potential important areas highlighted in the literature review and in previous interviews could also be discussed. The semi-structured format to the interviews allowed participants to talk freely about their experiences of and views about acute infective conjunctivitis but enabled important areas for discussion to be introduced if necessary.

Initially I considered undertaking focus groups in addition to individual interviews. Focus groups may have been able to provide rich data through discussion between participants. However I found that logistical reasons (particularly finding a suitable time to see participants) made arranging focus groups impractical.

I did not undertake in depth qualitative theory development, nor the use of theoretical sampling, as this was beyond the scope of this piece of work.

4.4: Rigor in qualitative research

All research should be conducted in a rigorous manner so that the results are reliable, valid and transferable. Qualitative research has often been criticised for lacking scientific rigor[88]. Mays and Pope[88] described the most common criticisms as being that it is merely an assembly of anecdote and personal impressions, strongly subject to researcher bias and that it lacks reproducibility and generalisability. However they also described how systematic and self conscious research design, data collection, interpretation and communication can be used to ensure rigor[88;89]. They suggested a range of questions to ask of a qualitative study to critically scrutinise its rigor:

1) Overall, did the researcher make explicit in the account the theoretical framework and methods used at every stage of the research?

2) Was the context clearly described?

3) Was the sampling strategy clearly described and justified?

4) Was the sampling strategy theoretically comprehensive to ensure the generalisability of the conceptual analyses (diverse range of individuals and settings, for example)?

5) How was the fieldwork undertaken? Was it described in detail?

6) Could the evidence (fieldwork notes, inter-view transcripts, recordings, documentary analysis, etc) be inspected independently by others; if relevant, could the process of transcription be independently inspected?

7) Were the procedures for data analysis clearly described and theoretically justified? Did they relate to the original research questions? How were themes and concepts identified from the data?

8) Was the analysis repeated by more than one researcher to ensure reliability?

9) Did the investigator make use of quantitative evidence to test qualitative conclusions where appropriate?

10) Did the investigator give evidence of seeking out observations that might have contradicted or modified the analysis?

11) Was sufficient of the original evidence presented systematically in the written account to satisfy the sceptical reader of the relation between the interpretation and the evidence (for example, were quotations numbered and sources given)?

I undertook reading and training into qualitative research techniques, was closely supervised by a qualitative supervisor with whom I was able to discuss points of methodology and

reflexivity and used the strategies suggested by Mays and Pope[88] ensure that the qualitative work was as well conducted as possible.

4.5: Method

4.5.1: Ethical approval

Ethical approval for the study was granted by the relevant local ethical committees (Southampton and Southeast Hampshire LREC no: 267/99 and Salisbury Ethics committees LREC no SA 27/99).

4.5.2: Constructing the sample

GPs and Practice Nurses from three GP surgeries in Hampshire and Wiltshire - one semi-rural, one urban and one cathedral city practice, asked patients presenting with acute infective conjunctivitis if they would be prepared to participate in the research. The patient was provided with a patient information sheet (approved by the local ethics committee) regarding the research (Appendix 2).

The patient information sheet gave a description of the study in simple language and explained that participants were free to withdraw from the research at any time without their medical care being affected. The patient read through the information sheet and if they were willing to be interviewed they signed the consent form which was then forwarded to me by post.

A maximum variety sample of twenty-five patients was constructed to include patients from a range of socio-economic groups, differing age and gender to capture a wide a range of views (Table 5) (however a predefined framework for sampling was not used).

I contacted the patients by telephone within one month of their attendance at the surgery to check if they were still willing to participate in the research and to arrange an interview time and place. The participant was given the choice as to the location and timing of the interview. Possible locations were a private area in the GP surgery, in the research department, or in the patients' own home. All participants choose to be interviewed at home.

4.5.3: Data Collection: The Interviews

4.5.3.1: Background

I undertook face to face semi-structured qualitative interviews in participants' homes between October 1999 and May 2001.

Prior to this study, I was inexperienced at qualitative interviewing. I am used to talking to patients as a GP but qualitative interviewing is a different skill[90]. I learnt about qualitative interview methods through reading and attended a qualitative methods course which included practicing interview technique. My supervisor assisted me with my qualitative interview skills by going through interviews and highlighting good interviewing and areas that may have been improved. I had also gained some experience with qualitative interviewing before undertaking this study by undertaking qualitative interviews with GPs for the GP survey (Chapter 3).

4.5.3.2: Interviewer/ interviewee relationship

The collection of data by qualitative interviewing depends on a relationship between the interviewer and interviewee. It is important to build a level of rapport and trust to be able to access participants' views and enable them to speak freely and honestly about the topic of discussion[91]. I was pleased that the participants chose to be interviewed in their own homes as I felt this may be a more relaxed and neutral setting for them to discuss their experiences than in a GP surgery or the research department.

I thought carefully about my approach to the interviews to try and place participants at their ease. I dressed tidily but not too smartly and initiated a casual conversation on arrival rather than heading into the interview too quickly. I emphasized that I was interested in the participant's story and that I was keen for them to tell it in their own words. I avoided medical terms and tried to use language that the participants would easily understand.

I am a young female GP and this affects the way people perceive and respond to me and my responses to them[92]. To ensure transparency in the research process I needed to consider my background and beliefs and the influences that this would have on my relationship with participants and data collection and analysis[91]. Mays and Pope[89] describe this as reflexivity. I come from the background of medical training which is bound to influence my beliefs about health, illness and healthcare. The results of this research must be viewed in this context. I tried to minimise the impact of my own assumptions and beliefs on the interviews by probing responses rather than assuming a shared understanding. I was also keen to minimise the effect of my medical background on the participants' responses. If participants were aware I was a doctor they may have felt that they had to respond to me in a certain way. For instance knowledge of my medical background may change the dynamics of the relationship and inhibit discussion of the treatment they received from their GP or Practice nurse, especially if they felt critical of the care they had received. Also they may have been more likely to give views that they though a doctor would expect or like to hear. Thus, I decided to introduce

myself as 'a researcher from the university' and not as a doctor[92] in an attempt to minimise bias. I decided to inform the participants that I was a doctor if they asked, but none of them did so.

4.5.3.3: Interview method

Interviews were 30 minutes to one hour long and were audio-taped and transcribed verbatim. I had secretarial support to transcribe the tapes, but I read through each transcript line by line whilst listening to the audiotape to ensure that the transcript was accurate. This also gave me an opportunity to reflect on the emerging data and on my interviewing technique.

During the interviews participants were encouraged to talk freely and describe their experiences of conjunctivitis. I developed an interview guide sheet to prompt me to explore areas of interest highlighted by the literature review or previous participant interviews (Appendix 3). However, I tried to let the participants' discussion lead the interview and the guide sheet was a secondary tool used to ensure that major areas of interest were not omitted.

After initial greetings and informal conversation to place the participants at their ease, I started the interview with some non-threatening basic questions such as how long they had been living in the area and the composition of their household. I then asked them to describe the episode that caused them to attend the surgery (with acute infective conjunctivitis) and encouraged them to talk freely about their experience. I undertook active listening to encourage them to tell their story in their own words. I then followed the participants' leads to encourage them discuss their ideas in greater depth. I attempted to be non-directive in my probing of participants' statements and to explore the basis for their beliefs. I asked open ended questions about the areas of interest highlighted on the interview guide that had not already emerged. Analysis and interviewing was undertaken concurrently (see below 4.7 for more discussion on analysis). Each interview was transcribed and reviewed and initial analysis started as soon as possible after the interview. This allowed for emerging concepts to be further explored in subsequent interviews. I continued to interview new participants until no further concepts were emerging and I had explored the concepts that had emerged (ie I attempted to reach data saturation to the level that was necessary to meet the objectives of this study). Saturation for my needs was different from what may be considered saturation for a study that aimed to develop a theory of patient responses to conjunctivitis.

Topics covered in the interviews included understanding of conjunctivitis and its diagnosis and management, experiences and knowledge of the condition, sources of information, experience of the consultation for conjunctivitis, beliefs regarding treatment, attitudes to

antibiotics, the effect of the condition on work and school, responses to different management strategies and attitude to future episodes of conjunctivitis.

Additionally, ideas regarding a patient information leaflet for conjunctivitis were explored. This was undertaken at the end of the interview to minimise any potential bias (see 4.6 development of the patient information leaflet below).

4.6: Development of the patient information leaflet

4.6.1: Background

The literature review revealed that there were no patient information leaflets regarding acute infective conjunctivitis that had been subject to research study (Chapter 2.5.3). One of the aims of this qualitative work was to gather information on what patients would like to see in a leaflet. This information could then be combined with the current research evidence regarding acute infective conjunctivitis to form a leaflet. The leaflet would then be shown to further participants to gain their views and the final leaflet would be assessed in the randomised controlled trial.

I wanted to develop a simple leaflet – just one side of A4 paper - that was accessible and easy to read. I wanted it to be amenable to being printed off from the computer within the GP consultation so that it could be handed to patients presenting with acute infective conjunctivitis. Issuing leaflets at the time of minor illnesses appears to have a greater impact on patients' attitudes than handing it out at other times[68;69]. Bearing these logistical restrictions in mind, I used suggestions from the published literature on developing patient information leaflets to guide the construction the leaflet[69]. This included considering the leaflets' layout, style, language, readability and clinical content. I decided not to include pictures and artwork on the leaflet as colour or complicated diagrams can take a long time to print. Artwork may make leaflets more appealing to read but I felt this could be forgone for the benefit of receiving an appropriate leaflet at the time of the consultation.

4.6.2: Method of leaflet development

I asked participants from the first five interviews how they would feel about receiving a patient information leaflet on acute infective conjunctivitis and what information should be included in a leaflet. This questioning was undertaken at the end of the interviews so as not to bias the rest of the interview.

I developed the leaflet in the light of these responses and the information from the literature review. I asked GPs within the research department to review the leaflet and give feedback on it. A question and answer format to the leaflet received good feedback from this process. I then showed the leaflet to subsequent participants in the qualitative interviews to gather their responses. The leaflet was modified in response to participants' comments and the final version of the leaflet (Appendix 4) was then assessed in the randomised controlled trial (Chapter 5).

4.7: Data Analysis

Content analysis was used to interpret the data[86;93] with a constant comparative approach informed by grounded theory. Each interview was deconstructed sentence by sentence by identifying key categories. These were compared across scripts and with established categories in the literature[37;60;61;64]. Data collection and analysis were iterative, constant comparison of the new data with previously collected data was undertaken to assess the integrity of the emerging categories and concepts. This required repeated rereading of scripts. To maximise sensitivity and rigour, the scripts were reviewed by both me and my supervisor, Dr. Satinder Kumar. Emerging concepts were discussed and debated between us in regular meetings and particular areas of interest were highlighted for further exploration in subsequent interviews. Thus concepts were explored in further detail to test their validity before being integrated into themes.

I considered using a software package to help analysis of the data and indeed went on a NUD*IST course but I found that manual manipulation of the data worked better for me.

4.8: Results

4.7.1: Study Group (Table 3)

All participants were white British, most were female, reflecting the preponderance of women attending and mothers attending with their children.

All social classes were represented but the index of multiple deprivation scores (2004)[78] for the postcode area of the participants (see table 5) shows that the participants lived in relatively less deprived areas of England that the general population. (see p.35 for more information on the index of multiple deprivation score (IMD))

The median scoring area in this study (score of 7.92) has a rank of 26,534 out of 32,482 lower layer super output areas for deprivation (with a rank of 1 being the most deprived area in

England and a rank of 32,482 the least deprived). The most deprived area in this study had a rank of 13,858 out of the 32,482 areas in England. Thus this study had no participants from areas of very high deprivation.

4.8.2: Table 5: Characteristics of participants

Characteristics of participants (n=25)		
Adult patients	13	male (3), female (10)
Parents of child patients	11	male (0), female (11)
Adolescent patient	1	female
Recruited by GP	12	
Recruited by Practice Nurse	13	
Age Range	13 to 90 years	
Index of multiple deprivation score (from postcode area of participant)	range 1.54 to 20.01, median 7.92, IQR 1.91 to 17.92	

4.8.3: Themes

Six themes were developed;

1) Perceptions of acute infective conjunctivitis,

2) Perceptions of medicines,

3) The consultation for conjunctivitis,

4) Responses to different management strategies for conjunctivitis,

5) Information wants and needs,

6) Different responses to conjunctivitis for oneself and for ones' child.

Each theme comprises a number of categories or subthemes. These themes are presented below supported by extracts from interview data and with a discussion of the underlying concepts.

4.8.3.1: Theme one - Perceptions of Acute infective conjunctivitis

4.8.3.1.1: Making a lay diagnosis

Most participants were confident in making a lay-diagnosis of an eye infection, using a range of symptoms and signs (e.g. red eye, eye discharge, eye irritation).

'he had a weepy eye, and um it, they both looked very red and I think it was it really, just the fact he had some sort of gunky stuff in them and a bit red, so in the end I assumed that it was conjunctivitis' (pt17p3)

'Well I woke up one morning and one eye was just scarlet and gummed up and that was the first indication anything was wrong, I hadn't known anything was wrong the previous evening, just there in the morning, so I thought um conjunctivitis, got to get it treated fast' (pt24 p1)

Responses when asked about the main features of conjunctivitis:

'Well, with my experience of it, it's been red eye first and rubbing a bit and then getting gooey and in the morning not being able to sort of open it straight away' (pt3p4)

'Um well discharge from the eye, um sort of golden discharge that are sticking the eyelashes together and the eyes look a bit crusty'(pt11p4)

Respondents drew on past experiences, both personal and of others to make this diagnosis. Most participants attended the GP surgery believing that their symptoms were due to an eye infection.

'...because I've had conjunctivitis in the past and because I'd seen cases of it I realised that this was the onset of it'(pt2 p1)

'I thought this could probably be conjunctivitis, so I wasn't surprised when he (the doctor) *said that's what it was'..... 'well I thought to myself this is conjunctivitis, I mean I've known of it for years and I've known people who've had it and what it looks like, so I just guessed it was' (pt12p4)*

'I've had experience of conjunctivitis in the family before so immediately I thought, aah, this looks like conjunctivitis, I'll take him down, so that's what I did' (pt14p1)

Most saw the terms 'eye infection' and 'conjunctivitis' as referring to the same condition and alternated between using the two terms. However a few were not certain what 'conjunctivitis'

meant or thought it was a more serious condition than they had experienced but they still recognised their symptoms were due to an 'eye infection'.

'It was an eye infection, but it wasn't as serious as conjunctivitis, it was just a bit of a sticky eye' (when asked directly if she thought it was conjunctivitis) – *' No I didn't think it was and they didn't think it was either, but I mean I don't know that much about conjunctivitis but.. I had the impression it was much worse and the whole eye ball was red and you know conjunctivitis was a much more serious looking condition and he certainly didn't seem as I say he had no real redness and no pain that I could see... So I assume that it's a mild eye infection and the Triage nurse certainly didn't say anything about conjunctivitis, she seemed to think it was an eye infection, if that's the right word' (pt10p5)*

(To the question: 'have you had experience of eye problems in the past?') *'No just minor infections um I've never had conjunctivitis as far as I can remember... ... I remember going to um see the optician, I was due to have um an examination, a few years ago and one of my eyes was a little bit inflamed and when he looked at it he just said 'oh it's just a minor infection' so it obviously wasn't conjunctivitis' (pt12p3)*

Receiving a diagnosis was not the main reason for attending in most cases.

'I go in without any necessity to enquire what's wrong because I recognise it, there (pointing to eye),.. *it's something you can see' (pt16p10)*

However, two participants did describe attending for reassurance that they had made the correct diagnosis.

*'I mean I went to the doctors really more for the reassurance that there was nothing in there that I couldn't see um or that it wasn't something other than an infection in the eye' (pt11p5) (*when asked if he expected antibiotics) *'No, uh I didn't really, no I went just expecting to have my eyes sort of examined and checked out'*

'as soon as I could go to the doctors I did, because I felt well you know I want them to say either yes.. you're right it's a mild eye infection or oops no it's something completely different but just looks like a mild eye infection. And I feel like I'm contradicting myself but I mean I wasn't worried but I didn't want to take any chances if that makes sense' (pt10p8)

Most participants stated they attended for advice, most expected a prescription (see Conjunctivitis – a minor illness that requires treatment 4.8.3.1.2 below).

'I just wanted his (the GPs) *advice' (pt1p1)*

' Did it need further treatment or did I need to just let it go away? ....I needed more information really' ' most of all I was expecting him to give me advice' (pt 5 p3)

Importantly, patients recognised that visual problems and pain in the eye were different from the usual symptoms of an eye infection, and could indicate a more serious condition.

'if it got worse, if he were getting problems with his sight I would go back straight away, no question of that' (pt17p6)

Indications that it might not be a simple eye infection: *'if they* (her eyes) *got worse, maybe puffy, or if she complained that her eyesight was a bit, you know, that she wasn't seeing properly' (pt8 p4)*

This suggests patients would continue to consult for serious *red eye* conditions if they self-care for conjunctivitis.

4.8.3.1.2: Conjunctivitis - a minor illness that requires treatment

Most patients perceived conjunctivitis as a minor condition - a nuisance or an inconvenience. It was not seen as sight threatening, distressing or disabling.

'Minor. I don't view it as a problem illness, I just view it as a niggly one that needs to be dealt with' (pt5p8)

'it's very minor, because I think it doesn't affect sight or anything, it's just that he looks horrible and it can be a bit irritating' (pt14p5)

'it's just sort of inconvenient more than anything' (pt3p6)

'it didn't seem to be bothering him over much, he wasn't in lots of pain or it wasn't irritating him a lot as far as I could see' (pt10p3)

'it didn't appear to be serious ..... he wasn't off his food, he wasn't crying, he wasn't having trouble sleeping, you know he was just as happy as anything' (pt10p8) 'it didn't look very serious, he didn't act like it was very serious'

However one mother perceived it as more of a problem:

'I'd hate my children to go through it.. because it's very painful and it's all the gunge stuff and what-have-you, you know it's not nice'(pt7 p8)

There was a strong belief in the need for treatment to clear an eye infection. Most patients expected a prescription and had not considered the consequences of leaving the condition untreated. Some expressed the idea that it might become more serious if left.

'the only way to get rid of it (conjunctivitis) *is antibiotics....That's why I decided to go and see a doctor'' (pt6p1)*

' I didn't really think about leaving it, it was conjunctivitis, it needed treating, get on and get it done, the sooner you treat it the sooner it will clear up' (pt24p3)

'I haven't a clue what it would actually do (if the conjunctivitis was not treated), *no I am just aware that it's not a good idea to leave something like that, I don't know what the repercussions, you know, what could happen' (pt17 p6)*

'I suppose if it's caught early not very serious really from my experience, 'cause it's always cleared up quickly... but saying that I don't know if it's left then perhaps it could be quite serious I don't know' (pt9p7)

Consequences if left: *'Probably would have got a lot worse and gone badly into the other eye as well I would imagine, it just wouldn't have cleared up' (pt9p3)*

Few patients had any notion that conjunctivitis might be self-limiting. Most felt it should be treated quickly and had sought an urgent appointment. This contrasted with their approach to a 'cold' which could be allowed to run its course without seeking medical advice.

'I have always thought that you, you know you have to sort of get it (conjunctivitis) *treated, I never realised that it would actually eventually disappear on it's own....(pt14p9) ..'I think you know it's one of those things that I assumed that you have to – you know go down and get cleared up'*

When challenged, patients acknowledged the paradox of believing conjunctivitis to be a minor condition but also feeling that it required urgent medical attention. The basis for the paradox appeared to be their lack of awareness of its self-limiting nature. So, although symptoms were mild, they still felt it required treatment as it might not get better or might get worse.

'it's like it (conjunctivitis) *isn't something that I would really panic about but then I know it's something that I must get cleared up, it's weird isn't it?. Yes I wouldn't.. I definitely would never leave it, no.. I just think get them to the doctors straight away really' ....' I don't know, I don't know where that came from, that's really weird, like conflicting there.. but, it's almost like it doesn't feel like it's that too bad a thing... and yet I know, and yet.. I 've got another feeling that it is and I need to get it treated and cleared up, and I don't know where that is come from really, yes quite bizarre' (pt17p11)*

Patients found it difficult to explain the urgency for seeking medical help but for most it appeared to be a learnt help-seeking behaviour. Past experiences of receiving immediate treatment at the GP surgery, advice to attend immediately from family, friends and pharmacists and the possibility of infecting others encouraged them to seek urgent treatment.

I don't know why I know not to leave it, um I don't know if it would be safe for me to treat it myself with salty water and just sort of clean it. ... Whether or not I could have tried that. I suppose I could have I'm not sure' (pt17p5)

'I though that he'd need drops because my sister, her little boy's a similar age had had it and she said I had to go and get drops from the doctor because it didn't clear up' (pt9p2)..... 'I am led quite a bit by my mum... she's probably a lot more knowledgeable... .I sort of get led by her and my sister' (pt9p6)

'I suppose, probably from when I was a child myself, I mean you get any eye problems treated, particularly if it looks like it's going to be conjunctivitis because it doesn't just clear up after a day or too, it can sort of go all through the family if you're not careful, so get it treated quickly' (pt24p3)

One participant (quote below) stated concern for his sight as a reason for seeking an urgent appointment but this was not a factor for the other participants.

'I have the .. the perception that it wasn't going to get better without any treatment, and so the sooner I saw the doctor the better um, I don't know I mean maybe it does go away if you don't treat it but all the same I value my left eye particularly after the accident I've had on my right eye and if anything happened to upset the vision I'd never get over it (laughs), uh so I was quite anxious to get something done quickly' (pt13p4)

4.8.3.2: Theme two – Perceptions of Medicines

4.8.3.2.1: Difference between beliefs and behaviour

Participants stated that they were careful and wary about taking medication and generally tried to avoid it because they believed it was *"better to fight off illnesses yourself"*. They emphasised self-care and not seeking medical help for other minor illnesses. Many felt that immunity to illness was improved if medicines, particularly antibiotics, were avoided.

'I'd rather wait and see if they're (her children) *going to get better first, without having antibiotics for your own healths' sake'.... 'I suppose if you're taking them* (antibiotics) *constantly, or a lot, then your own body never builds up resistance itself so I would rather they try and get over the problem on their own'(pt5p4)*

'.....well, I know that there's been a lot of publicity in recent years about the overuse of antibiotics, so I certainly agree that they shouldn't be given for things like may clear up on their own' (pt4p5)

'....you want to take as little medication as possible really. ....I don't want to have to take a drug unless I really have to' (pt11p5)

'I.. I think I'd be prepared to sweat it out rather than take antibiotics. If I knew I was going to get better, um so I'm not someone who goes to the doctor every time I get a cold and say I need an antibiotic (pt13p10)

'Well I know that it's best to try and fight it yourself without antibiotics, so I will you know, I'd prefer it if they (her children) *could fight any sort of infection without them but I wouldn't rule it out altogether... I think that just generally our society isn't, you know just isn't getting, building so much resistance, not building up the resistance*

that it needs to (illnesses) *and antibiotics need to be kept for things where it is really quite serious I think (pt19p5)*

However, in the context of conjunctivitis all these patients had sought medical attention, and had been prescribed and used topical antibiotics.

