The impact of chest radiography on the diagnosis, clinical management and outcome of acute lower respiratory infections in children

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Abstract

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Background. When available, chest radiography is widely used in acute lower respiratory infections in children. Its impact on clinical outcome is unknown.

Methods. A randomised controlled trial was performed of 522 children aged 2 to 59 months who met the World Health Organisation case definition for pneumonia. The main outcome was time to recovery, measured in a subset of 398 participants who offered a telephone number. Subsidiary outcomes included diagnosis, elements of clinical management and subsequent use of health facilities.

Findings. There was a marginal improvement in time to recovery, which was not clinically significant. The median time to recovery was seven days in both groups, 95% CI 6-8 days and 6-9 days in the radiograph and control groups respectively (p=0.50, log rank test). The hazard ratio for recovery was 1.08 (95% CI 0.85 to 1.34). This lack of effect was not modified by clinicians' experience and no sub-groups of children were identified in whom the radiograph had an effect. Pneumonia was diagnosed more often in the radiograph group (14.4% *vs.* 8.8%, p=0.03) and bronchiolitis less often (44% vs. 56%, p=0.005). Antibiotic usage was higher in the radiograph group (60.8% vs. 52.2%, p=0,05). There were no differences in subsequent health facility usage.

Interpretation. Despite a net change in diagnosis and an increase in antibiotic usage, chest radiography did not affect clinical outcome in outpatient children with acute lower respiratory infection. This lack of effect was independent of clinicians' experience. There were no clinically identifiable sub-groups of children within the World Health Organisation case definition of pneumonia who benefited from radiography. It is concluded that routine use of chest radiography is not beneficial in ambulatory children over two months of age with acute lower respiratory infection.

Summary

Background

Despite its widespread use, the utility of chest radiography in acute respiratory infections in children has not been fully examined. In uncontrolled before-after studies, chest radiography has had a small but clinically meaningful effect on diagnosis, antibiotic use and admission to hospital. No controlled trials of the effect of chest radiography on clinical management or outcome in children with acute lower respiratory infection have been performed.

Primary aim

To determine the effect of chest radiography on the diagnosis, management and clinical outcome of ambulatory children with acute lower respiratory infections.

Methods

Study design

Randomised controlled trial

Intervention

The intervention was the use of chest radiography (antero-posterior and lateral views). The control group received standard care, but without a chest radiograph. All management except radiography was entirely at the discretion of the clinician.

Participants

The participants were 522 children aged 2 to 59 months who met the World Health Organisation case definition for pneumonia. Additional exclusion criteria included symptoms for longer than 14 days or a household contact with active tuberculosis

Study setting

The trial took place in the general outpatients department of the Red Cross Children's Hospital. The clinicians interpreting the radiographs and managing the patients were 52 medical practitioners working full-time or part-time in the department.

Outcomes measured

The primary outcome was time from randomisation to recovery, measured in a subset of 398 participants who offered a telephone number. Subsidiary outcomes

included diagnosis, management and subsequent use of health facilities, measured by examination of hospital records.

Results

Participant flow and follow-up

There were no meaningful differences in baseline characteristics of radiograph and control groups. Telephone follow-up was 77.5% complete, and 99.2% of clinical records were reviewed.

Primary outcome

Chest radiography was associated with a marginal improvement in time to recovery, which was not clinically significant. The median time to recovery was seven days in both groups, 95% CI 6-8 days and 6-9 days in the radiography and control groups respectively (p=0.50, log rank test). The hazard ratio for recovery was 1.08 (95% CI 0.85 to 1.34). The effect of chest radiography was not modified by the following factors: age, weight for age, duration of symptoms before presentation, respiratory rate, clinicians' perception of the need for radiography, or clinicians' experience or possession of a post-graduate paediatric qualification

Subsidiary outcomes

Pneumonia was diagnosed more often in radiographed participants (14.4% *vs.* 8.4%, p=0.03), and bronchiolitis less often (43.6% *vs.* 55.9%, p=0.005).

Radiographed children received antibiotics more often (60.8% *vs.* 52.2%, p=0.05). Chest radiography was associated with an absolute reduction in antibiotic use of 15.8% in patients with a perceived need for radiography, and an increase of 11.1% in patients without a perceived need.

There were trends towards a higher proportion of radiographed patients being admitted to hospital at the first consultation or receiving follow-up appointments, but these were not statistically significant (p=0.14 and p=0.08 respectively). There was no difference in subsequent consultations, hospital admissions or radiographs performed within 28 days.

Interpretation

Chest radiography affected diagnosis in ambulatory children with acute lower respiratory infection. Pneumonia was diagnosed more often and bronchiolitis less often. Radiography also resulted in a small increase in antibiotic use.

These effects did not improve clinical outcome. The lack of effect of radiography on clinical outcome was independent of clinicians' experience and possession of a post-graduate paediatric qualification. This suggests that the findings are applicable to less experienced doctors in other settings. The lack of effect was also independent of any of the clinical variables measured, and of the clinicians' perception of the need for radiography. This suggests that there are unlikely to be clinically easily identifiable sub-groups of children within the World Health Organisation case definition of pneumonia who are likely to benefit from chest radiography.

Conclusions

Despite a net change in diagnosis and an increase in antibiotic usage, the use of chest radiography did not reduce time to recovery or subsequent health facility usage in children meeting the World Health Organisation case definition for pneumonia. This lack of effect was independent of clinicians' experience and there were no clinically identifiable sub-groups of children within this case definition likely to benefit from chest radiography.

Recommendations

Chest radiography is not indicated in the management of children over two months of age who meet the World Health Organisation case definition for pneumonia, who have been symptomatic for 14 days or less and who do not have a household contact with active tuberculosis.

The findings of this trial need to be confirmed in areas with a lower prevalence of wheeze.

Additional issues arising from the trial

The conduct of the trial provided opportunities to examine related aspects of acute respiratory infections in children, and aspects of the research methods.

1. *Chest radiography as a method of tuberculosis case finding in ambulatory children with acute lower respiratory infections.*

Routine chest radiography in the children allocated to the radiography arm of the study resulted in 12 (4.4%) of 273 patients having radiological findings suggesting tuberculosis. None of the children received antituberculous treatment as a result of the findings. It is concluded that chest radiography in ambulatory children with acute lower respiratory infections lasting 14 days or less and without a contact with active tuberculosis does not result in a meaningful increase in the diagnosis and treatment of tuberculosis.

2. *Telephone follow-up in a less developed country.*

Telephone follow-up offers an attractive option for follow-up in countries with some, but limited, telephone coverage; if it can be shown to be feasible, and the findings both valid and applicable to people without telephones. The telephone questionnaire contained three questions verifiable from hospital records. Data from hospital records were available for participants both accessible and not accessible by telephone.

Telephone follow-up was 77.5% complete. Using the clinical records as the reference standard, all three questions had a specificity above 98%. Sensitivity varied from 82% for the recording of a return visit to 56% for the recording of a subsequent chest radiograph. The effect of chest radiography on clinical management and use of hospital facilities in participants accessible by telephone did not differ significantly from that in inaccessible participants. This suggests that the trial findings measured by telephone follow-up are generalisable to patients in the same hospital population without telephones. It is concluded that telephone follow-up was practicable, and the findings were valid and applicable to participants in the same population without telephones.

3. *Determinants of clinical management decisions in acute lower respiratory infections.*

In a cross-sectional analysis of the trial database, potential determinants of the perceived need for radiography, actual antibiotic use and other management decisions were assessed in multiple logistic and linear regression models.

Clinicians' general experience and specific outpatient experience was associated with antibiotic use, but with the associations in opposing directions. The opposing associations of different forms of clinician experience with antibiotic use appeared to be part of a pattern of less active management as general medical experience increased, and more active decisions as specific outpatient experience increased, present across different clinical decisions and practice settings. A fuller understanding of the association of different forms of experience with clinical decisions could improve the effectiveness of interventions to improve knowledge and practice in a range of management decisions, and especially antibiotic use.

4. *Duration of illness in ambulatory children with a diagnosis of bronchiolitis.*

Time to recovery in bronchiolitis, a common lower respiratory infection of early childhood, has not been formally studied. The trial follow-up included an inception cohort of ambulatory children with a diagnosis of bronchiolitis.

The children recovered with few complications, but took longer than stated in standard textbooks. The median duration of illness was 12 days. Thirty nine percent were still ill after 14 days, 18% after 21 days and 9% after 28 days. Age, weight for age, gender and respiratory rate were not clinically useful predictors of time to recovery.

Fifty-five patients (39.3%) had subsequent unscheduled consultations within 28 days, mostly late in the illness. The high rate of unscheduled return visits that was observed in this cohort probably reflects parental concern regarding slow recovery. Counselling parents to expect gradual improvement over a period of up to three or four weeks could reduce these concerns.

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Table of Contents

List of Tables

Chapter 1

Chapter 2

Chapter 4

Appendices

Parameter estimates

List of Figures

Chapter 4

Chapter 6

Glossary

Absolute risk reduction

The difference between two groups in the rate of the outcome of interest (Sackett et al 1991)

Cronbach's alpha

An estimate of the correlation between the total score across a series of items from a rating scale and the total score that would have been obtained had a comparable series of items been employed (Last 1988).

Cumulative incidence

The number or proportion of a group of people who experience the onset of a health-related event during a specified time interval (Last 1988)

Collective effective radiation dose

The average effective dose to an exposed population multiplied by the number of people in the group. The unit of measurement is the man sievert (man Sv) (United Nations 1993)

DALYs

Disability-adjusted life years i.e. the sum of life years lost due to premature mortality and years lived with disability adjusted for severity.

Effective radiation dose

An indicator of the total detriment from radiation in an exposed individual and his or her descendants. The unit of measurement is the Sievert (Sv) (United Nations 1993)

Hazard ratio

The ratio of the rates of events in two groups, when time to the event is the outcome of interest. (Altman 1991)

Kappa

A measure of the degree of nonrandom agreement between observations or measurements of the same categorical variable. If the measurements agree more often than expected by chance, kappa is positive; if concordance is complete, kappa = 1; if there is only chance concordance, kappa = 0; if disagreement is more than expected by chance, kappa is negative (Last 1998)

The following are general interpretations of different values of kappa:

Kappa	*Strength of agreement*	
	Altman 1991	*Sackett et al 1991*
<0.20	Poor	Slight
0.21-0.40	Fair	Fair
0.41-0.60	Moderate	Moderate
0.61-0.80	Good	Substantial
0.81-1.00	Very good	Almost perfect

Kappa, weighted

When more than 2 categories are ordered, weighted kappa takes account of the degree of disagreement by giving weights to disagreements according to the size of the discrepancy in agreement. Weighted kappa is usually higher than unweighted kappa.

Likelihood ratio

The likelihood of given test result in a patient with the target disorder compared to the likelihood of the same result in a patient without that disorder. This summarises the clinical usefulness of a diagnostic test more meaningfully than sensitivity and specificity. It is a measure of how much a given diagnostic test result will raise or lower the pre-test probability of a disorder.

A rough guide to the interpretation is as follows:

1	No use at all
1-2 or 0.5-1	Small and rarely important change in diagnostic probability
2-5 or 0.2-0.5	Small but sometimes important change
5-10 or 0.1-0.2	Moderate change
>10 or <0.1	Large and often conclusive change

(Jaeschke, Guyatt and Sackett 1994; Sackett et al 1991)

Meta-analysis

The process of using statistical methods to combine the results of different studies (Last 1988).

Negative predictive value

The proprotion of individuals with a negative test who do not have the condition of interest (Sackett et al 1997)

Number needed to harm (NNH)

The number of individuals who need to be treated to produce one episode of harm (Sackett et al 1997)

Number needed to treat (NNT)

The number of individuals who need to be treated to prevent one adverse outcome. It is the inverse of the absolute risk reduction. (Sackett et al 1991). NNT(benefit) is synonymous with number needed to treat, and NNT(harm) is synonymous with number needed to harm (Altman 1998)

Odds

The ratio of the probability of an event to that of non-occurrence. For example, if 60 smokers develop a chronic cough and 40 do not, the odds are 60:40, or 1.5. In contrast the probability is 60:100, or 0.6 (Last 1998)

Odds ratio

The ratio of two odds. In the context of this thesis the disease- or risk-odds ratio is used. This reflects the ratio of the odds in favour of an event (e.g. antibiotic use) among the exposed (e.g. radiographed patients) to the odds in favour of the event in the unexposed (Last 1988)

Positive predictive value

The proportion of individuals with a positive test who have the condition of interest (Sackett et al 1997)

Relative risk

The ratio of the proportion of individuals with the outcome of interest in the treated or exposed group to that in the control group. In the context of this thesis, relative risk is synonymous with cumulative incidence ratio (Last 1988)

Relative risk reduction

The percent reduction in the outcome of interest in the intervention or exposed group, compared with the control group.

Sensitivity

The proportion of individuals with the condition of interest that are correctly identified by the test. (Altman 1991)

Specificity

The proportion of individuals without the condition of interest that are correctly identified by the test. (Altman 1991)

Abbreviations

ALRI	Acute lower respiratory infection
ARI	Acute respiratory infection
CI	Confidence interval
CRP	C-reactive protein
DALY	Disability-adjusted life year
GOPD	General Outpatients Department, Red Cross Children's Hospital
HIV	Human immunodeficiency virus
I-Q range	Inter-quartile range
man Sv	Man Sievert (see Glossary, "Collective effective radiation dose")
mSv	milliSievert (see Glossary, "Effective radiation dose")
NNT	Number needed to treat
RXH	Red Cross Children's Hospital
SD	Standard deviation
UNSCEAR	Nations Scientific Committee on the Effects of Atomic Radiation
URL	Uniform resource locator
WHO	World Health Organization

Chapter 1

Chest radiography in acute respiratory infections in children

Introduction

1.1 Acute lower respiratory infections in children

1.1.1 The magnitude of the problem

1.1.1.1 Internationally

Acute respiratory infection (ARI) is the leading cause of morbidity and mortality worldwide in children under five years. In 1990 an estimated 4.3 million children under five years died of acute respiratory infections (Garenne, Ronsmans and Campbell 1992). This represents approximately one third of all deaths in children under five (Garenne, Ronsmans and Campbell 1992). The great majority of such deaths are due to lower respiratory infections (Campbell 1995). The younger the child the greater is the mortality, with two thirds of ARI-related deaths under five years occurring in the first year of life (Leowski 1986).

The incidence of ARI appears to be similar in developed and developing countries, however the severity of lower respiratory infections is significantly greater in developing countries (Pio, Loewski and Ten Dam 1985). Ninety nine percent of ARI-related deaths occur in developing countries (World Bank 1993).

Respiratory infections have a massive impact on the burden of disease. In children under five years in developing countries, ARI was the leading cause of loss of disability-adjusted life years (DALYs) world-wide in 1990, accounting for the annual loss of approximately 93 million DALYs (calculated from World Bank 1993). This represents 18.0% of all such loss in this age group.

Apart from their acute effects lower respiratory infections may also cause chronic respiratory morbidity (Milner and Murray 1989; Woolcock and Peat 1985), but the size of this effect is not known.

Health services in developing countries carry a very large load from ARI. Between 30 and 60 percent of children attending outpatient health units have ARI, 70-80% of which are upper respiratory infections (Pio, Loewski and Ten Dam 1985). Of children

under 14 years admitted to hospital, approximately one third have ARI (Pio, Loewski and Ten Dam 1985).

The impact of the HIV epidemic on ARI-specific mortality has not yet been systematically reported. ARI was however the commonest clinical presentation in hospitalised children with HIV infection in West Africa, and proportionally a commoner mode of death than in non-HIV infected children (Vetter et al 1996). The importance of ARI for childhood mortality and the burden of disease thus appear more likely to increase than decrease with the spread of HIV infection.

1.1.1.2 In South Africa

South African mortality data are unreliable because of under-reporting and inadequate classification of cause of death (Bradshaw, Laubsher and Schneider 1995). In 1994, of 1998 deaths from ARI reported in children under five years, 1858 (93%) were from pneumonia (South Africa 1997). These deaths represent 8.9% of all deaths in this age group (and 10.2% of those with a specific reported cause).

Morbidity data are limited. Respiratory complaints represented 22.7% of all reported acute illness and injury in a household survey in a village in the Western Cape (Hoffman et al 1988). Acute respiratory infections and pneumonia accounted for 10.0% of all contacts in a representative sample of South African general practitioners (Bourne, Bloom and Sayed 1991). Unfortunately neither survey reported age-specific data. The number of infants requiring hospitalisation for ARI in South Africa each year has been conservatively estimated at 13 000 (Von Schirnding, Yach and Klein 1991).

1.1.1.3 In the context of this study

Cape Town is situated in the Western Cape Province, the Cape Town metropolis accounting for approximately 70% of the province's population (Provincial Administration of the Western Cape 1995). The mortality profile of this province differs somewhat from that of the rest of South Africa. In children under five years, ARI is a commoner cause of death than diarrhoea in the Western Cape. In South

Africa as a whole the ratio of ARI to diarrhoeal deaths is 0.60 (South Africa 1997), but in metropolitan Cape Town it is 1.22 (Von Schirnding, Yach and Klein 1991). In the general outpatients department of Red Cross Children's Hospital, 36% of unreferred children had acute respiratory infections, 60% of these having upper respiratory infections (unpublished routine hospital data).

1.1.2 Acute lower respiratory infections and their radiographic features

The two major forms of lower respiratory infection in young children are pneumonia and bronchiolitis.

1.1.2.1 Pneumonia

Pneumonia is defined as an inflammation of the parenchyma of the lungs, most often caused by micro-organisms (Prober 1996). Pneumonia is the dominant cause of death from acute respiratory infections in children under five years, accounting for 80-90% of ARI-related deaths in developing countries (Campbell 1995).

In developing countries approximately a half of hospitalised cases have a bacterial cause (World Health Organisation 1991). The majority of episodes of severe pneumonia are caused by two bacteria, Streptococcus pneumoniae and Haemophilus influenza, although mixed respiratory infections are common (Campbell 1995; Forgie et al 1991). In developed countries an estimated 5-15% of cases of pneumonia are caused by bacteria (World Health Organisation 1991), but some authorities have nevertheless recommended the routine use of antibiotics, because of the difficulty of excluding a bacterial cause (Isaacs 1989; Lancet 1988).

The characteristic clinical signs of pneumonia in older children and adults are less reliable in young infants, and in the developed world reliance has been placed on chest radiography in decisions regarding diagnosis and clinical management of infants. (Klein 1992; Courtoy, Lande and Turner 1989).

The radiological features of pneumonia vary with the age of the child, the extent of the disease and the aetiological agent. Consolidation, the hallmark of pneumonia in adults, occurs in children but less frequently than three other abnormalities:

generalised hyperaeration, irregular aeration (patchy consolidation) and bronchial wall thickening (Kuhn 1990a).

1.1.2.2 Bronchiolitis

Bronchiolitis is a clinical syndrome of acute viral lower respiratory tract illness occurring in the first 2 years of life and is diagnosed by a characteristic presentation of upper respiratory infection and signs of obstructive airway disease. Because bronchiolitis is a viral disease, antibiotics are not necessary (Welliver and Cherry 1992).

The radiological hallmark of bronchiolitis is generalised hyperinflation (Kuhn 1990b). Bronchial wall thickening is another typical finding. However the chest radiograph may be normal in some cases, and hyperinflation and bronchial wall thickening can also occur in pneumonia. Infiltrates and areas of atelectasis may occur, but are more common in pneumonia. The radiological dividing line between bronchiolitis and pneumonia is therefore indistinct (Kuhn 1990b).

1.1.2.3 Differentiation between bronchiolitis and pneumonia

The clinical and radiological presentation of acute lower respiratory infection (ALRI) in young children constitutes a continuum. This continuum extends from focal consolidation without signs of lower airway obstruction through to diffuse lung involvement without consolidation but with features of narrowed airways i.e. hyperinflation with radiological evidence of irregular aeration and bronchial wall thickening. The distinction between bronchiolitis (which does not require antibiotic treatment) and pneumonia (which usually does) may be very difficult.

1.1.3 The World Health Organisation (WHO) case management guidelines.

As part of a strategy to reduce childhood mortality, the WHO has developed guidelines for the case management of ARI in developing countries (World Health Organization 1990; World Health Organization 1995). The guidelines depend on simple clinical signs such as respiratory rate and chest indrawing to distinguish upper respiratory infections from the more serious lower tract infections. The diagnostic accuracy of tachypnoea in the diagnosis of pneumonia has been demonstrated in

cross-sectional studies in a wide variety of settings (Campbell et al 1989; Cherian et al 1988; Cherian et al 1997; Harari et al 1991; Margolis and Gadomski 1998; Mulholland et al 1991; Shann et al 1984). A stethoscope is not used. Cases are classified into one of three categories: i) upper respiratory infections, ii) pneumonia (mild lower respiratory infection) and iii) severe pneumonia (severe lower respiratory infection). Upper respiratory infections are managed supportively. Pneumonia is treated with an antibiotic at home, and severe pneumonia is managed in hospital. Implementation of the guidelines has been shown to reduce pneumonia-specific mortality in a wide variety of settings, in uncontrolled before-after studies (Mtango and Neuvians 1986; Roesin et al 1990) and in controlled before-after studies (Bang et al 1990; Datta et al 1987; Fauveau et al 1992; Khan et al 1990; Panday et al 1991). The guidelines make no use of chest radiography.

In South Africa, the WHO guidelines have been accepted in principle as national health policy. In the Western Cape Province implementation of the guidelines began in 1997, after minor adaptations to fit local circumstances (Provincial Reference Group 1997).

1.2 Chest radiography

1.2.1 Historical overview of the development and acceptance of chest radiography

On 28 December 1895, Wilhelm Conrad Roentgen reported the discovery of a new form of radiation (Roentgen 1895). These *x*-rays, as he named them, were able to pass through substances opaque to ordinary light. The excitement was immediate. Roentgen did not discuss any medical implications, but the first newspaper report eight days later was prophetic; "This could be of immeasurable help for the diagnosis of countless diseases other than those of bones." (Neue Freie Presse 1896). Within sixteen months FH Williams in Boston, Massachusetts, had produced more than 400 volumes of tracings of clinical chest fluoroscopy (Greene 1992). In England, within a year of the discovery, HS Ward (1896) had published a radiology handbook. The driving force for much of this activity was two-fold. Firstly, fluoroscopy offered unparalleled insight into the mechanics of respiration, which had been debated since

the time of Galen (Campbell 1958). Secondly, there was a medical imperative to detect and cure tuberculosis, and the hope that chest radiography provided the means to do so (Dally 1903; Wade 1896; Walsham 1901).

The excitement, though immediate, was not universal. The leader writer of the British Medical Journal spoke cautiously of "uneducated imagination" (BMJ 1896), and the Lancet of "all sorts of crude ideas" (Lancet 1896). Although Frenchman Antoine Béclère (1902), referring to the diagnosis of tuberculosis, stated that "examination by radioscope and radiography supersedes all other methods" and that this was now "universally recognised", the British Journal of Tuberculosis did not publish an illustrated paper on chest radiography until 1914 (Posner 1971).

The differences in attitudes to Roentgen rays and in the pace of development were partly due to differences in available equipment. Early equipment was unreliable and "it seemed at times as though gas tubes had been invented for the specific purpose of trying men's souls." (Hodges 1945) The invention of the hot-cathode high vacuum tube (Coolidge 1913) was a major technical advance, which led to much greater use of chest radiography (Posner 1971). By 1925, chest films had come to be "considered indispensable in the handling of pulmonary disease" (Hodges 1945).

Screening of apparently healthy people followed; "The most obvious field for these ultimate investigations of the human body is among the supposedly well who show no signs of trouble when subjected to ordinary physical routine . . .. X-rays should be utilized as a matter of routine where this is possible." (Fisk 1928). The development of microfilming (De Abreu 1939) opened the way for mass x-ray screening programmes for tuberculosis (Hodges 1945). During World War II, the US Army and Navy screened approximately 10 million personnel (Haygood and Briggs 1992) and as late as 1970 the city of New York took almost 300 000 chest radiographs in a year (Reichman 1975). Although mass chest radiography for tuberculosis case finding was abandoned because of low yield and high cost (Reichman 1975; WHO Expert Committee 1974; WHO Scientific Group 1983), routine chest radiography on admission to hospital or pre-operatively remained well established. It has been estimated that over 30 million such films were taken in hospitals in the United States

in 1980, with an associated $1.5 billion in charges to consumers (Hubbell et al 1985). It has been suggested that the development of health insurance hid the direct costs of the examination from the patient, and gave impetus to the widespread acceptance of chest radiography (Gurney 1995).

The development of the scientific basis for the use of chest radiography appears to have received less attention than technical advances. Recognition of the existence of inter-observer variation took almost 50 years, and widespread acceptance took even longer. A Board of Roentgenology was appointed in the USA in 1944 to investigate the relative diagnostic efficiency of the various roentgenographic and photofluorographic techniques used in mass survey work (Birkelo et al 1947). Each expert member of the board "found to his astonishment that not only did he differ from his colleagues in apparently simple interpretations, but that he even differed from himself" (Garland 1949). Ten years later Garland (1959) stated in a Mayo Foundation Lecture that "The mere existence, far less the extent, of the . . . . diagnostic error is little appreciated". A high proportion of missed diagnoses received attention only in the 1970s (Martin, Moskowitz and Milbraith 1979; Members of the Early Lung Cancer Cooperative Study 1984).

Reviewing the history of chest radiography in a prestigious radiological journal in the centennial of Roentgen's discovery, a radiologist was able to write; "As the most common radiographic examination, the chest radiographic examination rose to this position not on the basis of medical science but faith that technology in any form would aid in the care of patients. . . . . To my knowledge, whether the chest radiograph affected the outcome of patients with these diseases has never been studied and remains unknown today." (Gurney 1995).

1.2.2 Utilisation of chest radiography

1.2.2.1 Internationally

The Survey of Medical Radiation Usage and Exposures, performed in 1990-1 by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), details information on the usage of radiography in 50 countries (United

Nations 1993). Unless otherwise stated, the data quoted in this section are taken from the United Nations (1993) report. The information is based on often small and potentially biased samples of geographically and demographically heterogeneous populations. The data must thus be approached with caution, but provide a broad picture of utilisation.

A good correlation has been shown between the number of medical practitioners and the number of radiographic examinations per unit population (United Nations 1988). The report thus categorises countries into one of four levels according to the number of medical practitioners per 1000 population i.e.

Level I	more than 1 doctor per 1000 population
Level II	1 doctor per 1000-3000 population
Level III	1 doctor per 3000-10 000 population
Level IV	less than 1 doctor per 10 000 population

An estimated 1.6 billion diagnostic radiographs (excluding dental examinations) are performed annually worldwide with a mean utilisation of 300 examinations per 1 000 population per annum. Mean usage varies from 890 examinations per 1 000 in level I countries to 120, 67 and 9 examinations per 1 000 in level II, II and IV countries respectively. Chest radiographs comprise approximately 60% of all diagnostic examinations performed in level I countries and 70% in level II-IV countries. Thus, approximately 1 billion chest radiographs are performed annually. There was an unweighted average increase in radiograph usage in level II-IV countries of approximately 25% per five-year period during the 1980s, but no clear trend in utilisation in level I countries. The largest increase in level II-IV countries has been in chest radiographs.

For chest radiographs specifically, utilisation varies widely. The overall average rates for level I, II and III-IV countries are 527, 118 and 51 respectively (mass screening and fluoroscopy included). The annual rates per 1 000 population range from 440 in Japan to 4 in Rwanda (mass screening and fluoroscopy excluded).

Data on children are less readily available. Children under five years in the Netherlands have a rate of 87 chest radiographs per 1 000 per annum (calculated from data from Beentjies and Timmermans (1990)). This is 55% of the rate of 157 per 1000 in the general population in the same study. From data in a report of well children under five years attending a primary care continuation clinic in the United States of America 123 ambulatory chest radiographs were performed per 1 000 children per annum (Fosarelli and De Angelis 1987). This is 44% of the rate of 280 for the general population obtained from the United Nations (1993) report. Children under five years thus appear to have a utilisation rate of approximately half that of the general population.

1.2.2.2 In South Africa

The UNSCEAR report does not provide information from South Africa, neither was other published information located. South Africa has 0.57 doctors per 1 000 population (Health Systems Trust 1996), which is in the mid-range of the average rate for level II countries in the United Nations (1993) classification. Using the above good correlation between the number of medical practitioners and the number of radiography examinations per unit population (United Nations 1988), and thereby assuming that South Africa has an average utilisation rate for a level II country, approximately 120 chest radiographs per 1 000 population are performed annually. Assuming also that children under five years have half the utilisation rate of the general population (see Section 1.2.2.1 above) the rate for children under five years is approximately 60 per 1 000 children per annum. Given a population of 5 279 232 children under 5 years in South Africa (South Africa 1996), and assuming a chest radiograph rate of 60 per 1 000 per annum, an estimated 320 000 chest radiographs were performed in this age group in 1996.

1.2.2.3 In the context of this study

Information on radiograph utilisation in the specific context of this study is available from an unpublished audit of the usage of special investigations in patients attending the general outpatients department of the Red Cross Children's Hospital (personal communication, David Power). The survey was performed between 7am and 5pm on three consecutive weekdays in March 1996.. The patients were categorised by a team

of professional nurses into one of the following groups: emergency, acutely ill, non-urgent primary care, referral for secondary care, or follow-up visit.

The proportions of patients in whom chest radiography was performed are shown in Table 1.1

TABLE 1.1 Proportion of primary level paediatric patients at Red Cross Children's Hospital in whom chest radiography was performed[a].

		%	95% confidence interval
Acutely ill	26/145	17.9	11.7 to 24.2
Non-urgent, primary care[b]	31/590	5.3	3.5 to 7.3
Referred for secondary care	12 / 79	15.2	8.1 to 25.0
Follow-up visit	12/105	11.4	5.3 to 17.5

a Data from D Power, personal communication

b Non-urgent and could appropriately be managed at a primary care facility. Professional nurses made this judgement, as part of the audit.

The frequency with which chest radiography was performed relative to other radiographs and frequently performed tests is shown in Table 1.2.

Of acutely ill patients and those who (in a professional nurse's opinion) could appropriately have been managed at primary level facilities, chest radiography was the second most frequently performed investigation, being ordered in 17.9% and 5.3% of patients respectively. In referred patients and those brought back for follow-up it was the most common investigation, ordered in 15.2% and 11.4% of patients respectively.

Chest radiography accounted for 78.6% of all radiological procedures, similar to the 76.5% in the primary care continuation clinic in the United States of America (Fossarelli and De Angelis 1987). With the exception of "side-room" dipstix urinalysis, it was by far the most commonly ordered of all investigations.

TABLE 1.2 The frequency of performance of chest radiography and other diagnostic tests in primary level paediatric patients at Red Cross Children's Hospital[a].

	Chest radiograph	Other radiographs	Urine dipstix	Full blood count	Venous blood gasses	Chest radiographs as a proportion of all radiographs
Acutely ill n=115)	26	3	30	6	12	89.7%
Non-urgent, primary care[b] (n=590)	31	8	65	19	15	79.5%
Referred for secondary care (n=79)	12	5	8	10	0	70.6%
Appointment (n=105)	12	6	5	2	1	50.0%
Total (n=889)	81	22	108	37	28	78.6%

a Data from D Power, personal communication

b Non-urgent and could appropriately be managed at a primary care facility. A team of professional nurses made this judgement, as part of the audit.

The generalisability of the findings of this audit is limited because of the large variation in patient profile and availability of radiographic facilities at health facilities in the developing world. The precision of the estimates for acutely ill and referred patients is also low. Nevertheless these data document a substantial use of chest radiography in the context of this study and suggest frequent usage in ambulatory children when radiological facilities are accessible.

1.2.3 Exposure to ionising radiation

1.2.3.1 The extent of exposure

Global human exposure to medical radiation (including radiotherapy) is approximately one quarter that of radiation from natural causes such as radon, cosmic rays and terrestrial gamma rays. Man-made exposure is nevertheless important because it represents that component that can most easily be reduced or avoided. Medical exposure is the dominant component of man-made radiation exposure, comprising approximately 80% of all such exposure. Diagnostic medical radiation accounts for 45% of all man-made exposure (United Nations 1993).

Chest radiographs provide relatively small doses of radiation per examination. The average effective dose of an antero-posterior and lateral radiograph is 0.14 mSv, compared with 0.06 for a radiograph of the extremities, 1.1 for an abdominal radiograph, and 4.3 for computerised tomography. The estimated global collective effective dose (i.e. total human exposure) from chest radiographs represents 2.9% of the total collective effective dose of 1 610 000 man Sv annually for all diagnostic radiography. In the level II countries of the UNSCEAR survey, the estimated average collective dose from chest radiographs is 8 130 (8%) of 292 000 man Sv per year. These estimates exclude miniature chest films and chest fluoroscopy. If mini chest films and chest fluoroscopy are included, these three chest techniques account for 27.0% of the collective dose worldwide and 54.5% in level II countries (United Nations 1993).

1.2.3.2 Potential harmful effects

Exposure to high doses of ionising radiation is known to cause cancer (Godlee 1992, United Nations 1993). It has been suggested that the risk is higher in children because

of an increased radiosensitivity of their tissues (United Nations 1993) and a long life expectancy providing time for the development of cancer. Risk estimates of lower levels of exposure are highly uncertain and are repeatedly being revised (United Nations 1993). The risk is difficult to demonstrate by epidemiological methods because any such effect is very small (Godlee 1992) and the period between exposure and the development of cancer very long. The most recent estimate of risk is 0.05 cancer deaths per Sv of radiation for a population of all ages (United Nations 1993). If this estimate and the above estimates of exposure are accurate, approximately 80 000 deaths from cancer are caused annually by diagnostic radiation worldwide. Approximately 2 300 deaths would be attributable to chest radiography, and 22 000 to a combination of chest radiography, mini chests and chest fluoroscopy. From the perspective of an individual patient, one death from cancer would be expected from every 140 000 chest radiographs performed. These statistics must be interpreted with great caution. Given the uncertainty of the estimates of both exposure and the risks of exposure these calculations could be more than an order of magnitude too high or too low.

1.2.4 Cost implications of chest radiography

The cost implications will vary widely according to setting. The average cost to the health services of performing a chest radiograph at Red Cross Children's Hospital in 1996/7 was calculated as R58.75 ($12.95, £8.29 on 30 September 1996) (Appendix 1). This probably represents a minimum average cost to the health services, given the economies of scale in a large busy hospital dealing exclusively with children. The cost to patients, caregivers and society is not reflected in this calculation.

If radiological facilities are not available at the point of service and referral to another facility for the examination is necessary, the costs to the health services, the patient and society increase markedly. Transport to the referral facility becomes necessary, as does a repeat consultation by a doctor at the referral facility.

Given the estimated 320 000 chest radiographs annually (Section 1.2.2.2), the minimum annual cost to the health services of the performance of chest radiography on children under five years in South Africa is approximately R19 million ($4.2

million, £2.7 million on 30 September 1996). Many of these radiographs are performed on children admitted to hospital, or with chronic conditions. No data were found to allow an estimate of the proportion of these costs attributable to ALRI in ambulatory children.

1.3 Rationale for the use of chest radiography in ALRI

The rationale for the use of chest radiography in the initial assessment of acute lower respiratory infection rests on a number of assumptions.

i) clinical assessment plus radiography results in a more accurate diagnosis than clinical assessment alone

ii) the improved diagnosis leads to changes in clinical management

iii) changes in management result in benefit to the patient.

Potential benefits of chest radiography must be weighed against its costs and potential adverse effects. Potential adverse clinical effects include the effects of false positive and false negative findings, and exposure to ionising radiation. Although the hazards of radiography are uncertain, there is a clear indication to minimise risk by eliminating unnecessary examinations. Costs of radiography include the cost of the radiograph itself, the time spent waiting for radiography, the need to be seen again by a clinician and the additional load on a second clinician if the first has gone off duty. If travel to another facility for radiography is necessary, the cost is increased still further.

1.4 Implications of the use of chest radiography in ALRI

The impact of chest radiography on therapy and outcome thus has implications for:

i) individual clinicians' practice

ii) the development of clinical guidelines (including referral criteria)

iii) the cost of health care

The issues are perhaps particularly acute in middle income countries such as South Africa. The WHO case management guidelines do not recommend the use of chest radiography. They are however designed for "developing countries or areas with an infant mortality rate of over 40 per 1000 live births and limited resources i.e. hospitals where X-ray and laboratory facilities are limited or do not exist and where diagnosis

relies on clinical examination" (World Health Organization 1990). South Africa has an overall infant mortality rate of 40 per 1000 (Health Systems Trust 1995), which is on the threshold of applicability of the guidelines. Given relatively greater resources than most countries, additional inputs could result in improved clinical outcome. Because of the substantial costs of radiography it is important to know whether the use of chest radiography would increase the effectiveness of clinical management, by how much and at what cost.

1.5 Consensus statements on the indications for chest radiography

1.5.1 American College of Radiology

Indications for chest radiography in the American College of Radiology standard for the performance of paediatric and adult chest radiography include "Signs and symptoms potentially related to the respiratory, cardiovascular and upper gastro-intestinal systems . . . " (American College of Radiology 1995). No more specific guidance is given. Routine radiographs pre-operatively or on admission to hospital are not regarded as indications, if there are no symptoms or signs suggesting cardio-respiratory disease.

1.5.2 Royal College of Radiologists

The College guidelines state that chest radiography in acute chest infections in children is "Not necessary routinely" but that "If signs and symptoms suggest lung infection x-ray will show/rule out parenchymal involvement or collapse." (Royal College of Radiologists 1993)

1.5.3 WHO Scientific Group on the Indications and Limitations of Major X-ray Diagnostic Investigations

This group likewise does not recommend chest radiography in the absence of cardio-pulmonary symptoms, but makes no attempt to distinguish the situations in symptomatic patients in which radiography is or is not useful (WHO Scientific Group 1983).

1.5.4 WHO case management guidelines

The guidelines for the management of acute respiratory infections in children in developing countries do not include chest radiography: "Radiography can reduce the number of false positive diagnoses of pneumonia but is often not available and the expense does not justify its use in routine case detection of pneumonia. When a limited number of x-rays can be obtained, they are better used for the management of treatment failures and chronic cough." (World Health Organization 1990)

1.5.5 Summary

There appears to be broad agreement that radiographs are not useful in detecting clinically unsuspected disease. Little guidance is offered on which symptomatic children will benefit from radiography, when available.

Chapter 2

Diagnostic accuracy and the impact of chest radiography on clinical management and outcome

Systematic literature reviews

The beneficial impact of chest radiography requires all of the following:

a) improvement in diagnostic accuracy above that of clinical evaluation alone
b) the improved accuracy results in a change in clinical management
c) the change in management improves clinical outcome sufficiently to justify the cost and harmful effects of radiography.

If chest radiography improves diagnostic accuracy in acute lower respiratory infections, clinical benefit could occur by at least two mechanisms. Firstly children with pneumonia generally require antibiotics, while those without pneumonia generally do not (World Health Organization 1991). More accurate ascertainment of the presence of pneumonia will consequently result in a greater proportion of children with pneumonia receiving required antibiotics and a greater proportion of children without pneumonia avoiding unnecessary antibiotics. Secondly, a more accurate assessment of the severity of the pneumonia would enable more appropriate use of hospitalisation and oxygen therapy.

Diagnostic accuracy and the overall impact of a diagnostic test on clinical management and outcome are considered separately in the following reviews.

2.1 Diagnostic accuracy

The accuracy of chest radiography is best assessed by a cross-sectional study comparing radiological assessment of the presence or the severity of pneumonia with a credible reference standard. Accuracy is expressed as sensitivity, specificity or as likelihood ratios for positive and negative tests. In the case of pneumonia this study design is hampered by the lack of a suitable reference standard (such as histological or gross anatomical findings) against which to compare radiographic findings.

An alternative approach to assessing accuracy is to measure observer variation in the interpretation of radiographs. This may be done by cross-sectional studies measuring agreement between independent observers, or within a single observer when that observer views the same radiographs on two occasions separated by a period long enough to prevent recall of the previous assessment. Agreement is usually expressed as a kappa statistic, which reflects agreement over and above that expected by chance (Last 1988). Inter- and intra-observer agreement in the interpretation of the

radiographs is a necessary component of diagnostic accuracy, but it is not sufficient. High agreement does not necessarily equate with high validity (i.e. the observers can agree but both be wrong). Low agreement implies low validity, but gives little indication of the extent of inaccuracy. However low agreement could also be due to assessment of high validity by one observe and low validity by another.

The following three elements of the accuracy of chest radiography in acute lower respiratory infections in children are thus reviewed:

1. Observer variation in the interpretation of chest radiographs.
2. The radiological differentiation between bacterial and viral pneumonia.
3. The radiological assessment of the severity of pneumonia.

2.1.1 Observer variation in the radiological interpretation of lower respiratory infection

2.1.1.1 Objective

To quantify the agreement between and within observers in the detection of radiological features associated with acute lower respiratory infections in children.

2.1.1.2 Inclusion criteria for studies

All studies meeting the following criteria were included:

1. an assessment of observer interpretation of radiological features of lower respiratory infection, or of the radiological diagnosis of pneumonia
2. studies of children under 18 years of age or studies from which data on children under 18 years could be extracted
3. data presented that enabled the assessment of agreement between observers
4. independent reading of radiographs by two or more observers

2.1.1.3 Search strategy

1. Electronic databases

a) The MEDLINE database was searched from 1966 to 1997. The search strategy is outlined in Appendix 2. Possibly relevant studies reported in English or with English abstracts were evaluated further.

b) The HealthSTAR database was searched from 1975 to 1997, using Internet Grateful Med. The strategy used is detailed in Appendix 2.

2. The World Health Organization bibliography on acute respiratory infections (URL http://www.who.ch/chd/pub/ari/aripub/htm#oth_res) was searched manually.
3. Authors of identified studies were contacted with an enquiry about the existence of further studies, published or unpublished. A list of authors contacted appears in Appendix 3.
4. Reference lists of articles retrieved from the above searches were examined.

2.1.1.4 Data collection and analysis

Possibly relevant studies identified in the above search were evaluated by the investigator for appropriateness for inclusion, according to the above pre-stated selection criteria.

When no measures of agreement were reported, data were extracted from the reports and kappa statistics were calculated using the EpiTable programme in the Epi Info software package.

2.1.1.5 Description of studies

2.1.1.5.1 Studies included in the analysis

Six studies met the above criteria (Coblenz et al 1991; Davies et al 1996; Kramer, Roberts-Brauer and Williams 1992; Norman et al 1992; Simpson et al 1974; Stickler, Hoffman and Taylor 1984). Two studies by substantially the same authors appeared to be duplicate publications (Coblenz et al 1991; Norman et al 1992). The methods and materials used were indistinguishable, but the results differed in some respects. An attempt to contact the author of the later report to obtain clarification was unsuccessful. Both reports are included for comparison. The characteristics of the studies are summarised in Table 2.1.

Three studies used samples of hospital or emergency room populations, but the sampling methods were not described (Davies et al 1996; Kramer, Roberts-Brauer and Williams 1992; Simpson et al 1974). The other three studies were of purposively assembled collections of radiographs of abnormal and normal radiographs (Coblenz et al 1991; Norman et al 1992; Stickler, Hoffman and Taylor 1984). None of the studies stated explicitly whether the patients presented consecutively.

TABLE 2.1 Inter-observer agreement in the interpretation of chest radiography: characteristics of included studies.

Author	Subjects	Observers
Simpson[a] 1974	330 children under 14 years hospitalised with ALRI	2 radiologists
Stickler[a] 1984	34 children under 4 years with pneumonia 34 normal pre-operative radiographs, matched for age, sex, time of year	1 pediatric radiologist 1 radiology resident
Coblenz[b,c] 1991	25 children hospitalised with bronchiolitis 25 normal radiographs (from assessment of positive tuberculin skin tests or innocent cardiac murmurs)	3 pediatric radiologists
Kramer 1992	287 unreferred febrile children, aged 3-24 months, in an emergency unit	1 paediatrician 1 duty radiologist 1 "blind" pediatric radiologist
Norman[b] 1992	25 children hospitalised with bronchiolitis 25 normal radiographs (from assessment of positive tuberculin skin tests or innocent cardiac murmurs)	3 pediatric radiologists
Davies[b] 1996	40 children under 6 months, 25 with pneumonia and 15 with bronchiolitis, admitted to a tertiary care paediatric hospital	3 pediatric radiologists

a Kappa calculated from data extracted from the report

b Average weighted kappa

c Kappas for inter-observer variation read off a bar graph.

TABLE 2.2 Observer variation in the assessment of radiological features: kappa statistics (95% CIs)

Radiological features	Davies 1996[a]	Coblenz 1991[a,b]	Norman 1992[a,b]	Simpson 1974	Stickler 1984	Kramer 1992
Inter-observer variation						
Consolidation	0.79	0.41	0.33			
Pneumonia					0.68 (0.44-092)	0.46 (0.34-0.58) 0.47 (0.35-0.60)
Collapse/consolidation				0.83 (0.72-0.94)		
Collapse/atelectasis	0.78	0.46	0.41			
Hyperinflation/air trapping	0.83	0.60	0.48	0.78 (0.67-0.89)		
Peribronchial/bronchial wall thickening	0.55	0.42	0.35	0.55 (0.44-0.66)		
Perihilar linear opacities	0.82	0.40	0.28			
Intra-observer variation						
Consolidation	0.91	0.50	0.31-0.60			
Collapse/atelectasis	0.86	0.58	0.47-0.57			
Hyperinflation/air trapping	0.85	0.78	0.56-0.65			
Peribronchial/bronchial wall thickening	0.76	0.59	0.34-0.64			
Perihilar linear opacities	0.87	0.62	0.32-0.67			

a Individual data not available to calculate confidence intervals
b Possible duplicate studies

2.1.1.5.2 Studies excluded from the analysis

Three studies were excluded. In one, assessment by the observers was not independent and aggregate data on children and adults was presented (Franken et al 1995). In the second, observers were not independent (Kiekara et al 1996). In the third, the observers' independence was not described and appeared very unlikely in the context of the study, which was an audit of everyday practice (Fleischer, Ludwig and McSorley 1983).

2.1.1.6 Results

Agreement was expressed as a kappa statistic in four of the studies (Coblenz et al 1991; Davies et al 1996; Norman et al 1992; Simpson et al 1974) and was calculated from data extracted from the remaining reports. (Kramer Roberts-Brauer and Williams 1992; Stickler, Hoffman and Taylor 1984)

The kappa scores are shown in Table 2.2.

2.1.1.7 Discussion

Agreement was generally in the "moderate" (0.40-0.60) to "good" (0.60-0.80) range for both radiological features and diagnosis. This is similar to agreement in other radiological assessments (Coblenz et al 1991). The observers assessed were paediatricians and paediatric radiologists who are not necessarily representative of doctors throughout the world who manage ALRI.

Comparison of study findings is difficult. In the two largest studies with the most precise estimates of agreement (Kramer, Roberts-Brauer and Williams 1992; Simpson et al 1974) the same radiological features were not examined, and the clinical populations differed. The three studies that examined almost identical features (Coblenz et al 1991; Davies et al 1996; Norman et al 1992) were all small (samples of 50, 65 and 50 respectively), no confidence intervals were presented and insufficient data were reported from which confidence intervals could be calculated. It is thus not possible to assess whether any differences between these three studies were due to chance variation.

No meta-analysis was attempted because of insufficient data available for analysis from three studies, and the lack of common radiological features in the remaining three studies.

2.1.1.8 Conclusion

Radiological assessment of the presence of, or features of, lower respiratory infection is made with moderate to good inter- and intra-observer agreement, when assessed by expert observers.

2.1.2 Radiological differentiation between viral and bacterial lower respiratory infection

2.1.2.1 Objective

To quantify the accuracy of chest radiography in differentiating bacterial from viral lower respiratory infection in children

2.1.2.2 Inclusion criteria for studies

All identified studies meeting the following criteria were included:

1. an assessment of radiological differentiation of bacterial from viral pneumonia
2. studies of children under 18 years, or studies from which data on children under 18 years could be extracted
3. independent and blind assessment of radiograph and reference standards
4. use of credible reference standards for bacterial and viral infection. For the purpose of this review the following bacterial reference standards were regarded as credible, alone or in combination:

a) culture of bacteria from blood or pleural fluid
b) detection of bacterial antigen or DNA in blood or urine
c) rising antibody titre to a specific bacterium
d) culture of bacteria from nasopharyngeal secretions

The study of the differentiation of bacterial and viral pneumonia is hampered by the lack of a suitable bacterial reference standard (World Health Organization 1991). Culture of nasopharyngeal secretions is particularly problematic because of low specificity i.e. many bacteria causing pneumonia may also live harmlessly in the nose and throat (Congeni and Nankeris 1978; Jegathesan 1985) and be detected on naso-

pharyngeal culture even if they are not causing the disease. Studies using nasopharyngeal cultures were thus presented separately.

The following viral reference standards were regarded as credible:

a) nasopharyngeal culture
b) viral antigen detected in nasopharyngeal secretions
c) rising antibody titre to a specific virus

2.1.2.3 Search strategy

1. Electronic databases

a) The MEDLINE database was searched from 1966 to 1997. The strategy is outlined in Appendix 2. Possibly relevant studies reported in English or with English abstracts were evaluated further.
b) The HealthSTAR database was searched from 1975 to 1997, using Internet Grateful Med. The search strategy is detailed in Appendix 2.

2. The World Health Organization bibliography on acute respiratory infections (URL http://www.who.ch/chd/pub/ari/aripub/htm#oth_res) was searched manually.
3. Authors of identified studies were contacted with an enquiry about the existence of further studies, published or unpublished. A list of those contacted appears in Appendix 3.
4. Reference lists of articles retrieved from the above searches were examined.

2.1.2.4 Data collection and analysis

The investigator evaluated for inclusion potentially relevant studies identified in the above search, according to the pre-stated selection criteria. It was also recorded whether all radiographs had been verified by the reference standard.

When no measures of diagnostic accuracy were presented in the report, sensitivity, specificity and likelihood ratios were calculated from data extracted from the report (Jaeschke, Guyatt and Sackett 1994).

In making the calculations the following principles were followed:

1. mixed bacterial and viral infections were classified as bacterial. Identification of bacterial infections was considered the primary consideration, because they carry a higher mortality and morbidity (Campbell 1995) and are treatable with antibiotics.
2. infections by Chlamydia and Mycoplasma were excluded because they are neither bacteria nor viruses (Chirgwin and Hammerslag 1992; Cherry 1992)
3. cases with no demonstrated aetiology were excluded

2.1.2.5 Description and methodological quality of studies

2.1.2.5.1 Studies included in the analysis

The design and reporting of the nine potentially eligible studies are summarised in Table 2.3.

Six of the studies were included in the review (Bettenay, de Campo and McCrossin 1988; Courtoy, Lande and Turner 1989; Friis et al 1990; Korppi et al 1993; McCarthy et al 1981; Wahlgren et al 1984). One of the included studies did not specifically state that comparison with the reference standard was independent and blind (Courtoy, Lande and Turner 1989), but independent assessment was confirmed by personal communication with the author (Courtoy, Lande and Turner 1989). Three studies used nasopharyngeal culture as the reference standard (Eriksson et al 1986; Friis et al 1990; Wahlgren et al 1984). Characteristics of included studies are shown in Table 2.4, with studies with a questionable reference standard listed separately.

Reporting of the studies was generally poor. In only two of the six studies was the collection of the sample of patients clearly described in the report (McCarthy et al 1981; Wahlgren et al 1984), although in two studies (Courtoy, Lande and Turner 1989; Korppi et al 1993) further details were provided in a separate report (Turner et al 1987; Korppi et al 1991 respectively).

TABLE 2.3 Radiological differentiation between bacterial and viral lower respiratory infection: design and reporting of potentially eligible studies.

	Bacterial reference standard	Independent blind comparison	Sampling method described	All patients received reference standard	Clinically relevant test characteristics, with confidence intervals (CIs)
Bettenay, 1988	Culture (blood or pleural fluid) or urine antigen	Yes	No	No	None
Courtoy, 1989	Blood culture or urine antigen	Not reported[a]	No[b]	Not reported	Sensitivity and specificity. No CIs
Eriksson, 1986	Nasopharyngeal aspirate	Not reported	No	Not reported	Nonr
Friis, 1990	Nasopharyngeal aspirate	Yes	No	No	None
Isaacs, 1989	Culture (blood or pleural fluid)	Not reported	Yes	No	None
Korppi, 1993	Antigen in urine or serum, or rising antibody titre	Yes	No[b]	Not reported	Sensitivity, specificity, PPV, LR (pos). No CIs
McCarthy, 1981	Culture (blood or pleural fluid)	Yes	Yes	No	Sensitivity. No CIs
Wahlgren, 1984	Nasopharyngeal aspirate	Yes	Yes	Yes	No
Swishuk, 1986	Clinical assessment	Not reported[c]	Unclear	No	No

a confirmed to be independent and blind assessment on personal communication with author

b details in separate report

c subsequent correspondence revealed assessment not to be blind and independent

d PPV: positive predictive value, LR (pos): likelihood ratio for a positive test

TABLE 2.4 Radiological differentiation between bacterial and viral lower respiratory infection: characteristics of included studies.