A possible explanation for this difference between stated beliefs and actual behaviour is patients' lack of awareness of the self-limiting nature of conjunctivitis. Most patients believed it must be treated and were unaware of other potential options for managing the condition (eg self-care). They felt their general desire to avoid medication could not be realised for conjunctivitis. The issue of a prescription by a trusted health professional confirmed and reinforced the belief that treatment was necessary.

'the doctor wouldn't give them (antibiotics) *to you.. if he didn't think it was necessary' (pt7p13)*

'I realise it's best not to overuse them (antibiotics), *so unless it's really really necessary when someone is really ill would we consider going to the doctors to get antibiotics because I know they wouldn't give you it unless it's very bad anyway, so half the time you are wasting your time going down there with your child that doesn't feel well anyway. And you know that they are not going to be happy about giving you antibiotics unless its very serious really (pt17p5)*

Most participants were aware that the drops they received contained an antibiotic, but not all. They accepted the treatment readily and did not ask for (nor were they given) detailed information regarding the treatment. (see 4.8.3.5: Theme 5: Information wants and needs)

4.8.3.2.2: Topical versus tablet preparations

A possibility was that topical preparations could be perceived as a less concerning treatment than tablets and that this may explain participants' acceptance of it.

One patient did hold this view:

'....it doesn't seem so drastic somehow (laughs) Yes I'm unsure as to why I feel that, now if he was taking antibiotics orally I'd be oh god you know he's taking antibiotics I'd rather you didn't, whereas this just in the ointment, I was fine about that, I don't' know why that is'..... 'I guess it (antibiotic ointment) *must get into the body to work, some reason I just don't' seem to class it the same category for some reason and obviously it is, is just the same isn't it? Um,' (pt17p9)*

but most patients perceived no fundamental difference between the preparations.

'I can't really see that there could be much difference if that antibiotic is in a drop for your eyes um I can't see that there's any difference than it being in a, in a tablet form for you to take'(pt12p11)

4.8.3.3: Theme 3 -The Consultation for Conjunctivitis

Most participants sought an urgent appointment for conjunctivitis because they perceived this was the only way to access effective treatment.

Many participants had sought lay advice first (eg from family members, medical books, or the chemist), as seen in studies of lay decision making[94]. For almost all, the advice received was to seek an urgent medical opinion. Few had used over the counter treatments.
Patients were satisfied with their consultation for conjunctivitis, which they described as short with minimal information exchange. They asked few questions during the consultation.
Participants gave several reasons for this;

1) Receiving the expected treatment,

'I think that I just assumed that that's what it was, that's what he needed and it would just clear up straight away, which was what seems to always happen' (pt17p6)... 'it's always sort of happened like that and I just , I just assume they will again'

'Um, well um, I don't think DrX went into any detail about it um I think he assumed that I knew what conjunctivitis was um and he um confirmed what he thought um and suggested that I use these drops. ....Um I suppose if I'd asked him lots of questions he would have told me of course but I didn't really feel that there was much to say about it to be honest. Not as he was going to give me a treatment for it' (pt12 p6)

2) Conjunctivitis was a minor condition so they did not need more information,

'Well in this case I felt it was a fairly simple solution, but had it have been more complicated in nature, um I would have felt I would like more time(pt16p11)'

3) Trust in the health professional,

'I tend to sort of be led by the doctor and what they suggest... then I'll just go along with it really because you know I can be led by them' (pt9p6)

'I wouldn't go to see the doctor if I knew what to do by myself so I'll trust the doctor' (pt6p8)

'I just feel that whatever he's told me is right' (pt7p13)

'Yes I always take whatever the doctor says I I do usually, so I don't tend to argue with them' (pt14p7) 'I just assume they know better than I do at the end of the day that's why I go'

4) GPs time was pressured and asking questions would *"waste"* more time.

'I always feel I'm wasting time.....I only like to go down there if it's a real emergency' (pt3p3)

' I'm always conscious of the pressure on the doctor when you go to see them, I didn't engage in any chit chat other than putting the facts before him which he recognised at once the condition and wrote the prescription and I went'(pt16p10)

The result was acceptance of the treatment without question. Some participants were unaware that the treatment contained an antibiotic.

All the participants stated they would have accepted seeing *'a properly qualified nurse'* and those who had seen a practice nurse were happy with their consultation.

'As long as I reckoned the person I was talking with got enough experience or knowledge to give me the right opinion.. I would trust a nurse as well' (pt6p8)

'I'd be fine with a nurse run clinic ..because I don't think they would give the advice if they didn't have the back up from the doctor and they knew what they were doing'(pt8p16)

4.8.3.4: *Theme 4 - Patients response to different management strategies*

In general, participants stated that they were willing to accept advice during the consultation even if it varied from their expectations (i.e. to 'wait and see' or delayed prescription, rather than immediate antibiotics) because they recognised health professionals' greater knowledge of conjunctivitis.

'If the GP had said oh keep up the salt water baths, that will do the trick then I'd have accepted that, because I had a salt water bath, I got that from the chemist and it made it feel better. No no I don't, I don't sort of feel that the doctor isn't doing his or her job if they don't prescribe some 'goo' for the problem I think reassurance is just as important as uh a prescription really' (pt13p12)

Participants favoured the delayed prescription strategy because it might enable them to avoid medication and the perceived inconvenience of arranging a further appointment if the condition failed to resolve. Bathing the eye (e.g. with cooled boiled water) was seen as *'doing something'* and was more acceptable than just 'a wait and see' approach. Patients felt confident that they could decide when to start a delayed prescription and when and if to seek further medical advice.

'I would have been happy with that (a delayed prescription approach), *I'd have been quite, well if they'd said, well, go back home and bathe it , we'll try another couple of days just with the boiled water and then if that doesn't clear up come back for some ointment, I would have gone with that' (pt10p8)*

'if the doctor had said to me yes I think the best form of treatment for this is to use an antibiotic cream for a few days then fine I'm happy with that. Um, if he thinks that is truly the best way of treating it, if however he had said "look lets give it 2 or 3 days, washing it and cleaning up and if there's not an improvement come back I'd have been happy to do that equally yes' (pt11p5)

Regarding no prescription versus a delayed prescription strategy: *'I would have felt happier having a prescription to fall back on otherwise, 'cause otherwise, you have got the inconvenience of trying to get down there again and then you know, which is it, doesn't sound like it should be an inconvenience but it, you know I think that I'd have to go down again with him, I think that would have, I would have been happier doing that. I think it would have made more sense to me to know that I would have the integrity not to use it if I didn't need it.' (pt17p10)*

4.8.3.5: Theme 5 - Information wants and needs

4.8.3.5.1: Knowledge about Conjunctivitis

Patients did not feel knowledgeable about conjunctivitis. However they felt that they knew enough to manage the condition (i.e. recognise conjunctivitis and attend to receive treatment) and so did not seek or particularly want more information.

I don't really know much at all, just think I know what it looks like and how to get it treated. I would never leave it' (pt17p5)

'I've got enough knowledge to feel satisfied that it's not a threat .... but no I don't have a deep knowledge' (pt5p8)

Some were even unaware that the treatment they had been given contained an antibiotic.

Despite not seeking more information, all participants said they would have accepted and read a patient information leaflet on conjunctivitis.

'Yes I would read it yes I would pick up a leaflet if I find something relevant to what I've had or whatever, but I've never seen one on conjunctivitis' (pt14p7)

4.8.3.5.2: Response to a patient information leaflet on conjunctivitis

Later participants who were shown the draft patient information leaflet on conjunctivitis were positive:

'I felt it had quite a good flow to it , reading it. All the information was in the right order' (pt10p11)

'I think it covers everything that you need to know' (pt11p8) 'I think if that was in the GP surgery you'd find nearly every parent would take one'

'I think it explains it quite nicely actually, I wish I had seen one of these before (laughs)' (pt14p10)

They identified the self-limiting nature of conjunctivitis as the most useful information in the leaflet. Most participants found this surprising and said it altered their thoughts about conjunctivitis and how they would deal with it in the future. After reading the leaflet, most stated a preference to try and self care for the condition and 'wait and see' if it would clear for a few days before seeking medical help. Also, most felt that they would prefer not to use topical antibiotics even if the symptoms may last a few more days.

'... ... that's good to see that it actually, it doesn't damage the eyes in any way, is the first thing that's good to see, um the other thing is, well it's obvious now I that I read this that I shouldn't have panicked really and taken him down to the doctors I should have seen if it cleared up within two to three days, um so you know that's quite nice to know. I don't know where I got this 'get it down the doctors and get it treated straight away' from' (pt17p11)

4.8.3.6: Theme 6 – Different responses to conjunctivitis for oneself and ones' child

Eleven participants were parents who consulted for their child with conjunctivitis. They perceived a difference in their responses when their child rather than they themselves were affected. In general they said they would consult more quickly and ask more questions for their child because they felt parental responsibility and perceived that children are still developing (and thus may be more affected by conjunctivitis).

'.....being a mum.. for children's illnesses I think you need to know more because it does worry you more, just having a little bit of information can put your mind at ease'.. 'you don't tend to worry about your own health but you do for children because they don't sort of see themselves as being ill, they know they're ill but they don't know what to do about it so it's up to you to sort of look after them and know what's best for them.' (pt8p14)

'... the only reason that I went so soon really was because it was him' .. 'I just wanted to make sure that I was doing the right thing' (pt10p9)

'I suppose because they're still developing and you're not quite sure whether they can react to it in the same way and so I seek more of a professional advice for them' (pt8p7)

I also explored the possibility that concern about contagion and school/nursery attendance influenced parents' views.

Parents perceived conjunctivitis to be contagious and implemented simple hygiene measures (eg hand washing and separate towels).

'I do know it's contagious, very contagious.... 'he had his own towel and face cloth..... and he had 2 days off school with it' (pt3p4)

'I just did preventative things in terms of keeping her flannels and towels very separate and washing hands and that sort of thing' (pt19p1)

Parents said some schools excluded children with sticky eyes (and advised parents to seek a medical opinion) whereas others did not. (Current Health Protection Agency guidance for schools and nurseries is that no exclusion is required)[95]. However, for most parents, contagion and school attendance were not seen as major influences in seeking treatment. More important was the belief that conjunctivitis would not clear without treatment (see quotes 4.8.3.1.2 Conjunctivitis – a minor illness that requires treatment).

In general, parents were unhappy to give their children medicines unless it was really necessary (see 4.8.3.2 Perceptions of Medicines). Once aware of the self-limiting nature of conjunctivitis, their response was the same as the adult patients. Most stated a preference to *'wait and see'* and try bathing the eye before seeking treatment in the future - even if this resulted in a few more days of symptoms and time off school/nursery. Parents did not feel that potential childcare difficulties would influence this preference.

'I couldn't go back to work for some days because my childminder couldn't accept him because she couldn't let it pass on to other children, so I ended up staying at home' (HE: Is that a problem staying off work?) *No, they are really good, I mean, if I phone up and say I can't come in ... that's fine... I just book it in as a carers leave day... ' (pt21p9)*

One parent made a distinction between her children for her response to conjunctivitis (see below), feeling it was important her older son (10 years) avoided missing school and so she said she would seek an urgent appointment for him, where as she would prefer to 'wait and see' for her five year old.

'That (how quickly to seek medical advice) *would depend on which child it is, because my eldest son is due to start senior school and I think that is quite important, so I would prefer to get him checked out quicker'...'I mean at the moment he is doing lots of SATs practice and stuff' (pt14p10)*

4.9: Discussion

4.9.1: Background

This qualitative work provides useful information on the patients' perspective of acute infective conjunctivitis, an area on which there has been no previous research. It also contributes to the evidence on the management of minor illness and patients' information needs[37;60;64;72;96]. It highlights the importance of information sharing in the consultation, problems of medicalisation[37;57;58] and the potential usefulness of delayed prescription strategies[37;66;67] (see below 4.9.3 'Relationship of this work to the existing literature'). It has aided the development of a patient information leaflet for acute infective conjunctivitis and informed the development of the randomised controlled trial of management strategies for conjunctivitis.

4.9.2: Limitations of the study

Every effort was made to ensure a rigorously conducted study. I was inexperienced in qualitative research and so I undertook reading and courses in qualitative methods and was supervised by an experienced qualitative researcher to ensure I conducted the research in a suitable manner. I used the principles of Grounded theory and constant comparison to maximise validity and reliability[85].

I am used to talking to patients as a practicing GP. However qualitative interviewing is a different skill and I am unlikely to have been as proficient as experienced researchers. I believe I managed to undertake active listening well, and my interviewing skills improved during the course of the study, but nevertheless I found it more difficult to follow up all of the participants leads. The constant comparison technique and iterative nature of the study was helpful as it allowed me to reflect on the interviews already undertaken and explore emerging themes in subsequent interviews.

Recruitment was by health professionals (GPs and Practice nurses), no information is available for non-recruits, thus the study population could be biased to the patients that health providers felt would be willing participants. It is also biased to people with the time and inclination to participate in this type of research. This group may hold different views to the general population. I did however attempt to gain as wide a range of views as possible by constructing a maximal variety sample from 3 different types of practice (see 4.5: Method). This enabled a wide range of participants to be included in the study. However all participants were white British and they came from relatively less deprived areas than the general population and this may affect the transferability of the results.

All participants were attenders at the GP surgery for conjunctivitis. This group may be different from those who do not attend. For instance, it is likely that some individuals self-care for acute infective conjunctivitis and do not seek medical help. However, there is a benefit from interviewing attenders as it accesses the views of those utilising the health service for conjunctivitis. Researching this group provides relevant information for GPs and practice nurses to apply to their clinical practice.

All interviews occurred after the consultation. This could have influenced participants' views. For instance they may be more confident with their ability to self diagnose acute infective conjunctivitis when it had been confirmed by a medical professional than they would have been prior to the consultation.

My background as a general practitioner and the reading I undertook for the literature review is likely to have influenced the way I interacted with the participants' and interpreted their responses. My starting position was that little was known about participants ideas about acute infective conjunctivitis and that a greater understanding of this could enhance the doctor/patient relationship and patient care. I was keen for participants to tell of their experiences in their own words and I tried to follow up the leads they gave on their ideas, beliefs and concerns. However, a non-medical person may have followed up different leads from the participants and come to different conclusions when analysing the data. I attempted to reduce bias in the participants' responses by introducing myself as a researcher from the university rather than a doctor, by being as objective as possible when interpreting the data and by reviewing the data and emerging concepts with my supervisor (an experienced qualitative researcher).

4.9.3: Relation of this work to the existing literature

4.9.3.1: Consultation for minor illness

Previous research has found that seeking medical advice for minor illness depends on many factors including: the severity of the symptoms[59], the perceived serious of the condition[59-61], the illnesses impact on the patient's life[59], the potential treatments available[62], patients' expectations and the patient's perception of their ability to self-care for the condition[60;61].

This research reveals that patients who present with acute infective conjunctivitis do not perceive it as a serious condition. It has little impact on the patients' life. However, patients consult because they do not think that it will clear up without treatment, and some are worried that it might get worse. They do not feel they can self care for the condition, they believe they require treatment. This belief is reinforced by family and social networks. Many of the

participants had consulted family, friends, school or pharmacies and had been advised to seek urgent medical attention for treatment. Social networks have been found to be important influences in health care seeking behaviour in other studies[94;97;98]. Past experience of the condition and of receiving treatment from the GP for past episodes of conjunctivitis (learned help-seeking behaviour[98]) also influenced participants' decisions to seek medical help. Thus it appears that this minor self-limiting condition has been subject to medicalisation[37;58].

Patients also found it acceptable to see a practice nurse – a strategy identified as effective for other minor illnesses[99;100].

4.9.3.2: Information needs

Inadequate information sharing between GPs and patients has been highlighted as central to patients' problems in coping with minor illnesses[60;64;96]. The difficulties include limited time for information sharing during urgent appointments and the lack of incentive for GPs to do so if patients appear content with the treatment offered. This study highlights that although patients did not seek (or express a want for) more information on conjunctivitis, they in fact had an information need. They were unaware of the self-limiting nature of conjunctivitis and thus the potential for self-care. So despite their wishes - not to take medication if possible - they were seeking and receiving medication.

Providing patients with information – most importantly regarding the self-limiting nature of conjunctivitis - altered the way they thought they would manage conjunctivitis in the future. They said it reduced their desire for an urgent appointment, and topical antibiotics and increased their desire to self-care for conjunctivitis, even if this resulted in a few more days of symptoms. This suggests that providing information may increase self-management and reduce consultation and prescription rates for conjunctivitis (as has been found in studies of other minor illnesses[37;68;69]). Also it would enable patients to behave in a way that is consistent with their stated desires of avoiding the use of medication.

A patient information leaflet is a potential way of offering this information[69]. Information leaflets regarding minor illness have had variable success in past trials (see literature review 2.5.5). Some studies have shown that leaflets reduce reconsultation rates[101] but others showed no effect[72;73].

In general it seems that leaflets are most helpful if given in of context of the consultation for a particular complaint[68]. The feedback from my leaflet was positive and patients stated it changed their *'attitudes'*. I will assess the effect of the patient information leaflet on patients'

attitudes to attending the surgery with acute infective conjunctivitis in the future and their perception of the efficacy of antibiotics in the randomised controlled trial (Chapter 5).

4.9.3.3: A delayed prescription strategy for conjunctivitis

Patients perceived a delayed prescription as a good way of managing conjunctivitis. It may allow them to avoid medication and it avoids the inconvenience of arranging another appointment if symptoms are not resolving. They were happy to make the decision whether or not to start the medication. I will trial a delayed prescription approach[66;67] (which has been used successfully for sore throat[37]) in the randomised controlled trial (Chapter 5).

4.10: Conclusion

This study is the first to research the patients' perspective of acute infective conjunctivitis. It reveals that most patients are confident in recognising conjunctivitis and present for treatment because they are unaware of it self-limiting nature. Patients said they prefer not to take medication, and when informed that conjunctivitis is self-limiting, most said they would choose to wait a few days to see if it improved before seeking medical advice, even if this resulted in a few more days of symptoms.

Providing information on the self-limiting nature of acute infective conjunctivitis may increase self care and reduce the demand for urgent GP appointments. The patient information leaflet developed during this study will be trialled in the randomised controlled trial (Chapter 5).

Patients welcomed a delayed prescription strategy for acute infective conjunctivitis. This could prove a useful management strategy as it may reduce unnecessary treatment and encourage self care for future episodes of conjunctivitis.

Chapter 5: Randomised controlled trial of management strategies for acute infective conjunctivitis in general practice

5.1: Introduction

The literature review revealed a lack of evidence for the current management of acute infective conjunctivitis (see Chapter 2). I undertook this trial to help clarify the most appropriate way to mange acute infective conjunctivitis in general practice. Information collected from the GP survey (Chapter 3) and the Qualitative Study (Chapter 4) was used to inform the development of the trial.

5.2: Ethical Considerations and the Research Governance

Full ethical approval for the trial was obtained from the relevant ethical committees, Southampton and SW Hampshire LREC no. 267/99, Portsmouth and SE Hampshire LREC no. 09/99/894, Salisbury LREC no. SA 27/99 and Dorset LREC no. 46/03/S.

As discussed in the Ethical considerations section for the qualitative study, I adhered to the principals of the 'The Research Governance Framework for Health and Social Care'[102] published in 2001 when conducting the trial.

I used the principles from the MRCs Guidelines for Good Clinical Practice in Clinical Trials 1998[103] for the management of the trial. I did not initially have a Trial Steering Committee to oversee the trial but instituted one in 2003 just over half way through the trial to ensure the trial complied with the principals of Good Research Governance.

The Trial was registered with the International Standard Randomised Controlled Trial Register by the MRC in Jan 2003. Trial Registration no: ISRCTN32956955.

As PCTs (Primary Care Trusts) developed Research Governance roles I contacted the PCTs of GPs and Practice Nurses who were recruiting patients for the trial and provided them with information on the trial. As required by the PCTs, I obtained an Honorary Research Contract with one of the participating PCTs (New Forest PCT).

When the EU Directive on Clinical Trails was published and then brought into force in May 2004 I followed MRC guidelines on implementing the directive[104]. I contacted the Medicines and Healthcare products Regulatory Agency (MHRA)[105] and obtained the required paperwork for using chloramphenicol eye drops in a trial setting. I also arranged for the School of Medicine to act as Sponsor for the trial.

I applied for Adhoc funding from the Department of Health to be able to reimburse GPs for the extra time taken to recruit patients to the trial. This was granted for £3,300 in total (ie £10

per patient recruited). Normally a consultation regarding conjunctivitis takes a very short time (often less than 5 minutes) and GPs sometimes see it as a 'catch up' appointment where they can make up time if they are running late. However recruiting a patient takes 10 to 15 minutes and so it impacts on their surgery time. The GPs were sent a cheque quarterly, £10 for each patient recruited. Some put the money into practice funds, some kept it for themselves and others gave it to charity. I do not believe that the £10 per a patient was a great incentive to GPs to participate in the trial but feel it at least acknowledged that they were undertaking additional work load to help with the trial.

5.3 Rationale for a factorial open randomised controlled trial

Although observational studies can give estimates of treatment that are similar to randomised trials, the randomised controlled trial is the most powerful way to assess differences between treatments since it can control for confounding – both known and unknown[106;107]. Double blind trials give the best evidence for efficacy by controlling the placebo effect but the behaviour and perceptions of patients and doctors may not be generalisable to a normal clinical setting. Open trials more closely approximate everyday practice and thus can provide important evidence of effectiveness. They are essential when outcome measures include patients' perceptions and choices in response to different strategies, for example, whether "delayed" prescriptions are collected, the perceived efficacy of antibiotics, or the likelihood of future attendance when symptoms have resolved without treatment[44]. The main disadvantage of using an open approach is the possibility of bias due to the placebo effect. However it has been shown in previous trials[44;45] that the use of structured advice packages enable the general practitioner to support each proposed strategy and function as the placebo in each group (see Method for further information on the advice packages). This type of open randomised controlled trial design has been used successfully to research antibiotic prescribing in sore throat, otitis media and cough within this research department[44-46].