	Subjects	Observers	Aetiological profile (n)	Bacterial ref standard(s)	Viral ref standard(s)
McCarthy[a] 1981	128 consecutive children seen in an emergency room with infiltrates on chest radiography	1 general paediatrician 1 paediatric radiologist 1 general radiologist	Viral (16) bacterial (5) mycoplasma (9) unknown (98)	Blood or pleural fluid culture	Rising antibody titre
Bettenay 1988	107 children aged >100 days with strong clinical evidence of pneumonia. In-patients and outpatients.	2 radiologists viewing films together	Bacterial (11) viral (47) unknown/data incomplete (49)	Culture (blood or pleural fluid) or antigen in urine.	Naso-pharyngeal antigen or culture
Korppi[b] 1993	127 children hospitalised with definite alveolar or interstitial pneumonia.	2 radiologists (viewing films together?). Films used only if agreement on 2 separate occasions 3 years apart	Bacterial (20) viral (20) mixed (21) unknown/data incomplete (66)	Rising antibody titre or antigen in serum or urine	Rising antibody titre or naso-pharyngeal antigen

TABLE 2.4 (cont)

	Subjects	Observers	Aetiological profile (n)	Bacterial ref standard(s)	Viral ref standard(s)
Courtoy 1989	36 children with chest radiograph and aetiological diagnosis of pneumonia, of 98 paediatric outpatients aged 3-10 years	2 paediatricians 2 paediatric radiologists 1 paediatric immunologist	Viral (24) bacterial (12) unknown/data incomplete (62)	Blood culture or urine antigen	Rising antibody titre or naso-pharyngeal antigen or culture
Questionable bacterial reference standard					
Wahlgren 1984	66 with proven RSV infection of 135 children under 3 years hospitalised with respiratory symptoms	Not stated	RSV only (33) RSV plus bacterial (33)	Naso-pharyngeal culture	Naso-pharyngeal antigen or culture
Friis 1990	128 children aged 1 month-6 years hospitalised with clinical and radiological pneumonia	Radiologist	Viral (39) bacterial (25) mixed (37) unknown (27)	Naso-pharyngeal culture	Naso-pharyngeal antigen or culture

a No specificity presented because most cases were of unknown aetiology.
b A "few" cases of Mycoplasma and Chlamydia excluded and not reported.

All six studies used either a questionable reference standard i.e. nasopharyngeal secretions (Friis et al 1990; Wahlgren et al 1984) or a combination of standards e.g. combinations of a culture from one of multiple sites or a rising antibody titre or a bacterial antigen detected in the urine (Bettenay et al 1988; Courtoy, Lande and Turner 1989; Korppi et al 1993; McCarthy et al 1981). Despite relying on multiple bacterial and viral standards to increase sensitivity, approximately half of the cases in most studies were of unknown cause.

The application of all reference standards to all the patients was reported in one included study (Wahlgren et al 1984), was not reported clearly or not reported at all in two (Courtoy, Lande and Turner 1989; Korppi et al 1993), and did not occur in three (Bettenay et al 1988; Friis et al 1990; McCarthy et al 1981).

Studies excluded from the analysis

Three studies were excluded from the analysis. Two were excluded because assessment was not known to be independent and blind (Eriksson et al 1986; Isaacs 1987). A further study (Swischuk and Hayden 1986) was excluded because clinical assessment of aetiology was used as the reference standard and because it emerged in correspondence subsequent to publication that comparison with the reference standard had not been blinded (Leonidas 1987).

2.1.2.6 Results

Sensitivity and specificity were calculated from extracted data in all but one case (McCarthy et al 1981). In this case sensitivity was presented, but no data were provided for the calculation of specificity. One report that presented sensitivity and specificity included C-reactive protein (CRP) levels as a reference standard (Korppi et al 1993). In this case sensitivity and specificity were recalculated after patients with a raised CRP level alone had been reclassified.

Accuracy in the detection or exclusion of bacterial infection is shown in Table 2.5 for studies with a preferable bacterial reference standard, and in Table 2.6 for studies using nasopharyngeal bacterial culture.

TABLE 2.5. Radiological differentiation between bacterial and viral lower respiratory infection: test characteristics from studies using bacterial reference standards other than nasopharyngeal culture.

	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio (95% CI)		
			Positive test	*Indeterminate*	*Negative test*
McCarthy 1981[14]	60-80%	No data			
Bettenay 1988[8]	75% (35-97%)	63% (46-78%)	2.0 (1.1-3.6)	1.4 (0.46-4.41)	0.40 (0.12-1.3)
Korppi 1993[13, a]	49% (33-65%)	65% (41-65%)	1.4 (0.71-2.7)		0.78 (0.52-1.2)
Courtoy 1989[9]	42-58%[b]	54-83%[c]	1.1-3.4[d]		0.5-0.9[e]

a Intermediate readings excluded and not reported, therefore test accuracy overestimated

b Median 50% (95%CI 21-79%), five observers

c Median 75% (95%CI 53-90%), five observers

d Median 1.7 (95%CI 0.64-4.4), five observers

e Median 0.7 (95%CI 0.45-1.3), five observers

TABLE 2.6 Radiological differentiation between bacterial and viral lower respiratory infection: test characteristics from studies using nasophayngeal culture as the bacterial reference standard.

	Radiological feature	Sensitivity	Specificity	Likelihood ratio	
				Pos test	*Neg test*
Wahlgren	Infiltrates				
1984	interstitial	36%	64%	1.0	1.0
(n=66)	alveolar	18%	94%	3.0	0.87
	mixed	15%	78%	0.7	1.1
	Hyperinflation	27%	48%	0.5	1.5
Friis	Lobar pneumonia	48%	79%	2.3	0.66
1990	Bronchop'monia	8%	74%	0.32	1.2
(n=64)	Interstitial	42%	82%	2.3	0.71
	p'monia	37%	79%	1.7	0.79
	Peribronchitis	20%	85%	1.3	0.94
	Hyperinflation	11%	95%	2.2	0.93
	Atelectasis	6%	67%	0.19	1.4
	Normal X-ray				

The likelihood ratios for a positive test were similar across studies that used a preferable reference standard, ranging from 1.3 to 1.8. The only values above 2 were in studies using nasopharyngeal secretions as the reference standard. No likelihood ratio for a negative test was below 0.60

In studies in which multiple observers independently assessed films (Courtoy, Lande and Turner 1989; McCarthy et al 1981) sensitivity and specificity varied between observers by absolute differences of up to 20% and 29% respectively. Agreement between general paediatrician/paediatric radiologist, paediatrician/general radiologist and paediatric radiologist/general radiologist were all poor, with kappa statistics of 0.38, 0.26 and 0.32 respectively (McCarthy et al 1981).

2.1.2.7 Discussion

The usefulness of the studies is handicapped by the lack of a single suitably sensitive reference standard. An additional problem related to the reference standard(s) in the identified studies is that all standards were applied to all the patients in only one study (Wahlgren et al 1984). If failure to do tests on some patients was related to some unstated factors (such as clinical findings) that suggested that a particular infection was or was not present, overall test accuracy would probably be overestimated (Irwig et al 1995).

The generally haphazard sample collection and reporting thereof introduces potential selection biases and hampers generalisation of the findings. The generally poor quality of the studies could be ascribed partially to the fact that only one study appears to have been designed specifically to assess the accuracy of chest radiography and other tests in identifying the cause of pneumonia (Wahlgren et al 1984).

The large groups of cases of unknown aetiology that were excluded from the analysis raise questions regarding the applicability of the findings of this review to actual practice, where many patients represented by the "unknown" group are presumably infected by bacteria or viruses.

The likelihood ratio is a helpful summary measure of the clinical usefulness of chest radiography in differentiating bacterial for viral pneumonia. Ratios between 0.5 and 2 are rarely clinically useful (Sackett et al 1997). The studies reviewed showed a similar range of likelihood ratios below 2 for positive tests and above 0.5 for negative tests. This would indicate a level of accuracy in identifying bacterial pneumonia that is not clinically meaningful. These estimates of test accuracy should however be interpreted with great caution because of the abovementioned methodological limitations.

No meta-analysis was attempted because it was judged that the greater precision of the estimates generated would have little meaning in the presence of the large potential biases attributable to the methodological limitations of the available studies.

2.1.2.8 Conclusion

The diagnostic value of chest radiography in distinguishing bacterial from viral pneumonia is unknown, principally because of the methodological limitations of the available studies.

2.1.3 Radiological assessment of the severity of lower respiratory infection

2.1.3.1 Objective

To assess the accuracy of chest radiography in determining the severity of illness in acute lower respiratory infection in children.

2.1.3.2 Inclusion criteria for studies

All identified studies meeting the following criteria were included:

1. an assessment of association of radiological signs with severity of illness
2. studies of children under 18 years or studies from which data on children under 18 years could be extracted
3. use of a credible reference standard
4. independent and blind comparison between radiological assessment and reference standard

2.1.3.3 Search Strategy

1. Electronic databases
   a) The MEDLINE database was searched from 1966 to 1997. The strategy is outlined in Appendix 2. Possibly relevant studies reported in English or with English abstracts were evaluated further.
   b) The HealthSTAR database was searched from 1975 to 1997, using Internet Grateful Med. The strategy used is detailed in Appendix 2.
2. The World Health Organisation bibliography on acute respiratory infections (URL http://www.who.ch/chd/pub/ari/aripub/htm#oth_res) was searched manually.
3. Reference lists of articles retrieved from the above searches were examined.

2.1.3.4 Data collection and analysis

The investigator evaluated for inclusion, according to the pre-stated selection criteria, potentially relevant studies identified in the above search. It was also recorded whether all radiographs had been verified by the reference standard. When no measures of diagnostic accuracy were presented in the report, sensitivity, specificity and likelihood ratios were calculated from data extracted from the report. (Jaeschke, Guyatt and Sackett 1994).

2.1.3.5 Description and methodological quality of studies

Two studies met the inclusion criteria (Dawson et al 1990; Wilden, Chonmaitree and Schwischuk 1988). The characteristics of the studies are shown in Table 2.7.

Although assessment of radiographs and clinical severity was performed independently, the reference standards in both studies were questionable in that they included treatment outcomes such as mechanical ventilation and the use of intravenous fluids that could themselves have been determined partially by the interpretation of the radiograph.

Several additional shortcomings were present in the report of one study (Dawson et al 1990). Tables of raw data were provided for only two of the four radiological features assessed. In these there were differences between tables in the distribution of clinical severity in the same patients. The chi square test was used inappropriately for both tables in that they contained more than 20% of cells with expected frequencies of less than five (Altman 1991a).

2.1.3.6 Results

Test characteristics are summarised in Table 2.7. The presence of parahilar bronchial infiltrates and atelectasis had likelihood ratios between 2 and 4 for serious illness in viral respiratory infection. The likelihood ratios for the absence of the signs were above 0.5 (Wilden, Chonmaitree and Schwischuk 1988). It is not possible from the available data to assess the diagnostic value of combinations of radiographic signs.

There was minimal correlation between radiological and clinical severity scores in bronchiolitis (Dawson et al 1990).

TABLE 2.7 The association of radiological signs with severity of illness: summary of studies

Author	Subjects	Observers	Reference statndard	Radiological features	Test accuracy[a]			
					Sensitivity	Specificity	Likelihood ratios	
							Test Pos	Neg
Wilden 1988	128 children with viral upper and lower respiratory infection (microbiological evidence of infecton by a single virus). Age 1 week to 14 years. No lobar consolidation.	1 radiologist	"Serious" illness ": apnoea or mechanical ventilation or fatal outcome.	Normal	0.19	0.77	0.81	1.06
				Hyperexpansion	0.33	0.79	1.6	0.84
				Parahilar bronchial infiltrates	0.43	0.84	2.7	0.68
				Atelectasis,	0.62	0.75	2.5	0.51
				Lobar	0.57	0.83	3.4	0.52
				Segmental	0.48	0.87	3.7	0.60
				Adenopathy	0.05	0.88	0.41	1.08
				Diffuse interstitial infiltrates	–	–	–	–
Dawson 1990	153 sequential admissions with a final clinical diagnosis of bronchiolitis.	2 radiologists	Clinical score (1-3) incorporating need for oxygen, tube feeds, intravenous fluids, measures of respiratory distress and ICU admission	Severity score (0-3)	Rank correlation			
				Hyperinflation	0.07 (p=0.39)			
				Infiltrates	No data			
				Atelectasis	No data			
				Sum of scores	0.10 (p=0.24).			

a Calculated from data presented in the report

2.1.3.7 Discussion

The findings suggest little usefulness of chest radiography in assessing severity of illness in viral infections, except possibly for the presence of parahilar bronchial infiltrate and atelectasis helping to rule in serious illness.

These findings must be interpreted with caution because of poor methodological quality, particularly because of questionable reference standards. The use of treatment outcomes such as mechanical ventilation or use of intravenous fluids as part of the reference standard is however expected to result in an overestimation of the strength of any association, and a true association between radiological findings and severity thus appears unlikely.

2.1.3.8 Conclusions

The usefulness of chest radiography in the assessment of the severity of illness in viral respiratory infections is uncertain because of methodological limitations of the two available studies.

2.2 Impact of chest radiography on clinical management and outcome

When assessing the impact of a diagnostic test on clinical management and outcome, the test may be viewed as an intervention.

"Before-after" studies of this intervention have been used to measure differences between clinicians' stated intended management before a diagnostic test and actual management decisions once the test result is available. Such studies are susceptible to bias because the design assumes that the clinicians' stated management plans and actual clinical behaviour will match. However hypothetical management may differ from actual management even without radiography, and actual management may also be influenced by the prior act of recording intended management before the radiograph.

The least biased estimate of the effect of a diagnostic test as an intervention may be obtained by means of a randomised controlled trial, because of the randomised controlled trial's unique ability to minimise selection bias in assembling a control group (Altman 1991b). The randomised controlled trial also provides a direct assessment of impact on outcome. Drawbacks of randomised controlled trials include their generally high cost and the need to expose people to interventions of uncertain efficacy.

A further difficulty with the interpretation of the findings of a randomised trial of a diagnostic test is that a lack of effect of the test could be due to an inappropriate response to the test result of the clinicians involved, rather than poor performance of the test itself. However the effect of the test in usual clinical practice, rather than in ideal circumstances, is the more meaningful measure of a test's utility. A randomised controlled trial involving clinicians representative of those who would usually use the test thus gives the most meaningful assessment of the utility of a diagnostic test.

2.2.1 Objective

To quantify the effects of chest radiography on clinical management and clinical outcome of children with acute lower respiratory infections

2.2.2 Inclusion criteria for studies

All studies meeting the following criteria were included:

1. studies comparing clinical management or clinical outcome when managed with and without the use of chest radiography
2. studies of children under 18 years, or studies from which data on children under 18 years could be extracted

2.2.3 Search strategy

Two strategies were used:

2.2.3.1 To identify studies other than controlled trials

a) The MEDLINE database was searched from 1966 to 1997. The strategy is outlined in Appendix 2.

b) The World Health Organization bibliography on acute respiratory infections (URL http://www.who.ch/chd/pub/ari/aripub/htm#oth_res) was searched manually.

c) Reference lists of the articles retrieved from the above searches were examined.

2.2.3.2 To identify randomised controlled trials

a) The specialised trials register of the Cochrane Acute Respiratory Infections Group was searched, using the key words chest and (x-ray or radiograph or roentgenogram). No language restrictions were applied.

b) The Cochrane Library (1998) was searched using the key words chest and (x-ray or radiograph or roentgenogram). The search included the databases of the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness (DARE), and the Cochrane Controlled Trials Register.

c) The HealthSTAR database was searched from 1975 to 1997, using Internet Grateful Med. The strategy used is detailed in Appendix 2.

d) Experts in the field were contacted with an enquiry about the existence of studies, either published or unpublished, completed or in progress, dealing with the impact of chest radiography on therapy or outcome in acute lower respiratory infections in children. A list of those contacted appears in Appendix 3.

e) Reference lists of articles retrieved from the above searches were examined.

2.2.4 Data collection and analysis

The investigator evaluated for inclusion, according to the pre-stated selection criteria, articles identified in the above search.

2.2.5 Description of studies and methodological quality of studies

No randomised controlled trials involving children were identified. The only trial identified was excluded because all participants were adults.

Three before-after studies (one unpublished) examined the impact of chest radiography on management (Alario et al 1987; Grossman and Caplan 1988; Leventhal 1979). All were performed in the United States on children already identified as needing a radiograph, rather than in those with a specific case definition. The characteristics of these studies are summarised in Table 2.8. In one study only gross (rather than net) changes in diagnosis and treatment were reported (Grossman and Caplan 1988). An attempt to contact the author for further information was unsuccessful.

Changes in diagnosis, antibiotic treatment and admission to hospital were studied, but not changes in clinical outcome. All three studies followed an uncontrolled "before-after" design that assumes that clinicians' stated management plans and actual clinical behaviour will match, and that all changes over time are due to the intervention.

2.2.6 Results

The findings are summarised in Table 2.8. Each study found a moderate or small, but nevertheless clinically meaningful, change in diagnosis, antibiotic use and hospital admission. The changes in diagnosis were greater than changes of treatment (antibiotic use or admission to hospital).

TABLE 2.8 Before-after studies of the impact of chest radiography on management (95% confidence intervals in brackets)

	Leventhal 1979	Alario 1987	Grossman 1988
Clinicians	Paediatric residents	8 experienced paediatricians	A range from medical students to specialist paediatricians
Patient population	Children aged over 8 weeks Suspected pneumonia	1mth-18yrs. Suspected pneumonia (identified by paediatric residents)	Under 19yrs. Suspected pneumonia
Sample size	n=136	n=102	n=155
% admitted	11%	13%	17%
% with pneumonia	26%	36%	33%
Diagnosis of pneumonia			
Ruled in	3/127 2% (0.5-7%)	17 17% (9-24%)	
Ruled out	40/127 31% (23-40%)	2 2% (0.2-7%)	
Total change	43/127 34% (26-42%)	19 19% (11-22%)	
Net change	Ruled out 37/127 29% (21-37%)	Ruled in 15 15% (8-22%)	
Antibiotic use			
Ruled in	8/120 7% (3-13%)	9 9% (4-16%)	12%
Ruled out	9/120 7% (3-14%)	4 4% (1-10%)	10%
Total change	17/120 14% (8-20%)	13 13% (6-12)	22%
Net change	Ruled out 1/120 1% (0-5%)	Ruled in 5 5% (2-11%)	Ruled in 2%
Hospital admission			
Ruled in	3/120 2.5% (0.5-7%)	1 1% (0-5%)	
Ruled out	3/120 2.5% (0.5-7%)		
Total change	6/120 5% (2-11%)	1 1% (0-5%)	12%
Net change	0 0% (0-3%)	Ruled in 1 1% (0-5%)	
Comments	136/322 (42%) eligible patients had questionnaires completed.		Raw data not provided

The proportion of cases in which diagnosis was changed was similar in the two studies where data were provided (19% and 34%), but the net direction of change differed widely between studies. Pneumonia was ruled in in 15% (95% CI 18-22%) of cases in one study and ruled out in 29% (95% CI 21-37%) in the other. The net directions of change in antibiotic use and admission to hospital ranged from 0% to 5%, concealing total changes ranging from 13-22% for antibiotic use and from 1-12% for hospitalisation.

2.2.7 Discussion

A meaningful effect was found of chest radiography on diagnosis, antibiotic use and possibly admission to hospital. This effect was to rule diagnosis and management options both in and out, but the net direction of the effect was not consistent. Given the 95% confidence intervals for the changes in diagnosis in different directions in the studies by Leventhal (1979) and Alario et al (1987), the difference between studies is unlikely to be due to chance. The 95% confidence intervals for all but one estimate of change in antibiotic use (Table 2.8) do not include zero. This suggests that the estimates are unlikely to differ from zero by chance, although the differences between the studies could be due to random error.

The before-after study design used in all three studies is susceptible to bias and has been found in other situations to overestimate therapeutic impact, when compared with randomised controlled trials (Guyatt et al 1986). In situations where a before-after design shows therapeutic impact it has been recommended that a randomised controlled trial be performed (Guyatt et al 1986).

Although not included in the systematic review, the single randomised controlled trial of the use of chest radiography identified in the search is of interest. This was a trial of 1502 adults with cough for less than one month. It failed to show an effect of radiography on antibiotic use, scheduling of a return visit or the duration of eight symptoms or measures of limitation of activity. There were however significant threats to the validity of the report. These included a follow-up rate of 66% for duration of symptoms, the lack of reporting of allocation concealment or blinding of outcome assessment, and the lack of a power calculation.

2.2.8 Conclusions

1. No controlled trials of the effect of chest radiography on clinical management or outcome in children with acute lower respiratory infection were identified.
2. In uncontrolled before-after studies, chest radiography had a small but meaningful effect in both directions on diagnosis, antibiotic use and possibly admission to hospital.
3. The net effects of the bi-directional changes in diagnosis were not consistent, while those for changes in management were small.
4. The findings are probably overestimates, given the uncontrolled before-after study design.
5. The impact of chest radiography on clinical outcome in children with ALRI has not been studied.

2.3 Summary of conclusions of systematic reviews

There is great uncertainty about the value of chest radiography in ALRI in children. Diagnostic accuracy in the detection of pneumonia is unknown because of the lack of a credible reference standard. Agreement between and within expert observers in the interpretation of chest radiographs is "moderate" to "good", but that of less expert observers has not been studied. The diagnostic value of radiography in distinguishing bacterial from viral pneumonia and in assessing severity of illness is unknown because of inadequate reference standards and methodological limitations of the available studies.

Although part of the uncertainty about the value of chest radiography is due to the inadequacy of the methodology of available studies, but much of it is due to the absence of a randomised controlled trial of the effect of chest radiography. A randomised controlled trial is the study design that provides the strongest evidence of the effect of an intervention. It also enables a direct assessment of clinical benefit, which is the underlying reason for performing the radiograph.

Chapter 3

A trial of chest radiography

Methods

3.1 Aims and objectives

3.1.1 Purpose

To evaluate the impact of chest radiography on the diagnosis, management and outcome of acute lower respiratory infection (ALRI) in children.

3.1.2 Aim

To compare the diagnosis, management and outcome of children with ALRI managed with and without the use of chest radiography.

3.1.3 Objectives

To determine in children with ALRI who, according to World Health Organization (WHO) case management guidelines, may be treated as outpatients:

i the difference in the distribution of diagnoses when chest radiography is used and is not used

ii. the difference in management options exercised in the above circumstances

iii. the difference in clinical outcome when chest radiography is used and is not used

iv. the difference in the effect of chest radiography on clinical outcome when radiography is used by doctors with different levels of experience.

3.2 Study design

Randomised controlled trial

3.3 Participants

The participants were consecutive children aged 2 to 59 months who presented to the Red Cross Children's Hospital (RXH) as their first contact on weekday mornings. They were eligible for this study if they met the WHO case definition for pneumonia i.e. cough and tachypnoea but with the child drinking well and without chest indrawing, cyanosis, abnormal level of consciousness or stridor (World Health Organisation 1995). Tachypnoea was defined as a respiratory rate of 50 breaths or more per minute (measured over one minute) in children aged 2 to 11 months, and 40 breaths or more per minute in children aged 12 months or more. The WHO case

management guidelines recommend that this group of children be treated with an antibiotic at home. Exclusion criteria were a cough of more than 14 days duration, a history of a current household contact with active tuberculosis, a localised wheeze, clinical signs of cardiac failure or the clinician's view that a chest radiograph was mandatory.

3.4 Study setting

3.4.1 Outpatients department and patient population

The Red Cross Children's Hospital is a children's teaching hospital providing primary, secondary and tertiary level care. The study was conducted in the general outpatients department (GOPD). At the time of the study approximately 12 000 patients attended the GOPD per month. Unreferred patients (the participants in this study) accounted for 85% of patients. In a survey performed shortly before this study 85% of the unreferred patients could, in the judgement of the consulting doctor, have been appropriately seen at a community-based primary health care facility (Power et al 1997). Care was provided free of charge. Malaria is a very uncommon illness in the patient population in question.

3.4.2 Clinicians

The clinicians were 52 medical practitioners working full-time or part-time in GOPD. Seventeen (33%) possessed a postgraduate paediatric qualification, mostly the Diploma in Child Health (South Africa). Five (10%) were registrable in South Africa as specialist paediatricians. Twenty-nine (56%) had worked in the outpatients department for less than one year and 10 (19%) for more than five years.

3.5 Study plan and measurement

3.5.1 The intervention

The intervention was the use of a chest radiograph, antero-posterior and lateral views. The radiograph was viewed by the clinician. A routine report supplied by the duty paediatric radiologist or radiology registrar was available to the clinician.

3.5.2 The control

The control group received standard care, but without a chest radiograph. All management except radiography was entirely at the discretion of the clinician.

3.5.3 Outcome measures

3.5.3.1 Primary outcome

The primary outcome measure was time to recovery, defined as the number of days from randomisation to the first day that the child was judged by the caregiver to be completely well.

3.5.3.2 Subsidiary outcomes

Subsidiary outcomes were:

a. the frequency distribution of diagnoses
b. management options exercised at the first visit
    i. the proportion of participants in whom additional tests were ordered
    ii. the number of drugs per prescription
    iii. the proportion of participants in whom an antibiotic was prescribed
    iv. the proportion of participants admitted to hospital at the initial consultation
    v. the proportion of participants given an appointment for a return visit within 28 days
c. clinical outcome
    i. the proportion of participants making subsequent visits to RXH or elsewhere for health care within 28 days
    ii. the proportion of participants subsequently admitted to RXH within 28 days
    iii. the proportion of participants subsequently receiving a chest radiograph at RXH within 28 days

d. consultation time

i. total consultation time i.e. the total time spent by the participant in the consulting room with the clinician, including review after radiography or other procedures

ii. total patient time i.e. time from start to end of the consultation, including time during radiography or other procedures. It did not include time spent waiting to see the doctor before the consultation or time waiting for medicines after the consultation.

3.5.4 Enrolment and random allocation

3.5.4.1 Procedure

Patients were enrolled from 12 September to 1 December 1995 and from 13 February to 29 September 1996, avoiding a seasonal lull in the number of eligible patients. An experienced registered professional nurse, fluent in English and Afrikaans, who had received training in the eligibility criteria for the study screened all patients waiting to see a doctor, and selected those eligible for enrolment in the study. Eligible patients (i.e. those patients who satisfied the WHO case definition, who had been coughing for 14 days or less and who did not have a history of a current household contact with tuberculosis) were enrolled. Participant details were registered sequentially in a record book, together with date and time of enrolment. Unique participant identity numbers were allocated according to the order in which participants were entered into the register. Baseline information included age, weight, duration of symptoms before presentation, and respiratory rate. The data capture sheet is attached (Appendix 4). The nurse attached to the consultation sheet a sealed sequentially numbered envelope made from 80g manilla paper containing the treatment allocation generated in advance by the investigator (by tossing a coin).

Caregivers were asked whether they could be contacted by telephone. From 11 March to 6 June 1996 only subjects who offered a contact number were enrolled, to reduce the load on the temporarily short-staffed clinicians.

"Enrolled" participants were then seen by a clinician. Following clinical history and examination, the clinician recorded whether he or she would have performed a chest radiograph if the patient had not been part of the trial. The clinician excluded any patient with an exclusion criterion detectable on clinical examination (localised wheeze, clinical signs of cardiac failure or the clinician's view that radiography was mandatory). The clinician then entered the remaining participants into the trial by opening the sealed manila envelope attached to the clinical record. The envelope contained a self-adhesive sticker indicating the allocation. The sticker was placed by the clinician on the clinical record sheet. If a participant was excluded before randomisation the clinician returned the sealed randomisation envelope to the investigator by placing it in a receptacle provided for the purpose in each consulting room. The investigator discussed the randomisation procedure individually with each clinician before participation in the study, and instructions regarding the randomisation process were prominently displayed in each consulting room (Appendix 5). It was stressed during the discussion with the clinician that participation in the trial and entry of patients was entirely voluntary. It was also stressed that, if the clinician was unwilling to withhold a radiograph from a specific patient, that that patient should be excluded without opening the allocation envelope.

Reasons for exclusion were recorded by the clinicians. The investigator collected allocation envelopes of excluded patients, examined the clinical records (as described in Section 3.5.5.2) and discussed apparent departures from the protocol with the clinician involved. In the early stages of the trial several allocation envelopes were reportedly inadvertently opened because they were thought to be referral letters. From case number 161, a sticker with the following wording was placed on each envelope:

CXR Trial
Do not open before seeing Dr.
DOCTOR: If CXR essential please
place unopened envelope in
plastic sleeve.

Apart from the use of chest radiography, all management was entirely at the discretion of the clinician. Clinical notes were recorded on the pro forma consultation sheet routinely used in the department (Appendix 6).

The clinicians' perception of the need for the radiograph, whether the patient had been excluded (with the reason) and the final diagnosis were recorded by ticking the appropriate blocks stamped on the routine consultation form (Appendix 7). Clinicians were not asked to record diagnosis or intended management before radiography, for fear of influencing final diagnosis and management.

3.5.4.2 Audit of allocation concealment

3.5.4.2.1 Allocation procedure

The register of enrolled patients was examined for unallocated identity numbers, deletions or alteration of participant details, and for dates and times of registration that were not in chronological sequence.

To assess possible differential exclusion, the proportions of patients excluded from radiograph and control groups were compared.

3.5.4.2.2 Impact of potential loss of concealment

To assess whether any differential exclusion had resulted in allocation groups with different prognoses, excluded patients allocated to radiograph and control were compared for differences in baseline characteristics, time to recovery and subsidiary outcome measures.

To assess the impact of possible differential exclusion on the study findings, the primary analysis was repeated with excluded patients included in the proportional hazards regression model. The excluded patients were analysed in the groups in which they would have been allocated, had they been included.

3.5.5 Measurement of outcome

3.5.5.1 Time to recovery and visits other than to Red Cross Children's Hospital

Time to recovery (the principal outcome) and visits to other health care providers were recorded by telephone interview of the subset of participants who offered a telephone number. When participants were enrolled caregivers were asked whether they could be contacted by telephone. Details of all potential contact numbers were recorded, whether at home or via an employer or neighbour. The most convenient time to call (during or after working hours) and any further relevant contact information were recorded. Caregivers who offered an employer's telephone number were given a letter to the employer explaining the reason for the calls (Appendix 8). Participants were contacted twice weekly until recovery, or for 28 days. A participant was regarded as lost to follow-up after 3 successive unsuccessful attempts to establish contact at suitable times over a period of at least two days. The interviewer was a trained librarian fluent in English and Afrikaans who had no medical experience.

Respondents were asked, "Is (child's name) completely well yet?" If the answer was "Yes", the next question was "On what day was he/she last sick?" When a child had recovered since the previous telephone call, but the caregiver could not remember on which day the child had last been ill, the median of the intervening days (usually 2 or 3) was taken as the last day of illness. When there was an even number of intervening days, the earlier of the two middle days was taken.

The telephone questionnaire is attached (Appendix 9). Three questions included in the questionnaire (subsequent visits and admissions to RXH and subsequent chest radiographs at RXH) were verifiable by examination of the clinical records. Information on transport costs for the child's family and working days lost as a result of the child's illness were collected for a cost-effectiveness analysis, to be performed in the event of an effect of radiography being demonstrated. The questionnaire was pre-tested by the investigator in a pilot study of 40 patients. (For details of the pilot study, see Section 3.6 below.) The questionnaire was further refined in a second pilot

study of 10 patients who were recruited according to the study protocol, and interviewed by the same interviewer who conducted the study interviews.

3.5.5.2 Other subsidiary outcomes

Chest radiograph allocation, diagnosis, clinical management options used (additional tests ordered, number of drugs per prescription, antibiotic usage, follow-up appointment and immediate admission to hospital) and subsidiary clinical outcomes (return visits, subsequent hospital admissions and radiographs) were ascertained by examination of clinical records by the investigator, except for visits to facilities other than RXH which were measured by the above telephone interview. All patients were followed up by examination of the clinical records (whether accessible by telephone or not). Only prescriptions and management plans recorded explicitly on the usual consultation sheet were recorded. The data extraction form is attached as Appendix 10.

3.5.5.2.1 Consultation times

From 13 November to 1 December 1995 and 10 June to 29 September 1996, clinicians were asked to record the time at which the patients walked through the consulting room door at the start and end of the consultation and at any subsequent reviews. During this period an additional slip of paper was pasted to the record to facilitate recording of these times (Appendix 11). The periods of the trial when these times were recorded were limited so as to minimise disruption to the consultation process.

3.5.5.3 Reliability, validity and applicability of measurements

3.5.5.3.1 Validity of the telephone questionnaire findings

Validity of the trial findings measured by the questionnaire was tested by including questions on subsequent visits and admissions to RXH and subsequent chest radiographs performed at RXH. The effect of chest radiograph on these three outcomes measured by the telephone questionnaire was compared with the effect of radiography on the same outcomes measured from hospital records (in participants who offered a telephone number).

3.5.5.3.2 Applicability of telephone questionnaire findings

The effect of chest radiography on outcomes measured from hospital records in participants accessible by telephone was compared with the effect in those not accessible. Accessible participants were defined as those in whom initial telephonic contact was established. Non-accessible participants were those who either did not offer a contact number or in whom initial contact was not established.

3.5.5.3.3 Reliability of record review

Reliability was assessed by a second observer repeating the examination of the records in a ten percent random sample of records. The second observer was a specialist paediatrician familiar with the format of the clinical records but not a co-investigator in the study. Twelve items were assessed. These were: exclusion before randomisation, chest radiograph allocation, clinicians' perceived need for radiography, diagnosis, additional tests ordered (yes or no), number of drugs per prescription, antibiotic use, follow-up appointments within 28 days (yes or no), hospital admission at the first consultation (yes or no), subsequent visits to RXH within 28 days (yes or no), subsequent admissions within 28 days (yes or no) and subsequent chest radiographs within 28 days (yes or no).

3.5.5.4 Follow-up of excluded patients

Enrolled patients excluded by the clinicians before randomisation were followed up in identical manner to included participants

3.5.6 Masking

3.5.6.1 Time to recovery

The telephone interviewer was not informed of the study hypothesis, was blind to the randomisation status of the patients and had no contact with the hospital other than through the investigator. On informal enquiry at the end of the study the interviewer had guessed only that the study dealt with chest infections.

3.5.6.2 Data analysis

Coding, entry and cleaning of telephone questionnaire data was performed by the investigator on a separate data capture sheet, in a separate database and at a separate location (the investigator's home), without knowledge of allocation group.

3.5.6.3 Other

The participants, the clinicians and the investigator's examination of the hospital records could not be blinded to treatment allocation.

3.6 Sample size determination

Assuming a median time to recovery of six days in the control group, it was judged that a reduction of two days (to four days) would justify the expense and inconvenience of a chest radiograph. Assuming an exponential distribution for survival times, the ratio of medians in survival analysis is equivalent to the hazard ratio (Parmar and Machin 1995). A hazard ration of 1:1.5 was thus taken as the smallest clinically meaningful difference in outcome. The following differences in secondary outcomes were regarded as the smallest clinically meaningful differences: antibiotic use of 70% *vs.* 50%, hospital admission of 5% *vs.* 10%, return visits of 30% *vs.* 20%, means number of drugs prescribed of 3 *vs.* 1.5

A pilot follow-up study was performed on a sample of patients identified from the hospital computer database as having a contact telephone number and discharged home from GOPD with ALRI in the previous 3 days. Of 40 patients contacted by telephone 39 were followed till recovery, or for a minimum of 28 days. From the survival data from this pilot study, the sample size required to detect a ratio of median time to recovery of 1:1,5 with 95% confidence and 90% power (using the log rank test) was 153 in each group (determined using the Egret software package).

The projected proportion of patients accessible by telephone, estimated from a review of telephone numbers recorded in the hospital database, was 50%. In the time taken to enrol 306 patients with telephones a further 306 patients without telephones were thus expected to be enrolled. It was calculated that the total of 612 cases would allow

detection of the following differences in rates of subsidiary outcomes with 95% confidence and 90% power: antibiotic use, 70% vs. 82%; admission, 5% vs. 13%; return visits, 30% vs. 20%; mean number of drugs prescribed, 3 vs. 2,5. With the exception of hospital admission, these differences were regarded as smaller than clinically meaningful i.e. a null hypothesis of no clinically meaningful difference could be accepted with at least 90% power. It was decided not to increase sample size merely to increase the power in detecting a difference in hospital admissions.

The target sample size was thus 306 participants accessible by telephone.

3.7 Data analysis

Analysis was by intention to treat.

The investigator entered the data into an electronic database, using the Epi Info software package. The investigator performed the analysis with the Epi Info and Statistica packages on a personal computer. Z-score for weight for age was determined using the anthropometric module of the Epi Info package.

3.7.1 Time to recovery

Survival analysis was performed using the Statistica software package. Time to recovery was compared by inspection of Kaplan-Meier survival curves and the log rank test. In addition, to adjust for any imbalances between the allocation groups in baseline prognostic variables, the analysis was repeated using Cox proportional hazards regression. The prognostic variables included in the model were age, Z-score for weight for age, duration of symptoms before presentation, respiratory rate, clinicians' possession of a postgraduate paediatric qualification, clinicians' time spent working in the outpatients department and clinicians' perception of the need for radiography. Potential modifiers of the effect of chest radiography on time to recovery were sought by testing for an interaction with chest radiography in a proportional hazards regression model. The proportional hazards regression analysis was repeated including clinicians time since qualification, which had not been included in the a priori regression model.

3.7.2 Subsidiary outcomes

Normally distributed continuous data were compared using the t test and other continuous data with the Kruskal Wallis test. Approximate 95% confidence limits for medians were determined from tables (Altman 1991a). Confidence intervals for proportions were calculated using the exact binomial method provided in the EpiTable calculator of Epi Info. Categorical data were compared using the uncorrected chi squared or Fisher's exact tests.

If an effect of chest radiography on a secondary outcome was demonstrated, modifiers of that effect were sought by testing for an interaction in a logistic regression model of radiograph use with the same variables as those tested in the proportional hazards regression model. Logistic regression was used rather than bivariate analysis because of the continuous variables tested. Logistic regression was performed using SAS on an alpha platform. If a significant categorical effect modifier was identified, the magnitude of the effect was expressed as a risk ratio, using stratified contingency tables.

3.7.3 Validity and applicability of questionnaire findings

Interactions of categorical variables with the effect of radiography were tested with a chi-square test provided in the Epi Info package and described by Rothman (1986). An interaction of the number of drugs per script with the effect of radiography was tested using linear regression.

3.7.4 Reliability

Inter-rater agreement was expressed as a kappa statistic, calculated using the method described by Fleiss (1981) and featured in the EpiTable calculator of Epi Info. Confidence intervals were calculated using the method described by Altman (1991a)

3.7.5 Level of significance

A two-tailed alpha level of 0.05 was regarded as significant.

3.8 Ethics

Written informed consent was obtained by the nurse from the caregiver before enrolment in the study (Appendix 12). All clinicians consented verbally to participation. The study was approved by the Ethics and Research Committee of the University of Cape Town.

Of potential ethical concern is the fact that controls did not receive a chest radiograph, even if the clinician would ordinarily have ordered a radiograph. Justification for this approach includes:

i. Three "before-after" studies in children had found small but meaningful changes in clinical management. The "before-after" study design has tended to overestimate therapeutic impact, when compared with the results of randomised controlled trials (Guyatt et al 1986), and it is not known whether the management changes were in fact beneficial. If a "before-after" study shows therapeutic impact it has been recommended that a randomised controlled trial be performed (Guyatt et al 1986).

ii. The World Health Organisation case management guidelines for doctors in developing countries do not include the use of chest radiography for patients with this clinical presentation.

iii. The exclusion criteria cover the circumstances in which failure to perform a radiograph could be dangerous to the patient.

Chapter 4

A trial of chest radiography

Results

4.1 Participant flow and follow up

The trial profile and follow-up are summarised in Figure 4.1.

4.1.1 Enrolment and allocation

4.1.1.1 Enrolment

Five hundred and eighty one eligible patients were identified by the registered nurse. The caregivers of all eligible patients consented to inclusion in the study.

4.1.1.2 Allocation concealment and exclusions

4.1.1.2.1 Allocation procedure

No deletions or alterations were found in the register of patients enrolled by the nurse. There were nine disruptions of the chronological sequence of entry (Figure 4.2). Of the nine disruptions, two resulted in a participant receiving a radiograph he/she would otherwise not have received, four resulted in a change from a radiograph to a control allocation, and three in no change in allocation.

4.1.1.2.2 Exclusions

Fifty-nine participants (26 accessible by telephone) were excluded by the clinicians before randomisation. The stated reasons for the exclusions are shown in Table 4.1.

4.1.1.2.3 Allocation concealment

The status of envelopes of excluded patients, and the stated reasons for exclusion are shown in Table 4.2. All but nine of the 59 exclusions were excluded for reasons of severity or protocol. Of the nine remaining exclusions for "administrative" reasons, two reportedly had allocation envelopes inadvertently opened before the consultation (because they were mistaken for referral letters) and seven were reported to have been lost before the consultation.

The proportion of eligible patients who were excluded decreased during the progress of the trial (Table 4.3).

FIGURE 4.1 Trial profile and follow-up.

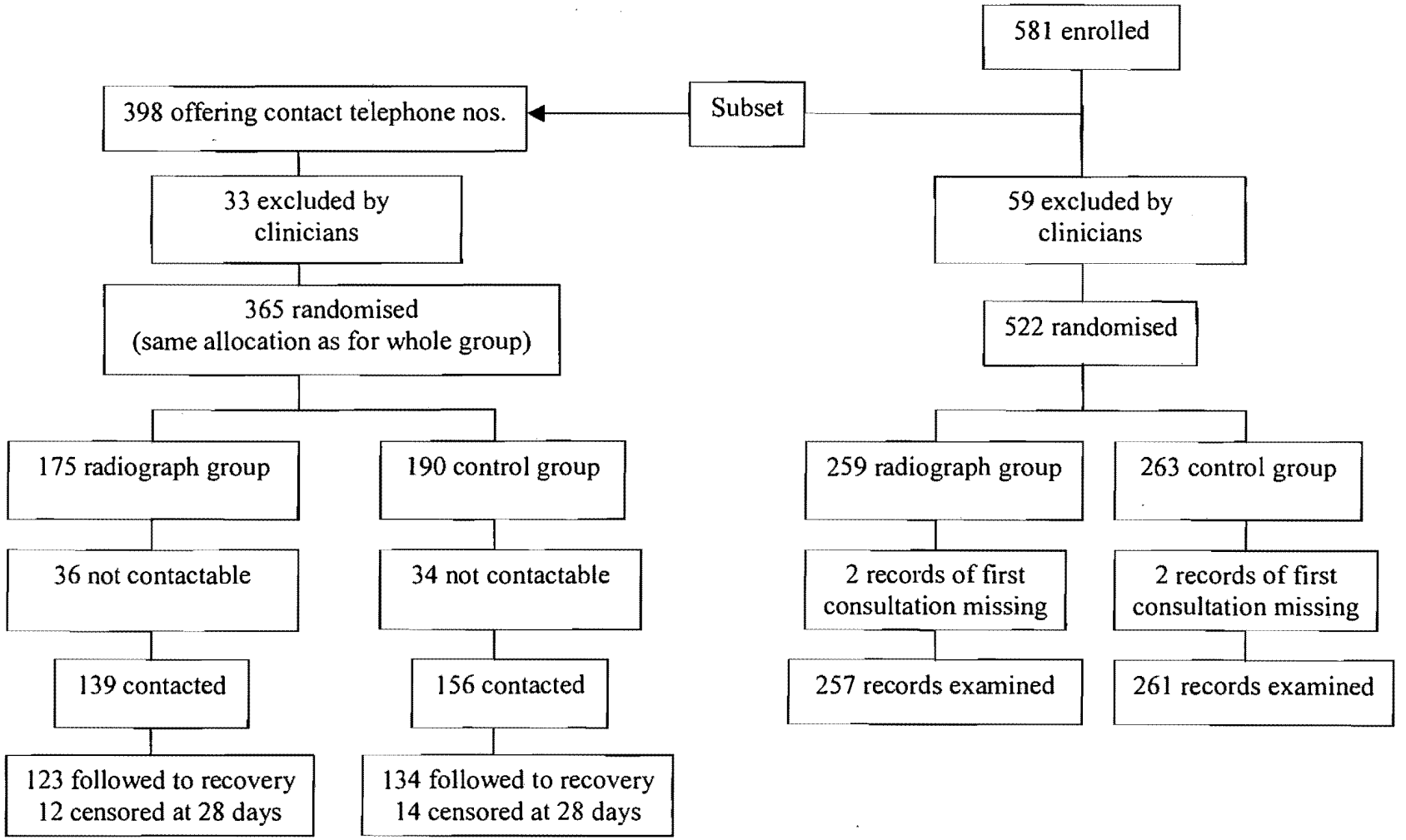


FIGURE 4.2 Adherence to the allocation procedure.

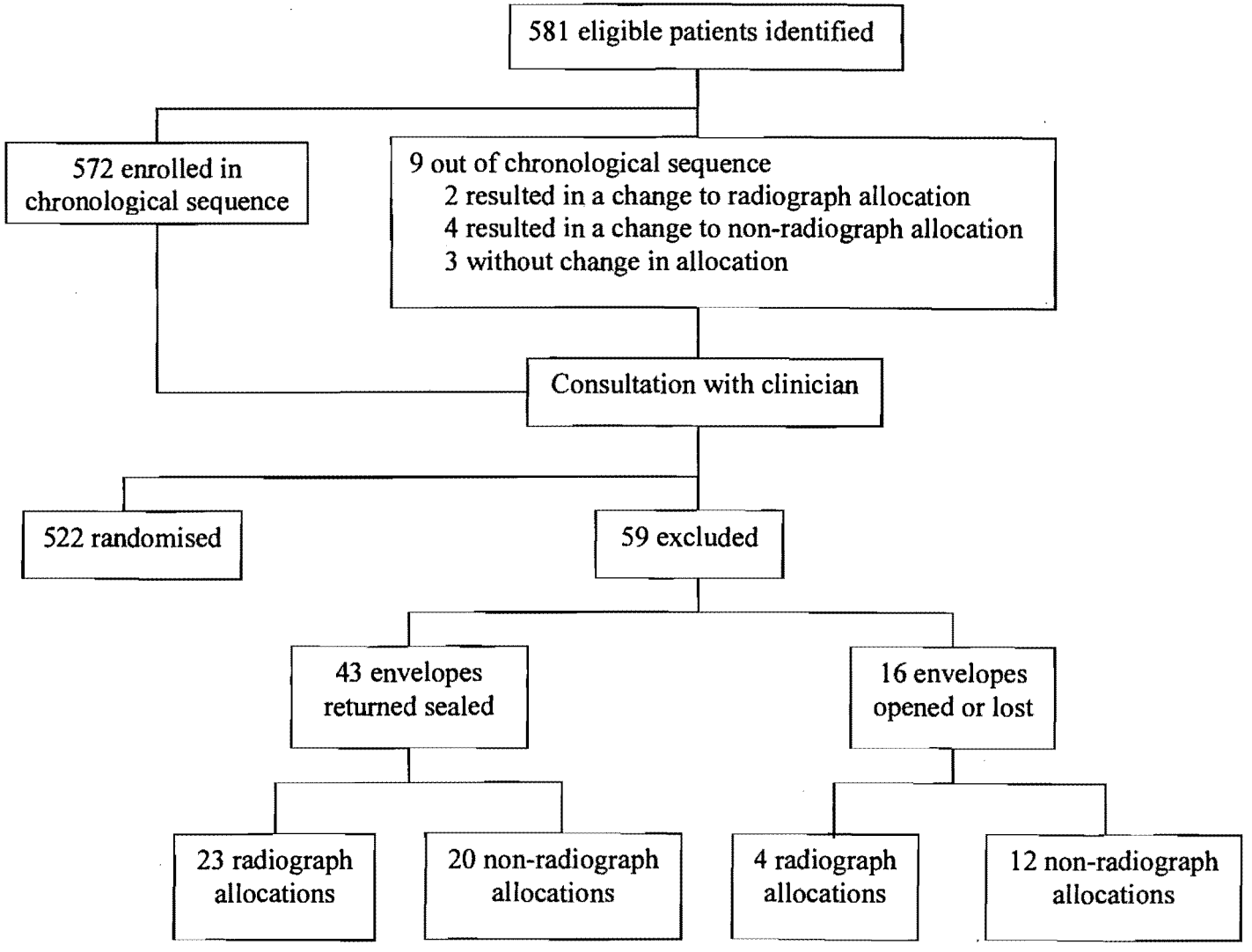


TABLE 4.1 Patients excluded before randomisation: stated reasons for exclusion.

Stated reason	Total	Subset accessible by telephone
Too ill	18	5
Not ill enough	11	7
"Administrative"	9	4
Unilateral wheeze[2]	4	3
No response to therapy[1]	2	1
Cough longer than 2 weeks[1]	2	1
Stridor[1]	1	0
TB contact[1]	1	0
Cardiac failure[2]	1	0
Congenital heart disease	1	1
Hypertension	1	1
Haemoptysis	1	0
Chronic lung disease	1	0
Poor growth	2	0
"Recurrent problem"	1	1
Too young (2 months)	1	0
Unknown	2	2
TOTAL	59	26

[1] Predetermined criterion for exclusion before initial enrolment.

[2] Predetermined criterion for exclusion before randomisation

TABLE 4.2 Patients excluded before randomisation: stated reasons for exclusion, and the status of allocation envelopes.

Stated reasons	Total		Status of envelope					
			Sealed		Opened		Lost	
	Radiograph	*Control*	*Radiograph*	*Control*	*Radiograph*	*Control*	*Radiograph*	*Control*
Too ill	10	8	10	4		3		1
Not ill enough	6	5	6	4		1		
"Administrative"	3	6				2	3	4
Predetermined exclusion criteria	7	4	6	3		1	1	
Other clinical reasons	1	7	1	7				
Unknown		2		2				
TOTAL	27	32	23	20	0	7	4	5

TABLE 4.3 Patients excluded before randomisation during the progress of the trial.

		Patients excluded
First	100 patients	15
Second	100 patients	11
Third	100 patients	13
Fourth	100 patients	7
Fifth	100 patients	6
Final	81 patients	7
Chi-square for linear trend		4.43
p		0.04

Stated reasons for exclusion in patients with opened or lost envelopes are shown in Table 4.4. In total, 16 envelopes were opened or lost. Four of the envelopes had radiograph allocations (1.4% of 286 allocations) and 12 (4.1% of 295 allocations) had control allocations (p=0.05). This discrepancy between allocation groups in lost and opened envelopes was not present in participants offering a telephone number (Table 4.5). The proportion of excluded patients who had opened or lost envelopes diminished during the course of the trial (Table 4.6).

4.1.1.3 Allocation

Five hundred and twenty two participants were entered in the trial, 259 to the radiograph group and 263 to the control group. Four (1.5%) of the radiograph group did not receive the intervention. Seven (2.7%) of the control group received a radiograph on the day of randomisation; two of these when a clinician changed his/her mind about the necessity of a radiograph, two when the patient returned for second consultation later in the day, and three for unknown reasons.

TABLE 4.4 Patients excluded before randomisation: stated reasons for exclusion when allocation envelopes were opened or lost before randomisation.

	Radiograph	Control	TOTAL
All cases			
Too ill	0	4	4
Not ill enough	0	1	1
"Administrative"	3	6	9
No response to therapy[1]	0	1	1
Stridor[1]	1	0	1
TOTAL	4	12	16
Subset accessible by telephone			
Too ill	0	0	0
Not ill enough	0	1	1
"Administrative"	3	1	4
No response to therapy[1]	0	0	0
Stridor[1]	0	0	0
TOTAL	3	2	5

[1] Predetermined criterion for exclusion before initial enrolment.

TABLE 4.5 Patients excluded before randomisation: status of envelopes.

	Radiograph	Control	TOTAL
All cases			
Envelope returned sealed	23	20	43
Envelope opened	0	7	7
Envelope lost	4	5	9
TOTAL	27	32	59
Subset offering a telephone number			
Envelope returned sealed	11	10	21
Envelope opened	0	1	1
Envelope lost	3	1	4
TOTAL	14	12	26

TABLE 4.6 Patients excluded before randomisation: status of allocation envelopes of patients excluded during the progress of the trial.

		Patients excluded	Envelopes opened or lost (% of excluded patients)
First	100 patients	15	9 (60%)
Second	100 patients	11	3 (27.3%)
Third	100 patients	13	1 (7.7%)
Fourth	100 patients	7	2 (28.6%)
Fifth	100 patients	6	1 (16.7%)
Final	81 patients	7	0 (0%)

Chi-square for linear trend 8.49 (5th and final groups of patients merged to avoid empty cell)

p 0.004

4.1.2 Clinicians

All 52 clinicians who worked in the department during the course of the study gave verbal consent to participation. Their professional experience, possession of a postgraduate paediatric qualification and the number of patients seen are shown in Table 4.7. The median time (25^{th} – 75^{th} centile) spent working in GOPD was 12 months (1-38 months) and since qualification 5 years (2-17.5 years). Spearman rank order correlation between time spent in GOPD and time since qualification was 0.64.

Three clinicians were withdrawn from participation by the investigator, as a result of monitoring the allocation process. The withdrawals were made after one clinician excluded 4 of 5 patients for apparently trivial reasons, a second excluded 3 of 4 patients, and the third ignored the allocation procedure in both patients seen.

4.1.3 Follow-up

4.1.3.1 Telephone interviews

Two hundred and eighty three (77.5%) of the 365 participants offering a telephone number were followed till recovery or for 28 days. There was no significant difference in follow-up between treatment groups (Table 4.8).

TABLE 4.7 Clinicians' general and specific experience, and possession of a postgraduate paediatric qualification.

	Number of clinicians	Number with a postgraduate qualification	Total number of patients seen
Experience in general outpatients department[a]			
Less than 1 year	25	5	157
1-5 years	15	9	190
More than 5 years	11	6	171
TOTAL	51	20	518[b]
Experience since qualification[a]			
Less than 3 years	15	0	123
3-5 years	12	3	99
6-10 years	7	6	119
More than 10 years	17	11	177
TOTAL	51	20	518[b]

a Completed years at mid-point of clinician's participation in trial.

b Missing data in 4 participants

TABLE 4.8 Completeness of telephone follow-up.

	Radiograph		Control	
		%		%
	n=175		n=190	
Telephone contact established	139	79.4	156	82.1
Following contact	n=139		n=156	
Recovered	123	88.5	134	85.6
Censored at 28 days	12	8.6	14	9.0
Lost to follow-up	4	2.9	8	5.1

The reasons for failure to establish initial telephone contact are shown in Table 4.9. The reasons for failure to maintain contact, once established, are shown in Table 4.10.

TABLE 4.9 Reasons for failure to establish telephone contact (among participants offering a contact number).

	No.	%
Not living at or unknown at that number	31	40.2
No contact after 3 attempts	26	33.8
Access refused by telephone owner	10	13.0
Language problem	6	7.9
Discontinued telephone account	3	3.9
Unknown	1	1.3
TOTAL	77	

TABLE 4.10 Reasons for failure to maintain telephone contact (once contact established)

	No.	%
No subsequent reply	3	23.1
Refused further access by telephone owner	4	30.8
Moved, no further contact	2	15.4
Discontinued telephone account	2	15.4
Left employment, no home number	1	7.7
Unknown	1	7.7
TOTAL	13	

4.1.3.2 Record review

The full clinical records of the first consultation of 518 (99.2%) of the 522 randomised participants were retrieved. Of the remaining four cases, the consultation sheets were missing in three and there was no record of review after radiography in the fourth. The inclusion in the trial of the 3 patients without consultation sheets could not be confirmed because this information was recorded on the consultation sheet. None had randomisation envelopes returned so it was assumed that they had been entered into the trial. One was in the radiograph group and 2 in the control group.