A factorial design[107;108] was chosen for the trial because it has the major advantage of enabling a number of possible management strategies to be assessed at the same time, ie issues relevant to medicalisation and self management (antibiotic strategies, patient information, microbiological testing). Montgomery et al in their paper[108] on the design, analysis and presentation of factorial trials describe the advantages of factorial trials over the standard parallel-groups design: '(factorial trials) enable efficient simultaneous investigation of two (or more) investigations by including all participants in the analyses'. Thus the sample size is smaller than would otherwise be required. The main disadvantage of a factorial trial is that

unless it is specifically powered to assess interactions between the strategies (which can involve a prohibitively high sample size), moderate interactions can be missed. The investigation of the interactions is a secondary analysis and may have poor precision[108]. Thus, the possibility of undetected interactions must be considered when drawing conclusions from the trial.

5.4: Trial Design

A 3x2x2 factorial design was chosen to enable assessment of the effect of antibiotic prescription, a patient information leaflet and of performing eye swabs.

See the literature review – 2.5: Potential management strategies for acute infective conjunctivitis – for more information on the current research evidence behind the potential strategies.

The patients were randomised to receiving one of 3 treatments:

1) Immediate topical antibiotic eye drops (Chloramphenicol eye drops).
2) No antibiotic prescription.
3) A delayed prescription of antibiotic eye drops (to be collected from the surgery at the parents' or patients' discretion after three days).

As discussed in the literature review (and confirmed by the GP survey[19]) the most commonly used management strategy for acute infective conjunctivitis in general practice is a prescription for immediate topical antibiotics (topical chloramphenicol eye drops are most often prescribed in the UK). Thus any trial must compare other potential management options to this. An alternative option for managing a minor self-limiting illness is no prescription. Probably only half of the cases of acute infective conjunctivitis that present to general practice are bacterial in origin[14] and thus have the potential to respond to antibiotics. The Cochrane review[6] for acute bacterial conjunctivitis revealed that 64% of cases of confirmed acute bacterial conjunctivitis resolve by day 2-5 without treatment. Thus I decided to include a no prescription group was in the trial.

The delayed prescription approach has been shown to be successful and acceptable to patients for other minor self-limiting illnesses[44;45] and patients interviewed in the qualitative study[109] supported this as a possible management option. It has the potential to reduce the unnecessary use of antibiotics and reduce medicalisation of self-limiting illnesses[37]. Thus it was included in the trial. A decision was required as to how long the delay should be before the patient collected the prescription. Three days was chosen because, according to the literature[6], there

was a reasonable likelihood that some cases of conjunctivitis may have settled by that time but it was not too long a time to ask the patients to wait for treatment if they still had symptoms.

The patients were also randomised to receive a patient information leaflet (developed in the qualitative part of this study – see 'Development of the patient information leaflet' Section 4.6, Appendix 4) or not to receive a leaflet. The leaflet was handed to the patient in the GP consultation for them to read and take home. Leaflets can provide patients with relevant information and have been shown to be able to change consulting behaviour in some studies (see the Literature review 2.5.3 for discussion of the use of patient information leaflets).

The final component of the factorial design was randomisation to have an eye swab sent for culture, or not to have an eye swab. Those that had swabs taken would provide microbiological information about the cohort. Determination of the proportion of acute infective conjunctivitis cases that have a bacterial aetiology in the general practice setting would enable an assessment of the proportion of patients that could potentially benefit from antibiotic prescription. Viral culture is technically more difficult and more expensive than bacterial culture and thus was not within the scope of this study.

The reason for performing the swabs in only half the participants was to assess whether taking a swab had an effect on participants' beliefs in the need to seek medical advice for future episodes of conjunctivitis. It may be that performing a test (eye swab) has a medicalising effect on participants and encourages them to feel they need to attend for medical advice.

Summary of the randomisation:

Thus, in total there were 12 groups that the participants were randomised to:

Group 1	Immediate topical antibiotics, no eye swab, no patient information leaflet
Group 2	Delayed topical antibiotics, no eye swab, no patient information leaflet
Group 3	No antibiotics, no eye swab, no patient information leaflet
Group 4	Immediate topical antibiotics, eye swab, no patient information sheet
Group 5	Delayed topical antibiotics, eye swab, no patient information sheet
Group 6	No topical antibiotics, eye swab, no patient information sheet
Group 7	Immediate antibiotics, eye swab, patient information sheet
Group 8	Delayed topical antibiotics, eye swab, patient information sheet
Group 9	No topical antibiotics, eye swab, patient information sheet
Group 10	Immediate topical antibiotics, no eye swab, patient information sheet
Group 11	Delayed topical antibiotics, no eye swab, patient information sheet
Group 12	No topical antibiotics, no eye swab, patient information sheet

Also see the trial consort diagram (Figure 3)

5.5: Outcome measures

The proposed outcome measures were duration and severity of symptoms, satisfaction and compliance with the treatment, use of antibiotics, perceived efficacy of antibiotics and perceived importance of seeing the doctor.

After discussions with the Trial Steering Committee, 3 main outcome measures were agreed on: Duration of moderate symptoms, severity score for the first 3 days of symptoms and belief in the efficacy of antibiotics for acute infective conjunctivitis (see below 5.6: Sample size calculation for further information).

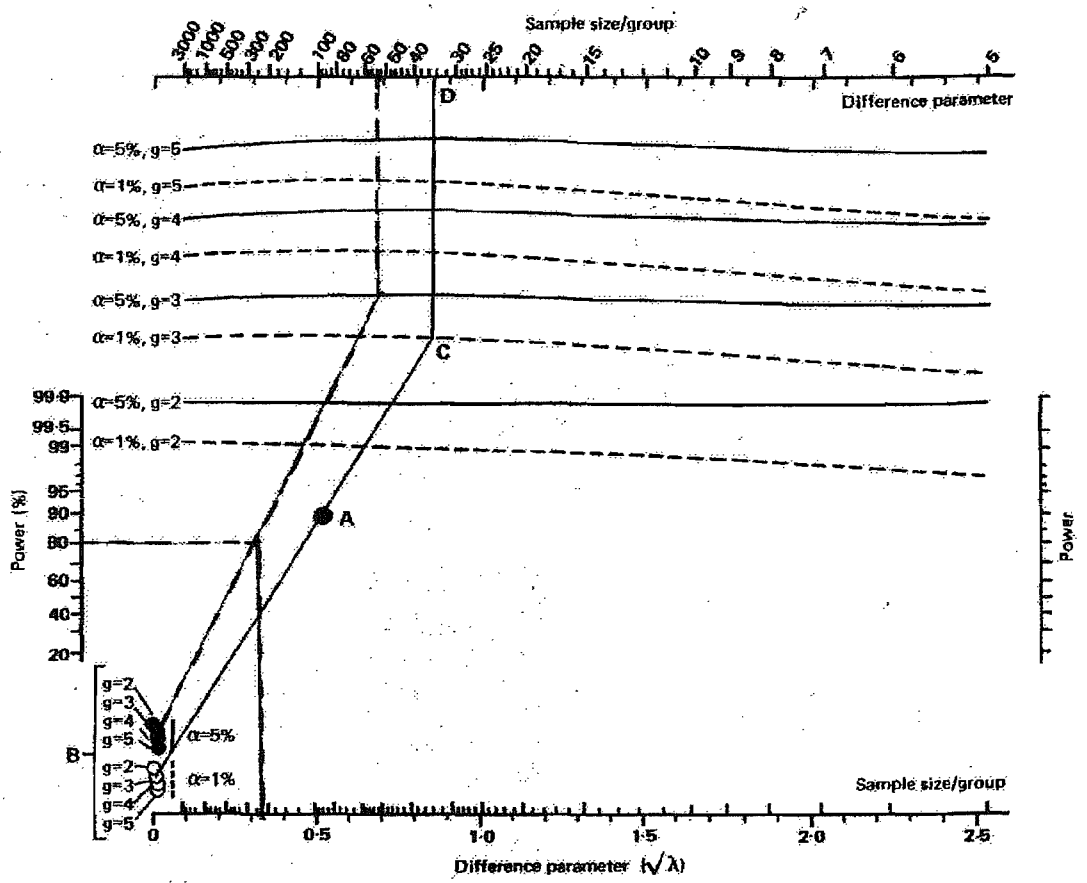
5.6: Sample size calculation

The initial sample size calculation estimated that 204 patients would be required to detect a one day difference in symptom resolution and a 25% difference in belief in antibiotics[44] for 80% power and 5% level of significance. This was based on the estimate that symptoms would settle on average by 5 to 6 days (Standard Deviation (SD) 3) and assumed a one day difference between resolution between the groups (No Antibiotics = 6 days, Delayed prescription = 5 days, Immediate Antibiotics = 4 days). These figures were based on data from previous trials[6]. The sample size allowed for a 20% loss to follow-up based on previous studies[44]. It also assumed no interactions between prescribing strategies, receiving a leaflet and the effect of performing an eye swab. Calculation was by nomogram for multiple groups in a factorial trial[110] for the symptom resolution (see Figure 1 below) and Spida 1.6 version computer package for the belief in antibiotics.

As there was limited previous research data on which to base the estimates it was felt prudent to undertake an interim sample size calculation part way through the trial.

A target for recruitment of 300 patients was determined to allow for some leeway in the assumptions and to possibly enable assessment of potential subgroups from secondary analysis (e.g. based on severity of symptoms on day 1).

5.6.1: Figure 1: Nomogram for comparing up to five independent samples. (Reproduced with the permission of the BMJ from 'Sample size and power for comparing two or more treatment groups in clinical trials' Day, S.J. and Graham, D. F., Br Med J 1989;299:663-5.)



Nomogram for comparing up to five independent samples (g=number of groups) of continuous variable relating power, group sample size, difference parameter (√λ), and significance (α). Points (A-D) relate to determining sample size required to show difference between means of 85, 95, and 100 mm Hg with standard deviation 15 mm Hg (√λ=0·509) at 1% significance with 90% power (see text for details)

For 3 groups (immediate, delayed and no offer of antibiotics) for 80% power and 5% level of significance with a difference parameter of 0.33, the nomogram showed a required sample size of 54 per group (hashed line added on to nomogram). Assuming an 80% response rate, 68 would be needed per group or 204 in total.

Interim sample size calculation

The required sample size was recalculated part way through the trial, when 200 patients had been recruited. Data was available on symptom duration and severity for the entire sample but was not divided by treatment received. This data revealed a mean of 6.3 days of symptoms (SD 3.57) until all symptoms were scored as very little or no problem. Assuming 1 days difference between groups (i.e. 7.3, 6.3, 5.3 days) this would require a sample size of 64

patients for each treatment group or 240 in total for 80% power and 5% significance (including the 20% loss to follow up).

Discussion with the Trial Steering Committee regarding the best principal outcomes for the study resulted in further calculations of sample sizes for the duration of moderate symptoms and severity of symptoms in the first three days.

The discussions resulted in the adoption of 3 principle outcomes all at a significance level of 1% which resulted in the following sample size calculations:

1) Duration moderate symptoms (a day between each group) – sample size 234.

The mean number of days of moderate symptoms after seeing the Dr /Nurse was 3.75 days (SD 3.06) This very skewed data required transformation to enable a sample size calculation. Some values were zero so log transforming was not appropriate, but the square root transformation of this variable was suitable: mean 1.76 (SD 0.81). Transforming back from square roots gave information on the difference in days to moderate symptom resolution that could be detected. To detect a difference of 1 day of moderate symptoms required detection of square root means of 1.45, 1.76 and 2.02 (squared means = 2.10,3.09,4.08 i.e. roughly a day between each), this required 150 in total for a 5% level of significance and 234 for 1% significance.

2) Severity of symptoms (0.33 between each group) – sample size 264.

Patients have the worst symptoms in the few days after seeing the doctor. Taking the mean of days 1 to 3 for each symptom, factor analysis suggested that 5 symptoms loaded strongly onto one factor, with power 80% and a mean item score of 2.3 (i.e. on average at least one symptom rated a moderate problem), SD 1.03.

An effect size of 0.66 is equivalent to more than half items being rated a slight rather than a moderate problem (a similar effect size was agreed by the Trial Steering Committee of the MRC cough trial). To detect a difference of 0.66 (the delayed prescription group 0.33 lower and the immediate antibiotic group 0.66 lower than the no Antibiotic group) requires 48 per group or 180 in total, for a significance level of 1% 264 are needed.

3) Beliefs in antibiotics (15% difference between each group) – sample size 246.

Assuming beliefs in the importance of antibiotics correspond to previous studies[37;44] (85% Immediate antibiotic group, 70% Delayed antibiotic group , 55% No Antibiotic group) then 36 per group are required or 138 in total for a 5% level significance. For 1% significance 198 are

needed. If the percentage believing in the importance in antibiotics is evenly spaced (85%, 70%, 55%) for a significance level of 1% the sample size is 246.

Thus, after the interim sample size calculations, a minimum sample size of at least 264 was agreed on with the MRC Steering Committee for the trial.

5.7: Study Group

Patients aged one year and over, presenting with presumed acute infective conjunctivitis (red, inflamed discharging eyes) to their general practitioner or practice nurse were included in the trial. There was no upper age limit. Infants under one year were excluded to avoid those with ophthamia neonatorium or blocked tear ducts. The plan was to include as large a proportion of those that present to general practice as was practical.

Exclusions were patients who were systemically unwell and required oral antibiotics, patients who had received antibiotics in the previous 2 weeks, patients with chronic infective eye disease eg blepharitis, patients who had recently had eye surgery (ie in the last month) and those who were known to be allergic to chloramphenicol. These exclusions only involve a small proportion of those presenting to general practice, thus the results should be generalisable to majority of patients that present to GPs.

5.8: Method

5.8.1: GP and Practice nurse recruitment

The literature review suggested that a full time GP would see a case of acute infective conjunctivitis approximately once a week[1-4]. However, with Practice nurses undertaking minor illness clinics in some surgeries, I could not be sure how many potential trial participants each GP or Practice Nurse would see. Information from recruitment from previous similar trials[44;45] suggested that only a small proportion (20 to 30%) of GPs or Practice nurses who agreed to try and recruit would ever actually recruit a patient and that many of these would only recruit one or two patients. Based on previous studies from the Southampton group, I estimated that recruitment of between 50 and 100 GPs or Practice Nurses was a reasonable target throughout the life of the trial.

I contacted general practitioners on the Health Authority lists in the Southampton, Portsmouth and Salisbury areas by letter to ask if they would like to participate in the trial. They returned a reply slip if they would like more information. I then arranged a meeting at the practice to discuss the trial further and show them the trial paperwork. In some practices all the partners

and practice nurses were interested in attending the meeting but more commonly just one or two GPs or nurses from a practice wished to be involved. Each meeting took 20 to 40 minutes. Nearly all of the GPs visited agreed to try and recruit patients for the trial and I provided them with a small number of recruitment packs (3 to 4 per GP) to keep in their consulting room and open if they saw a patient with acute infective conjunctivitis. As packs were used I sent out more by post. I also sent quarterly update letters about the trial progress to GPs to remind them about the trial and try and encourage them to recruit patients.

To try and collect some data on patients not entering the trial, I provided each GP with a 'Not Entered Book' to fill in brief details of those not entered (age, sex, the reason for not entering the trial and the severity of conjunctivitis - see Appendix 9). I collected these books at the end of the trial to explore any differences between those entered and not entered.

5.8.2: Patient Recruitment and Randomisation

Patients were recruited opportunistically by GPs and Practice Nurses when they presented to general practice. Patients were asked if they were prepared to participate in "study looking at how quickly eye infections settle". If they were willing to participate they received the patient information sheet about the trial (see Appendix 6). If they were still happy to participate after reading the patient information sheet, they were asked to sign the consent form (Appendix 7). Parents gave consent for children under 16yrs, for those aged 12 to 16yrs both parental and child written consent was obtained. To minimise contamination between the groups, general practitioners were asked not to discuss the efficacy of antibiotics before randomisation. Randomisation occurred during the consultation by the general practitioner opening a numbered sealed opaque envelope (a recruitment pack) containing one of the twelve randomised advice package sheets (see Appendix 11). This method of randomisation only works well if the recruiting GP/nurse has equipoise – hence the importance of robust information and agreement at the practice recruiting stage. The method was used successfully with no evidence of selection bias in previous studies undertaken in this research department [44;45]. Block randomisation (block size of 12) was used to ensure equal sample sizes in each group.

The GP used the advice sheet to provide the patient with the structured advice package including the designated treatment. Each advice sheet had boxes to tick once the statement had been read or explained. This was a pragmatic trial and if the patient requested a different treatment from that they were randomised to, the GP was able to provide the treatment (eg immediate rather than delayed antibiotics). The GP noted on the advice sheet if this was the

case and the patient continued in the trial. Their results were analysed on an intention to treat basis – as described in the data analysis section (Section 5.9).

5.8.3: Trial Documentation and Procedure

5.8.3.1: Introduction

Each Trial pack contained a patient information sheet and consent form, one of the twelve randomised advice package sheets, a patient information leaflet (if appropriate), eye swab documentation (if appropriate), a GP clinical signs sheet and a freepost return envelope. Additionally, each pack contained another envelope that was to be handed to the patient, containing the patients'diary, patients' questionnaire about eye symptoms and a freepost return envelope (see Appendix for all the documentation). Each pack had a unique identification number that was on every piece of paperwork. I assembled the packs in large batches, using randomisation tables to randomise the advice sheets. GPs and Practice Nurses were initially given 3 to 4 packs to have in their consulting room. As these were used I re-supplied them with further packs by post.

Each GP/practice received an index card box to keep in reception to hold the scripts from the delayed prescription strategy group.

After patient recruitment, the GP returned the consent form, the advice package sheet and GP clinical signs Sheet, in the freepost envelope provided, to the administrative centre for monitoring. Eye swabs were placed in the normal transport system to go to the microbiology laboratory. The patient took home the envelope containing the questionnaire and diary and they posted them to the administrative centre in the freepost envelope once they were completed.

Patients randomised to immediate antibiotics received a prescription during the consultation to take to a pharmacy to receive their medication. Prescriptions for those in the delayed prescription strategy group were printed off and signed and placed in a box behind reception. These patients were advised that they could return to collect a script for topical antibiotics from reception, if required, but to try and wait three days before doing so.

The trial paperwork and systems were piloted by 5 GPs and Practice Nurses with 10 patients to ensure that there were no technical or administrative problems. A larger pilot was not undertaken because the mechanisms of this trial were so similar to previous trials[44;45] that most of the systems and potential problem areas had already been addressed.

5.8.3.2: Advice packages

The structured advice sheets randomised the patients to their treatment groups and enabled the general practitioner to support each proposed strategy and function as the placebo in each group. They were based on the same format as had been used successfully in previous trials[44;45]. Information collected during the literature review and obtained during the tape recorded interviews (five with general practitioners as part of the GP survey and 25 with patients/parents of patients presenting with acute conjunctivitis as part of the qualitative study) was used to inform the content of the packages.

The proposed packages were also reviewed by three GPs and one Practice Nurse with an interest in minor illness research who had agreed to recruit for the trial.

A standard advice package was developed for each randomisation group (see Appendix 11). Each package had six to nine standard statements supporting the particular strategy including advice to bathe the eyes with cooled boiled water and to return for follow up if symptoms were not resolving or if concerning symptoms such as pain, redness, eyelid swelling or reduced vision were present. The GP or Practice Nurse was asked to document whether the patient had left the consultation with a prescription and to note any additional questions or areas of concern that the patient expressed. The advice package sheet also had a question asking the recruiter how well they thought the patient had accepted the advice strategy. This is important as management strategies that are unpopular with patients are unlikely to be successful outside a trial situation.

5.8.3.3: Patient information leaflet

'Development of the patient information leaflet' (Section 4.6 in the qualitative chapter) describes how the leaflet was developed. (See Appendix 4 for patient information leaflet)

The advice package sheet indicated whether patients should receive a patient information leaflet. Patient information leaflets were included in the recruitment packs for those randomised to receive a leaflet. The GP handed the leaflet to the patient to read and take home. They also checked if the patient had any questions about the content of the leaflet.

5.8.3.4: Eye swabs

Those randomised to have eye swabs taken had the microbiology laboratory paperwork included in the recruitment pack. The eye swabs were not included in the packs as it would have been possible to feel the swab through an unopened pack and thus reveal randomisation. The required swabs were standard charcoal swabs that were available in every GP surgery.

The GP sampled the eye discharge from the most severely affected eye or if there was no visible discharge they rolled the swab along the lower eye lid of the most affected eye. I demonstrated the required swab technique to GPs when they were recruited to the trial. If young children were not compliant with performing the eye swab, it was not taken but they were entered into the trial on an intention to treat basis. The GPs completed the eye swab paperwork and placed the eye swab on the next available transport to the microbiology laboratory. The swab was stored at room temperature.

Microbiological laboratories in the U.K. have standardised procedures for analyzing eye swabs[111]. The research literature investigating acute bacterial conjunctivitis reveals a number of methods for analyzing eye swabs but the Cagle and Abshire method[24] or modifications of this, are the most prominent. This method is quite similar to the standardised laboratory procedures undertaken in the local microbiology laboratories. I took advice from the microbiological consultant and the head of the microbiology laboratory in Southampton to finalise the eye swab protocol for the trial (see Appendix 8 for the protocol).

To maximise consistency in eye swab analysis I used just one laboratory to analyze the specimens despite the fact that recruitment was occurring from a wide geographical area. There was good transport between the laboratories in the study area so most swabs were able to reach the laboratory for analysis on the same day as they were taken. However, it was not normally possible to analyse eye swabs within a suitable time frame for patients recruited on a Friday afternoon surgery because of transport difficulties. This would also have been the case if local laboratories were used.

The staff at Southampton microbiology laboratory used the trial eye swab protocol procedures to analyse the swabs and then forwarded the results to the administrative centre. Eye swabs are not routinely performed for conjunctivitis, so I gave the recruiting clinicians the option of whether they would like a copy of the results sent to them. Most did so and they were free to act on any results received if they felt it was clinically appropriate. Information on any further treatment the GP initiated was picked up on the notes review at the end of the trial.

5.8.3.5: GP Clinical Signs Sheet

The general practitioners completed the clinical signs sheet during the consultation. (Appendix 10). The clinical signs sheet gathered information on the duration of the eye infection, which eye was affected, physical signs, and whether they though the infection was viral or bacterial and their confidence with the diagnosis.

The sheet was based on one devised by Dr Aziz Sheikh who conducted the Cochrane Systematic Review for Acute Bacterial Conjunctivitis[6]. We planned to collect the same information so that it would be comparable if we went on to develop a symptom scoring system to try and discriminate between viral and bacterial conjunctivitis. The signs and symptoms on the sheet were based on information on diagnosis of acute infective conjunctivitis gathered during the literature review. The GPs were asked to score the severity of the clinical signs: conjunctival injection, conjunctival oedema, subconjunctival haemorrhage and eye discharge on a 0 to 6 scale (0 = normal, 6 = as severe as it could be).

5.8.3.6: Patient Questionnaire

The Patient Questionnaire about eye infections (Appendix 12) was designed to collect baseline data on the signs and symptoms of the eye infection from the patients' perspective. Development of the questionnaire was based on information from the literature review and the qualitative study. Patients were asked to score the severity of their symptoms and signs on a 0 to 6 scale in the same way as was required for the patient diary. It enabled information to be collected on many symptoms and on the use of home remedies and previous eye infections without requiring more time during the medical consultation.

5.8.3.7: Patient Diary

The patient diary (Appendix 13) was based on a previously validated diary devised by this research department for similar trials on sore throat[44] and cough[45] which have been shown to have good reliability, criterion validity and sensitivity to change. Information gathered from the literature review, the GP survey and the qualitative study was used to inform the development of the diary. The symptoms scored in the diary: ie red eye, eye discomfort or itchiness, waking with a sticky eye, eye discharge during the day, eye lid swelling, altered vision and how unwell the participant felt, were a combination of the signs and symptoms used to diagnose acute infective conjunctivitis, to discriminate it from other conditions and the symptoms that patients felt were important to them. Patients were asked to score their symptoms on a 0 to 6 scale (0 = normal, 6 = as severe as it could be).

Further validation of the dairy specific to this trial was planned by comparing the symptom scores to the MYMOP[112] symptom scoring system. Unfortunately there were logistical problems with contacting patients quickly enough to enable comparison of symptom resolution between the diary and MYMOP so it was not possible to collect this data. A combination of factors contributed to this: time taken for the recruitment information to be

received at the management office (ie time of the information in the post), that acute infective conjunctivitis is a rapidly resolving condition and so the participants' symptoms had frequently resolved by the time I managed to contact them and difficultly getting hold of patients (as they did not take time off work for this condition).

Patients were given the envelope containing the questionnaire about eye infections and the diary at the end of the consultation and asked to open it when they got home and to start filling it in that day. The diary was completed daily to avoid recall bias in the recording of symptom severity. A self-completed questionnaire has advantages over repeated review appointments to gather information on symptom resolution because it reduces the amount of clinician time, administration time, cost and inconvenience to the patient that is required for data collection. It also minimises the bias that could result from a researcher administered questionnaire.

The signs and symptoms of acute infective conjunctivitis are visible and relatively straightforward for a non medical person to assess. The end point of 'no symptoms' should be relatively clear, so the duration of the illness should be able to be documented quite accurately by patients themselves. However, it can be argued that patient scoring of symptoms may not be as objective and reliable as that undertaken by a clinician. A self-completed questionnaire relies on the patients' perception of the severity of their illness. Each individuals' assessment of their symptoms may vary and may be influenced by external factors (such as their confidence with the treatment they receive and family and social pressures). Thus self-completed questionnaire reflects the impact of the symptoms on the patient in the wider context of the patients' life and the management strategies used to treat the illness. Nevertheless, this is arguably the most valid measurement tool for a minor self-limiting illness where it is the patients' perceptions of the illness that determines presentation for medical care, and thus patients' perceptions that should determine illness severity and resolution.

The diary was filled in each day until patients were both free of symptoms and had finished their medication up to a maximum of 2 weeks. In the case of children under 12 years the parent was asked to help complete the diary (as used successfully in previous studied undertaken by this group[44]). Parental recording of child symptoms has been shown to be valid in previous trials[45].

Patients also answered written questions on six point Likert scales (extremely, very, moderately, slightly, not very, not at all) at the beginning of treatment, and at the end of the diary. The initial questions were about worries, satisfaction, and "legitimation" (attending the doctor to explain the illness to others) as used in previous studies[44;45]. Those at the end of the

diary were about other symptoms, antibiotic use, perceived efficacy, future intentions, time off work and school and socio-demographic details.

Within three days of the consultation, patients were contacted by a research assistant to check that there were no problems with filling in the diary. Patients who had not returned their diaries two weeks after entry into the study were reminded to return the dairy by letter or by a telephone call. If the diaries were not returned, they were telephoned to ask for information on symptom resolution. The validity of information gathered by questionnaire and by telephone has been shown to be comparable in this type of trial[44].

5.8.3.8: Post Recruitment Questionnaire

At the end of the study general practitioners were sent a questionnaire asking them to rank a list of reasons for non-recruitment, to comment on whether participating in the trial had influenced their management of acute infective conjunctivitis and for any other comments they had regarding the trial (see Appendix 14).

5.8.4: Review of patients notes

Once the trial had closed to recruitment, the patients' notes were reviewed by me or their recruiting GP or Practice Nurse to check if they had re-attended with acute infective conjunctivitis, suspected conjunctivitis or for Upper Respiratory Tract illnesses (URTI) within 1 year of trial recruitment or in the year before recruitment. Information was collected on the number of attendances, whether they received further treatment and on any referrals to secondary care. This was undertaken to enable assessment of the different management strategies on re-attendance rates. (See Appendix 15 for Notes Review form)

5.9: Data Entry and Analysis

The patient diary was formatted so that it could be scanned for data retrieval. FORMIC was used to design the diary and scan the data. It was then converted to an SPSS or STATA file for analysis. Other information (eg from the GP Clinical Signs Sheet and the patient questionnaire) was hand entered into SPSS files. All hand entered data was double entered. All the data was cleaned and checked for accuracy by looking for unusual and outlying results and by randomly sampling 50 records and checking the SPSS record of the results against the original paper version.

Data analysis

The plan of analysis was agreed with the MRC Trial Steering Committee.

Data were analysed on an intention to treat basis using STATA. Factor analysis was used to determine which symptoms contributed to the symptom severity score; the internal reliability of the score was assessed using Cronbach's alpha statistic. Primary outcome measures (symptom severity score for first 3 days of the diary, duration of moderate symptoms, belief in antibiotics for conjunctivitis) were compared for the different intervention groups. Logistic regression was used for discrete outcomes (i.e. % belief in antibiotics) and multiple regression for continuous outcomes i.e symptom score (multiple linear regression) and duration of symptoms (Poisson regression). Interactions between the intervention variables were assessed, but since no interactions were found the estimates for each factor are presented, mutually controlling for other factors. Potential confounders were also assessed – assessing whether any variable was associated with the randomisation group. Clustering of effect by recruiting GP was also explored (although this effect was minimised by individual rather than practice randomisation, and the use of structured advice packages).

5.10: Results

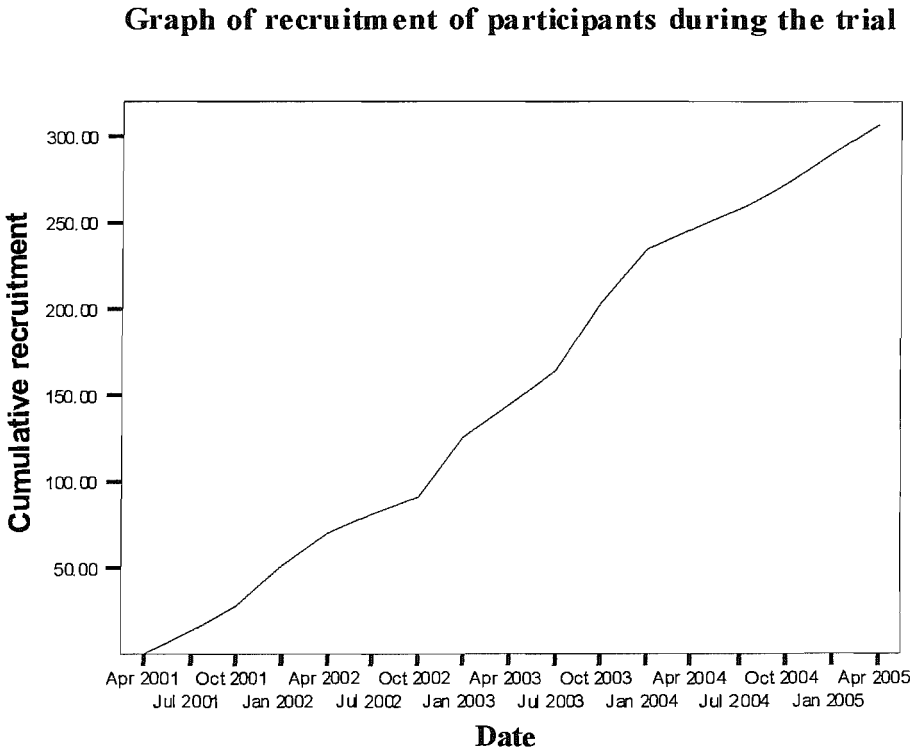
5.10.1: Recruitment

During the study period (April 2001 to April 2005), 307 participants were recruited to the trial. 92 GPs and Practice Nurses from 48 practices agreed to try and recruit patients for the trial. Of these, 38 GPs and Practice Nurses from 30 practices actually ever recruited a patient. The number of patients recruited ranged from one to 52 patients. A small number GPs and Practice Nurses recruited high numbers of patients (15 or more). 66% (203/307) of the participants were recruited by 7 GPs and Practice Nurses.

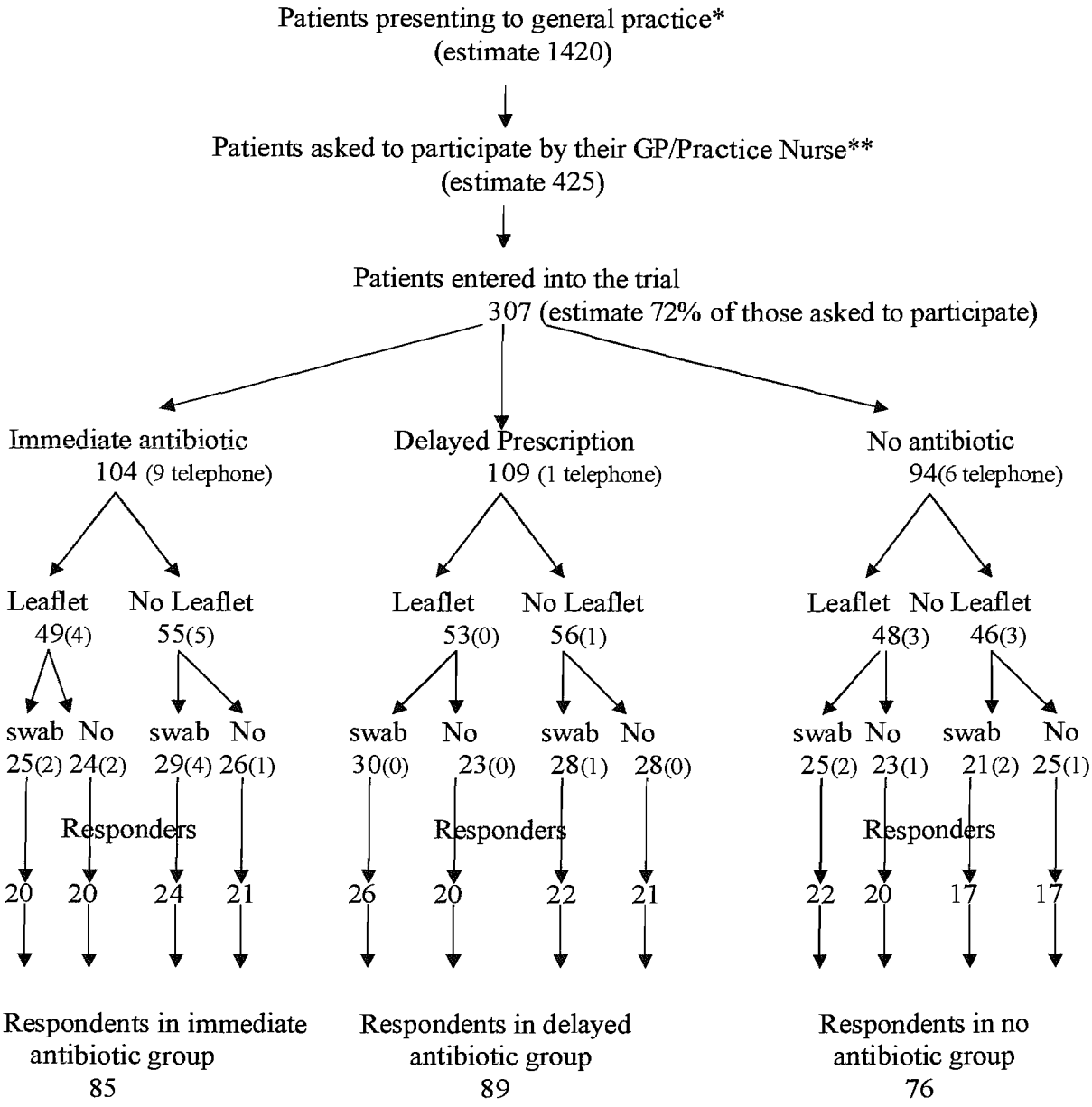
Patient recruitment was fairly steady during the trial period (see 5.10.2: Figure 2: Graph of recruitment (below)). This was achieved by continuing to recruit GPs and Practice nurses during the trial.

Recruitment of 307 participants to the trial with an 80% response rate increases the power of the trial from the original 80% in the sample size calculation, to more than 90% for duration of moderate symptoms, 87% for symptom severity for days 1 to 3, and 89-90% power for belief in the effectiveness of antibiotics.

5.10.2: Figure 2: Graph of recruitment of participants during the trial



5.10.3: Figure 3: Trial Consort Diagram



*The number of patients presenting to general practice was calculated from the number each GP/practice nurse recruited and their estimate of the proportion of patients presenting with acute infective conjunctivitis that they recruited (data collected on the post recruitment questionnaire). **GPs were also asked to record the number of eligible patients they asked who refused to participate.
( ) numbers in brackets indicate telephone response rather than postal return of the diary

5.10.4: Baseline characteristics (Table 6)

The mean age of recruits was 27.6yrs (Range 1.0 to 85.7yrs). 45.0% (138/307) recruits were children (aged 12yrs or under). 56.7% (174/307) recruits were female. 99.1% (216/218) respondents described their ethnic background as white.

There were no statistically significant differences in baseline characteristics of recruits between randomization groups (Table 6).

The response rate for diary outcomes was 81.4% 250/307, of these 5.2% (16/307) were telephone responses. See the trial consort diagram (5.10.3: Figure 3) for a detailed picture of the groups in the trial.

There was no significance difference in response rates between randomization groups (no antibiotic group 76/94 (80.9%), immediate antibiotics group 84/104 (81.7%) delayed antibiotic group 89/109 (81.7%) (p=0.888). Although responders were older than non responders (mean 29.5yrs (sd 28.4) versus 18.3yrs (sd 18.7)) and had lower deprivation scores (mean 12.7 (sd 9.8) versus 15.9 (sd 11.5), including these variables in the models did not alter the estimates of effectiveness.

5.10.5: Antibiotic use

99% of those in the immediate antibiotic group, 53% of the delayed prescription group and 30% of the no antibiotic prescription group reported using antibiotics during this episode of acute infective conjunctivitis (as this was a pragmatic trial, patients in the no antibiotic group were free to re-consult and GPs were free to treat patients in subsequent consultations as they felt appropriate).

5.10.6: Table 6: Baseline Characteristics of trial recruits

	No Antibiotics n=94	Immediate Antibiotics n=104	Delayed Antibiotics n=109
Age			
Mean	27.2	27.2	28.2
(SD)	(27.6)	(25.1)	(25.9)
Children ≤12yrs	46/94	43/104	49/109
(%)	(48.9%)	(41.3%)	(45.0%)
Sex			
Number of males	39/94	45/104	49/109
(%)	(41.5%)	(43.3%)	(45.0%)
No. Male children ≤12yrs (% of all children)	26/49 (53.1%)	25/43 (58.1%)	26/46 (56.5%)
No. Males >12yrs	13/45	20/61	23/63
(% of all adults)	(28.9%)	(32.8%)	(36.5%)
Deprivation Score (imd)			
Mean	14.4	12.6	13.1
Standard deviation	(11.6)	(10.2)	(8.7)
Clinical Features*			
Unilateral	42/93 (45.2%)	59/103 (57.3%)	62/109 (56.9%)
Moderate to severe conjunctival injection	37/92 (40.2%)	43/101 (42.6%)	47/108 (43.5%)
Discharge present	74/91 (81.3%)	84/102 (82.4%)	86/108 (79.6%)

*The denominator is slightly different from the number recruited due to a small number of incomplete GP clinical signs sheets.

5.10.7: Outcome measures

Factor analysis revealed that all seven symptoms scored on the diary loaded onto one factor (Cronbach's alpha = 0.84) and thus all symptoms were used to calculate the symptom severity score, and the duration of symptoms.

5.10.7.1: Symptom Severity Score

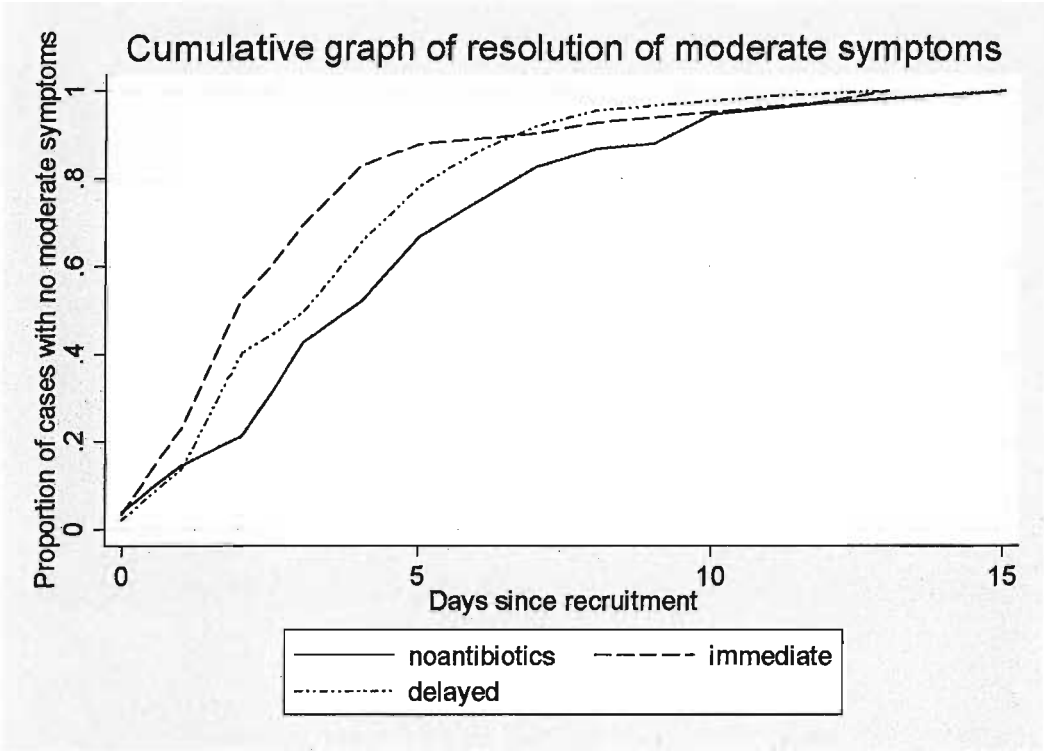
Provision of a patient information leaflet or performing an eye swab did not significantly affect symptom severity or any of the other main outcome measures (Table 8 and 9).
The average severity of symptom score for the first three days was not significantly different between the three antibiotic groups (Table 7). No evidence of confounders, interactions or clustering by GP was found for this outcome.

5.10.7.2: Duration Moderate symptoms

Duration of moderate symptoms (i.e. the number of days when at least one symptom scored as moderately bad or worse) was shorter in the immediate (mean = 3.26 days (sd 2.81)) and delayed (mean = 3.86 (sd 2.54)) antibiotic groups than the no antibiotic group (mean = 4.83 days (sd 3.24). The rate ratio (RR) was 0.67, p=0.001 for immediate antibiotic group and RR= 0.79, p=0.002 for delayed antibiotic group compared to the no antibiotic group (Table 7).
A borderline significant interaction was found between immediate antibiotic prescription and having an eye swab performed (p=0.068) suggesting the possibility of a longer duration of illness for patients receiving both immediate antibiotics and an eye swab.
The data was explored for a clustering effect by GP for all outcome measures and was found to be present in the duration of symptoms. Clustering for moderate symptoms (sigma=0.25 SE 0.08, 95% CI 0.14; 0.47, p=0.001). The importance of this finding is uncertain since it is confined to just one outcome measure, thus I have not allowed for clustering in Table 7 (Main outcomes by antibiotic group for responders). However, if p values and confidence intervals are calculated allowing for clustering (with the use of robust standard errors (SE)), it makes a difference to the confidence intervals, but no difference to the interpretation of the results. RR (using robust SE) for immediate compared to no antibiotic group = 0.67 (95%CI 0.53 to 0.87) p=0.002, RR (using robust SE) for delayed compared to no antibiotic group = 0.79 (95% CI 0.65 to 0.96) p=0.019.
Figure 4 shows cumulative graph of resolution of moderate symptoms. The curves converge so that there is no significant difference in presence of moderate symptoms between the antibiotic groups by day 8 after seeing the doctor (OR for cure by day 8 of moderate

symptoms for immediate antibiotic group compared to no antibiotic group =1.14, 95% CI 0.22 to 5.89, p=0.875, for delayed compared to no antibiotic group =1.78, 95% CI 0.29 to 11.00, p=0.535)

5.10.7.2.1: Figure 4: Cumulative graph of resolution of moderate symptoms



5.10.7.3: Belief in antibiotics and intention to re-attend for acute infective conjunctivitis

The immediate antibiotic group were more likely to believe antibiotics were effective, and more likely to state their intention to re-attend (OR = 3.15, p=0.001) compared to no initial offer of a prescription (or a delayed prescription) (table 7). A patient information leaflet or eye swab had no significant effect on patients' belief in antibiotics, nor plans to re-attend with subsequent eye infection (table 8 and 9).