The folders of all 522 patients were located to ascertain subsequent visits.

4.2 Analysis

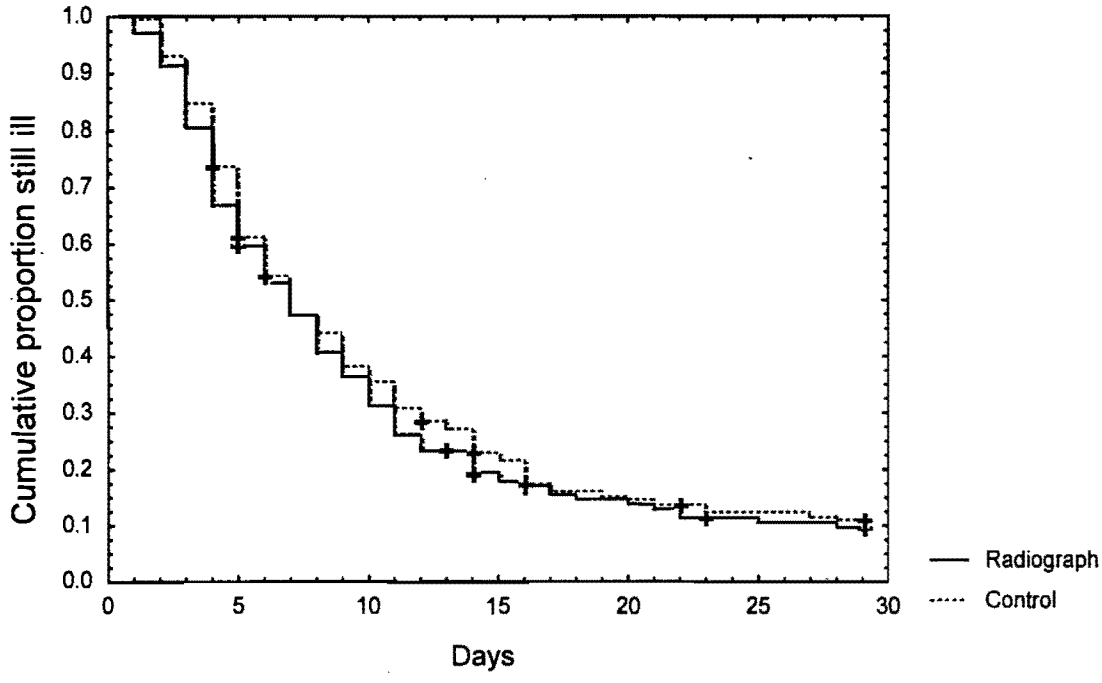
4.2.1 Baseline comparability

The baseline characteristics of the radiograph and control groups and of excluded participants are shown in Table 4.11. There were no meaningful differences between groups.

4.2.2 Time to recovery

The median time to recovery was 7 days in both groups (95% confidence intervals 6 to 8 days in the radiograph group and 6 to 9 days in the control group, log rank test statistic 0.68, p=0.50). Kaplan-Meier survival curves for radiograph and control groups are shown in Figure 4.3.

FIGURE 4.3 Time to recovery: comparison of radiograph and control groups.



Using Cox proportional hazards regression the unadjusted hazard ratio (i.e. the relative risk for the instantaneous probability of *recovery*) for the radiograph group compared with control was 1.08 (95% confidence interval 0.85 to 1.34). None of the following factors were associated with time to recovery: age, Z-score for weight for age, duration of symptoms before presentation, respiratory rate, clinicians' possession of a postgraduate paediatric qualification, clinicians' time spent working in GOPD

TABLE 4.11 Baseline comparability.

	All randomised patients		Subset accessible by telephone		Patients excluded before randomisation
	Radiograph	Control	Radiograph	Control	
Median (n, I-Q range) respiratory rate (per minute)	59 (253, 54-64)	58 (262, 52-64)	59 (136, 54-62)	58 (155, 52-62)	58 (59, 52-66)
Median (n, I-Q range) age (months)	7.3 (259, 4.3-14.3)	8.4 (263, 4.6-14.8)	7.4 (139, 4.6-13.5)	8.3 (156, 4.9-14.95)	10.4 (59, 5-19.2)
Mean (n, SD) weight for age (Z score)	0.0 (259, 1.43)	0.0 (263, 1.24)	-0.1 (139, 1.28)	0.1 (156, 1.26)	-0.4 (59, 1.58)
Median (n, I-Q range) duration of symptoms before presentation (days)	3 (256, 2-6.5)	3 (261, 2-5)	3 (138, 2-7)	3 (155, 3-5)	3 (59, 2-7)
Accessible by telephone	139/259 (54%)	156/263 (59%)	-	-	26/59 (44%)
Clinicians with a postgraduate qualification	107/257 (42%)	116/261 (44%)	53/139 (38%)	64/155 (41%)	22/55 (40%)
Median (n, I-Q range) clinicians' outpatient experience (months)	15 (257, 7-62)	19 (261, 8-60)	14 (139, 4-39)	16 (155, 8-39)	13.5 (52, 7-37)
Clinician's perceived need for radiography	51/242 (21%)	47/252 (19%)	28/129 (22%)	27/150 (18%)	-

and clinicians' perception of the need for chest radiography. The hazard ratio was not changed by adjustment for these variables (adjusted hazard ratio 1.08, 95% confidence interval 0.84 to 1.38) (Appendix 13). Post hoc addition to the model of clinician's time since qualification did not meaningfully alter the hazard ratio (1.07, 95% CI 0.84 to 1.38).

4.2.3 Diagnosis

The clinicians' final diagnoses are shown in Table 4.12. There was a statistically significant difference between radiograph and control groups (chi-square 13.73 df 6 p=0.03). A higher proportion of radiograph patients were diagnosed as having pneumonia (14.4% *vs.* 8.4%, p=0.03), and a lower proportion as having bronchiolitis (43.6% *vs.* 55.9%, p=0.005).

TABLE 4.12 Clinicians' final diagnoses.

	Radiograph		Control	
	n	%	n	%
Bronchiolitis	112	43.6	146	55.9
Pneumonia	37	14.4	22	8.4
Upper respiratory infection	43	16.7	32	12.3
Asthma, recurrent wheeze	15	5.8	20	7.7
Non-specific lower respiratory	31	12.1	27	10.3
Other	6	2.3	8	3.1
No diagnosis	13	5.1	6	2.3
TOTAL	257	100	261	100

Chi-square 13.73
p 0.03

4.2.4 Management

Clinical management at the first consultation is shown in Table 4.13.

TABLE 4.13 Clinical management at the first consultation: comparison between radiograph and control groups.

	Radiograph	Control	Relative risk	95% CI
Additional tests ordered	24/257 (9.3%)	26/261 (10.0%)	0.94	0.55 to 1.59
Antibiotic use [a]	149/245 (61%)	133/255 (52%)	1.17	1.00 to 1.36
Follow-up appointments within 28 days[a]	33/245 (13%)	22/255 (8.6%)	1.56	0.94 to 2.60
Hospital admission	12 /257 (4.7%)	6/261 (2.3%)	2.03	0.77 to 5.33
			Difference between means	
Mean (SD, n) no. of drugs per prescription[a]	3.2 (0.98, 245)	3.2 (0.99, 255)	0	-0.17 to 0.17

[a] Admissions to hospital excluded

4.2.4.1 Antibiotic use

While 149 (60.8%) of 245 radiograph children received antibiotics, only 133 (52.2%) of 255 control children did (p=0.05).

4.2.4.2 Other management

There were trends towards a higher proportion of radiograph patients being admitted to hospital at the first consultation or receiving follow-up appointments, but these were not statistically significant (p=0.14 and p=0.08 respectively). The numbers needed to treat (NNTs) i.e. the number of interventions necessary to prevent one adverse event are listed in Table 4.14.

4.2.5 Subsequent consultations, admissions and chest radiography.

The number of participants with subsequent consultations, hospital admissions or radiographs performed within 28 days in each group is shown in Table 4.15. No differences were found. The most favourable of the 95% confidence limits for a NNT of any of the outcomes was 38 radiographs to prevent one subsequent hospital admission (Table 4.16).

4.2.6 Consultation times

Of 158 eligible participants, complete time data were recorded in 101 (63.9%). These data were available for 42 (56.0%) of 75 radiograph participants and 59 (71.1%) of 83 control participants.

Total time elapsed from the start of the consultation to the end of the final review was available in 109 (69.0%). Adequate data were available in 50 (66.7%) of 75 radiograph participants and 59 (71.1%) of 83 controls.

Total consultation time (the time spent by the patient in the consulting room) and total patient time (the time between the start of the consultation and the end of the final review) are shown in Table 4.17. Median consultation time was 22% longer in the radiograph group and median total patient time 214% longer in the radiograph group.

TABLE 4.14 Clinical management: The number of radiographs needed to prevent one adverse event (NNT).

	NNT[a]	95% confidence interval[b]
Additional test ordered	NNT(benefit) 167	NNT(harm) 22 to ∞ to NNT(benefit) 18
No. of drugs per script	N/A	N/A
Antibiotic use	NNT(harm) 11	NNT(harm) 6 to 61728
Follow-up appointment within 28 days	NNT(harm) 21	NNT(harm) 10 to ∞ to NNT(benefit) 154
Hospital admission	NNT(harm) 42	NNT(harm) 18 to ∞ to NNT(benefit) 127

a NNT(benefit) represents the number of radiographs needed to prevent one adverse event, while NNT(harm) represents the number of radiographs needed to cause one adverse event (equivalent to the number needed to harm, NNH). Because of their lack of effect on clinical outcomes, management options exercised are categorised as adverse events.

b Confidence intervals are expressed as recommended by Altman (1998).

TABLE 4.15 Hospital-based clinical outcome: comparison between radiograph and control groups.

	Radiograph	Control	Relative risk	95% CI
Subsequent visit to RXH within 28 days	85/259 (33%)	85/263 (32%)	1.02	0.79 to 1.30
Subsequent visit elsewhere within 28 days	21/139 (15%)	18/156 (12%)	1.31	0.73 to 2.35
Subsequent admission within 28 days	9/259 (3.5%)	9/263 (3.4%)	1.02	0.41 to 2.52
Subsequent radiograph within 28 days	20/259 (7.7%)	24/263 (9.1%)	0.85	0.48 to 1.49

TABLE 4.16 Hospital-based outcome: the number of radiographs needed to prevent one adverse event (NNT).

	NNT[a]	95% confidence interval[b]
Subsequent visit to RXH within 28 days	NNT(harm) 200	NNT(harm) 12 to ∞ to NNT(benefit) 13
Subsequent visit elsewhere within 28 days	NNT(harm) 28	NNT(harm) 9 to ∞ to NNT(benefit) 24
Subsequent admission within 28 days	NNT(harm) 1890	NNT(harm) 32 to ∞ to NNT(benefit) 32
Subsequent radiograph within 28 days	NNT(benefit) 71	NNT(harm) 30 to ∞ to NNT(benefit) 16

a NNT(benefit) represents the number of radiographs needed to prevent one adverse event, while NNT(harm) represents the number of radiographs needed to cause one adverse event (equivalent to the number needed to harm, NNH).

b Confidence intervals are expressed as recommended by Altman (1998).

TABLE 4.17 Consultation times: comparison between radiograph and control groups.

	Radiograph		Control		95% CI for difference	p
		95% CI		*95% CI*		
Total consultation time (minutes)	n=42		n=59			
Median	11	9-14	9	7-10		0.003
Mean	13.5	10.8-16.2	11.1	8.4-13.7	-1.4 to 6.3	
Total patient time from start till final review (minutes)	n=50		n=59			
Median	132	125-152	42	25-57		0.000001
Mean	145	129-162	46	36.5-55.4	81.7 to 118	

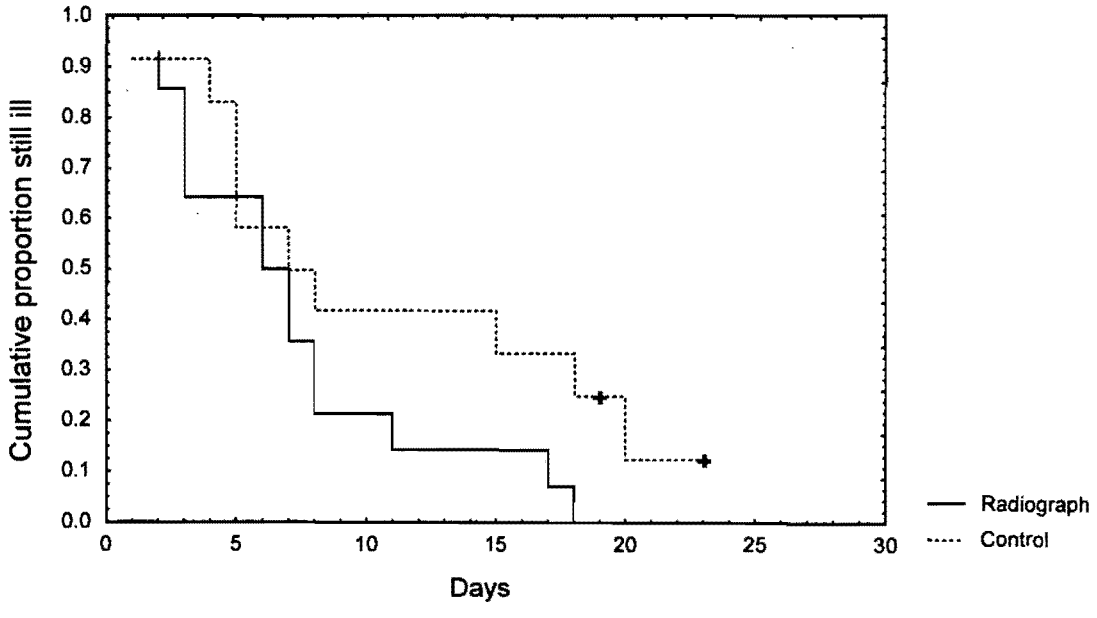
4.2.7 Excluded patients

4.2.7.1 Impact of potential loss of concealment

There was no difference between excluded radiograph and control patients in baseline characteristics (Table 4.18).

In excluded patients, there was no statistically significant difference between those with radiograph and control allocations in time to recovery (Figure 4.4). The hazard ratio (the relative risk for instantaneous *recovery*) of all excluded patients with radiograph allocations compared with controls was 1.92 (95% CI 0.81 to 4.53). The hazard ratio in excluded patients with lost or opened envelopes was 0.49 (95% CI 0.07 to 3.5).

FIGURE 4.4 Time to recovery of participants excluded before randomisation: comparison of radiograph and control groups (n=26).



Log rank statistic 1.57, p= 0.12

When the primary analysis was repeated, with excluded patients included in the model and analysed according to their allocated treatment, the hazard ratio increased from 1.08 (95% CI 0.85 to 1.34) to 1.13 (95% CI 0.89 to 1.43).

TABLE 4.18 Patients excluded before randomisation: baseline characteristics of patients with radiograph and control allocations.

	Radiograph	Control	p
	n=27	n=32	
Median (I-Q range) respiratory rate per minute	58 (50-66)	58 (52-64)	0.96
Median (I-Q range) age in months	10.9 (5.0-16.9)	10.3 (5.25-30.1)	0.55
Mean (SD) Z score for weight for age	-0.19 (1.62)	-0.51 (1.55)	0.44
Median (I-Q range) days of symptoms before presentation	4 (2-6)	3 (2-7)	0.68
Accessible by telephone (%)	14 (51.9%)	12 (37.5%)	0.27
Clinicians with a postgraduate qualification (%)	11 (42.3%)[a]	11 (37.9%)[b]	0.74
Median (I-Q range) months of clinicians' outpatient experience at RXH	15.5 (7-16)[a]	12.5 (7-39)[c]	0.65
Cases judged "too well" for a CXR (%)	6 (22%)	5 (15.6%)	0.59

a Missing data in 1 case

b Missing data in 3 cases

c Missing data in 6 cases

TABLE 4.19 Patients excluded before randomisation: management and outcome of patients with radiograph and control allocations.

	Radiograph	Control	p
	n=27	n=32	
Management			
Additional tests ordered	3 (14.3%)[a]	5 (17.9%)[b,c]	0.74
Mean (SD) no. of drugs per prescription	3.3 (1.23)[a]	3.2 (1.18)[b]	0.90
Antibiotic use	15 (71.4%)[a]	18 (62.1%)	0.49
Follow-up appointments within 28 days	3 (14.3%)[a]	7 (25.0%)[b,c]	0.36
Hospital admission	6 (22.2%)	3 (9.7%)[c]	0.19
Outcome			
Subsequent visits to RXH within 28 days	8 (29.6%)	9 (28.1%)	0.90
Subsequent visits elsewhere within 28 days[d]	4/14 (28.6%)	1/12 (8.3%)	0.19
Subsequent admissions within 28 days	1 (3.7%)	1 (3.1%)	0.90
Subsequent radiographs within 28 days	3 (11.1%)	5 (15.6%)	0.61

a 6 admissions to hospital excluded
b 3 admissions to hospital excluded
c Missing data in 1 case
d Patients accessible by telephone only

There was no significant difference between excluded patients with radiograph and control allocations in clinical management or subsequent use of hospital facilities (Table 4.19).

4.2.8 Participants lost to telephone follow-up

Radiograph and control participants lost to telephone follow up were very similar with respect to baseline characteristics and clinical management (Table 4.20).

The effect of chest radiography on clinical management and the three hospital-based outcomes did not differ between participants lost to telephone follow-up and those successfully followed up (Table 4.21).

TABLE 4.20 Participants lost to telephone follow-up: baseline characteristics, management and outcome of radiograph and control groups.

	Radiograph	Control	p
	n=40	n=42	
Baseline			
Median respiratory rate per minute (n, I-Q range)	60 (39, 52-64)	56 (42, 52-62)	0.35
Median age in months (n, I-Q range)	7.3 (40, 4.2-15)	10.2 (42, 6.6-17)	0.24
Mean Z score for weight for age (n, SD)	0.12 (40, 1.33)	-0.24 (42, 1.14)	0.18
Median days duration symptoms before enrolment (n, I-Q range)	3 (39, 2-7)	3 (42, 2-5)	0.51
Perceived need for radiograph (%)	7/36 (19.4%)	6/40 (15.0%)	0.61
Management			
Additional test ordered (%)	4/37 (10.8%)	3/41 (7.3%)	0.59
Number of drugs per prescription (mean, SD)	2.9 (37, 1.10)	3.2 (41, 0.96)	0.25
Antibiotic use (% of cases)	18/37 (48.6%)	14/41 (34.1%)	0.19
Follow-up appointment within 28 days (%)	5/37 (13.5%)	1/41 (2.4%)	0.07
Hospital admission (% of cases)	3/40 (7.5%)	1/42 (2.4%)	0.35
Outcomes (within 28 days)			
Subsequent visit to RXH (%)	10/40 (25.0%)	11/42 (26.2%)	0.90
Subsequent admission (%)	1/40 (2.5%)	2/42 (4.8%)	0.56
Subsequent radiograph (%)	4/40 (10.0%)	3/42 (7.1%)	0.42

TABLE 4.21 Validity of telephone follow-up: comparison of the relative risks of radiography for hospital-based outcomes measured from clinical records and from telephone follow-up (in participants offering a telephone number).

	Record review Relative risk (95%CI) n=365	**Telephone follow-up** Relative risk (95%CI) n=283[1]	**p for interaction**
Subsequent visit[2] (95%CI)	1.09 (0.82-1.44)	0.88 (0.51-1.50)	0.49
Subsequent admission[2] (95%CI)	1.30 (0.40-4.19)	0.73 (0.12-4.31)	0.59
Subsequent radiograph[2] (95%CI)	1.16 (0.58-2.34)	1.53 (0.50-4.72)	0.68

1 82 participants lost to follow-up

2 Within 28 days

TABLE 4.22 The impact of accessibility by telephone on trial findings: comparison of the relative risks of chest radiography for hospital based outcomes in participants accessible and not accessible by telephone.

	Accessible Relative risk (95% CI) n=295	Not accessible Relative risk (95% CI) n=227	p for interaction
Management			
Antibiotic use[a,b]	1.15 (0.94-1.40)	1.20 (0.94-1.54)	0.78
Further tests[a,b]	1.22 (0.56-2.68)	0.73 (0.33-1.59)	0.36
No. of drugs per prescription[a,b,c]	-	-	0.64
Admission at first consultation[b]	0.90 (0.25-3.28)	7.13 (0.91-56.03)	0.10
Follow-up appointment[a,b]	1.27 (0.66-2.44)	2.16 (0.93-5.04)	0.33
Outcome			
Subsequent visit[d]	1.06 (0.79-1.43)	0.99 (0.64-1.53)	0.78
Subsequent admission[d]	1.40 (0.38-5.12)	0.71 (0.20-2.59)	0.47
Subsequent radiograph[d]	0.95 (0.44-2.05)	0.73 (0.31-1.69)	0.65

a Patients admitted to hospital at the first consultation excluded (9 patients in each groups).

b 4 records missing (2 accessible and 2 inaccessible)

c Tested by linear regression

d Within 28 days

4.2.9 Participants not accessible by telephone

For hospital-based outcomes, there was no difference in the effect of chest radiography in participants accessible by telephone compared with those not accessible (Table 4.22).

4.2.10 Subgroup analyses

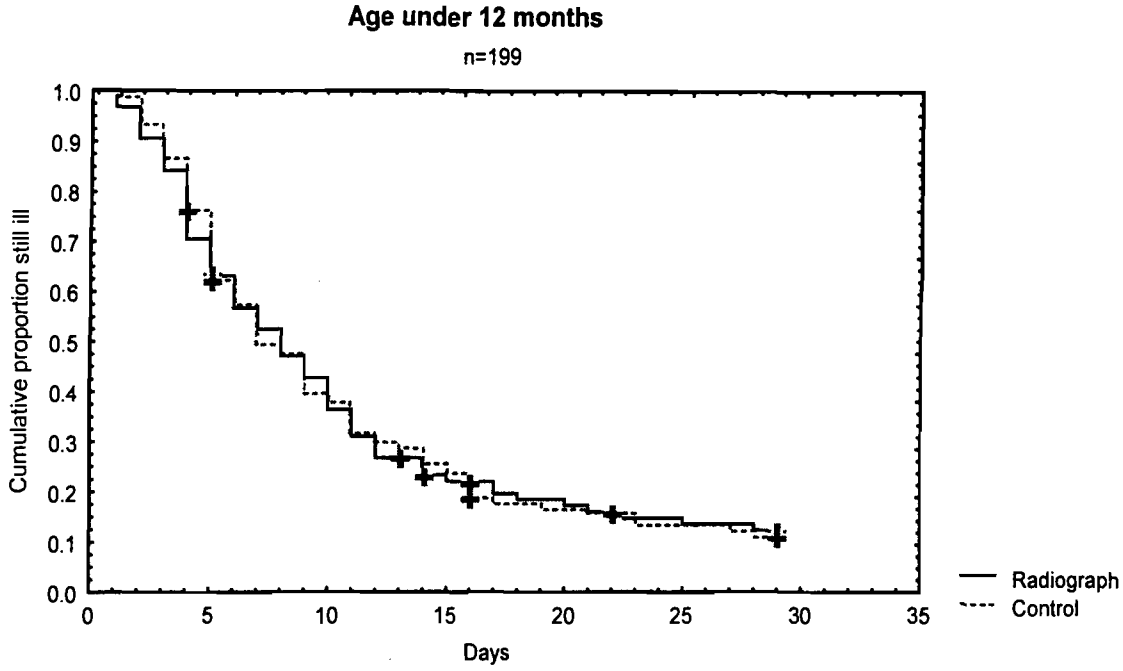
4.2.10.1 Time to recovery

There were no significant interactions of the effect of chest radiography with the following variables: age, Z-score for weight for age, duration of symptoms before presentation, respiratory rate, clinicians' possession of a postgraduate paediatric qualification, clinicians' time spent working in GOPD and clinicians' perception of the need for radiography (Appendix 13).

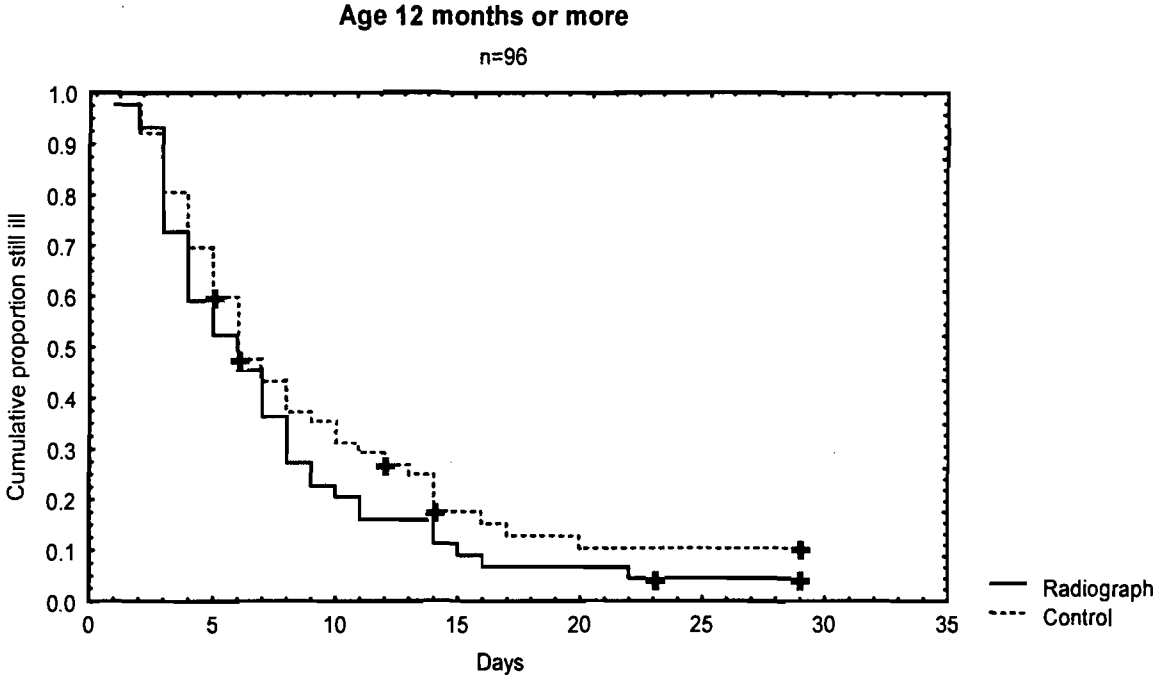
Kaplan-Meier survival curves comparing radiograph and control participants stratified for age, z-score for weight for age, duration of symptoms before presentation, respiratory rate and clinician's possession of a post-graduate paediatric qualification are shown in Figures 4.5 - 4.9. There were no significant differences between radiograph and control groups in any of these sub-groups.