5.10.7.4: Duration of mild symptoms

Duration of mild symptoms (at least one symptom scored as a slight problem or worse) showed a similar pattern to the duration of moderate symptoms. Duration of mild symptoms

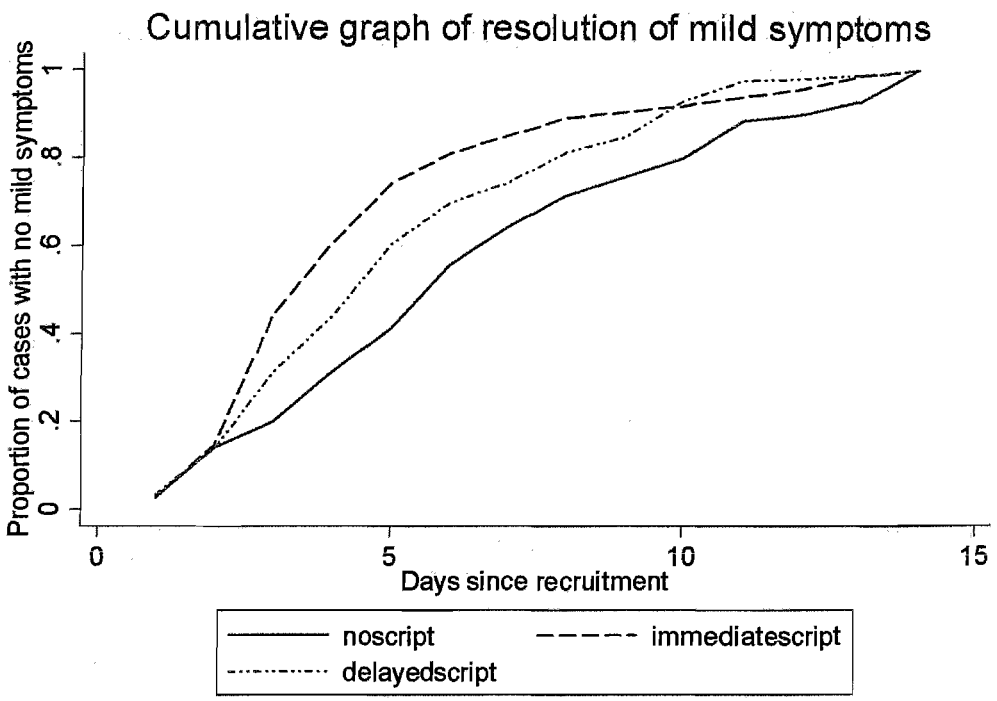
was shorter in the immediate and delayed antibiotic groups than the no antibiotic group (Table 7).

A significant interaction was found between immediate antibiotic prescription and having an eye swab performed (p=0.014) suggesting a longer duration of illness for patients receiving both immediate antibiotics and an eye swab.

A clustering effect by GP was found to be present for the duration of mild symptoms (sigma=0.19 SE 0.05 95% CI 0.11; 0.32, p=0.001). As for the duration of moderate symptoms, if p values and confidence intervals are calculated with the use of robust standard errors (SE), it makes a small difference to the confidence intervals and no difference to the interpretation of the results. RR for immediate compared to no antibiotic group (using robust SE) = 0.71, 95% CI 0.58 to 0.86, p=0.001 and for delayed compared to no antibiotic group RR = 0.81, 95% CI 0.68 to 0.94, p=0.008.

Figure 5 shows cumulative graph of resolution of mild symptoms. Similar to the duration of moderate symptoms the curves converge, in this case after day 10. There is no significant difference between the immediate and no antibiotic groups by day 13 and a borderline significant difference between the delayed and no antibiotic groups at day 13 (OR for cure by day 13 of mild symptoms for immediate antibiotic group compared to no antibiotic group = 2.50, 95% CI 0.61 to 10.28, p=0.203, for delayed compared to no antibiotic group = 4.91, 95% CI 0.97 to 24.83, p=0.05).

5.10.7.4.1: Figure 5: Cumulative graph of resolution of mild symptoms



5.10.7.5: Table 7: Main outcomes by antibiotic group for responders (adjusted for patient information leaflet and eye swab)

	No Antibiotic Prescription Group n=76	**Immediate antibiotic Prescription group n=85**	**Difference (Immediate from no antibiotics)**	**Delayed prescription Group n=89**	**Difference (Delayed from no antibiotics)**
Average symptom score (days1-3) Mean (sd) Difference 95% CI	2.08 (0.91)	1.87 (0.94)	-0.20 (-0.54; 0.10) p= 0.187	1.97 (0.98)	-0.11 (-0.41;0.18) p=0.449
Duration of moderate symptoms Mean (sd) (days) Rate ratio 95% CI	4.83(3.24)	3.26(2.81)	0.67 (0.57;0.79) p=0.001	3.86(2.54)	0.79 (0.68;0.92) p=0.002
Duration of mild symptoms Mean (sd) (days) Rate ratio 95% CI	6.79(3.81)	4.80(3.03)	0.71 (0.61;0.81) p=0.001	5.50(3.04)	0.81 (0.71;0.92) p=0.001
Belief in antibiotics Extremely or very effective Odds Ratio 95% CI	23/49 (46.9%)	47/70 (67.1%)	2.35 (1.10; 5.00) p=0.027	36/65 (55.4%)	1.43 (0.68; 3.02) p=0.351
Likelihood to reattend with future eye infection Extremely or very likely to reattend Odds Ratio 95% CI	26/65 (40.0%)	49/72 (68.1%)	3.15 (1.56;6.36) p=0.001	34/84 (40.5%)	1.01 (0.52;1.95) p=0.981

5.10.7.6: Table 8: Main outcomes by patient information leaflet group for responders (adjusted for antibiotic group and eye swab)

	No Patient Information Leaflet Group n= 119	**Patient Information Leaflet group n=122**	**Difference (Leaflet from no leaflet)**
Average symptom score (days 1-3) Mean (sd) Difference 95% CI	1.93 (0.96)	2.02 (0.96)	0.07 (-0.17; 0.31) p= 0.565
Duration of moderate symptoms Mean (sd) (days) Rate ratio 95% CI	3.88(2.87)	4.05(3.03)	1.01 (0.78;1.31) p=0.939
Duration of mild symptoms Mean (sd) (days) Rate ratio 95%CI	5.62(3.19)	5.71(3.54)	0.99 (0.89;1.11) p=0.895
Belief in antibiotics Extremely or very effective Odds Ratio 95% CI	51/88 (58.0%)	55/96 (57.3%)	1.02 (0.90; 1.16) p=0.784
Likelihood to reattend with future eye infection Extremely or very likely to reattend Odds Ratio 95% CI	57/107 (53.3%)	52/114 (45.6%)	0.77 (0.44;1.33) p=0.346

5.10.7.7: Table 9: Main outcomes by eye swab group for responders (adjusted for antibiotic group and patient information leaflet)

	No Eye swab Group **n=117**	**Eye swab Group** **n=127**	**Difference (Eye swab from no eye swab)**
Average symptom score (days1-3) Mean (sd) Difference 95% CI	1.89 (0.90)	2.05 (0.98)	0.17 (-0.07; 0.41) p= 0.172
Duration of moderate symptoms Mean (sd) (days) Rate ratio 95% CI	3.76(2.89)	4.15(3.00)	1.10 (0.98;1.26) p=0.111
Duration of mild symptoms Mean (sd) (days) Rate ratio 95% CI	5.52(3.26)	5.81(3.48)	1.06 (0.95;1.18) p=0.291
Belief in antibiotics Extremely or very effective Odds Ratio 95% CI	56/95 (59.0%)	50/89 (56.2%)	0.86 (0.48; 1.57) p=0.634
Likelihood to reattend with future eye infection Extremely or very likely to reattend Odds Ratio 95% CI	53/109 (48.6%)	56/112 (50.0%)	1.10 (0.64;1.91) p=0.729

5.10.7.8: Effect of age on outcome measures

Age was not a confounder nor an effect modifier for any of the outcome measures, but duration of symptoms does seem to be related to age.

The duration of mild and moderate symptoms was shorter in children (12yrs or under) than in the over 12yrs. Mean duration of moderate symptoms for children (12yrs and under) = 3.44 days (sd 2.37) compared to 4.3 days (sd 3.29) over 12yrs, (RR= 0.76, 95% CI 0.69 to 0.85, p=0.001). For mild symptoms mean duration in children = 4.66 days (sd 2.7) compared to 6.44 (sd 3.64) for the over 12yrs, (RR= 0.71, 95% CI 0.64 to 0.79, p=0.001) (adjusted for prescribing group, patient information leaflet and eye swab). Thus children are likely to have a shorter duration of symptoms with acute infective conjunctivitis but prescribing has the same effect size in children as the over 12yrs.

5.10.8: Eye swab analysis

158 participants were randomized to an eye swab but in 20 swab results were unavailable: in 11 the swab was not taken due to recruitment on a Friday afternoon, uncooperative children or the GP forgetting and 9 swabs were rejected by the laboratory because of transport problems and a delay in analysis making results invalid. Swab analysis was undertaken using a modified Cagel and Abshire technique[24]. Significant bacterial growth was detected in 69/138 (50%) of swabs. The main organisms were Haemophilus influenzae 26/69 (37.7%), Streptococcus pneumoniae 16/69 (23.2%) and Staphylococcus aureus 11/69 (15.9%). None were resistant to chloramphenicol.

There was no significant difference in outcome measures between those with and without bacterial growth. For example, in the immediate antibiotic group, mean duration moderate symptoms if swab positive = 3.47 days, if swab negative = 3.50 days (p=0.975).

5.10.8.1: Predictors of a positive bacterial swab result

The sex of the participant, deprivation score, recruitment by a high recruiting GP, unilateral symptoms, conjunctival injection, lymphadenopathy or a history of previous episodes of acute infective conjunctivitis did not predict a positive swab result for bacterial growth, nor did a presumptive diagnosis of bacterial conjunctivitis (as opposed to viral conjunctivitis) by the recruiting GP (see Table 10). However, being a child and the presence of discharge did have a positive relationship with a positive swab result. 63% (42/67) of swabs taken in children (12yrs and under) were positive for bacteria compared to 38% (27/71) in those aged over 12yrs (OR (adjusted for presence of discharge) = 2.31 p=0.021 95% CI 1.14 to 4.72). In those

with discharge 57% (63/111) were swab positive compared to 25% (6/24) in those with no visible discharge (OR (adjusted for being a child) =3.50 p=0.016, 95%CI 1.26 to 9.68). The significance of these findings for clinical management are unclear since neither being a child nor having a positive swab result interacted with treatment group.

5.10.8.1.1: Table 10: Potential predictors of a positive bacterial swab result (adjusted for child and discharge present)

Variable	**Odds ratio**	**95% Confidence interval**	**P value**
Child (12yrs or under) (baseline: over 12yrs)	2.31	1.14 to 4.72	0.021
Discharge present (baseline: no discharge present)	3.50	1.26 to 9.86	0.016
Unilateral Symptoms (baseline: bilateral)	0.85	0.41 to 1.75	0.657
Conjunctival Injection: moderate or worse (baseline: no/slight conjunctival injection)	1.55	0.73 to 3.29	0.249
Lymphadenopathy - present (baseline: not present)	1.04	0.34 to 3.25	0.94
Sex: female (baseline: male)	1.38	0.65 to 2.93	0.406
Deprivation score, imd >10 (baseline: imd ≤10)	0.71	0.34 to 1.50	0.361
High recruiting GP (baseline: low recruiters)	1.54	0.75 to 3.15	0.241
History of previous episodes of conjunctivitis (baseline: no previous episodes)	0.73	0.32 to 1.65	0.448
Presumptive diagnosis of bacterial infection by GP (baseline: viral diagnosis)	1.00	0.47 to 2.10	0.996

5.10.9: Re-attendance

57/307 (18.9%) re-attended the surgery for conjunctivitis in the year following recruitment (either for the same episode or a new episode), 26 (8.5%) re-attended within 2 weeks. Those in the delayed prescription group were less likely to re-attend within 2 weeks than the no prescription group (OR 0.33 (0.11 to 0.98) p=0.046), but there was no significant difference between the immediate and no prescription groups (OR 0.65 (0.26 to 1.63) p=0.357).

There was no significant difference in re-attendance rates over the year of follow up between the immediate and the no prescription group OR = 0.83 (95% CI 0.42 to 1.63, p=0.589). However, there was a borderline significant reduction for the delayed prescription group compared to no prescription group OR = 0.51 (95% CI 0.24 to 1.07, p=0.074).

5.10.10: Initial diary questions

Participants answered 5 questions at the start of the diary regarding: their concern/worry about the eye problem, how well the doctor dealt with their worries or concerns, how satisfied they were with the consultation, the importance of seeing the doctor to be able to continue to go work or school and how satisfied they were with the information they were given regarding eye infections.

The results are summarised in table 11, 12 and 13.

None of the responses were related to the treatment group to which the patient had been randomised (immediate, delayed or no antibiotics) (Table 11).

However, the answers to the questions give interesting information about participants' attitudes to acute infective conjunctivitis and the use of patient information leaflets and eye swabs.

They reveal:

1) Satisfaction with the amount of information given about eye infections was greater in those receiving a patient information leaflet (OR 2.43 (95% CI 1.31; 4.49) p=0.004)

A patient information leaflet may also increase the patient's perception that the doctor addressed their concerns and worries extremely or very well and may increase the patients' satisfaction with the consultation, but these results were of borderline significance (Table 12).

2) Performing an eye swab seems to increase concern and worry about acute infective conjunctivitis (OR 1.71 (95% CI 1.00; 2.96) p=0.050). This may be due to increased uncertainty in the patients mind about the diagnosis (Table 13).

3) The perceived need to go to the doctor or nurse to enable return to work or school was not related receiving a patient information leaflet or eye swab. (Table 12 and 13) (Nor was it related to the participant being a child (OR for 12yrs or under compared to over 12yrs = 1.42 (95% CI 0.82; 2.46) p=0.205). Some schools and nurseries have an exclusion policy for those with conjunctivitis, so this may have been relevant).

5.10.10.1: Table 11: Responses to initial diary questions by antibiotic group (adjusted for eye swab and patient information leaflet)

Initial Diary Question	No antibiotic group	Immediate antibiotic group	OR (immediate to no antibiotics)	Delayed antibiotic group	OR (delayed to no antibiotics)
Concern/ Worry about the eye problem *Extremely, very or moderately worried* Odds Ratio (95% CI)	30/70 (42.9%)	29/73 (39.7%)	0.89 (0.46;1.76) p=0.747	30/83 (36.1%)	0.73 (0.38;1.41) p=0.349
How well did the doctor deal with the participants' worries or concerns? *extremely or very well* Odds Ratio (95% CI)	54/71 (76.1%)	59/73 (80.8%)	1.38 (0.62;3.10) p=0.429	67/83 (80.7%)	1.33 (0.61;2.89) p=0.476
Satisfaction with the consultation *extremely or very satisfied* Odds Ratio (95% CI)	53/71 (74.7%)	61/73 (83.6%)	1.81 (0.79;4.13) p=0.161	67/84 (79.8%)	1.36 (0.63;2.91) p=0.429
Importance of seeing a Doctor /Nurse to enable one to go to school/nursery *extremely or very important* Odds Ratio (95% CI)	34/67 (50.8%)	44/71 (62.0%)	1.58 (0.80;3.12) p=0.185	33/82 (40.2%)	0.65 (0.34;1.25) p=0.200
Satisfaction with the amount of information given about eye infections *extremely or very satisfied* Odds Ratio (95% CI)	55/71 (77.5%)	55/73 (75.3%)	0.93 (0.43;2.01) p=0.864	58/84 (69.1%)	0.64 (0.31;1.34) p=0.238

5.10.10.2: Table 12: Responses to initial diary questions by patient information leaflet group (adjusted for antibiotic group and eye swab)

Initial Diary Question	No Patient information leaflet Group	Patient information leaflet Group	OR for leaflet group compared to no leaflet
Concern/ Worry about the eye problem *Extremely, very or moderately worried* Odds Ratio (95% CI)	38/106 (35.9%)	51/120 (42.5%)	1.31 (0.76;2.26) p=0.328
How well did the doctor with the participants' worries or concerns? *extremely or very well* Odds Ratio (95% CI)	79/107 (73.8%)	101/120 (84.2%)	1.90 (0.99;3.67) p=0.054
Satisfaction with the consultation *extremely or very satisfied* Odds Ratio (95% CI)	80/108 (74.1%)	101/120 (84.2%)	1.91 (0.99;3.67) p=0.053
Importance of seeing a Doctor/Nurse to enable one to go to school/nursery *extremely or very important* Odds Ratio (95% CI)	52/102 (51.0%)	59/118 (50.0%)	0.99 (0.57;1.69) p=0.956
Satisfaction with the amount of information given about eye infections *extremely or very satisfied* Odds Ratio (95% CI)	70/108 (64.8%)	98/120 (81.7%)	2.43 (1.31;4.49) p=0.004

5.10.10.3: Table 13: Responses to initial diary questions by eye swab group (adjusted for antibiotic group and patient information leaflet)

Initial Diary Question	No Eye Swab Group	Eye Swab Group	OR for Eye Swab compared to No eye swab
Concern/ Worry about the eye problem *Extremely, very or moderately worried* Odds Ratio (95% CI)	37/112 (33.0%)	52/114 (45.6%)	1.72 (1.00;2.96) p=0.050
How well did the doctor with the participants' worries or concerns? *extremely or very well* Odds Ratio (95% CI)	88/112 (78.6%)	92/115 (80.0%)	1.07 (0.56;2.06) p=0.827
Satisfaction with the consultation *extremely or very satisfied* Odds Ratio (95% CI)	90/113 (79.7%)	91/115 (79.1%)	0.96 (0.50;1.83) p=0.891
Importance of seeing a Doctor/Nurse to enable one to go to school/nursery *extremely or very important* Odds Ratio (95% CI)	55/108 (50.9%)	56/108 (50.0%)	1.01 (0.59;1.74) p=0.959
Satisfaction with the amount of information given about eye infections *extremely or very satisfied* Odds Ratio (95% CI)	81/113 (71.7%)	87/115 (75.7%)	1.23 (0.67;2.25) p=0.505

5.10.11: Prevalence of concurrent symptoms

Participants were asked to record in the patient questionnaire and diary what other symptoms they experienced during their episode of acute infective conjunctivitis. 55.7% (127/228) of those who returned the diaries experienced a runny nose, 43.8% (98/224) a cough, 35.9% (79/220) a sore throat and 12.6% (28/223) diarrhoea. Other symptoms reported included headache and earache.

5.10.12: Use of over the counter medication

41% (93/227) used some form of temperature or pain relief (most commonly paracetamol or ibuprofen) during the episode of acute infective conjunctivitis. 17.4% used over the counter eye medication from the pharmacist prior to attending the GP surgery (most commonly Brolene, Optrex and Golden Eye Ointment). 86.7% (196/226) bathed the eyes with cooled boiled water during the illness (this strategy was advised to the patients as part of the advice packages). 36.9% 76/206 stated they took some time off work or school during this episode of illness.

5.10.13: History of previous episodes of acute infective conjunctivitis

57.2% (131/229) of those returning the diaries said they had had a previous eye infection. 30.1% (34/113) had one, 57.5% (65/113) two and 12.4% (14/113) three or more previous infections. 12.7% (14/110) of those who had experienced a previous infection had not attended the GP surgery before for an eye infection, 32.7% (36/110) had attended once before, 48.2% (53/110) two to four times before and 6.4% (7/110) five times or more.

5.10.14: Post recruitment questionnaire

At the end of the study recruiting GPs and Practice Nurses were sent a Post recruitment questionnaire (Appendix 14) to obtain feed back on trial recruitment.

34 of the 38 GPs and Practice Nurses who recruited patients for the trial returned the questionnaire. 46% (15/33) reported that they entered less than 10% of patients who presented with acute infective conjunctivitis into the trial, 9% (3/33) entered 10-29%, 12% (4/33) entered 30-49%, 12% (4/33) entered 50-69%, 12% (4/33) entered 70-89% and 9% (3/33) entered 90% or greater. These figures were used, along with numbers actually recruited, to calculate the estimate of the number of patients presenting to the GPs and Practice nurses for the Trial Consort diagram (Figure 3).

Only 24 GPs and Practice Nurses answered the question about how many eligible patients they asked about the trial refused to participate. 9/24 (38%) said no one refused to participate, 4/24 (17%) said they had one refusal, 9/24 (38%) had 2 to 6 refusals and 2/24 (8%) had 10 to 20 refusals.

The GPs and Practice Nurses were asked to rank their main reasons for not entering patients in the trial. 18/29 (62%) said lack of time was their main reason for not entering patients into the trial, 5/29 (17%) said it was patient refusal. More information on those not entered is described in the next section (5.10.15: Patients not entered into the trial: Information from 'not entered' books).

18/33 (55%) of the GPs and Practice Nurses felt they had changed their management of acute infective conjunctivitis as a result of participating in the trial. The main change they specified was using a 'wait and see' or delayed prescription approach more frequently.

5.10.15: Patients not entered into the trial: Information from 'not entered' books

Fifteen not entered books were returned at the end of the study from the 38 GPs and Practice Nurses who had recruited patients to the trial – the other books were reported as being mislaid. Four of the returned books had no entries and two had only one entry. Thus a limited amount of data was available on those not entering the trial. This type of information is often difficult to collect. Opportunistic recruitment during normal GP surgeries allows little time for recruitment let alone documentation of those not recruited. Thus, even those books with entries are likely to be incomplete. However, information on those not entered is important to try and collect.

I will present the data available. 101 not entered patients were documented in the 11 books returned that had an entry. The mean age of those not entered was 27.6 (sd 30.2), median 8.8, range 3 months to 101 years (calculated from the 95 entries with a specified age). 52.3% (46/88) were male. The mean score for the severity of the conjunctival injection was 2.3 (sd 1.18) and 2.0 (sd 1.19) for amount of discharge (0 to 6 scale with 0 =normal and 6 = as severe as it could be).

Thus, on the information available, those not entered appeared to be similar to those entered into the trial. Their mean age was the same (27.6 yrs for both groups), 50.5% were children (12yrs or under) compared to 45% in the recruited group, 47.7% were female compared to 56.7% in the recruited group and the signs and symptoms were being scored as slight to moderate for both groups.

The reasons the GPs and Practice Nurses documented for the non-recruitment of those listed in the 'not entered' books were: Lack of time for the doctor 24.8% (25/101), Patient refusal 27.7% (28/101), Patient too unwell 6.9% (7/101), Parental anxiety 5.9% (6/101), Antibiotics for conjunctivitis in the last 2 weeks 5% (5/101), Chronic infective eye condition 3% (3/101), Recent eye surgery 1% (1/101), Other 25.7% (26/101). Most of the 'Other' category probably fall into the patient refused category (comments included: 'about to go on holiday', 'work commitments', 'worried may end up with more days off nursery', 'already left it for one week and not prepared to take the risk of not getting antibiotics', 'not interested', 'wants prescription as it worked last time'), but there were also two non-English speakers and four patients who were extremely elderly and frail who were not recruited.