In the subgroup of patients perceived by clinicians to need a radiograph the hazard ratio was 0.91 (95% CI 0.52 to 1.60). Kaplan-Meier survival curves comparing radiograph and control participants perceived by clinicians to need chest radiography are shown in Figure 4.10.

FIGURE 4.5 Sub-group analysis of time to recovery by age: comparison of radiograph and control groups.

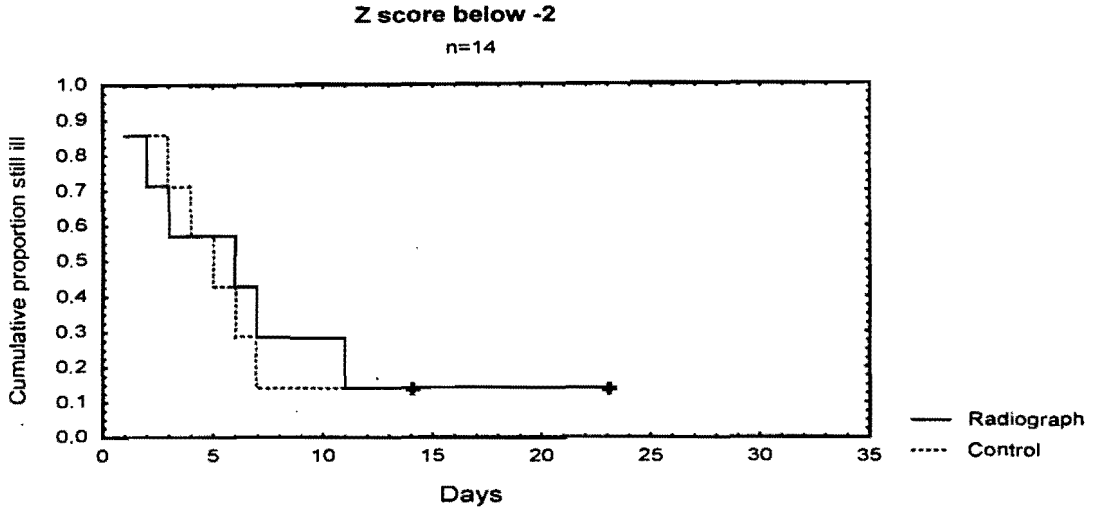


Log rank statistic 0.016, p=0.99

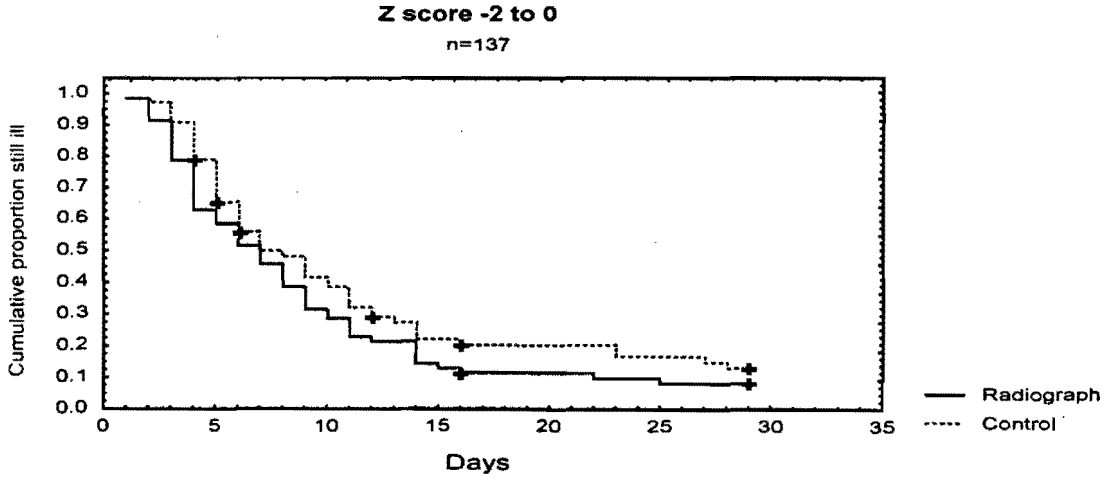


Log rank statistic 1.23, p=0.22

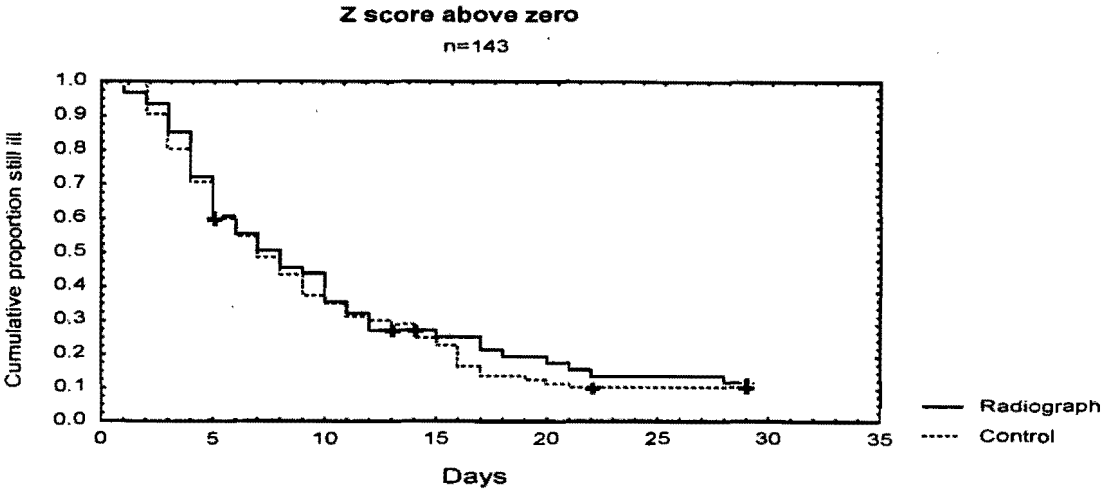
FIGURE 4.6 Sub-group analysis of time to recovery in participants stratified by z-score for weight for age: comparison of radiograph and control groups.



Log rank statistic -0.18, p=0.86

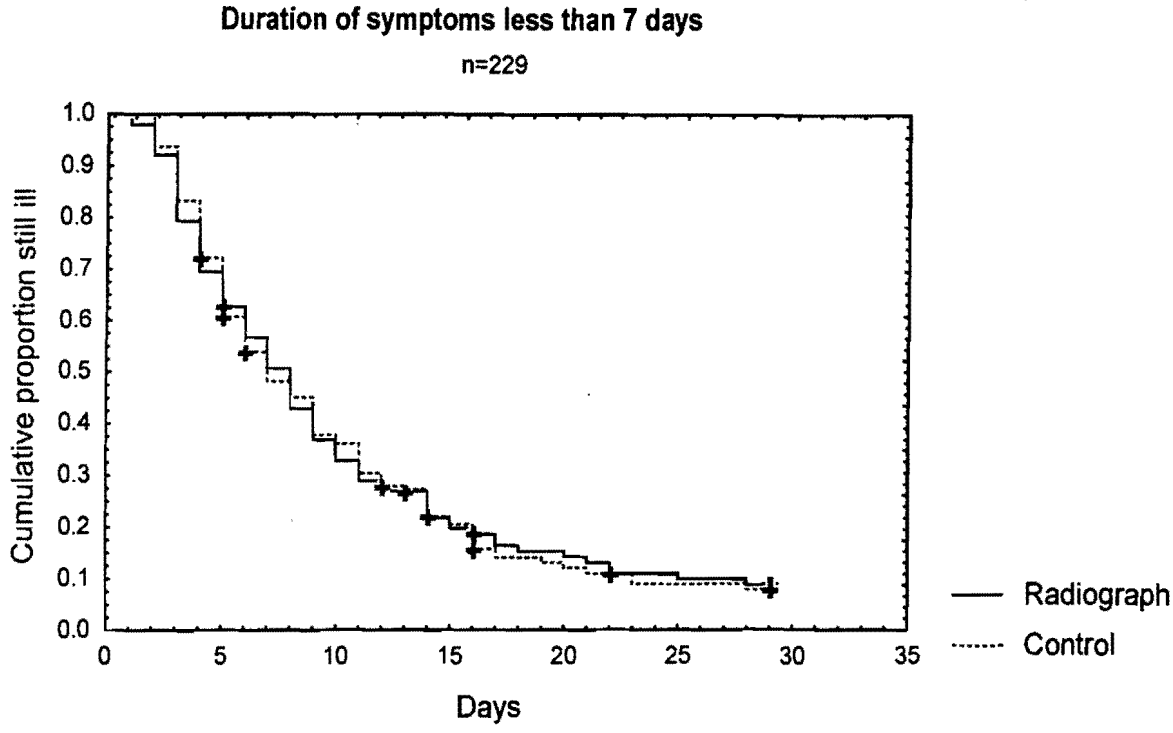


Log rank statistic 1.47, p=0.14

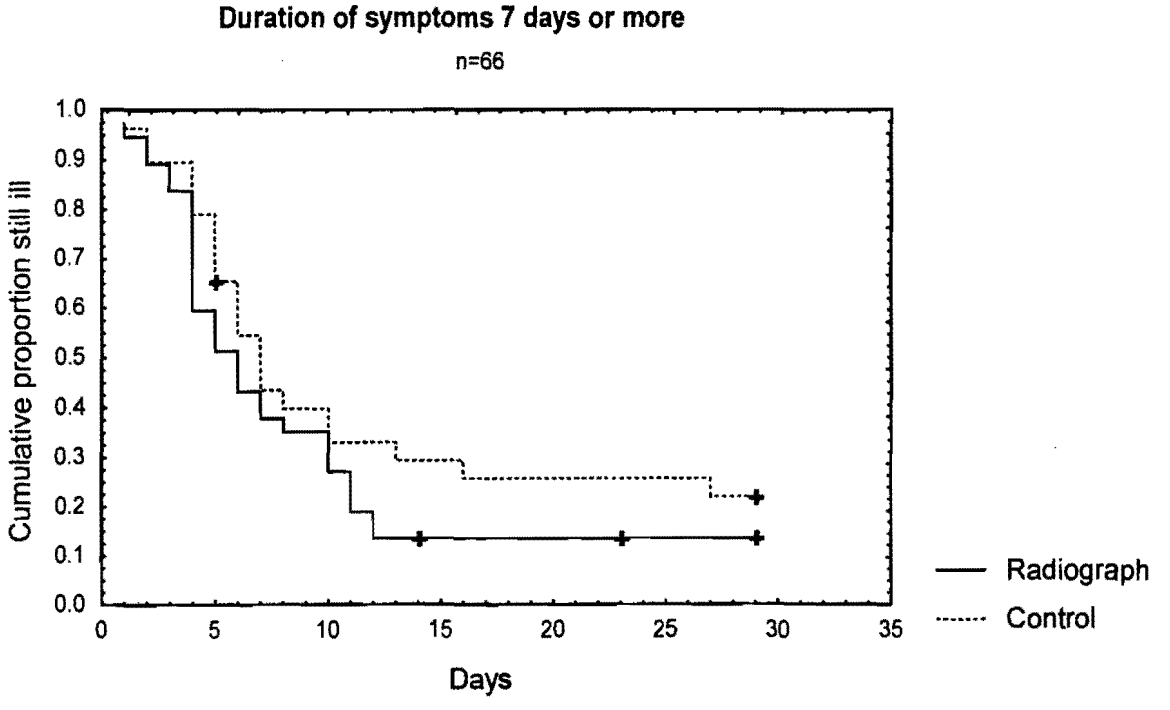


Log rank statistic -0.52, p=0.60

FIGURE 4.7 Sub-group analysis of time to recovery in participants stratified by duration of symptoms before presentation: comparison of radiograph and control groups.

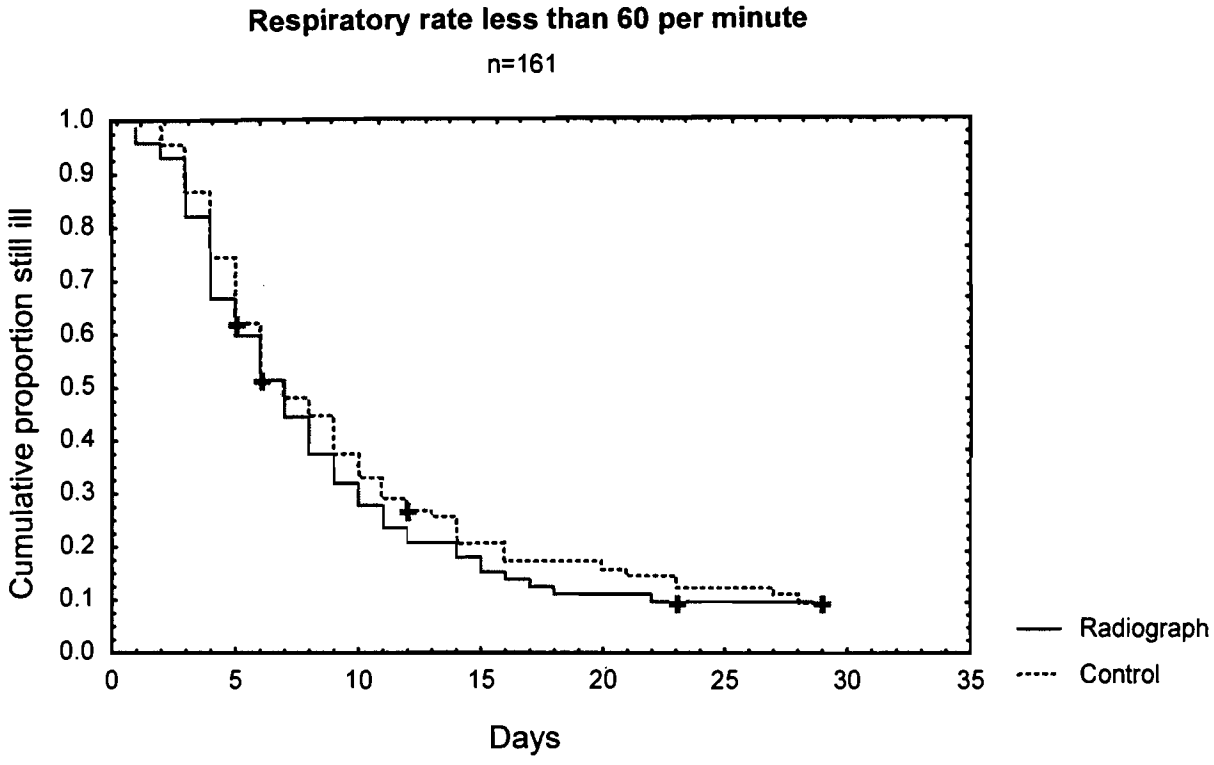


Log rank statistic -0.15, p=0.99

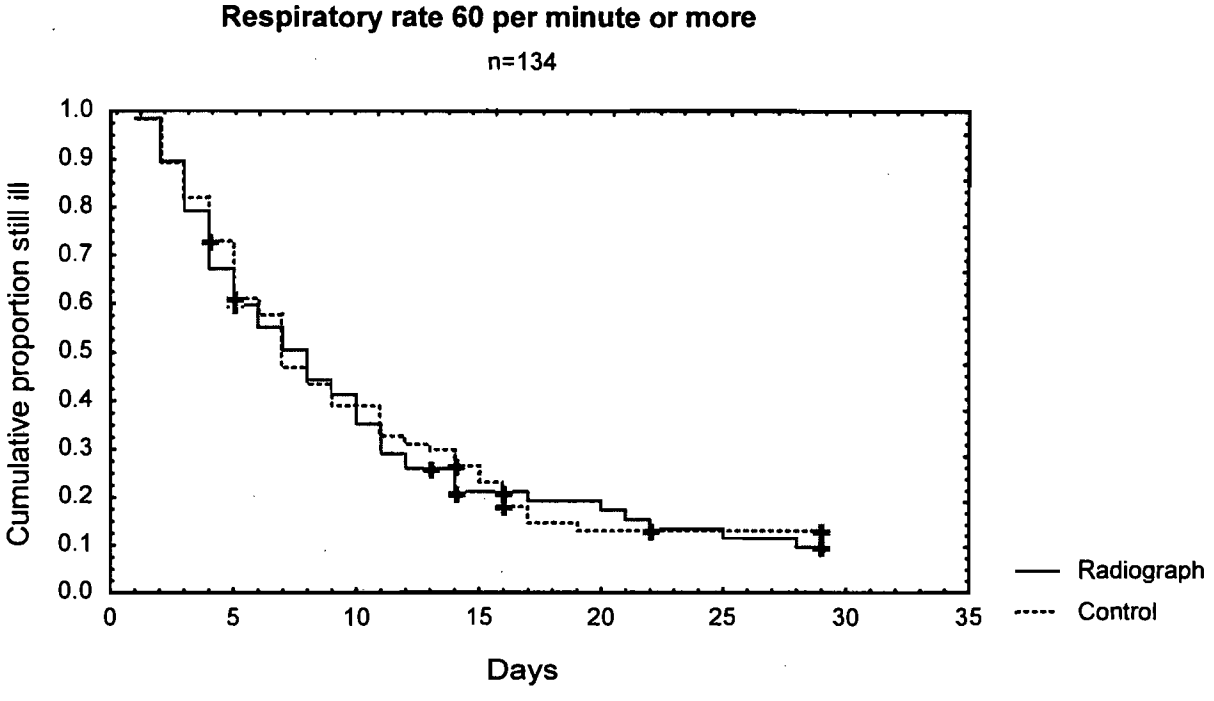


Log rank statistic 1.22, p=0.22

FIGURE 4.8 Sub-group analysis of time to recovery in participants stratified by respiratory rate: comparison of radiograph and control groups.

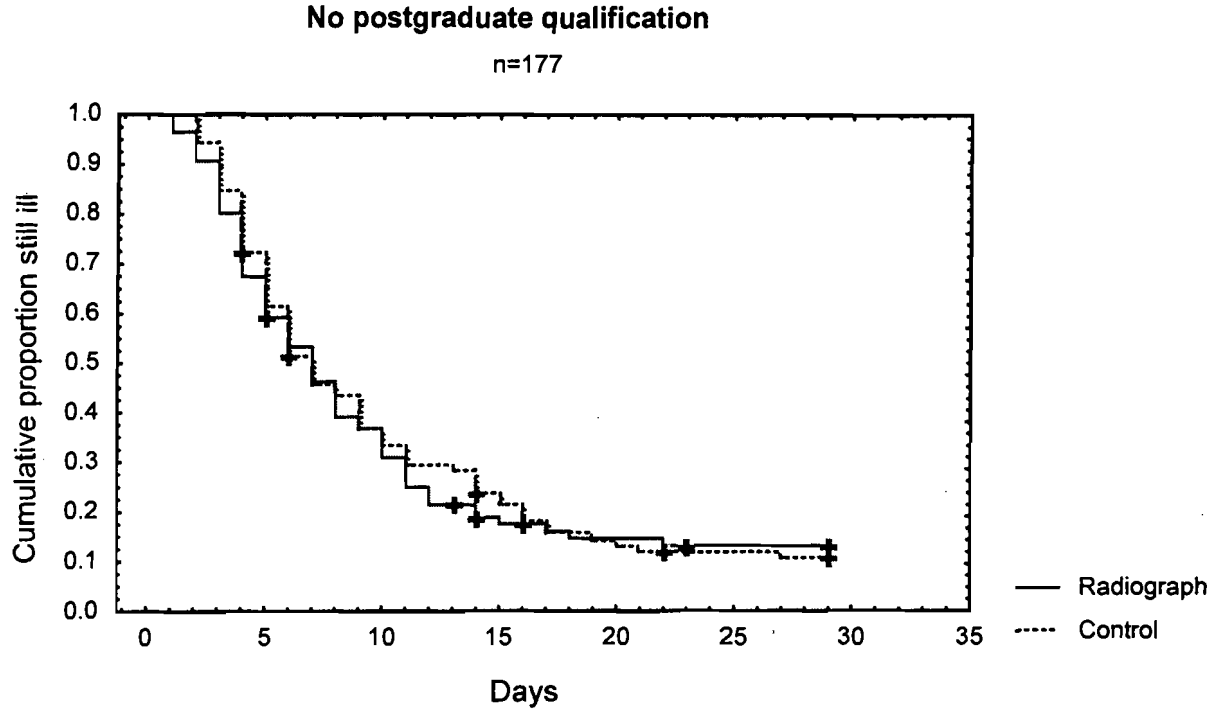


Log rank statistic 0.70, p=0.49

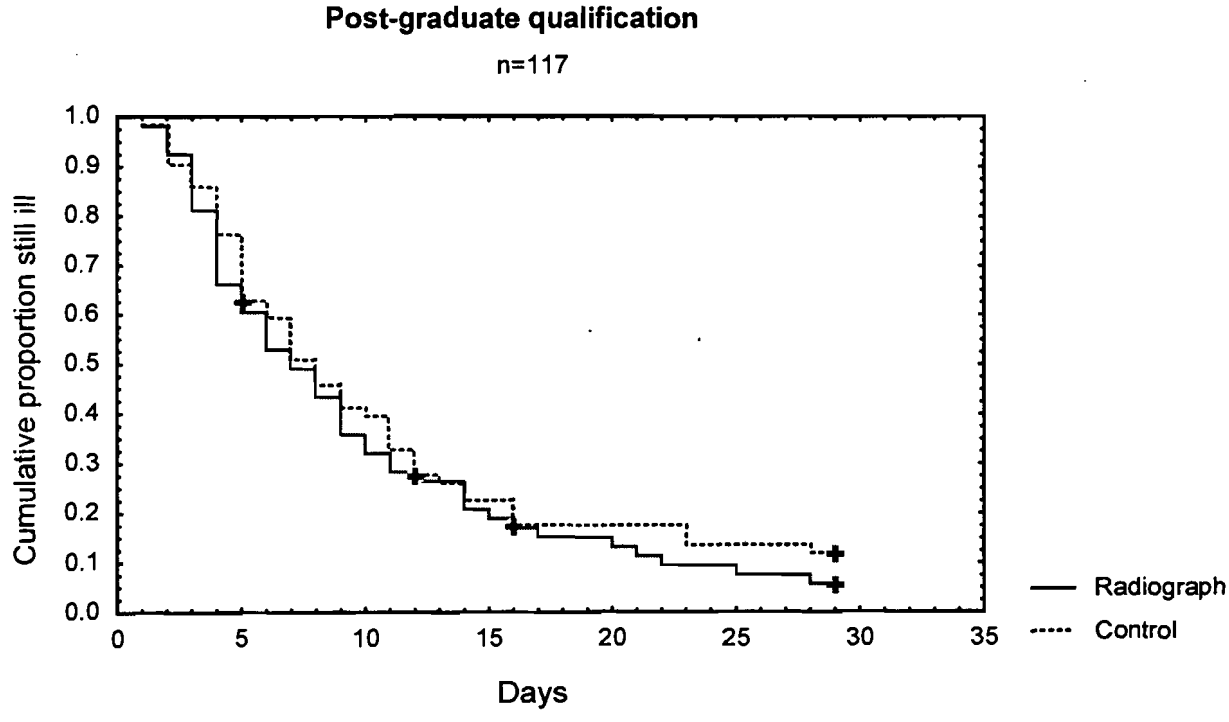


Log rank statistic 0.31, p=0.76

FIGURE 4.9 Sub-group analysis of time to recovery in participants managed by clinicians with and without a postgraduate paediatric qualification: comparison of radiograph and control groups.

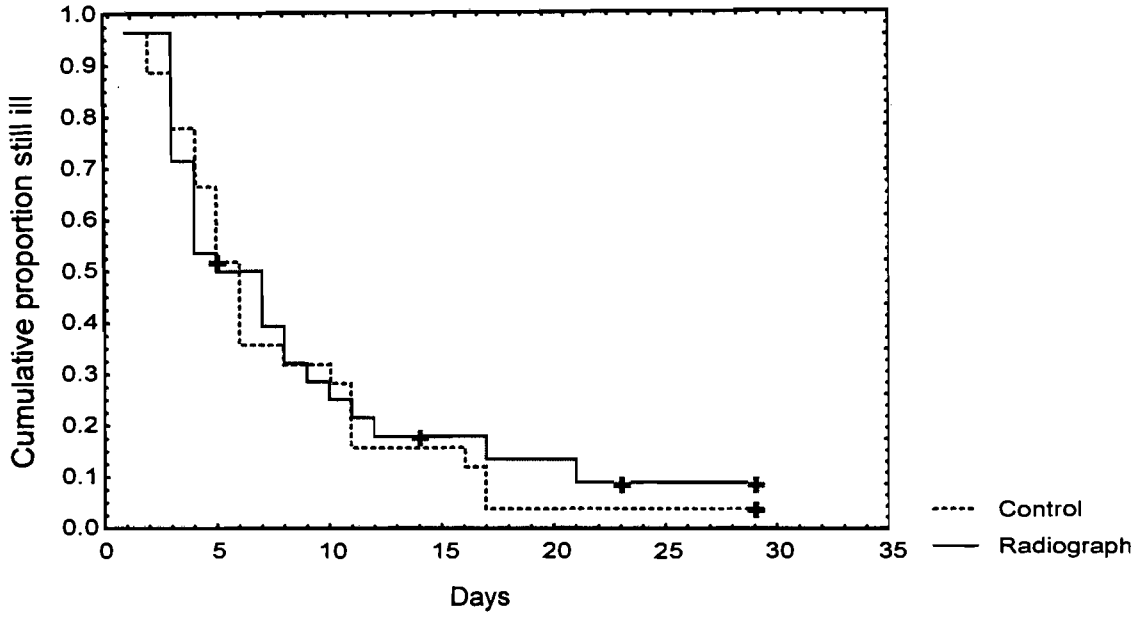


Log rank statistic 0.25, p=0.80



Log rank statistic 0.89, p=0.37

FIGURE 4.10 Sub-group analysis of time to recovery in participants perceived by clinicians to need chest radiography: comparison of radiograph and control groups (n=55).



Log rank statistic –0.348, p=0.73

4.2.10.2 Antibiotic use

The logistic regression model did not converge when all the variables and their interactions with radiograph use were included in the same model. When each interaction was individually tested, the only significant interaction was with the clinicians' perception of the need for radiography (p=0.01) (Appendix 13).

In a stratified contingency table analysis, the relative risks for antibiotic use in those with and without a perceived need for radiography were 0.83 (95% CI 0.71 to 0.98) and 1.26 (95% CI 1.20 to 2.39) respectively (chi-square 9.40, p=0.002) (Table 4.23). Chest radiography resulted in an absolute increase in antibiotic use of 11.1% in patients without a perceived need for radiography and a reduction of 15.8% in patients with a perceived need (Table 4.24). In participants with a perceived need for radiography, six radiographs (95% CI 3-44) would need to be performed to avoid one course of antibiotics.

TABLE 4.23 Relative risk for antibiotic prescription with and without a perceived need for chest radiography.

	Calculated from contingency tables	Calculated from logistic regression model[a]
Relative risk		
Perceived need for radiograph	0.83	-
No perceived need	1.26	-
p value for interaction	0.002	-
Odds ratio		
Perceived need for radiograph	0.19	0.19
No perceived need	1.57	1.89
p value for interaction	0.01	0.03

a Adjusted for potential confounding factors

TABLE 4.24 Rates of antibiotic prescription with and without a perceived need for chest radiography.

	Antibiotic prescription (%)	Absolute risk difference with radiography
Perceived need for radiography		
Radiograph use	35/44 (79.5%)	
Control	41/43 (95.3%)	
		15.8%
No perceived need		
Radiograph use	101/187 (54.0%)	
Control	87/203 (42.9%)	
		11.1%

TABLE 4.25 Examination of hospital-based clinical records: inter-observer agreement in a 10% random sample.

	n	kappa
Baseline data		
Exclusion before randomisation	56	0.84
Clinicians' perceived need for chest radiography	47	1.00
Treatment allocation	51	1.00
Diagnosis	55	0.60
Management		
Additional test ordered (yes or no)	52	1.00
No. of drugs per prescription (weighted kappa)	53	0.99
Antibiotic use	58	0.93
Follow-up appointment within 28 days (yes or no)	53	1.00
Hospital admission (yes or no)	58	1.00
Outcomes		
Subsequent visit to RXH within 28 days (yes or no)	58	0.89
Subsequent admission within 28 days (yes or no)	58	1.00
Subsequent radiograph within 28 days (yes or no)	55	0.88

4.2.11 Validity of questionnaire findings

In participants offering a telephone number, the effect of chest radiography on the three hospital-based outcomes, measured by telephone interview, did not differ significantly from that measured from hospital records (Table 4.21)

4.2.12 Reliability of record review.

Kappa scores for inter-observer agreement in examination of 58 clinical records are shown in Table 4.25. Of the twelve items examined, kappa was 1.0 for six items, above 0.9 in a further two and above 0.8 in another three. The only score below 0.8 was for diagnosis (0.60).

4.3 Summary of main results

Baseline comparability

1. There were no meaningful differences in baseline characteristics of radiography and control groups.

Completeness of follow-up

2. Completeness of follow-up was 77.5% for telephone follow-up, and 99.2% for the review of clinical records.

Diagnosis

3. Radiographs resulted in pneumonia being diagnosed more often (14.4% *vs.* 8.4%, p=0.03), and bronchiolitis less often (43.6% *vs.* 55.9%, p=0.005).

Clinical management

4. Radiographed children received antibiotics more often (60.8% *vs.* 52.2%, p=0.05). Chest radiography resulted in an absolute reduction in antibiotic use of 15.8% in patients with a perceived need for radiography, and an increase of 11.1% in patients without a perceived need.
5. There were trends towards a higher proportion of radiograph patients being admitted to hospital at the first consultation or receiving follow-up appointments, but these were not statistically significant (p=0.14 and p=0.08 respectively).

Clinical outcome

6. The median time to recovery was 7 days in both groups (95% confidence intervals 6 to 8 days in the radiograph group and 6 to 9 days in the control group, p=0.50).
   - The effect of chest radiography did not depend on age, Z-score for weight for age, duration of symptoms before presentation or respiratory rate.
   - The effect of chest radiography did not depend on clinicians' possession of a postgraduate paediatric qualification, clinicians' time spent working in GOPD and clinicians' perception of the need for radiography.
7. There was no difference in subsequent consultations, hospital admissions or radiographs performed within 28 days.

Consultation time

8. Median consultation time was 22% longer in the radiograph group and median total patient time 214% longer in the radiograph group.

Chapter 5

A trial of chest radiography

Discussion

5.1 Background

Despite the widespread use of chest radiography, its impact on the management and outcome of respiratory disease has received little attention, and specifically not in acute lower respiratory infection (ALRI) in children.

Cross-sectional studies to determine the sensitivity and specificity and likelihood ratios of chest radiograph findings for pneumonia are of limited usefulness, for a number of reasons. Firstly there is no acceptable reference standard (other than biopsy or autopsy) against which to validate radiological findings. Secondly, even if high diagnostic accuracy is demonstrated this does not necessarily imply a change in treatment.

Studies of changes of treatment due to radiography in children with ALRI have been limited to those with a before-after design. These studies are susceptible to bias in that they do not control for a potential discrepancy between clinicians' stated management plans and actual clinical behaviour, and have been found in other situations to overestimate therapeutic impact, when compared with randomised controlled trials (Guyatt et al 1986). The randomised controlled trial reported here is to the investigator's knowledge the first to be performed on the impact of chest radiography in acute respiratory infections in children. It offers substantial advantages over the previous before-after studies:

i. Of current clinical study designs, the randomised controlled trial is widely recognised as the definitive method of evaluating the effect of an intervention on clinical outcome. This is because of the unique ability of random allocation to minimise selection bias (Altman 1991b).
ii. The net impact on clinical outcome is examined, rather than management changes that may or may not affect clinical outcome.

The case definition for the participants studied included a mixed group of patients with upper and lower respiratory infections and cardiac failure.

5.2 The findings

5.2.1 The effect of chest radiography on clinical outcome

The main finding of the trial is that time to recovery and the subsidiary clinical outcomes were not affected by the use of chest radiography in acute lower respiratory infection in ambulatory children.

Before accepting a null hypothesis of no effect of chest radiography, it is necessary to establish that a meaningful difference has not been missed because of inadequate statistical power (type II error). One approach to deciding this (with 95% confidence) is to decide whether the 95% confidence interval for the difference between groups includes a clinically meaningful difference (Detsky and Sackett 1985).

5.2.1.1 Primary outcome

In this study the upper confidence limit for a reduction in time to recovery due to chest radiography is 3 days. This "saving" of 3 days of relatively trivial symptoms, at the 95% confidence limit most favourable to chest radiography, must be balanced against costs and harmful effects of radiograph. These might be judged by the point estimates of increases in occurrence of the following outcomes (with the relative increase in brackets):

i	hospital admission at first consultation	2.4% (104%)
ii.	follow-up appointments	4.8% (56%)
iii.	subsequent visits elsewhere	3.6% (31%)
iv.	total duration of consultation	90 min (214%).

The only beneficial effects of radiography were a 1.4% (15%) reduction in subsequent radiographs (if the intervention itself may be regarded as a negative outcome) and 0.6% (6%) reduction in other tests ordered. Further costs of a chest radiograph include:

i the cost to the health service of a 22% increase in clinicians' time, and the cost of the radiograph itself.

ii the cost of the additional consultations and admissions, listed above

iii. the cost to the child's family of the extra time taken, and of possible additional visits to health care facilities.

iv. the time and expense of transport and of consultation with a second clinician, when referral for radiography is necessary.

It is difficult to assign comparative values to these benefits and costs, and the values will in any case vary with the availability of health care resources and access to radiographic facilities and transport. It is nevertheless suggested that the most optimistic estimate of effect of chest radiography does not justify the cost, inconvenience and potential adverse events associated with radiography in most circumstances, and especially not where health care resources are limited.

5.2.1.2 Subsidiary clinical outcomes

When assessing the clinical meaningfulness of the effect of an intervention the difference in the risk of a categorical outcome has little intuitive value. The effect is better expressed as the "number needed to treat" (NNT) i.e. the number of interventions which, on average, would be necessary to prevent one adverse event (Sackett et al 1997). This number is the reciprocal of the absolute risk reduction. From the NNTs listed in Table 4.16, the most favourable of the 95% confidence limits for a NNT for any of the outcome variables appears to be 32 for subsequent admission. That is, at the most optimistic confidence limit for an effect of chest radiography on any of the outcomes, 32 radiographs would need to be performed to prevent one subsequent admission. It is arguable which option is preferable. Thus, even in an outcome with very wide confidence intervals (i.e. with an upper 95% confidence limit of 32 radiographs to cause one admission), the most optimistic estimate of clinical impact of chest radiography is, at best, of questionable benefit.

It is concluded that there are reasonable grounds for accepting the null hypothesis of no beneficial effect of chest radiography on the outcomes measured.

5.2.1.3 Rare but serious outcomes

This study does not address the effect of radiography on rare but serious morbidity or mortality. The sample size is insufficient to provide adequate power to detect differences in rare harmful effects, or even to detect rare events themselves. The upper 95% confidence limit for the probability of an event occurring in one or other

group, even when no such event was recorded, is 1.4%. It is thus not possible to exclude an effect of chest radiography in reducing rare events.

5.2.1.4 An alternative statistical approach: the study as a equivalence trial

An alternative statistical approach would be to regard this study formally as an equivalence trial. The aim would be to show that withdrawal of an established technology, while providing substantial benefits in terms of cost and convenience, does not excessively jeopardise patient outcome (Com-Nougue, Rodary and Patte 1993). A null hypothesis of non-equivalence may thus be tested:

H_O: clinical outcome is improved when chest radiography is used

This is a one-sided hypothesis, which may be tested (at a two-tailed alpha level of 0.05) by calculating only the 90% confidence limit most favourable to radiography. Because the 95% confidence intervals in this study did not include meaningful differences, the narrower 90% confidence intervals will not do so either.

5.2.2 The effect of chest radiography on diagnosis and clinical management

5.2.2.1 Diagnosis

The overall pattern of diagnosis was changed by chest radiography. Pneumonia was diagnosed more frequently (14.4% *vs.* 8.4%), and bronchiolitis less often (43.6% vs. 55.9%). This suggests that the effect of radiography on diagnosis is to rule in pneumonia in favour of bronchiolitis.

5.2.2.2 Clinical management

5.2.2.2.1 Antibiotic use

Antibiotic usage was increased by 8.6% by chest radiography. The increase in antibiotic usage was relatively small, and could represent a chance finding. A total of nine outcome measures were assessed. When nine individual outcomes are assessed the probability is 0.37 that one or more p values will be 0.05 or below.

In any event, whatever increase of antibiotic use did occur, it did not improve clinical outcome. On the contrary, the effect of radiography on antibiotic use is likely to be harmful, given the side-effects of antibiotics and the bacterial resistance associated with such use (Gleckman and Borrega 1997; Seppälä et al 1997; Wise et al 1998).

5.2.2.2.2 Other management

Chest radiography had no significant effect on other management outcomes. From the NNTs listed in Table 4.14 the most beneficial impact of radiography on management appears to be in the case of subsequent hospital admissions. In this case the most favourable 95% confidence limit for the NNTs is 127 radiographs to prevent one subsequent hospital admission.

5.2.2.3 Net versus gross changes in management and diagnosis

The changes in diagnosis and management reflect net changes. These net changes could conceal a greater number of changes in opposite directions (e.g. antibiotics added in some cases and withdrawn in a similar number of others). Such bi-directional changes were found to varying degrees in the before-after studies of the impact of chest radiography on diagnosis and outcome, particularly with antibiotic use. In the case of antibiotic use the net and total changes respectively were 1% and 14% (Leventhal 1979), 5% and 13% (Alario et al 1987) and 2% and 22% (Grossman and Caplan 1988) case. The differences found in this study thus probably underestimate the gross impact of chest radiograph on diagnosis and management. The net impact on management is nevertheless of public health importance as it represents the impact on resource utilisation.

It would have been possible during the trial to ask clinicians to record their intended diagnosis and management before randomisation, and to compare this with final management. This would have allowed measurement of the total effect on management and an analysis of individual changes in management. It would also have offered the opportunity to establish baseline comparability of treatment groups with respect to pre—radiography diagnosis and management. Further, it would have provided the chance of a subgroup analysis of the effect of chest radiography in individuals in whom management was and was not changed. This was however not

done; for fear that recording diagnosis and management plans before radiography would influence plans after viewing the radiograph.

5.2.2.4 Consultation times

Median consultation time was two minutes longer in the radiography group, presumably because of the additional time spent requesting and reviewing the radiograph. The difference is statistically highly significant despite the smaller sample size in which consultation times were measured.

Because the consultation times do not fit a normal distribution, mean times are not appropriate for hypothesis testing, but do give an indication of the effect of chest radiography on human resource utilisation. The absolute and relative differences in mean times are similar to that of median times and represent a more than 20 % increase in consulting time. This is a meaningful difference, because doctors' time is expected to account for the large proportion of the cost of a consultation that usually requires few special investigations or expensive drugs.

Data on consultation time should nevertheless be interpreted with caution. There was a low and differential response rate, with the lower response in the radiograph group. The low overall response is understandable, given the large number of recordings that needed to be made at a specific moment at the beginning and end of each contact in the consultation. The lower rate in the radiograph group is probably because of the greater number of reviews in the consultation. This differential response rate negatively affects validity, but appears likely to underestimate the difference between groups. It is expected that the patients lost to follow-up were those who were reviewed more often, and whose consultations consequently lasted longer. The lower response rate thus probably resulted in an underestimate of consultation time in radiograph patients.

Another reason for caution in interpreting consultation times is that the nature of the consultation was artificial. The clinician did not know whether a radiograph would be performed until after examining the patient. In usual clinical practice the clinician might decide early in the consultation to order a radiograph and consequently spend

less time on history and clinical examination because of superior information expected from the radiograph.

There was a greatly prolonged time from the start of the consultation to the final review in the radiograph group. This finding is expected, given the time spent while a radiograph is performed and then waiting to be seen again. The mean additional wait of 99 minutes represents both inconvenience and additional time spent waiting with other ill children, adding to the risk of cross-infection. The size of the effect on time till final review cannot be generalised beyond this specific outpatients department (on a workday morning) because the waiting time is dependent on many local factors such as workload and staffing.

5.3 Threats to validity

5.3.1 Allocation concealment

The unique benefit of random allocation in eliminating bias in a clinical trial depends on the person enrolling a patient being unaware of the intervention allocation, until enrolment is irrevocable (Schulz et al 1995; Chalmers et al 1983). Inadequate concealment of the allocation has been shown empirically to exaggerate the effect of interventions by 40% overall, compared with an exaggeration of 17% for inadequate blinding (Schulz et al 1995; Moher et al 1998). Allocation concealment therefore has the largest known single impact on the validity of a randomised controlled trial.

If concealment is breached, allocation can be subverted by adjusting the sequence of enrolment to obtain a preferred allocation for a specific participant, or by unnecessarily excluding a participant when an allocation is felt to be inappropriate. Reports of breaches of concealment are rare (Schulz 1996) but subversion of randomisation appears to be common (Schulz 1995). Breaches of concealment include illicit opening of sealed envelopes (Schulz et al 1995; Johnson and Lilford 1990; Pocock 1982; Friedman; Furberg and DeMets 1985), transillumination of envelopes with a bright light (Schulz 1995; Carleton, Sanders and Burack 1960) and the nocturnal rifling of the principal investigator's records (Schulz 1995)! Even when a breach of concealment is unproven, the absence of a watertight system of concealment can lead to the results of a trial being questioned (Bailar and MacMahon 1997). As a

result, it has been recommended that random allocation in clinical trials should be managed in a manner that makes tampering impossible, such as central randomisation (Boyd 1997).

This may not be easy to integrate into a normal work setting. This issue is particularly important in a trial of a diagnostic test, where the effect of the test depends on the clinician's response to the result. Since it is the usefulness of the test in normal clinical settings that is most relevant, it is important to perform such a trial in a manner that minimally disrupts usual clinical behaviour. Unfortunately such usual circumstances are frequently less than ideal for the rigorous conduct of a trial.

Patients could be enrolled in this trial only after exclusion criteria had been ruled out on clinical examination. This meant that randomisation had to take place in mid-consultation. The process had to be as non-intrusive as possible, to avoid interference with clinical behaviour. A sequentially numbered sealed manila envelope attached to the clinical record was deemed to be the most effective method of concealment that did not substantially interfere with the consultation. Central telephone-in randomisation would have interrupted consultation flow, as would automatic computer randomisation in a setting with limited access to computers.

A number of features of the design of this trial provided an opportunity to study the feasibility, security and validity of local, envelope-based allocation concealment in a busy outpatients department:

i. The nurse performed preliminary enrolment and collection of baseline data independently of the clinician, but the decision regarding exclusion from the trial was made by the clinician. Baseline data were thus available for all patients seen by a clinician.
ii. The audit of allocation concealment identified cases in which concealment might have been breached.
iii. All excluded patients were followed up.

These factors allowed an analysis of patterns of exclusion from the trial when concealment was suspect, and also a comparison of excluded patients with radiograph and control allocations with respect to baseline characteristics and outcome.

In this study, the most likely effect of loss of concealment is that ill patients with control allocations would be excluded from the trial because the person deciding on enrolment believed that a chest radiograph was necessary. In contrast, ill patients with chest radiograph allocations would be included. This would result in the treatment group being more severely ill on average at baseline, with a worse outcome. This would consequently reduce any measured beneficial effect of radiography.

5.3.1.1 The security of allocation concealment

Nine discrepancies in the sequence of registration of cases led to six changes in the original allocations. The slight preponderance of changes to control allocations is not only compatible with chance ($p=0.34$) but is in the opposite direction to that expected if changes in sequence were motivated by a prior belief that chest radiographs were desirable in some patients. There is thus no evidence of differential allocation attributable to violations of the enrolment sequence.

Some loss of allocation concealment did occur. Seven envelopes of excluded patients were opened and another nine were not accounted for. Open envelopes were explained by the clinicians as having been opened before the consultation. This is a plausible explanation, given a tendency of staff in the department to unthinkingly open envelopes on the assumption that they were referral letters. The preponderance of control allocations among the 16 excluded cases with opened or lost envelopes is unlikely to have happened by chance ($p=0.05$). This imbalance in allocation suggests that some subjects may have been excluded from the study because their control allocations were known, whereas similar patients with radiograph allocations may have been included. However, the number of opened envelopes is small and did not affect the conclusion of the trial.

Concealment breaches from closed envelopes are potentially more dangerous. Envelopes made from 80g manilla paper and containing the allocation written on a

self-adhesive sticker were used to conceal the allocation. The allocations could not be seen through the envelope when held up to a window or everyday lights. However, during preparation of this report, the allocation was found to be visible when held against the radiograph viewing box in the passage of the outpatients department, a few metres from the consulting rooms in which the doctors were working. This potentially serious oversight in planning does not appear to have resulted in actual loss of concealment or in differential allocation. In 43 excluded patients with sealed envelopes the small majority (23) contained radiograph allocations. This differs from the large majority of non-radiograph allocations (12 of 16) when envelopes were lost or opened.

5.3.1.2 Impact of loss of concealment

The preliminary registration of eligible cases by the nurse meant that baseline data were available for all potential trial participants presented to the clinicians. Follow-up data were also collected on patients excluded by the clinicians. This permitted an assessment of whether excluded patients with radiograph allocations were different from those with control allocations, not only for baseline characteristics but also for treatment and clinical outcome.

Any differential allocation that did occur did not result in a difference in the prognosis of radiograph and control groups. Baseline characteristics of excluded patients with radiograph and non-radiograph allocations were similar. In excluded patients there was no significant difference in time to recovery between allocation groups. The trend was in the opposite direction to that expected if concealment had been lost, and differential exclusion had been based on a prior belief in the need for radiography. This lack of difference between groups in primary outcomes was also present in the secondary outcomes. Finally the overall effect of any loss of concealment did not meaningfully change the findings of the trial. When excluded patients were included in the proportional hazards regression model there was a clinically insignificant increase in the relative risk for recovery (i.e. benefit from chest radiograph) from 1.08 to 1.13.

Further indirect evidence supporting these conclusions is that the sub-group of patients whom the clinicians considered to need a chest radiograph did not benefit from radiography (Fig 4.5). This suggests that any selection bias introduced by the nurse's or clinicians' perceptions of the need for radiography would not have selected a group more likely to benefit from a radiograph.

5.3.1.3 Feasibility and acceptability of concealment by sealed envelopes

Envelopes have been regarded as less than the ideal for allocation concealment (Boyd 1997). They were nevertheless judged to be the only feasible method in this study setting that would not so disrupt the consultation as to destroy the circumstances of an effectiveness study. Clinician recruitment was complete and 94% of the 52 recruits performed the randomisation procedure without difficulty. Informal comments from the clinicians were favourable and at face value the process had minimal impact on clinical behaviour.

If sealed envelopes are used, important precautions are necessary. Envelopes must be opaque to extraordinary attempts at transillumination. Methods recommended to ensure opacity include writing the allocation on opaque card and placing cardboard or aluminium foil in the envelope (Schulz 1995). Pre-trial testing of such opacity using the brightest available light is necessary. The randomisation process should be carefully monitored (Schulz 1995). An additional tactic is to require that participant particulars be written on the envelope before opening, with pressure-sensitive paper or carbon paper providing a permanent record on the enclosed allocation (Schulz 1995).

The effect of monitoring the quality of trial conduct, with feedback to clinicians, was not systematically assessed in this study but it is the investigator's strong impression that it was indispensable to the smooth conduct of the trial. The reduction as the study progressed in the proportion of envelopes that were opened or lost presumably represents increasing familiarity of clinicians and other staff with the study process.

5.3.1.4 Conclusions

In summary, a small degree of loss of concealment occurred in the early stages of the trial when envelopes were opened, mistakenly or otherwise, before randomisation. This loss of concealment probably resulted in a degree of differential exclusion from

the non-radiograph group but did not affect the findings of the study. The use of sealed opaque envelopes with careful monitoring of the concealment process may be appropriate for trials of diagnostic tests in other settings where centralised randomisation is not feasible.

5.3.2 Follow up

5.3.2.1 Clinical records

All patients' clinical folders were traced and the consultation sheets of 99.5% of enrolment consultations were identified. The high rate of recovery of the initial consultation sheets suggests that identification of consultation sheets of subsequent visits was similarly complete. Bias due to differential follow-up of clinical records was thus not significant.

5.3.2.2 Telephone follow-up

Of those subjects who offered a telephone number 77.5% were followed until recovery or for 28 days. This study is unusual in that three subsidiary outcomes were measured by two methods in the same participants for the same duration. In the second method, follow-up of records of patients offering telephone numbers was 99.2%. This enables comparison of the effect of chest radiography on the same outcomes when measured by the two methods. In patients offering a telephone number, there was little meaningful difference in the effect of chest radiography when measured with complete and incomplete (telephone) follow-up (Table 4.21). This finding suggests that there was no difference between radiograph and control patients with respect to the prognosis of patients lost to follow-up, and that loss to follow-up did not affect the estimate of effect of radiography on time to recovery.

Additional less important factors supporting the conclusion that loss to follow-up did not materially affect the trial findings are:

i. Follow-up rates were similar in both groups (Table 4.8). The numerically similar loss to follow-up could conceal attrition for different reasons, with effects in opposing directions, resulting in eventual groups that are similar in number but different in character. Although this possibility is not excluded, the

numerical similarity between groups makes bias less likely than if follow-up were numerically differential.

ii. There is no clear reason to expect the intervention to result in differential follow-up. Other interventions (such as a drug) could affect follow-up by their effectiveness (because participants recover sooner) or side-effects. The radiograph however was not effective and it is difficult to conceive of a "side-effect" of the radiograph that would affect telephone follow-up.

The follow-up rates for the primary outcome in this study is marginally below the 80% level generally regarded as acceptable (Annals of Internal Medicine 1994; Evidence-Based Medicine 1998). Empirical evidence to support this cut-off level is difficult to find. The Cochrane Collaboration Handbook, a manual for the performance of systematic reviews of randomised trials, with rigorous critical appraisal, offers no empirical evidence that loss to follow-up leads to bias, let alone data to support a specific cut-off level. The Users' Guides to the Medical Literature, an authoritative series of articles on critical appraisal, likewise offers no evidence or cut-off level (Guyatt, Sackett and Cook 1993). A search of the Review Methodology Database of the Cochrane Library (1998) for the test word "follow" produced only one relevant reference (Schulz et al 1995). This study failed to show a difference in the estimates of effects of similar trials with and without reported exclusion after randomisation, although this failure could have been due to incomplete reporting.

Given the internal evidence that significant bias due to loss to follow-up is very unlikely in this study, and the lack of evidence to support an 80% cut-off level, the follow-up rate below 80% does not compromise the validity of this study.

5.3.3 Information bias

5.3.3.1 Participants

Patients and caregivers could not be blinded to radiograph status. Interpretation of complete recovery could thus have been affected by caregivers' perceptions of the value of chest radiography. To minimise this bias, consent to inclusion in the study was phrased so as not to reveal the study hypothesis (Appendix 12). It was not

possible to assess the presence, direction or size of any bias resulting from lack of blinding of participants or caregivers to the intervention.

5.3.3.2 Telephone interviewer

The assistant administering the telephone questionnaire was blind to radiograph status, was not informed of the study hypothesis and had no contact with the hospital other than via the investigator. On informal enquiry at the end of the study, the interviewer had guessed only that the study dealt with chest infections. Blinding was thus apparently successful.

5.3.3.3 Examination of the clinical records

This examination could not be blinded to radiography status because details of the performance of a radiograph were prominently and inextricably featured in the records. The investigator, with a clear interest in the outcome of the study, examined the records. This was necessitated by the lack of alternative resources, but increased the possibility of bias in the collection of data. However consultations in the outpatients department, including drug prescriptions and management plans, are routinely recorded on a separate, single, pro forma sheet of paper. This is expected to have reduced the potential for a differential search for, or oversight of, data.

The very high level of inter-observer agreement in the examination of clinical records provides reassuring evidence of a low level of bias in the collection of the data. If bias were present the high level of agreement would require the second disinterested observer to have been significantly biased in the same direction and to a virtually identical degree in measuring all twelve variables. This appears very unlikely

5.3.3.4 Analysis

Data from telephone interviews were coded and captured in a separate database at a separate location, and were merged with other data only after preliminary data cleaning. Interpretation and cleaning of telephone data were thus performed without knowledge of the patients' allocation status.

5.3.4 Confounding

The following potential confounders were hypothesised during planning:

i. Severity of illness - iller children were judged more likely to receive a chest radiograph and could take longer to recover.

ii. Age of patient - younger children were judged more likely to receive a radiograph and could take longer to recover.

iii. Duration of symptoms before enrolment – longer-standing symptoms were judged more likely to result in a radiograph and could be due to a more chronic disease which would take longer to recover.

iv. Nutrition - malnourished children were judged more likely to receive a radiograph and could take longer to recover.

v. Contact with tuberculosis - contact with tuberculosis was expected to prompt a radiograph and symptoms attributable to tuberculosis were expected to take longer to resolve.

Patients with a household contact with active tuberculosis and those with duration of symptoms greater than 14 days were excluded before randomisation. Although this was done primarily with an eye to the applicability of the results, it also had the effect of excluding potential confounders. The main means of controlling for confounding was random allocation. The relatively large sample size is expected to have resulted in the equal distribution between treatment groups of known and unknown confounders. As a further control for chance imbalances between groups, the proportional hazards regression was repeated including seven potential confounders. None were identified as confounders and the relative risk for recovery was not affected by the inclusion of these variables in the model. This supports the conclusion that there was no systematic or random imbalance of confounders between groups.

5.3.5 Validity of telephone follow-up

Comparison of the effect of chest radiography measured by telephone interview with that measured from hospital records in participants offering a telephone number enabled an assessment of overall validity of telephone follow-up, including the impact of loss to telephone follow-up. There was little meaningful difference in the findings. The confidence intervals for the relative risk for one of these outcomes, subsequent

admissions, was wide. This reflects low power of the hypothesis test to detect interactions of radiograph effect with follow-up status. However the distribution of the three p values, 0.49 or above, supports a tentative conclusion that variation in the results is due to chance.