5.10.16: Comparison High versus Low Recruiter

I compared patients from high recruiters (GPs indicating they recruited over 70% of cases they encountered) with low recruiters. There was no difference in severity of presenting symptoms, sex of recruits or proportion of children, but higher recruiters recruited older participants (respectively mean age 31.6yrs vs 24.6yrs, difference = 7.0 yrs, 95% CI 1.1 to 12.1, p=0.02) and participants with lower deprivation scores (index multiple deprivation 11.4 vs 14.8, difference -3.4, 95% CI -5.7 to -1.1, p=0.004) which is likely to be a function of the practice populations of the respective doctors. However, there was no evidence of a difference in the outcome measures according to recruitment status of the patient (i.e. from a high or low recruiting doctor).

5.10.17: Complications

One patient in the immediate antibiotic prescription group developed orbital cellulitis (hospital admission 11 days after recruitment). This patient scored extremely high symptom scores for the diary, unlike the rest of the study participants. If the analysis is redone excluding her data it does not effect the conclusions of the trial.

Not other complications were recorded. However several of the diaries noted that it was not easy to administer eye drops to young children and that this lead to the medication being discontinued.

5.11: Discussion

5.11.1: Principal findings

The different prescribing strategies did not affect symptom severity in the first 3 days, but duration of moderately bad symptoms was less with antibiotics. Compared with no initial offer of antibiotics, antibiotic use was higher in the immediate prescription group, as was belief in the effectiveness of antibiotics and intention to re-consult.

A patient information leaflet or an eye swab had no affect on the main outcome measures. However, performing an eye swab may increase concern about acute infective conjunctivitis. A patient information leaflet increases satisfaction with the amount of information received and may increase satisfaction with the consultation and the perception that the doctor addressed patients concerns about conjunctivitis.

5.11.2: Strengths and limitations

The pragmatic open trial design allows assessment of management strategies in a setting that closely resembles normal general practice, and allows assessment, not only of symptom resolution, but also patients' responses to different strategies, belief in the efficacy of antibiotics, use of antibiotics, and intention to consult. The placebo effect has been minimised by using standard advice packages; allowing the GP to support each strategy and act as the 'placebo' in each group (ie provide the same advice to patients during the consultation apart from the randomised interventions), which has been used successfully in previous trials where little or no placebo effect has been detected [44-46].

Selective overall recruitment could limit generalisability. Most GPs did not recruit every patient they saw with conjunctivitis. The main reasons they gave for this were lack of time, patients declining to participate and exclusion criteria (children under 1yr or chronic eye conditions such as blepharitis being the main factors). However, the data available from the 'not entered books' suggests that those not recruited were similar to the recruits.

Patients from high recruiting doctors differed in age and deprivation score from low recruiters. This is likely to be a function of the practice populations of the respective doctors.

Recruitment status of the patient (i.e. from high versus low recruiting GPs) did not predict any outcome nor affect the estimates of effectiveness of interventions.

Similarly, although respondents were older and had lower deprivation scores than non-respondents, neither of these altered the effect size.

The delayed prescription strategy used in this trial involved participants returning to the surgery to collect their prescription. This may have reduced antibiotic use compared to a

strategy of providing the prescription within the consultation and advising a delay before obtaining the medication.

5.11.3: Discussion of main results and relationship to the literature

The different management strategies did not affect symptom severity in the first three days after seeing the doctor. On average, symptoms were scored as slight to moderate during this time - consistent with my qualitative work[109] where patients describe the symptoms of acute infective conjunctivitis as being 'minor' and 'niggly' rather than troublesome. However, 53% of the delayed prescription group and 30% of the no antibiotic prescription group stated they used antibiotics. This is probably due to a belief in the need for antibiotics to clear the infection even though the symptoms are mild[109]. Whatever the reasons, no initial offer of antibiotics will still result in significant use of antibiotics. Thus, a no prescription approach, as suggested by Rose[41] and Rietveld[28], may not be as effective (in terms of reducing antibiotic use) as one may initially presume. Additionally, patients may re-attend the GP surgery to obtain the antibiotics and thus GP consultations may actually be higher when there is no initial offer of antibiotics.

In my study population, the difference between the immediate and no antibiotic groups was 1½ days of moderate symptoms, and for the immediate compared with the delayed antibiotic group ½ a day. The percentage cured within the antibiotic groups converges so there is no significant between the groups by day 8 (Figure 4). This result varies with results published by Rose et al[41] who found a consistent 0.3 of a day difference in symptoms between their chloramphenicol and placebo arms between day 2 and day 7. The greater benefit, in the current study, of immediate antibiotic drops compared to Roses' recent study[41] may have a number of explanations: a) a greater placebo effect is possible, but unlikely, as previous studies using identical methodology have found very similar estimates from open trials compared to blinded trials[44-46]; b) the Rose study[41] underestimated the effect of drops (my study provides estimates closer to the Cochrane reviews[6;42]) possibly due to the effect in adults being greater than children; c) different outcome measures were used (duration of moderate symptoms was not measured by Rose et al[41]); or d) there may be a non specific mechanical effect of drops providing lubrication and helping flush out pathogens (both arms in the Rose study[41] had drops).

One to two days reduction in moderately bad symptoms (comparing immediate with no offer of antibiotics) might be worth a prescription of antibiotic drops; however it is debatable whether it is worth prescribing immediate antibiotics to all patients when the benefit compared

with delayed antibiotics is likely to be half a day reduction of moderate symptoms. It may well depend on the individual patients' circumstances (ie ability of children to attend day care).

Immediate prescribing of antibiotics seems to 'medicalise' patients with acute infective conjunctivitis – as seen in research on other respiratory infection[44;45]. Those receiving immediate antibiotics were much more likely to indicate they would re-attend with their next eye infection than those receiving no antibiotics or a delayed script.

Delayed prescribing gives the GP the opportunity to discuss the natural history of acute infective conjunctivitis with the patient. My qualitative work[109] indicated that patients lack of awareness of the self-limiting nature of acute infective conjunctivitis was an important reason for them attending for antibiotics. It also revealed that they were happy with a delayed prescription approach and were comfortable with the decision to start the antibiotics or not.

The provision of a patient information leaflet or performing an eye swab did not affect any of the main outcome measures. However, patients were more satisfied with the information provided and possibly more satisfied with the consultation, and felt they had their concerns better addressed, when a leaflet was given. This suggests that providing a patient information leaflet within the GP consultation for acute infective conjunctivitis may be more beneficial than a brief explanation of the natural history and symptomatic management. Past studies assessing the effectiveness of leaflets in general practice[46;70-72;113] have shown variable results, with some showing a change in consulting behaviour or antibiotic use after receiving a leaflet[70;71]. However, some show little or no effect on outcome measures[46;72]. Providing a leaflet specific to the presenting condition within the consultation, as was done in my trial, seems to be most likely to have an effect[68]. A possible explanation for the lack of effect on the main outcome measures in this trial (particularly the belief in the effectiveness of antibiotics for acute infective conjunctivitis and intention to re-attend with subsequent episodes of conjunctivitis questions) is that the leaflet used in my study was deliberately neutral as to the best management strategy for acute infective conjunctivitis. This was necessary as it was being given to all three treatment groups. If the wording of the leaflet were changed, in light of the new research evidence[28;41;42], to highlight the marginal benefit for antibiotics and the possibility of a 'wait and see' approach then a greater effect may be seen.

Undertaking an eye swab had no effect on the main outcome measures. However, patients who had an eye swab seemed to be more worried about their eye problem. The borderline

significant interaction between immediate prescribing and having an eye swab for the duration of moderate symptoms and the significant interaction for mild symptoms, suggests further studies could explore the hypothesis that an investigation may create uncertainty in patients minds and possibly effect perceived symptom resolution[114;115]. In everyday general practice eye swabs are rarely used[19] because of the cost and time delay in receiving a result. However, diagnostic testing prior to prescribing[116] has been suggested for a range of illness as a way of reducing antibiotic use. If bacterial conjunctivitis could be distinguished from viral conjunctivitis, prescribing could potentially be reduced by 50% - so is it worth considering increased use of eye swabs for acute infective conjunctivitis? My trial and Roses' trial[41] showed no difference in clinical cure rates between antibiotic and no antibiotic groups, even in those with a positive bacterial swab result. However Rietvelds[28] trial did show a greater effect of antibiotics in those who are swab positive for bacteria. Taking the marginal effect of antibiotics, the potential for increased worry, and the cost and delay of performing swabs into account, it would not seem appropriate to recommend increased use of eye swabs for acute infective conjunctivitis in general practice.

The uncertainty as to whether antibiotics have a greater benefit in those with a bacterial aetiology also raises the question as to whether a symptom score to discriminate bacterial from viral conjunctivitis has any value. If the benefit of antibiotics is marginal, and the condition is self-limiting, then discriminating bacterial from viral conjunctivitis becomes unnecessary.

Re-attendance at the GP surgery at two weeks was less in the delayed antibiotic prescription group than the immediate and no prescription groups. Additionally, there was a borderline significant reduction in re-attendance in the year following the initial consultation for the delayed prescription group compared to the other groups. This suggests that a delayed prescription policy may reduce actual re-attendance rates in the longer term (consistent with the results from the 'intention to re-consult with future episodes of conjunctivitis' question in the patient questionnaire and with the results of previous studies[37;45]). Thus delayed prescribing may have longer term benefits on GP workload and patient self-care for acute infective conjunctivitis. A larger trial would be needed to confirm this.

5.12: Conclusion

The different prescribing strategies (immediate, delayed or no antibiotics) did not affect symptom severity in the first three days after attending the surgery, but duration of moderately bad symptoms was less in the immediate and delayed antibiotic prescription groups. Immediate prescribing appeared to medicalise acute infective conjunctivitis but this was not seen with delayed prescribing. Not offering a prescription of antibiotics at the initial consultation still resulted in 30% of patients eventually receiving a prescription for that episode of conjunctivitis.

Eye swabs and patient information leaflets did not affect the main outcome measures. However, eye swabs may increase patients' worries about their eye problem and a patient information leaflet may increase satisfaction with the consultation and the amount of information received and the patient's perception that the doctor addressed their concerns well.

The delayed prescribing approach may be the best approach to use overall – it has the advantage of reducing antibiotic use by nearly 50%, showed no evidence of medicalisation, provides similar symptom control to immediate prescribing, and reduces re-attendance in the short term compared with no offer of antibiotics.

Chapter 6: Summary

The management of acute infective conjunctivitis in general practice was a poorly researched area. Information was lacking on GPs current management and diagnosis of acute infective conjunctivitis, the most appropriate way to manage the condition in the general practice population and on patients' understanding of conjunctivitis and their concerns and worries about the condition. My work and other recently published papers[14;26;28;41;42] have greatly improved the evidence base for managing acute infective conjunctivitis in general practice.

My GP survey[19] revealed that most GPs still prescribe immediate topical antibiotics for most cases of acute infective conjunctivitis and that GPs feel confident in diagnosing acute infective conjunctivitis but few feel they can discriminate bacterial from viral conjunctivitis. Most prescribed immediate topical chloramphenicol first line and did not use a delayed prescription strategy, a patient information leaflet or perform eye swabs.

The qualitative work[109] revealed that most patients regarded conjunctivitis as a minor illness but were not aware of its self-limiting nature. Patients stated a preference not to take medication but believed that conjunctivitis would not clear without treatment. However, they were open to alternative management approaches (e.g. delayed prescription approach) because they trusted their GPs' judgement.

The randomised controlled trial revealed that the different prescribing strategies (immediate, delayed or no offer of topical antibiotics) did not affect symptom severity in the first three days, but duration of moderately bad symptoms was less with immediate or delayed topical antibiotics than no offer of antibiotics. Antibiotic use was higher in the immediate prescription group than the delayed prescription and the control group. Belief in the effectiveness of antibiotics and intention to re-consult were higher with immediate antibiotics than a delayed prescription or no offer of antibiotics. A patient information leaflet or an eye swab had no affect on the main outcome measures. However, the diary questions revealed that a patient information leaflet may increase satisfaction with the consultation, the amount of information received and the patient's perception that the doctor addressed their concerns well. Conversely, eye swabs may increase patients' worries about their eye problem.

The two recently published trials of topical antibiotics for acute infective conjunctivitis in general practice[28;41] (one exploring topical chloramphenicol[41] and the other topical fusidic acid[28]) found no benefit for antibiotics over placebo and suggested that there was no evidence to support continued prescription of topical antibiotics. However the updated Cochrane review

and meta-analysis[42] still found a benefit at days 2 to 5 for topical antibiotics after incorporation of these two new trials (RR=1.24, 95% CI 1.05 to 1.45).

My trial has results consistent with the Cochrane review[42], showing some benefit for topical antibiotics for acute infective conjunctivitis. However, the benefit is relatively small and acute infective conjunctivitis is a self-limiting minor illness.

An important feature of my trial is its ability to look at patients' behaviour in response to the different management strategies as this should give an indication of what would happen if GPs changed their management of acute infective conjunctivitis in light of the new research evidence. No initial offer of antibiotics may seem like a reasonable strategy, but GPs may find resistance to this among patients who have been used to receiving topical antibiotics. Additionally, my study shows that 30% of patients randomised to no initial offer of antibiotics ended up receiving antibiotics and that they re-attended more in the two weeks following the initial consultation that those receiving a delayed prescription.

Issuing a delayed prescription provides an opportunity to discuss the natural history of acute infective conjunctivitis and the new research results[28;41;42] (regarding the limited potential benefit from antibiotics) with the patient. The patients' 'knowledge gap' (their lack of awareness that acute infective conjunctivitis is self-limiting[109]) can be addressed. Providing this information would allow them to make a more informed choice as to whether they would prefer to have antibiotics or not. Delayed prescribing also empowers the patient by allowing them to decide whether to and/or when to start the medication. The qualitative study showed that patients found the delayed prescription strategy acceptable and that that they were comfortable with the decision to start the antibiotics or not.

Thus, a delayed prescription seems an appropriate strategy for GPs to adopt. It provides similar symptom control to immediate prescribing but has the advantage of reducing antibiotic use by nearly 50%. Additionally, it shows no evidence of medicalisation, and reduces re-attendance in the short term compared with no offer of antibiotics.

A patient information leaflet had no affect on the main outcomes from the trial but did seem to increase satisfaction with the consultation, the amount of information received and the patients' perception that the doctor dealt with their concerns. It also received positive responses in the qualitative study. Thus, it would seem reasonable that GPs should use a leaflet alongside the delayed prescribing approach.

6.1: Over the Counter Chloramphenicol

A recent and important development in the management of acute conjunctivitis in primary care is that chloramphenicol eye drops were made available over the counter in the summer of 2005. It is the first antibiotic to be available over the counter in the UK.

Patients now have access to it without the need to consult their GP. The qualitative research revealed that many patients sought advice from pharmacies regarding their eye condition prior to attending the GP surgery. Most had been advised by the Pharmacist to see their GPs for advice and treatment. If pharmacies now offer these people over the counter topical chloramphenicol, patients may not attend the GP surgery and acute infective conjunctivitis could become a less common presentation to general practice. Thus, any change in management by GPs may not lead to an overall reduction in antibiotic use. Additionally the potential to educate patients regarding the self-limiting nature of acute infective conjunctivitis and the marginal benefit of topical antibiotics may be lost.

Thus, it will be important to disseminate the results of the recent trials to pharmacists as well as GPs, so that they can give customers appropriate advice and not just recommend topical antibiotic for all those presenting with acute infective conjunctivitis.

6.2: Further Research

Development of a scoring system to try and discriminate viral from bacterial conjunctivitis could potentially be useful to better target antibiotic prescribing. Rietveld et al[26] have looked at this and have developed a score but it lacks specificity and they have not validated their measure (see 2.2.3.1: Discriminating between bacterial and viral conjunctivitis). In my randomised controlled trial, being a child and having discharge from the eye were associated with a positive swab result for bacteria but other features were not. A larger trial with more power would be needed to explore this further. However, the benefit of using of a symptom score to identify bacterial cases is debateable as the Rose et al trial[41] and my trial found no association between a positive swab result for bacteria and the outcome measures (though the subgroups in my trial may have been too small to detect a difference).

A larger open trial of different prescribing strategies would be needed to assess if delayed prescribing reduces re-attendance at the GP surgery in the longer term and to explore the possible interaction between performing an eye swab and immediate prescription of antibiotics.

Another important area, that lacks evidence, is that of complications following acute infective conjunctivitis. Complications appear to be rare but potential complications such as orbital

cellulitis, keratitis and panophthalmitis are mentioned in the literature. Antibiotic prescribing has been widespread and if this is to be reduced, then the possibility that complications may increase should be considered. The most appropriate method to investigate rare occurrences such as this would be a case control study. The cases and the controls should both be taken from a general practice population so a database such as the General Practice Research Database (GPRD) would be appropriate. The GPRD collects prescribing, diagnostic and background data from about 3 million GP patients in the UK.

Further research is also needed to explore the area of school and nursery attendance in children with acute infective conjunctivitis, as some of these institutions have exclusion policies for those with conjunctivitis and this may influence parents' acceptance of a delayed prescribing or no prescribing approach. Presumably an exclusion policy is designed to prevent spread of acute infective conjunctivitis to other children, but is this necessary for a minor self-limiting illness? – most schools and nurseries do not exclude children with a common cold. The Health Protection Agency website states that there is no need for exclusion[95]. A study could survey schools and nurseries to assess their current policies regarding acute infective conjunctivitis and then provide information and follow up to see if policies change.

Additionally, a survey of pharmacists regarding their knowledge of the management of acute infective conjunctivitis and their current recommendations to customers would be valuable as they are an important source of patient information and they can now offer over the counter topical chloramphenicol.

Research into acute infective conjunctivitis must be taken in the context of the conditions of the time, i.e. the level of infections in the community, the organisms causing those infections and the management of the infections by professionals and lay people. All these aspects can change over time. Ongoing programmes of research will be required to cope with the dynamic nature community infections.

Appendix

Appendix 1 GP Survey about Acute Infective Conjunctivitis

GP Name ---------- Practice name----------
Male / Female------ Years as a GP -------- Practice list size----------
No. of GP sessions worked per week -------- MRCGP? Y/N
Do you have any specialist experience in ophthalmology? Y/N If Yes - what?----------
---

1) What features do you use to diagnose acute infective conjunctivitis?

Red eye	Y/N	Eye discharge	Y/N
Eyelashes stuck together in morning	Y/N	Irritation/grittiness of eye	Y/N
Swollen eye lid	Y/N	History of contact with conjunctivitis	Y/N
Conjunctival injection	Y/N	Conjunctival Oedema	Y/N

Other Y/N please specify----------

2) What examination do you usually perform? – if any
Visual inspection Y/N Corneal staining Y/N
Ophthalmoscopy Y/N Other Y/N please specify----------

3) How confident do you feel with diagnosing acute infective conjunctivitis?
very confident / confident / neutral / not very confident / not confident

4) Do you feel you can discriminate viral from bacterial infection? Y/N
If yes: Do you use:
History of a 'cold' Y/N
Other features of the history Y/N If yes what?----------
Type of discharge (ie watery or sticky) Y/N
Amount of discharge Y/N
Bilateral versus unilateral infection Y/N
Other Y/N if yes please specify----------

5) What proportion of the cases of acute infective conjunctivitis that you see do you think are bacterial? <10% 10-29% 30-49% 50-69% 70-89% >90%

6) Do you usually prescribe for this condition? Y/ N
If yes: What do you usually prescribe first line and for how long?----------
---
Are there patients where you are happy not to prescribe? Y/N
If Yes: In what proportion of patients? <10% 10-29% 30-49% 50-69% 70-89% >90%
What are the characteristics of these cases?----------

7) Do you ever use a 'delayed prescription' strategy for infective conjunctivitis? Y/N
If Yes: In what proportion of patients? <10% 10-29% 30-49% 50-69% 70-89% >90%

8) Do you ever take eye swabs for acute infective conjunctivitis? Y/ N
If Yes: In what proportion of cases? <10% 10-29% 30-49% 50-69% 70-89% >90%
What are the commonest reasons for doing so?----------
---

9) Do you have a patient information leaflet about acute infective conjunctivitis? Y/N
If Yes: What proportion do you give it to? <10% 10-29% 30-49% 50-69% 70-89% >90%

Please use the back of this sheet for any other comments you have about the management of acute infective conjunctivitis.

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE
Please return in the Freepost envelope provided to: Dr Hazel Everitt, MRC Fellow,
Primary Medical Care, Aldermoor Health Centre, Aldermoor Close, Southampton, SO16 5ST

Appendix 2: Qualitative Study Information Sheet and Consent form

University of Southampton

EYE INFECTION STUDY
Patient information sheet

We feel it is important to find out about patients views about illnesses. This research project is trying to find out what you feel about eye infections. This includes your concerns about eye infections, the sorts of available treatment and what you feel about the way your infection has been managed.

The study involves taking part in a confidential tape-recorded interviewer with a researcher. The information will be recorded for research purposes only and will only be identified by an identification number. The tape recording of your interview will be destroyed within one year.

All the information that you give us will be keep fully confidential. Even your GP will not see it. Your/your child's name will not appear on any documents or reports.
You can withdraw yourself/your child from the study at any time without it affecting you/your child's treatment in any way.

If you have any queries please contact:

Hazel Everitt
Primary Medical Care,
University of Southampton,
Aldermoor Close,
Southampton
SO16 5ST
(Tel 02380 241079 – 24 hr ansaphone)

Date:---------- Doctors Name: ----------
Name: Mrs/Mr/Miss----------
Childs Name: (if appropriate)----------
Address:----------
----------Postcode:----------
Telephone no:----------
Signature:----------

Appendix 3:Conjunctivitis Qualitative Study Interview Guide

This guide was continually updated and adapted as interviewing progressed. It acted as an aide memoir to remind me of areas that might be interesting to pursue. This version is from 19/01/01 approximately half way through the interviewing and thus includes areas that I thought may be interesting prior to starting the interviews but also much more that emerged as the interviews progressed.

Background – age
marital status
occupation
family

Describe eye problem went to doctor with
Recognising illness- home diagnosis- how?- confidence with this
Making decisions
Duration
Symptoms
Self medication
Concerns/worries
Preceeding health status
Relationship with Dr
Expectations from consultation
Satisfaction with consultation
Advice given by GP
What if no prescription?/delayed

Cause of infection- viral/bacterial? Is it important to know?

How see illness- serious or minor- what would happen if not treated?

Why went to dr/nurse? - decision to consult
Advice
treatment

Decision to consult for oneself or for child – decisions

Confidence with advice from doctor/nurse

Treatment – What is in ointment /drops?
How does it work
Is it important to know how it works?
When is it important to know?
What would happen if not treated –natural hx of disease

Difficulty accessing treatment
Getting appt/script
Concerns re wasting GPs time
?nurse clinic

Past experiences of eye infection
- Advice
- Previous treatment
- Antibiotics

Sources of knowledge

Knowledge from others ie other parents/school/drs

Home management

Contagiousness/ sources of infection

Effect on school and work and rest of family

Sources of information
- Family?
- Pharmacy?
- etc

Attitude to antibiotics
- Usefulness -benefits
- Side effects
- ?overuse
- Resistance
- Tablets vs drops
- Internal vs external
- Use of antibiotics for other illnesses
- Natural immunity/building up

Attitude to PIL
- How well informed do they feel?
- ?want information
- What sort of information

Appendix 4: Patient information leaflet for conjunctivitis

Patient information leaflet for conjunctivitis

What is conjunctivitis?

Conjunctivitis is a common infection of the outer lining of the eye. It is caused by an infection with a virus or bacteria. It usually gets better within one week.

Who gets conjunctivitis?

Anyone can get conjunctivitis but it is most common in school-aged children. It can come on at the same time as a cold and can be spread by close (touching) contact.

How do I know that I (or one of my family) have conjunctivitis?

-Red eyes - One or both of your eyes may be red.
-The surface of the eye may feel itchy or irritated (not pain deep in the eye).
-You may have a sticky or watery discharge from the eye (yellow or green).
-Your eyelashes may be stuck together by the discharge when waking in the morning.
-Your vision should not be affected (once you have wiped away any discharge).
-You may also have a cold or a runny nose.
-You may have been in contact with someone who has had conjunctivitis recently.

Signs that my eye problem may not be conjunctivitis

A few other eye problems can look a bit like conjunctivitis – if you have any of the following symptoms you should not assume that you have conjunctivitis – ring you GP surgery for advice or an appointment:

-Pain in the eye (not just irritation on the surface of the eye)
-Problems with your vision (once you have wiped away any discharge)
-Swollen eye lids (they may be slightly puffy with conjunctivitis but should not be swollen)

Can conjunctivitis damage the eye?

No. Although it doesn't look nice conjunctivitis only affects the outside lining of the eye and does not damage it.

Do I need to go to the GP if I think I have conjunctivitis?

If you think that you have conjunctivitis and do not have eye pain, visual problems or swollen eyelids it is safe to allow a few days to see if the conjunctivitis will clear by itself. If you are not sure or it is not clearing then you should make an appointment to see the GP.

Do you need eye drops to clear conjunctivitis?

Your GP may or may not prescribe antibiotic eye drops.
Most conjunctivitis gets better by itself within a week without any treatment.
Research shows that antibiotic drops may reduce the length of time you have conjunctivitis by one to two days compared with having no treatment (in those cases of conjunctivitis that are caused by a bacterial infection).
Antibiotics do not work on viral infections so the conjunctivitis that is caused by viruses (probably at least half of all conjunctivitis) will not be helped by antibiotics.

What can I do to help treat myself at home?

You can clear any discharge from the eye with a piece of cotton wool soaked in cooled boiled water. This will help soothe the eye and can be done as often as necessary.

How can I prevent the spread of conjunctivitis?

Avoid touching or rubbing your eyes if you have conjunctivitis or make sure that you wash your hands afterwards.
Do not share your flannel or towel with others (sharing with the rest of the family can help the infection to spread).

Primary Medical Care, University of Southampton September 2001

Appendix 5: Trial Protocol

Conjunctivitis Trial Protocol

1.1 Title

Open Randomised Controlled Trial of Management Strategies for Acute Infective Conjunctivitis in General Practice

1.2 Principal Investigator

Dr Hazel Everitt
Primary Medical Care
Aldermoor Health Centre
Aldermoor Close
Southampton
SO16 5ST

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Email: hae1@soton.ac.uk
Fax: 023 80701125

2 The need for a trial

Patients with acute infective conjunctivitis are commonly seen in general practice. 2 to5 % of general practice consultations are related to eye conditions and approximately 40% of these are concerned with conjunctivitis. Thus, on average, GPs see a patient with infective conjunctivitis every week. However, the most appropriate management strategy for GPs to employ for acute infective conjunctivitis is uncertain.

Traditionally, bacterial conjunctivitis has been treated with topical antibiotic preparations (eg chloramphenicol eye drops). The difficulty distinguishing bacterial from viral conjunctivitis has meant that most patients who present with conjunctivitis are treated with antibiotics empirically. Thus, a significant number of patients with viral conjunctivitis are likely to be given antibiotics unnecessarily.

Even in confirmed bacterial conjunctivitis there is some uncertainty regarding the role of antibiotics. Bacterial conjunctivitis is as a self-limiting illness, resolving in most cases in 5 to 7 days without treatment. Antibiotics have been used in an attempt to reduce the duration and severity of symptoms and the likelihood of relapse and complications (eg orbital cellulitis). However, the evidence for this is weak, as few randomised controlled trials have been published comparing the effect of antibiotics with placebo. Most of the trials have taken place in the USA in secondary care, none in general practice.

Further evidence is needed to confirm the most appropriate management strategy for acute infective conjunctivitis.

2.1 Problem to be addressed

To assess the effect of common management strategies for acute infective conjunctivitis in general practice.

2.2 What is the hypothesis to be tested?

The Null hypothesis is that for patients presenting to general practice with acute infective conjunctivitis, there is no difference in clinical outcome or belief in antibiotic effectiveness in those treated with immediate antibiotics compared to management without antibiotics or with delayed antibiotics.

2.3 Why is a trial needed now?

It is now recognised that use of antibiotics should be restricted as far as possible to cases of proven need and benefit. The emergence of increasing resistance in common bacteria and the acknowledgement of the potential harmful effects of antibiotics has focused attention on reducing antibiotic prescribing wherever possible, particularly for acute self-limiting infections.

Also, concern has emerged regarding the possible medicalising effects of prescribing antibiotics - prescribing reinforcing patients belief in antibiotics and the intention to seek medical help (as has been demonstrated for prescribing in sore throat). This may lead to increased pressure on already stretched primary care resources.

.

2.4 Has a systematic review been carried out and what where its findings?

A Cochrane review looking at antibiotics for acute bacterial conjunctivitis was published in April 1999. It found 3 RCTs that fulfilled eligibility to be included in the review. They concluded that: 'Acute bacterial conjunctivitis is frequently a self-limiting condition but the use of antibiotics is associated with significantly improved rates of clinical cure and microbiological eradication. These results however cannot be generalised to a primary care based population.'

2.5 How will the results of this trial be used?

This trial will help to clarify which strategies are most appropriate for the management of acute infective conjunctivitis in general practice.

2.6 Please detail any risks to the safety of participants involved in the trial

None

3 The Proposed Trial

3.1 What is the proposed trial design?

The trial will be an open randomised controlled trial with a 3x2x2 factorial design.

.

3.2 What are the planned trial interventions?

The patients will be randomised to receiving one of 3 treatments:

4) topical antibiotic eye drops for 7days.
5) no prescription.
6) a delayed prescription of antibiotic eye drops after 3 days.

These groups will be further randomised to receive a patient information leaflet (which has been developed in the qualitative study allied to this trial).

Half the patients in each group will have eye swabs sent for culture. This will give microbiological information about the cohort.

3.3 What is the proposed duration of treatment period?

Treatment as detailed above. The diary will be used to record symptoms for a maximum of 14days

3.4 What are the planned inclusion/exclusion criteria?

Inclusion criteria: Patients aged 1 year and over presenting with presumed acute infective conjunctivitis (red, inflamed discharging eyes) to their general practitioner or practice nurse.

Exclusion criteria: Patients who are systemically unwell and require oral antibiotics, patients who have had antibiotics in the previous 2 weeks, patients with chronic infective eye disease eg blepharitis and patients having recently had eye surgery ie in the last one month.

3.5 What are the proposed outcome measures?

Primary: 3 primary outcomes:
Symptom severity score (mean item score for 5 main symptoms over first 3 days of the diary) - Main outcome
Duration of moderately severe symptoms
Belief in the efficacy of antibiotics for conjunctivitis

Secondary: Duration of minor symptoms
Relapse of symptoms
Compliance with the treatment
Use of antibiotics
Perceived importance of seeing the doctor.

3.6 Will Health service research issues be addressed?

Health economic issues are not being addressed
Quality of life measures are being assessed in the diary.

3.7 What is the proposed frequency/duration of follow up?

Participants will complete diaries for a maximum of 14 days after recruitment.

3.8 How will the outcome measures be measured at follow-up?

GP information sheet
The general practitioner will fill in a documentation sheet during the consultation showing duration of illness, signs and symptoms and treatment offered.

Patient Questionnaire and Diary
Patients will be given a daily dairy in which to record symptoms and will be asked to continue the diary until they are both free of symptoms and have finished their medication (up to a maximum of 14 days). In the case of children under 12 the parent will be asked to complete the diary (as used successfully in previous studied undertaken by this group). Parental recording of child symptoms has been shown to be valid in previous trials. The design of the diary is similar to those used in previous trials. The symptoms recorded in the diary has been determined by a search of the literature and from information gathered in the associated qualitative study (face and content validity). Construct validity of the diary will be checked by asking 30 patients to complete a MYMOP questionnaire at Day1 and Day3 – thus enabling comparison of the diary with a validated measure of symptom severity recording. Patients will be

contacted within 3 days of the consultation to check that there are no problems filling in the diary.
Patients will also be asked to answer written questions using a validated Likert scale at the beginning of treatment - regarding worries, treatment option and satisfaction – and at the end - regarding antibiotic use, perceived efficacy, future intentions and time off work or school.
It is anticipated (based on experience from similar trials within the group) that at least 75 % of the diaries will be returned. Patients who fail to return the diary within 2 weeks of entry to the study will be telephoned to ask the questions addressed by the diary. The validity of information gathered by questionnaire and by telephone has been shown to be comparable in this type of trial.

3.9 What are the proposed practical arrangements for allocation participants to the trial groups?

Participants will be randomised by the opening of a sealed numbered opaque envelope in the consultation as to which treatment they will receive (used successfully with no evidence of selection bias in previous studies undertaken by this group). Balanced randomisation will be used to ensure equal sample sizes in each group.

3.10 What are the proposed methods for protecting against other sources of bias?

Blinding is not appropriate for this trial. An open trial design is essential to assess patients' perceptions and choices in response to different management strategies. It is a design that closely represents the behaviour every day general practice (this type of trial has been used successfully to research antibiotic prescribing in sore throat, otitis media and cough within this research group). The main disadvantage of using this approach is the possibility of bias due to the placebo effect. However it has shown in previous trials that the use structured advice packages to enable the general practitioner to support each proposed strategy means that the general practitioner can function as the placebo in each group.

3.11 What is the proposed sample size and what is the justification for the assumptions underlying the power calculations?

The original calculations based on information on symptom duration and the effect of antibiotics from the literature, estimated that a sample size of 200 patients will be required to detect a 1 day difference in symptom resolution and a 25% difference in belief in antibiotics. This was calculated by nomogram for multiple groups in a factorial trial for the symptom resolution and Spida 1.6 version computer package for the belief in antibiotics. Because of the uncertainty behind the assumptions made for the sample size calculation (lack of available evidence) a sample size of 300 was set as the working target.

Assessment of severity and duration data from 126 diaries (Jan 2004) has allowed recalculation of the sample size.(using NQuery multiple group sample size program)
For an alpha of 0.01:
Duration moderate symptoms (a day between each group) 234 are needed
Severity of symptoms (0.33 between each group) 264 are needed
Beliefs in antibiotics (15% between each group) 246 are needed

After discussion with the TSC a sample size of 260 to 300 will be aimed for to allow for some sub group analysis.

3.12 What is the planned recruitment rate?

75 patients per year for 4 years = 300 participants.

3.13 Are there likely to be any problems with compliance?

Unlikely

3.14 What is the likely loss to follow up rate?

It is anticipated (based on experience from similar trials within the group[18]) that at least 75 % of the diaries will be returned (thus a loss to follow up of 25%).

3.15 How many centres will be involved?

One centre – Southampton – but many GP practices (50 to 100) will recruit patients from Southampton, Salisbury, Portmouth and Dorset LREC areas.

3.16 What is the proposed type of analysis?

Data will be analysed on an intention to treat basis by logistic regression for the factorial study for discrete outcomes (eg % belief in antibiotics) and Anova for continuous outcomes (eg symptom resolution).

3.17 What is the proposed frequency of the analysis?

Analysis will occur after data collect is complete.

3.18 Are there any planned sub group analyses?

Yes. Regression modelling will be used to determine factors that predict adverse outcome (severe/prolonged symptoms) and assess if this subgroup predicts benefit from antibiotics. Potential factors may include severity of presenting symptoms, bilateral vs unilateral disease, presence/absence of other (non eye related) symptoms, age.

3.19 Has any pilot study been carried out using this design?

Yes. The other trials successfully undertaken by this group (eg sore throat, otitis media) have had very similar design. Also small pilot to assess paperwork and swab analysis was undertaken.

4 Trial Management

4.1 What are the arrangements for day to day management of the trial.

Dr Hazel Everitt is responsible for day to day management of the trial including recruiting GPs , managing paperwork and data handling.

4.2 What will be the responsibilities of the applicants?

Dr Everitt -Day to day management of the trial

4.3 What will be the responsibility of the staff employed on the grant?

Dr Everitt -Day to day management of the trial

4.4 What will be the role of the named collaborators?

N/A

4.5 Who is the trial statistician?

Professor Paul Little is supervising the statistics for the trial.

4.6 Trial steering committee

Prof Chris Butler (chair) Cardiff University, Dr Hazel Everitt (trial manager) Southampton University, Prof Paul Little (trial supervisor) Southampton University, Rebecca Cannings (statistician) Cardiff University, Dr Alastair Hay (independent committee member) Bristol University.

Ethical approval

Patients will give informed consent to be included in the trial (parents will give consent for children under 16yrs). Competent children (ie those aged 10-16yrs) will also be asked for consent along with their parent and will sign the consent form

Full Ethical approval has been sought and gained for this research project from Southampton (no: 267/99), Portsmouth (no: 09/99/894) and Salisbury (no: SA27/99) and Dorset (no:46/03/S) LRECs.

Trial registration number: ISRCTN32956955

Appendix 6: Patient information sheet for the Randomised Controlled Trial

University of Southampton

EYE INFECTION STUDY
Patient information sheet

This research project is trying to find out what you feel about the different sorts of available treatment and advice GPs give about eye infections. It will also give us valuable information about how quickly you/your child gets better from eye infections, what other symptoms you/your child experienced and what causes eye infections.

What the study involves for you:

- answer a brief questionnaire today
- you/your child may be asked to have an eye swab performed today by your GP
- complete the diary of you/your child's symptoms and answer a few questions and then return it in the Freepost envelope provided
- the research assistant may ask you to consider talking confidentially about concerns you have about eye infections: this information will be recorded for research purposes only and remains strictly confidential
- your/your childs' notes may be checked by the researcher after the study to see if you have had any further problems with eye infections

At any time during the study you are free to withdraw yourself/your child without giving any reason and without affecting your/your child's future treatment in any way.
All the information that you give us will be keep fully confidential. Even your GP will not see the diary or questionnaires. Your/your child's name will not appear on any documents or reports.

If you have any queries please contact:

Hazel Everitt
Primary Medical Care,
University of Southampton,
Aldermoor Close,
Southampton
SO16 5ST
(Tel 02380 241079 – 24 hr ansaphone)

March 2003

Appendix 7: Consent form for the Randomised Controlled Trial

University
of Southampton

LREC number:

Patient ID no:_____

EYE INFECTION STUDY
CONSENT FORM

Please initial box:-

1. I confirm that I have read and understand the information sheet for the eye infection study and have had an opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw myself/my child from the study at any time, without giving any reason, without my medical care or legal rights being affected.

3. I agree to take part in the above study.
   Or I agree for my child _____to take part in the study.

Your name Mr/Mrs/Miss/Ms _____

Your signature _____ Date _____

Child's signature (if appropriate) _____

Address _____

_____

Postcode _____ Telephone no. _____

Name of person taking consent _____ Date _____

Signature of person taking consent _____

March 2003

Appendix 8: Eye Swab Protocol for Conjunctivitis Trial

1. Specimen Collection

a) Clinical samples are collected using calcium alginate swabs and placed into Amies transport medium with charcoal.
b) Collection of the material is by sampling any visible pus or by rolling the swab along the lid margin.
c) One swab is taken per trial participant randomised to swab collection. If both eyes are affected the sample is taken from the more severely affected eye.
d) Swabs are held at ambient temperature until processed.
e) Swabs are sent on the usual laboratory transport from the GP surgery to the Southampton microbiology laboratory were processing occurs
f) All swabs are processed within 48 hours (preferably within 24hours) of collection.

2. Removal of bacteria from swab

a) The swab is removed from its container and the tip of the swab cut off into 3ml of sterile 0.9% saline.
b) The tube containing the swab tip and saline is vortexed for 2 minutes to remove any bacteria from the swab.

3. Culture of specimens

a) 100ul and 10ul samples are spread onto blood agar and chocolate agar. Culture plates are incubated at 37°C for 48 hours in a 5% enriched CO_2 atmosphere.

b) Colony counts are then performed on the cultures to give the number of colony forming units.

c) Cultures are identified using standard bacteriological techniques. Appropriate sensitivity tests are performed when necessary.

Appendix 9: 'Not Entered' Book Information

GPs or Practice nurses were asked to note any patients presenting with acute infective conjunctivitis that were not entered into the trial. They noted the patients age, sex, the reason for not entering the trial (see list below) and the severity of the conjunctivitis (conjunctival injection and amount of eye discharge – scoring system below)

REASON FOR PATIENT NOT ENTERING STUDY

1) No time (doctor)
2) Patient refused
3) Parental anxiety
4) Patient too unwell
5) Antibiotics for conjunctivitis in last 2 weeks
6) Problems following previous conjunctivitis
7) Chronic infective eye condition (eg blepharitis)
8) Recent eye surgery (in last month)
9) Other

SEVERITY OF THE EYE INFECTION – Please score the level of conjunctival injection and the amount of eye discharge

0=normal, 1=very little, 2=slight, 3=moderate, 4=bad, 5=very bad, 6=as severe as it could be

Appendix 10: GP Initial Clinical Signs Sheet from the Randomised Controlled Trial

EYE INFECTION STUDY
Initial Clinical Signs Sheet

Patient's Name _____

Date of Birth ___/___/___ Date Entered into study ___/___/___

1. **Duration of eye infection (days)** _____

2. **Which eye affected?** Right / Left / Both

3. **Clinical signs present on examination:**
   Please indicate the severity of the sign by placing a number in each box from 0 to 6. (0=normal, 1=very little, 2=slight, 3=moderate, 4=bad, 5= very bad, 6= as severe as t could be)

   a. **Conjunctival injection** ☐

   b. **Conjunctival oedema** ☐

   c. **Subconjunctival haemorrhage** ☐

   d. **Eye discharge** ☐

   If present, is the discharge: i) Clear /yellow /green /bloody
   ii) Sticky/ watery
   iii) large amount/ small amount

   e. **Neck lymphadenopathy** ☐

   If present, is it: (please circle) Pre-auricular/ cervical/ other

   f. **Other symptoms present with this illness?** ☐

   Please specify _____
   (eg sore throat, cough, fever, headache)

4. **What is your clinical diagnosis?** (Please tick box)
   Bacterial conjunctivitis ☐
   Viral conjunctivitis ☐
   Other _____

5. **How confident are you of the diagnosis?** ☐
   0=not at all, 1=very little, 2= slightly, 3 =moderately, 4=quite, 5=very, 6=certain.

Thank you!

Appendix 11: GP Advice Sheets for the Randomised Controlled Trial

These randomised the participants to the treatment they were to receive and ensured that the GPs provided a standard advice package for the participants. There were 12 randomisation groups.

Summary of the randomisation:

Sheet 1	Immediate topical antibiotics, no eye swab no patient information leaflet
Sheet 2	Delayed topical antibiotics, no eye swab no patient information leaflet
Sheet 3	No antibiotics, no eye swab no patient information leaflet
Sheet 4	Immediate topical antibiotics, eye swab, no patient information sheet
Sheet 5	Delayed topical antibiotics eye swab, no patient information sheet
Sheet 6	No topical antibiotics, eye swab, no patient information sheet
Sheet 7	Immediate antibiotics, eye swab, patient information sheet
Sheet 8	Delayed topical antibiotics, eye swab, patient information sheet
Sheet 9	No topical antibiotics, eye swab, patient information sheet
Sheet 10	Immediate topical antibiotics, no eye swab, patient information sheet
Sheet 11	Delayed topical antibiotics, no eye swab, patient information sheet
Sheet 12	No topical antibiotics, no eye swab, patient information sheet

ID No:_____

ADVICE SHEET 1

Please follow this advice sheet as near verbatim as possible. After the patient has left please tick only the items that you mentioned and answer the questions at the end.

		Essential Points	*Suggested Wording*
☐	1.	**This is an eye infection**	known as conjunctivitis.
☐	2.	**Antibiotic eye drops could help**	you/your child's **symptoms to settle** and **prevent** any **complications.**
☐	3.	**I will give you/your child a prescription**	for antibiotic drops. It is very important that you/your child take the antibiotic drops for the **full course.** (Prescription of Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	4.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. They may be cleaned as often as is required with a piece of wet cotton wool.
☐	5.	**Follow up**	If you/your child has pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come for a check-up appointment. Also come back if it is not settling after one week.
☐	6.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 1.

Please include this sheet with the Initial Clinical Signs sheet and the Consent Form and return in the freepost envelope provided.

ID No:_____

ADVICE SHEET 2

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐	**1. This is an eye infection**	known as conjunctivitis. Usually your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐	**2. Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. Your/your childs' eyes may be cleaned as often as is required with a piece of wet cotton wool.
☐	**3. Most patients get better without antibiotic drops**	Antibiotics are not usually needed for eye infections. They are not **painkillers**.
☐	**4. Antibiotic drops may cause side effects**	can cause allergy and can lead to antibiotic resistance
☐	**5. Antibiotic drops may still be prescribed if:**	you are not starting to improve in **3 days** (explain that a **red eye** and **discharge for a few days** is normal and does not mean antibiotics are needed). A prescription will be left for you in reception. (Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	**6. Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come of a check-up appointment. Also come back if it is not settling after one week
☐	**7. To recap most get better so try and wait 3 days**	before collecting the prescription. **NB Remember to state you are in the eye infection study if you collect a prescription.**
☐	**8. Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 2.

Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided.

ID No:_____

ADVICE SHEET 3

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐ 1.	**This is an eye infection**	known as conjunctivitis. Your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐ 2.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes –especially in the mornings. This is not harmful but may be irritating and may be cleaned as often as is required with a piece of wet cotton wool
☐ 3.	**Most patients get better without antibiotic drops**	Antibiotics are not needed for eye infections. They are **not painkillers**.
☐ 4.	**Antibiotic drops can also cause side effects**	can cause allergy, and can lead to antibiotic resistance.
☐ 5.	**Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or the vision is affected please come for a check up. (*explain that a **red eye** and **discharge** for a few days is normal)*. Also come back if it is not settling after one week.
☐ 6.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 3.

Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided.

ID No:_____

ADVICE SHEET 4

Please follow this advice sheet as near verbatim as possible. After the patient has left please tick only the items that you mentioned and answer the questions at the end.

		Essential Points	*Suggested Wording*
☐	1.	**This is an eye infection**	known as conjunctivitis.
☐	2.	**Antibiotic eye drops could help**	you/your child's **symptoms to settle** and **prevent** any **complications.**
☐	3.	**I will give you/your child a prescription**	for antibiotic drops. It is very important that you/your child take the antibiotic drops for the **full course**. (Prescription of Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	4.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. They may be cleaned as often as is required with a piece of wet cotton wool.
☐	5.	**I would like to take a swab from your eye**	This will be sent to the laboratory to see if any bacteria are present. The results will be available in 5 to 7 days time.
☐	6.	**Follow up**	If you/your child has pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come for a check-up appointment. Also come back if it is not settling after one week.
☐	7.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 4.

Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature.

Please include this sheet with the Initial Clinical Signs sheet and the Consent Form and return in the freepost envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 5

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐	1. **This is an eye infection**	known as conjunctivitis. Usually your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐	2. **Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. Your/your childs' eyes may be cleaned as often as is required with a piece of wet cotton wool.
☐	3. **Most patients get better without antibiotic drops**	Antibiotics are not usually needed for eye infections. They are **not painkillers**.
☐	4. **Antibiotic drops may cause side effects**	can cause allergy and can lead to antibiotic resistance
☐	5. **Antibiotic drops may still be prescribed if:**	you are not starting to improve in **3 days** (explain that a **red eye** and **discharge for a few days** is normal and does not mean antibiotics are needed). A prescription will be left for you in reception. (Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	6. **I would like to take a swab from your eye**	This will be sent to the laboratory to see if any bacteria are present. The results will be available in 5-7days time.
☐	7. **Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come of a check-up appointment. Also come back if it is not settling after one week
☐	8. **To recap most get better so try and wait 3 days**	before collecting the prescription. **NB Remember to state you are in the eye infection study if you collect a prescription.**
☐	9. **Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 5.
Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature.
Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 6

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐ 1.	**This is an eye infection**	known as conjunctivitis. Your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐ 2.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes –especially in the mornings. This is not harmful but may be irritating and may be cleaned as often as is required with a piece of wet cotton wool
☐ 3.	**Most patients get better without antibiotic drops**	Antibiotics are not needed for eye infections. They are **not painkillers.**
☐ 4.	**Antibiotic drops can also cause side effects**	can cause allergy, and can lead to antibiotic resistance.
☐ 5.	**I would like to take a swab from your eye**	This will be sent to the laboratory to see if there are any bacteria. The result will be available in 5-7 days time.
☐ 6.	**Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or the vision is affected please come for a check up. (*explain that a **red eye** and **discharge** for a few days is normal).* Also come back if it is not settling after one week.
☐ 7.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 6.

Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature.

Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 7

Please follow this advice sheet as near verbatim as possible. After the patient has left please tick only the items that you mentioned and answer the questions at the end.

		Essential Points	Suggested Wording
☐	1.	**This is an eye infection**	known as conjunctivitis.
☐	2.	**Antibiotic eye drops could help**	you/your child's **symptoms to settle** and **prevent** any **complications.**
☐	3.	**I will give you/your child a prescription**	for antibiotic drops. It is very important that you/your child take the antibiotic drops for the **full course.** (Prescription of Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	4.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. They may be cleaned as often as is required with a piece of wet cotton wool.
☐	5.	**I would like to take a swab from your eye**	This will be sent to the laboratory to see if any bacteria are present. The result will be available in 5-7 days time.
☐	6.	**Follow up**	If you/your child has pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come for a check-up appointment. Also come back if it is not settling after one week.
☐	7.	**Here is a patient information leaflet**	It contains information to help you manage the conjunctivitis. Please read it carefully and keep it in a safe place.
☐	8.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 7.
Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature.
Please include this sheet with the Initial Clinical Signs sheet and the Consent Form and return in the freepost envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 8

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐	**1. This is an eye infection**	known as conjunctivitis. Usually your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐	**2. Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. Your/your childs' eyes may be cleaned as often as is required with a piece of wet cotton wool.
☐	**3. Most patients get better without antibiotic drops**	Antibiotics are not usually needed for eye infections. They are not **painkillers**.
☐	**4. Antibiotic drops may cause side effects**	can cause allergy and can lead to antibiotic resistance
☐	**5. Antibiotic drops may still be prescribed if:**	you are not starting to improve in **3 days** (explain that a **red eye** and **discharge for a few days** is normal and does not mean antibiotics are needed). A prescription will be left for you in reception. (Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	**6. I would like to take an swab from your eye.**	This will be sent to the laboratory to see if any bacteria are present. The result will be available in 5-7 days
☐	**7. Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come of a check-up appointment. Also come back if it is not settling after one week
☐	**8. To recap most get better so try and wait 3 days**	before collecting the prescription. **NB Remember to state you are in the eye infection study if you collect a prescription.**
☐	**9. Here is a patient information sheet**	It contains information to help you manage conjunctivitis. Please read it carefully and keep it in a safe place.
☐	**10. Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 8.

Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature. Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 9

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐ 1.	**This is an eye infection**	known as conjunctivitis. Your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐ 2.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes –especially in the mornings. This is not harmful but may be irritating and may be cleaned as often as is required with a piece of wet cotton wool
☐ 3.	**Most patients get better without antibiotic drops**	Antibiotics are not needed for eye infections. They are **not painkillers**.
☐ 4.	**Antibiotic drops can also cause side effects**	can cause allergy, and can lead to antibiotic resistance.
☐ 5.	**I would like to take an swab from your eye.**	This will be sent to the laboratory to see if there are any bacteria. The result will be available in 5-7 days.
☐ 6.	**Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or the vision is affected please come for a check up. (*explain that a **red eye** and **discharge** for a few days is normal*). Also come back if it is not settling after one week.
☐ 7.	**Here is a patient Information sheet**	It contains information to help you manage conjunctivitis. Please read it carefully and keep it in a safe place.
☐ 8.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 9.

Label the eye swab and microbiology form (include patients name, date of birth, address & IDno) and place in todays transport to microbiology at SGH. Store at room temperature.

Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 10

Please follow this advice sheet as near verbatim as possible. After the patient has left please tick only the items that you mentioned and answer the questions at the end.

		Essential Points	*Suggested Wording*
☐	1.	**This is an eye infection**	known as conjunctivitis.
☐	2.	**Antibiotic eye drops could help**	you/your child's **symptoms to settle** and **prevent** any **complications.**
☐	3.	**I will give you/your child a prescription**	for antibiotic drops. It is very important that you/your child take the antibiotic drops for the **full course**. (Prescription of Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	4.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. They may be cleaned as often as is required with a piece of wet cotton wool.
☐	5.	**Follow up**	If you/your child has pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come for a check-up appointment. Also come back if it is not settling after one week.
☐	6.	**Here is a patient information leaflet**	It contains information to help you manage the conjunctivitis. Please read it carefully and keep it in a safe place.
☐	7.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 10.

Please include this sheet with the Initial Clinical Signs sheet and the Consent Form and return in the freepost envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 11

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐	**1. This is an eye infection**	known as conjunctivitis. Usually your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐	**2. Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes – especially in the mornings. This is not harmful but may be irritating. Your/your childs' eyes may be cleaned as often as is required with a piece of wet cotton wool.
☐	**3. Most patients get better without antibiotic drops**	Antibiotics are not usually needed for eye infections. They are **not painkillers**.
☐	**4. Antibiotic drops may cause side effects**	can cause allergy and can lead to antibiotic resistance
☐	**5. Antibiotic drops may still be prescribed if:**	you are not starting to improve in **3 days** (explain that a **red eye** and **discharge for a few days** is normal and does not mean antibiotics are needed). A prescription will be left for you in reception. (Chloramphenicol eye drops 0.5% 10ml, 2 drops in the affected eye every 2 hours for 2 days then 2 drops four times a day, continue for 48hours after healing)
☐	**6. Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or your/your childs' vision is affected please come of a check-up appointment. Also come back if it is not settling after one week
☐	**7. To recap most get better so try and wait 3 days**	before collecting the prescription. **NB Remember to state you are in the eye infection study if you collect a prescription.**
☐	**8. Here is a patient information sheet**	It contains information to help you manage conjunctivitis. Please read it carefully and keep it in a safe place.
☐	**9. Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 11.
Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

ID No:_____

ADVICE SHEET 12

Please follow this advice sheet as near verbatim as possible. After patient has left please tick only the items that you mentioned and answer the questions at the end.

	Essential points	*Suggested wording*
☐ 1.	**This is an eye infection**	known as conjunctivitis. Your/your child's body will fight the infection and heal itself over the next week without the need for antibiotics.
☐ 2.	**Sticky eyes can be relieved by bathing with cooled boiled water**	Conjunctivitis often causes sticky eyes –especially in the mornings. This is not harmful but may be irritating and may be cleaned as often as is required with a piece of wet cotton wool
☐ 3.	**Most patients get better without antibiotic drops**	Antibiotics are not needed for eye infections. They are **not painkillers.**
☐ 4.	**Antibiotic drops can also cause side effects**	can cause allergy, and can lead to antibiotic resistance.
☐ 5.	**Follow-up**	if you/your child have pain in the eye (opposed to a gritty feeling) or increasing swelling or redness around the eye or the vision is affected please come for a check up. (*explain that a **red eye** and **discharge** for a few days is normal).* Also come back if it is not settling after one week.
☐ 6.	**Here is a patient Information sheet**	It contains information to help you manage conjunctivitis. Please read it carefully and keep it in a safe place.
☐ 7.	**Any questions?**	Can I put your mind at rest about any concerns or questions you have? *(Please make a note of these below)*

Did the patient leave the surgery with a prescription for antibiotics? Y N

How well did you feel the patient accepted the advice strategy?

Extremely well	Very well	Moderately well	Slightly well	Not very well	Not at all well
☐	☐	☐	☐	☐	☐

Make a note on patient's notes that they have been entered into the study and that they have been given Adv Pkg 12.

Please include this sheet with the Initial Clinical Signs sheet and Consent form and return in the stamped addressed envelope provided to Primary Medical Care.

Appendix 12: Patient Questionnaire about Eye Infections

Questionnaire about Eye Infections

Your Name: _____ Date: _____

Sex: M / F Date of birth: _____

Please complete these questions about your eye infection:

Which eye is affected? Right/Left/Both eyes
How long has it been affected? (**before** this consultation): _____days.

How bad are each of the following symptoms today?
Put a number in every box from 0 to 6 corresponding to how bad each symptom is. (If you don't have the symptom put 0.)
0 = normal 1 = very little problem 2 = slight problem 3 = moderate problem 4 = bad 5 = very bad 6 = as bad as it could be

1. Fever? ☐
2. Red eye/eyes? ☐
3. Eye pain or discomfort? ☐
4. Itchy eye/eyes? ☐
5. Altered vision? ☐
6. Dislike of bright lights? (photophobia) ☐
7. Eyelid swelling? ☐
8. Waking with sticky eyes? ☐
9. Eye discharge during the day? ☐ discharge? a) clear/yellow/green/bloody
   b) sticky/watery
10. Runny nose? ☐
11. Cough? ☐
12. Sore throat? ☐
13. Other? _____
14. Have you used any medications or remedies at home to treat this eye infection? Y / N
    If yes please specify: _____
15. Have you/your child had an eye infection before? Y / N
    If yes how many?_____ and how many have you been to the doctor for an eye infection? _____

Thank you for completing this questionnaire. Please check that you have answered all the questions and hand it into reception today.

Appendix 13: Patient Diary for the Randomised Controlled Trial

Diary of Symptoms

Eye Infection Study

Primary Medical Care

University of Southampton

Eye Infection Study - Patients' Diary

office use only

IDno ☐☐☐☐

TODAY *Please answer the following questions by the ticking the appropriate box:*

Q1 **How worried are you about your/your child's eye problem?**

Extremely worried	Very worried	Moderately worried	Slightly worried	Not Very worried	Not at all worried
☐	☐	☐	☐	☐	☐

Q2 **How well did the doctor/nurse deal with your worries or concerns?**

Extremely well	Very well	Moderately well	Slightly well	Not Very well	Not at all well
☐	☐	☐	☐	☐	☐

Q3 **How satisified are you with the consultation you had with the doctor/nurse?**

Extremely satisfied	Very satisfied	Moderately satisfied	Slightly satisfied	Not Very satisfied	Not at all satisfied
☐	☐	☐	☐	☐	☐

Q4 **How important was it for you to see a doctor/nurse on this occasion to enable you/your child to continue to go to work/school?**

Extremely important	Very important	Moderately important	Slightly important	Not Very important	Not at all important
☐	☐	☐	☐	☐	☐

Q5 **How satisfied are you with the amount of information you were given about eye infections?**

Extremely satisfied	Very satisfied	Moderately satisfied	Slightly satisfied	Not Very satisfied	Not at all satisfied
☐	☐	☐	☐	☐	☐

Please fill in the diary on the next page starting this evening

Eye Infection Study DIARY OF SYMPTOMS

Please fill in the diary below by choosing the most appropriate number from the code box for each question.
You can see from the example below how to write the numbers in the boxes. Read **down** the list of symptoms for each day. Fill in one day at a time. Please complete the chart each evening. The questions refer to how you (or your child) has felt during the last 24 hours. **Continue using the chart until you no longer have any symptoms.** If this diary is for your child, please fill in this diary together.

IMPORTANT: All categories are for the last 24 hours.

Please put your/your childs initials at the top of each page.

Code box:

0 = Normal / not affected	4 = bad
1 = Very little problem	5 = Very bad
2 = Slight problem	6 = As bad as it could be
3 = Moderately bad	

From the example given it can be seen that the patient had a 'slightly' red eye; 'moderately bad' eye discomfort; waking with a sticky eye was 'very bad' ; eye discharge during the day was 'moderately bad': eye lid swelling was "very little problem"; vision was 'not affected' and the patient found feeling unwell 'very little problem'.

	Example Day
Red eye	2
Eye discomfort or itchiness	3
Woke with sticky eye	5
Eye discharge during day	3
Eye lid swelling	1
Altered vision	0
How unwell you/your child is feeling	1

Eye Infection Study Diary of Symptoms WEEK 1

Initials:

Please fill in
Date chart started D D / M M / Y Y

IDno
office use only

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Red eye	☐	☐	☐	☐	☐	☐	☐
Eye discomfort or itchiness	☐	☐	☐	☐	☐	☐	☐
Woke with sticky eye	☐	☐	☐	☐	☐	☐	☐
Eye discharge during the day	☐	☐	☐	☐	☐	☐	☐
Eye lid swelling	☐	☐	☐	☐	☐	☐	☐
Altered vision	☐	☐	☐	☐	☐	☐	☐
How unwell you/ your child feels	☐	☐	☐	☐	☐	☐	☐

Please continue the diary on the next page. When you/your child are completely better please go to the next section

Eye infection Study Diary of Symptoms Week 2 Initials

	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
Red eye	☐	☐	☐	☐	☐	☐	☐
Eye discomfort or itchiness	☐	☐	☐	☐	☐	☐	☐
Woke with a sticky eye	☐	☐	☐	☐	☐	☐	☐
Eye discharge during the day	☐	☐	☐	☐	☐	☐	☐
Eye lid swelling	☐	☐	☐	☐	☐	☐	☐
Altered vision	☐	☐	☐	☐	☐	☐	☐
How unwell you/your child is feeling	☐	☐	☐	☐	☐	☐	☐

Even if your eye problem is not better by day 14, please go on to the next section.

Eye Infection Study IDno ☐☐☐☐
office use only

FINALLY after you/your child are completely better please answer the following questions by filling in the spaces or ticking the appropriate answer.

Q1 Did you/your child experience a runny nose during the illness?

Yes ☐ ☐ No If Yes, how many days? ☐☐

Q2 Did you/your child experience a cough during the illness?

Yes ☐ ☐ No If Yes, how many days? ☐☐

Q3 Did you/your child experience a sore throat during the illness?

Yes ☐ ☐ No If Yes, how many days? ☐☐

Q4 Did you/your child experience a diarrhoea during the illness?

Yes ☐ ☐ No If Yes, how many days? ☐☐

Q5 Did you/your child have some form of pain/temperature relief e.g. paracetemol/calpol/ Junifen?

Yes ☐ ☐ No If Yes, what was its name? ☐

Q6 Did you/your child use any medication/drops/ointment from the pharmacist?

Yes ☐ ☐ No If Yes, what was its name? ☐

Q7 Did you/your child bathe the affected eye/eyes in cooled boiled water?

Yes ☐ ☐ No If yes, For how many days? ☐☐

Q8 Were you/your child given an antibiotic ointment/eye drop prescription?

Yes ☐ ☐ No

Q9 If Yes to Q8, did you/your child use the eye ointment/drops?

Yes ☐ ☐ No

Q10 If Yes to Q9, which day did you/your child start taking the eye ointment/drops (please state which day of the diary e.g. Day 3) ☐☐

Q11 How many days did you/your child take them for? ☐☐

PLEASE TURN OVER AND CONTINUE WITH THE QUESTIONS

Q12 **Do you think antibiotic eye ointment/drops are effective in treating eye infections?**
(please answer whether you/your child had antibiotics this time or not).

Extremely effective	Very effective	Moderately effective	Slightly effective	Not very effective	Not at all effective
☐	☐	☐	☐	☐	☐

Q13 **How likely are you to go/take your child to the doctor/nurse with a future eye infection?**

Extremely likely	Very likely	Moderately likely	Slightly likely	Not very likely	Not at all likely
☐	☐	☐	☐	☐	☐

Q14 **Did you take/your child take any time off work or school?** Yes ☐ ☐ No

Q15 **If yes to Q12 which day did you/your child return. (*please state which day of the diary e.g. day 4)***

Day ☐☐

Q16 **As a result of the visit to the doctor/nurse and advice you have been given, do you feel you are?**

	much better	better	same or less
Able to cope with your/your childs life?	☐	☐	☐
Able to understand your/your childs illness?	☐	☐	☐
Able to cope with your/your childs illness?	☐	☐	☐
Able to keep yourself/your child healthy?	☐	☐	☐

	much more	more	same or less
Confident about your/your childs health?	☐	☐	☐
Able to help yourself/your child?	☐	☐	☐

Please turn to the next page

Q17 **Date of birth** D D / M M / Y Y Y Y

Q18 **Sex** Male ☐ ☐ Female

(If you are completing this questionnaire for your child please answer the following questions as they relate to yourself)

Q19 **Marital Status:**

- Single ☐
- Married (or living with partner) ☐
- Widowed ☐
- Divorced/separated ☐

Q20 **How would you describe your ethnic background**

- Afro-caribbean ☐
- Indian ☐
- Pakistani ☐
- Bangladeshi ☐
- Chinese ☐
- White ☐
- Other ☐

Q21 **At what age did you leave full time education?** ☐☐

Q22 **What are your highest formal educational qualifications?**

- No formal educational qualifications ☐
- CSEs/O'levels or similar ☐
- A Levels (or similar) or ONC/OND ☐
- Diploma (non degree) e.g. HNC, HND ☐
- Degree ☐
- Postgraduate Degree ☐

Please turn to the next page

Q23 **Employment History**

Pick one statement below, that best explains your current employment status

- Full time employee ☐
- Part time employee ☐
- Self employed ☐
- Homemaker ☐
- Retired ☐
- Not in paid employment due to disability ☐
- Not in paid employment due to long-term sickness ☐
- Unemployed for less than one year ☐

What is the title or description of your current job OR the job you last had when your were in paid employment (please explain clearly)

Q24 **In the job stated above where you (are you) either**

- A manager ☐
- A foreman ☐

Please return this questionnaire in the freepost envelope provided.

Thank you for all your help.

Appendix 14: GP post recruitment questionnaire

Conjunctivitis Trial

Post-Recruitment Questionnaire

Name:_____ Date_____

1. **What proportion of patients with acute infective conjunctivitis that saw you during the trial period do you think were entered into the trial?**

   <10%, 10-29%, 30-49%, 50-69%, 70-89%, >90%

2. **How many eligible patients that you asked about the trial refused to participate? --**

3. **What were the main reasons for not entering patients into the trial? Please rank the below in order, 1 being the most likely and 10 the least**

   No time (doctor) _____
   Patient under 1yr old _____
   Patient refused _____
   Parental anxiety _____
   Patient too unwell _____
   Antibiotics for conjunctivitis in last 2 weeks _____
   Problems following previous conjunctivitis _____
   Chronic infective eye condition (eg blepharitis) _____
   Recent eye surgery (in last month) _____
   Other (please specify) _____

4. **Has your management of acute infective conjunctivitis changed as a result of participating in the trial?** Yes/No

   If Yes, please specify

   _____

   _____

5. **Any other comments?** (Please continue on reverse of paper if necessary)

   _____

   _____

   _____

Thank you!

Please return this in the freepost envelope with your 'Not entered' book and any unused scripts from the delayed prescription box.

Appendix 15: Notes review form for the Randomised Controlled Trial

University of Southampton

Conjunctivitis Study Patient Follow-up

IDno:

Patient:	**Date of Birth:**
Recruiter:	**Date of study entry:**
Date:	**Completer of this form:**

1)	Has the patient re-attended since the recruitment date with Conjunctivitis or suspected conjunctivitis? (see above for recruitment date)	Yes		No

If yes, please give dates and details below and state whether they received antibiotics. Please also note any referrals to secondary care for eye related symptoms.

2)	Has the patient re-attended since the recruitment date with other URTIs?	Yes		No

If yes, please give dates and details below and state whether they received antibiotics.

3)	Did the patient have any consultations for conjunctivitis or suspected conjunctivitis in the year prior to recruitment?	Yes		No

If yes, please give dates and details below and state whether they received antibiotics. Please also note any referrals to secondary care for eye related symptoms.

4)	Did the patient have any consultations for other URTIs in the year prior to recruitment?	Yes		No

If yes, please give dates and details below and state whether they received antibiotics.

Please continue below if you need more space.
THANK YOU FOR YOUR TIME AND HELP IN COMPLETING THIS QUESTIONNAIRE
PLEASE RETURN IN THE FREEPOST ENVELOPE

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