5.3.6 Reliability of questionnaires

5.3.6.1 Telephone questionnaire

Inter-observer agreement was not assessed because of practical difficulties in its assessment, given the rapidly changing symptoms. To do so would have required two observers to call the same caregiver on the same day in randomly or systematically determined order. Even if this had been achieved, it would have been of questionable validity because the caregiver would have had insufficient time to forget the response to the first call. Delayed repeat interviews would have had little face validity, because of loss of recall of inconstant symptoms between telephone calls.

5.3.6.2 Clinical records

There was a very high level of agreement between two observers examining a wide range of variables. This is attributed to the structured consultation sheet and the high quality of clinical record keeping.

The only variable with low agreement (kappa 0.60) was diagnosis. This could be explained by the lack of a complete list of specified diagnoses for the clinician to tick. Specifically, upper respiratory infection was not offered as an option, and a diagnosis was not always recorded under "other". The observers thus needed to exercise more judgement than for other variables to decide on the final diagnosis from the routine notes.

5.4 Applicability of the findings

5.4.1 Subgroups who might benefit

Rather broad inclusion criteria were used for this study, encompassing almost all children with suspected acute lower respiratory infection who might be treated as outpatients. Sub-groups could exist in this sample in which use of chest radiography is

effective, but where the effect was missed because of dilution in the sample as a whole.

5.4.1.1 Time to recovery

Using proportional hazards regression there was no interaction between radiograph use and the following potential modifiers of the effect of radiography: age, z score for weight for age, duration of symptoms before presentation, respiratory rate (a proxy for severity of illness) and the clinicians' perception of the need for radiography. Inspection of Kaplan-Meier survival curves also failed to show clinically meaningful differences in time to recovery in sub-groups. This suggests that, within the WHO case definition of pneumonia, there are no sub-groups with respect to age, nutrition, severity of illness and duration of symptoms (up to 14 days) in whom chest radiography is useful. The lack of association of an effect with clinicians' perception of the need for a radiograph further suggests that no other factors taken into account (intuitively or otherwise) during clinical assessment modify the effect of radiography. These sub-group analyses however involve smaller samples than the main analysis and thus lack sufficient statistical power to exclude clinically meaningful differences in subgroups.

5.4.1.2 Antibiotic use

The effect of chest radiography on antibiotic use in the randomised trial was modified by the clinician's perception of the need for the x-ray. In those patients with a perceived need, radiography resulted in a reduction in antibiotic usage, compared with an increase when the radiograph was judged not to be clinically indicated (Table 4.23). This difference is presumably due to the exclusion of suspected conditions which prompt chest radiograph use and the detection of clinically unsuspected conditions in a radiograph which would not normally have been performed. This finding does not imply that chest radiography should be performed when it is perceived to be necessary. The reduction in antibiotic usage is too small to justify performing a radiograph in order to avoid antibiotic use. Six (95% CI 3 to 43) radiographs would need to be performed to avoid one course of antibiotics. Of greater importance, the use of chest radiography in children with a perceived need for the investigation did not improve clinical outcome (Section 4.2.10.1).

5.4.2 A teaching hospital as the site for the trial

The findings of a study performed at a large teaching hospital such as the Red Cross Children's Hospital are not necessarily applicable to other health care settings. This is particularly true for applicability to primary care settings where the findings have the greatest implications. The participants, the clinicians and the technical quality of the radiographs are all expected to be different.

5.4.2.1 The participants

Patients attending a large teaching hospital might not represent the population attending primary care facilities.

However a survey at around the time of the trial found that 85% of unreferred children seen in the general outpatients of the hospital could have been seen more appropriately at community health centre level (Power et al 1997). Only such unreferred children were included in the trial. Furthermore, the case definition excluded the children with more severe disease who would be expected to be over-represented in a sample of patients attending RXH.

If the patients attending RXH are not representative of a primary care population, they are expected to differ by having more severe disease or less typical clinical presentations. They are thus more likely to benefit from radiography and to increase rather than neutralise an effect of radiography.

5.4.2.2 The clinicians

The effect of radiography could depend on the individual clinician who interprets and acts on the radiograph. As a group, the doctors at RXH are expected to have far more paediatric clinical experience than most other primary care clinicians. The greater experience of a clinician might either increase or reduce the benefit derived from a radiograph, and such a modification of effect would greatly affect the applicability of the findings.

The 52 clinicians in the study nevertheless represent a wide range of experience from recently qualified doctors with no previous paediatric outpatient experience to specialist paediatricians with many years of experience in this specific clinical setting.

Across this range, neither duration of experience in the RXH outpatients department, nor the possession of a postgraduate paediatric qualification, nor the perception of the need for chest radiography modified the effect of the radiograph. This suggests that the findings of this study are applicable to primary care doctors in general.

The findings cannot confidently be generalised to clinical nurse practitioners. This is of little relevance as clinical nurse practitioners are seldom trained in the interpretation of radiographs.

5.4.2.3 The quality of the radiographs

Children's radiographs are likely to be of higher quality in specialist paediatric institutions and are thus likely to maximise the beneficial impact on outcome. Given the lack of effect of chest radiography at RXH, such radiography is even less likely to have a beneficial effect in settings with poorer quality films.

5.4.2.4 An alternative site

Despite the above reasons for believing that the findings are applicable to a primary care population, it might have been preferable to perform the study in a primary care facility. This was not possible for practical reasons. The very large number of primary level patients seen at RXH at the time meant that relatively few patients were seen at other primary level facilities in Cape Town. Heideveld Community Health Centre, one of the larger primary care facilities in Cape Town, was initially investigated as a potential site for the study. The very much smaller number of children seen at that facility would have required an assistant to spend prohibitively long periods at the facility in order to recruit sufficient cases. The following were additional advantages of using RXH as the site:

i. The investigator was an employee in the Red Cross Hospital Ambulatory Unit. This greatly increased the chance of obtaining the clinicians' co-operation and avoided the potentially incapacitating problem of supervision, at a distance and over a prolonged period, of a trial with a relatively complicated enrolment and randomisation procedure.
ii. The structured routine consultation sheet at RXH resulted in very reliable record review.
iii. The excellent record retrieval system enabled almost complete follow-up.

5.4.3 Exclusions before randomisation

The inclusion criteria for the study follow the WHO guidelines for pneumonia for children aged 2 months to 5 years, except that children with prolonged symptoms, contact with active tuberculosis, those with clinical features of cardiac failure, foreign body or a unilateral wheeze were excluded. In addition to patients excluded on those grounds 48 children (8.4% of the remaining 570 eligible patients) were excluded for other reasons, including 21 (7.2%) of 290 patients contactable by telephone. These exclusions could represent the patients within the case definition who were selected out of the study precisely because of their potential to benefit from radiography.

However, participants who were perceived by the clinicians to need a radiograph but were not excluded from the study did not benefit from the radiograph. In fact, they did marginally worse (hazard ratio for recovery 0.91, 95% CI 0.52 to 1.60). The clinicians were thus unable to identify randomised patients who would benefit from radiography. This suggests that those excluded from the study because of a similar perception also did not benefit. The upper 95% confidence limit for the hazard ratio above 1.50 indicates however that a clinically meaningful benefit is not excluded.

5.4.4 Participants accessible by telephone

Accessibility by telephone could be related to a variety of socio-economic factors that could modify the effect of chest radiography. The use of telephone interviews could thus influence the applicability of the findings to a broader population.

Patients with and without telephones were followed up in identical manner with regard to clinical management and subsequent use of hospital facilities. This enabled comparison of the two groups with respect to the effect of chest radiography and also the frequency of treatment and hospital-based clinical outcomes.

There was no significant difference between accessible and non-accessible groups in the effect of chest radiograph on the eight hospital-based outcomes. The confidence intervals for the effect estimates for some outcomes were wide, especially treatment outcomes. A difference in the effect of radiography on these particluar outcomes can thus not be confidently excluded. However the eight p values for interactions are

distributed evenly between 0 and 1, suggesting chance variation. It thus appears that the finding of no effect of chest radiography on the primary outcome of time to recovery in participants accessible by telephone is generalisable to those not accessible.

Telephone follow-up is discussed further in Chapter 6.2.

5.4.5 Time to recovery as an outcome measure

The use of time to recovery as the primary outcome measure depended on the caregiver's assessment of complete recovery. This is highly subjective, and thus imprecise and of questionable repeatability. This outcome measure nevertheless has immediate clinical relevance and applicability. The resolution of symptoms as assessed by the person closest to the child is clinically meaningful; far more clinically meaningful than other measures of recovery such as the return to normality of a laboratory result.

Measurement of time to recovery alone is not sufficient to detect potential side effects of therapy that are not detectable from symptoms. This is however not an issue when assessing a diagnostic test such as chest radiography.

This outcome measure enabled the use of survival analysis, which is statistically more efficient than analysis of categorical variables (Peto and Peto 1972), and therefore requires a smaller sample. An additional important feature of time to recovery is that it can be measured by telephone interview. This offers considerable advantages in the feasibility and precision of measurement. These issues are discussed in Section 6.2.6.4.

5.4.6 The disease profile in Cape Town

Forty nine percent of subjects (who all satisfied the WHO case definition for pneumonia) were diagnosed as having bronchiolitis, rather than pneumonia, and only 54% of subjects received antibiotics. This high prevalence of viral illness reduces the potential to improve outcome by the use of antibiotics. This in turn reduces the potential of chest radiography to improve clinical outcome by modifying antibiotic use.

It is not clear what proportion of patients meeting the WHO case definition for pneumonia actually have bronchiolitis. The World Health Organisation cited four studies (two pre-publication) which supported the WHO clinical criteria for the diagnosis of pneumonia and which used chest radiography as the reference standard. (World Health Organization 1991; Campbell et al 1989; Cherian et al 1988; Redd et al 1994; Mulholland et al 1992). A further six studies were identified by the investigator in the literature search outlined in Section 2.3.1 which also used radiography as the reference standard and supported the WHO criteria (Dai et al 1995; Falade et al 1995; Harari et al 1991; Singhi et al 1994; Taylor et al 1995; Usha, Katariya and Walia 1990). Five of the above ten studies provide no specific radiological criteria for pneumonia (Dai et al 1995; Harari et al 1991; Mulholland et al 1992; Redd et al 1994; Taylor et al 1995) and another two include non-specific features such as "radiological abnormalities of the lungs" (Cherian et al 1988) and "hyperlucency" (Usha, Katariya and Walila 1990) as criteria sufficient in themselves for the diagnosis of pneumonia. Only three studies excluded bronchiolitis by the criteria specified for the reference standard (Campbell et al 1989; Falade et al 1995; Singhi et al 1994). As regards clinical findings, wheezing children were specifically excluded in only three of these studies (Harari et al 1991; Mulholland et al 1992; Taylor et al 1995). Wheezing children were included in four studies (Campbell et al 1989; Cherian et al 1988; Dai et al 1995; Falade et al 1995) and not mentioned in the remaining three (Redd et al 1994; Singhi et al 1994; Usha, Katariya and Walila 1990). Many of the children diagnosed with bronchiolitis in this study would thus probably be regarded as having pneumonia by the criteria of several of the aforementioned studies.

Seventeen percent of patients in this study were diagnosed as having an upper respiratory infection. This is similar to approximately 20% of such false positives in other studies of patients with this case definition (World Health Organisation 1991), suggesting a similar case profile with respect to the mix between upper and lower respiratory infection.

5.5 Conclusions

1. Chest radiography did not affect time to recovery, subsequent visits to RXH or elsewhere, admissions to RXH, or chest radiographs performed at RXH .
2. Statistically significant impacts of chest radiography were demonstrated on:
   Diagnosis: Radiographs resulted in pneumonia being diagnosed more often (14.4% *vs.* 8.4%), and bronchiolitis less often (43.6% *vs.* 55.9%).
   Antibiotic use: This was increased from 52.2% to 60.8%. Chest radiography was associated with an absolute reduction in antibiotic use of 15.8% in patients with a perceived need for radiography, and an increase of 11.1% in patients without a perceived need.
3. Chest radiograph use showed trends which closely approached, but did not reach, statistical significance with respect to an increase in follow-up appointments (from 8.6% to 13.5%) and admission to hospital at the first consultation (from 2.3% to 4.7%). No effect was found on test ordering or the number of drugs prescribed.
4. Clinicians' experience in GOPD and the possession of a post-graduate qualification in paediatrics did not modify the effect of chest radiography. This suggests that the findings are also applicable to less experienced doctors in other settings.
5. The effect of chest radiography was not modified by the following factors: age, weight for age, duration of symptoms, respiratory rate or physicians' perception of the need for radiography. This suggests that there are unlikely to be clinically easily identifiable sub-groups of children in the group studied who are likely to benefit from chest radiography.
6. The findings appear broadly applicable to children who fit the WHO case definition for pneumonia although doubt persists about the applicability of the findings to areas with a low prevalence of wheeze.
7. Chest radiograph increased consultation time by 22% and greatly increased time from start to finish of the consultation. The difference in consultation time is probably an underestimate, but the applicability of these findings to usual clinical practice is questionable.

In summary, despite a net change in diagnosis and an increase in antibiotic usage, the use of chest radiography did not reduce time to recovery or subsequent health facility usage in children meeting the WHO case definition for pneumonia. This lack of effect was not modified by clinicians' experience and there were no clinically identifiable sub-groups of children within this case definition likely to benefit from CXR.

5.6 Recommendations

1. Chest radiograph is not indicated in the management of children who fulfil the World Health Organisation case definition for pneumonia, who have been symptomatic for 14 days or less and who do not have a household contact with active tuberculosis.
2. The findings of this trial need to be confirmed in areas with a lower prevalence of wheeze.

Chapter 6

Issues arising from the trial

Chapter 6.1

Issues arising from the trial

Chest radiography in ambulatory children with acute lower respiratory infections: Effective tuberculosis case finding?

6.1.1 Background

Mass chest radiography of asymptomatic people for tuberculosis case finding has been abandoned because of the low yield and high expense (Reichman 1975; WHO Expert Committee 1974). The situation in patients with respiratory symptoms or signs is potentially different however, because of the higher probability of underlying tuberculosis. Tuberculosis is difficult to diagnose in children because of the non-specific symptoms and the infrequency of isolation of the organisms. Strong reliance is thus often placed on chest radiography (Coulter 1992). For these reasons, routine chest radiography in children with lower respiratory symptoms or signs could represent an effective means of the early identification of otherwise unsuspected cases of tuberculosis.

The trial found no improvement in clinical outcome from chest radiography, but benefit from the diagnosis of tuberculosis is unlikely to be detected in this short-term study, because of the relatively delayed effect of anti-tuberculous treatment.

Random allocation to chest radiography effectively provided a 50% random sample of consecutive patients who met the study case definition. This sample enabled a description of the impact of radiological findings suggestive of tuberculosis on management and clinical outcome in ambulatory children with a clinical case definition suggesting acute lower respiratory infection.

6.1.2 Aims

1. To determine the prevalence of radiological findings suggesting tuberculosis in chest radiographs performed routinely in ambulatory children with acute lower respiratory infection.
2. To determine the proportion of chest radiographs performed routinely in such children in which clinical management is changed as a result of radiological findings suggesting tuberculosis.
3. To determine the proportion of chest radiographs performed routinely in these children in which changes in clinical management could have resulted in improved clinical outcome.

6.1.3 Methods

6.1.3.1 Study design

Descriptive record review, with limited follow-up.

6.1.3.2 Population and sampling

6.1.3.2.1 Subjects

All eligible patients were included in this study (whether or not they were enrolled in the trial) if their predetermined treatment allocation was to receive a chest radiograph. Eligibility criteria are described in Section 3.3. In brief, they were children aged 2 to 59 months with cough and tachypnoea, but without chest indrawing. Exclusion criteria included a history of a current household contact with active tuberculosis, or symptoms for longer than 14 days before presentation.

6.1.3.2.2 Setting

The Western Cape, in which the hospital is situated, had a tuberculosis incidence rate of 702 per 100 000 population in 1993. This is extremely high. By comparison, the incidence for the rest of South Africa was 200 per 100 000. The incidence rate for children under five in South Africa as a whole was 179 per 100 000 (Department of Health 1995).

HIV infection, the other important cause of mediastinal lymphadenopathy and a risk factor for tuberculosis, was relatively uncommon in the Western Cape at the time of the study. The prevalence was 1.7% in antenatal clinic attenders in October 1995 (Department of Health 1996a).

6.1.3.2.3 Sampling

6.1.3.2.4 Radiography and management

Antero-posterior and lateral chest radiographs were performed. A report supplied by the duty paediatric radiologist or radiology registrar was available to the clinician. Apart from use of the chest radiograph, clinical management was entirely at the discretion of the clinician.

6.1.3.2.5 Measurement of outcome

6.1.3.2.5.1 Radiological findings suggesting tuberculosis

The investigator examined the radiologist's report and the clinician's notes to identify findings suggesting tuberculosis. Only comments written on the formal radiological report or by the clinician on the pro-forma consultation sheet were examined.

The following words or phrases describing radiograph findings were regarded as specifically suggestive of tuberculosis: lymph node enlargement, calcification, miliary pattern, mediastinal widening (not stated to be due to a thymus), pleural opacification, fibrosis, any mention of tuberculosis in the radiologist's report or any mention of tuberculosis in the clinician's notes that could have been prompted by the radiograph.

The following findings were regarded as not specifically suggesting tuberculosis, unless an interpretation by radiologist or clinician suggested otherwise: consolidation, pneumonia, patchy opacification, interstitial infiltration, reticular shadows, parahilar infiltration, perihilar changes, peribronchial infiltrates, bronchial wall thickening, hyperinflation/overexpansion/air trapping/hyperexpansion, atelectasis/collapse/volume loss/linear atelectasis, linear opacities. The phrase "prominent cardiothymic shadow" was regarded as normal unless further comment was offered.

6.1.3.2.5.2 Changes in clinical management

The consultation sheets were examined for any additional diagnostic tests that could have been ordered or any treatment that could have been instituted as a result of radiographic findings suggesting tuberculosis.

6.1.3.2.5.3 Follow-up

When a patient was referred to a community-based tuberculosis clinic for reading of a tuberculin skin test and possible consequent initiation of anti-tuberculous treatment, the clinic was contacted telephonically for details of tuberculosis treatment. According to national policy, all children under five years with a strongly positive skin test were treated for tuberculosis for three months with rifampicin, isoniazid and pyrazinamide

(Department of Health 1996b). The tuberculosis clinics did not routinely keep records of negative skin tests (which were recorded on a patient-held record) but did maintain records of treatment.

6.1.4 Results

Of 286 patients allocated to receive a chest radiograph 13 (4.5%) did not have the radiograph performed. Ten of the cases not radiographed were excluded from the trial before randomisation, five because they were judged too well for inclusion in the trial, four for administrative violations of the study protocol before randomisation and one because of a predetermined exclusion criterion (stridor). One of the remaining three cases not radiographed had no record of a consultation and two cases missed radiography for unknown reasons.

Of the 273 patients who received a radiograph as allocated, 12 (4.4%, 95% CI 2.3-7.6%) had radiological findings suggesting possible tuberculosis. Nine of the findings were noted by the radiologist; three were recorded only by the clinician. The impact of these findings on further investigation and management is shown in Table 6.1.1.

TABLE 6.1.1 Radiological findings suggesting tuberculosis, and their impact on further investigation and management

	n	Clinician action on findings	Further tests	Change in diagnosis	Change in treatment	Potential benefit
Lymphadenopathy						
suspected[a]	8	7	7	0	0[a]	0[a]
calcifying	1	0	0	0	0	0
Prominent right hilum	2	0	0	0	0	0
Fibrotic strand	1	1	1	0	0	0
TOTAL	12	8	8	0	0[a]	0[a]

a Loss to follow up in 1 case

Nine of the 12 patients were noted to have mediastinal lymphadenopathy (one with early calcification), six by radiologists and seven by clinicians. Agreement between radiologists and clinicians on the presence of mediastinal lymphadenopathy (with the clinician having access to the radiologist's report) is shown in Table 6.1.2.

TABLE 6.1.2 Agreement between radiologists and clinicians on the presence of mediastinal lymphadenopathy (with the clinician having access to the radiologist's report).

		Radiologist Lympadenopathy		
		Present	Absent	TOTAL
Clinician Lymphadenopathy	Present	4	3	7
	Absent	2	264	266
	TOTAL	6	267	273

With one exception (noted by the clinician alone) all findings of lymphadenopathy were equivocal. Five radiological reports mentioned "? adenopathy" (or very similar), one stated that adenopathy "may be present" and another that it "cannot be excluded".

Of the nine cases, two were ignored by the clinician (including the case with calcification). The remaining seven patients had tuberculin skin tests performed. Of the seven skin tests, three were negative and three children were referred to community based tuberculosis clinics for reading of the tests and further management. There was no record of these patients having received treatment at the clinics to which they were referred. The final patient, with suspected lymphadenopathy noted by the clinician but not the radiologist, was due to leave for another town before the test could be read. She was given a referral letter and was lost to study follow up.

The only other radiological finding that was acted upon was a fibrotic strand in the right upper lobe. A tuberculin skin test was negative and the child was not treated for tuberculosis.

6.1.5 Discussion

The chest radiography trial was an effectiveness trial in which clinical management was entirely at the clinician's discretion. No extraordinary attempts were thus made to ensure that patients with radiological signs suggesting tuberculosis were fully investigated, or that tuberculin skin tests were read. The findings thus represent the impact of chest radiography in conditions of actual practice rather than in ideal conditions. The situation of the outpatient department in a teaching children's hospital and the clinical management in the context of a controlled trial nevertheless make it likely that investigation was fuller than usual. The study conditions were thus probably more favourable for investigation of tuberculosis than in many other settings where tuberculosis is common.

In order to minimise interference with usual clinical behaviour, routine clinical notes and radiological reports were studied. As a result, not all radiological or management changes were necessarily recorded in the notes, and some could have been overlooked by the investigator, thereby under-assessing the impact of chest radiography. The use of a formal radiologist's report and pro-forma routine clinical consultation sheet is expected to have reduced, but not eliminated the non-recording or oversight of findings. Additional factors that aided the retrospective retrieval of data were the specific nature of the diagnosis of tuberculosis, and of the use of a specific skin test as the standard next step in the investigation of children with radiographically suspected tuberculosis (Department of Health 1996b).

Routine chest radiography in this study resulted, at best, in minimal impact on the diagnosis and treatment of tuberculosis. Eight (2.9%) of 273 children were investigated for tuberculosis. At most, one patient received treatment for tuberculosis. This patient, with equivocal lymphadenopathy noted only by the clinician, was lost to follow-up, and could have had the skin test read in another town. She could thus have received treatment, but this seems unlikely. Had this child received treatment, the 95% confidence interval for the number of radiographs necessary to detect and treat one case of tuberculosis would extend from 50 to 16 393. If this patient had not been treated, the most favourable 95% confidence limit for the number of radiographs necessary to detect and treat one case of tuberculosis would be 75. This suggests that

chest radiography in ambulatory children with ALRI in the study setting does not lead to the detection or treatment of tuberculosis in a clinically meaningful proportion of cases. Given the extremely high prevalence of tuberculosis in the population of which the study children are a part (Department of Health 1995), chest radiography is unlikely to be more useful in other settings.

These findings do not necessarily apply to children with symptoms lasting longer than 14 days or to those with a household contact with active tuberculosis, who were excluded from the study. The findings also do not necessarily apply to children without signs of lower respiratory infection e.g. children with cough but no tachypnoea.

It is possible that some children without specific radiological signs suggesting tuberculosis were later diagnosed because of non-resolution of pneumonia detected on the initial radiograph. The diagnostic and therapeutic yield of chest radiography for persistent respiratory symptoms or of follow-up radiographs of pneumonia was not addressed by this study.

6.1.6 Conclusions

1. Initial chest radiography in ambulatory children with acute lower respiratory infections lasting 14 days or less and without a contact with active tuberculosis did not result in a meaningful increase in the diagnosis and treatment of tuberculosis.
2. Given the very high incidence of tuberculosis in the setting in which this study was performed, it is unlikely that chest radiography will be beneficial in children with the same case definition in other settings.

Chapter 6.2

Issues arising from the trial

Telephone follow-up in a less developed country: feasibility, validity and representativeness

6.2.1 Introduction

In industrialised countries telephone follow-up offers many potential advantages of cost and feasibility, when compared with face-to-face interviews. In less developed countries there are obvious constraints to telephone follow-up. These include the questionable feasibility of establishing and maintaining telephone contact, and doubts about the validity of the information obtained and the applicability of the information to people without telephones.

All forms of follow-up are nonetheless difficult in less developed countries, and telephone follow-up remains an attractive option if it can be shown to be feasible, valid and representative. Growth of telephone access is very rapid in less developed countries. For example, the number of telephone lines increased by 29% in South Africa between 1994 and 1998 (Telkom SA Ltd 1998).

The attractions of telephone follow-up are particularly pertinent to clinical trials, which are not as dependent on a representative sample as community surveys. The degree to which the sample in a trial represents the study population does not affect its validity, although it may be important for the applicability of the findings (Sackett et al 1997).

The telephone follow-up rate in this trial was marginally below the 80% generally regarded as acceptable (Section 4.1.3.1), although the trial findings appear both valid (Section 5.3.2.2) and applicable to patients in the same population without telephones (Section 5.4.4).

The trial offered an opportunity to study several further questions regarding telephone follow-up in a community with some, but limited, access to telephones.

6.2.2 Systematic literature review

6.2.2.1 Inclusion criteria for studies

Studies included in this review were all those identified that described telephone interviews that collected health related information, and that provided information on one or more of the following subjects:

1. A comparison of response rates of telephone and other questionnaire modes.
2. A description of the reliability or validity of the questionnaire, with or without a comparison with other modes.
3. A comparison of the costs of telephone interview with other questionnaire modes.
4. The association of socio-demographic factors with response rates or telephone interview findings.

6.2.2.2 Search strategy

Potentially relevant articles were identified using the MEDLINE search strategy described in Appendix 2. Potentially relevant citations in the articles thus identified were examined.

6.2.2.3 Results

All the studies identified were performed in the industrialised world.

6.2.2.3.1 Response rates

Six reports of response rates were identified (Hochstim 1967; Lam, Kleevans and Wong 1988; Nebot et al 1994; O'Toole et al 1986; Siemiatycki 1979; Weeks et al 1983). The characteristics of these studies are summarised in Table 6.2.1. Initial contact rates were in each instance lower for telephonic response rates than for personal interview, but higher than for mail. The response rates to individual questions were similar between questionnaire modes.

6.2.2.3.2 Reliability

Four studies examined test-retest agreement of telephone interviews findings and/or agreement between telephone and face-to-face interviews (Korner-Bitensky and Wood-Dauphinee 1995; O'Toole et al 1986; Stein et al 1996; Weinberger et al 1994). The characteristics of these studies are summarised in Table 6.2.2.

TABLE 6.2.1 Literature survey: response rates to telephone, mail and face-to-face interviews

Author	Participants	Questionaire content	Contact rate	Comparison mode(s): contact rate	Reponse rate to individual questions	Comparison mode(s): individual questions
Nebot 1994	Women aged 17-35 years. Inner city Baltimore	Sexual and HIV risk behaviour	66%	Face to face, street sample 77.0%		
O'Toole 1986	Australian Vietnam war veterans	General, including medical			99.6%	Mail 99.4% Home interview 99.8%
Weeks 1983	Community samples, Tampa Bay	Household health data	65%	Home 84%		
Siemiatycki 1979	Community sample, Montreal	Household health data	74%	Mail 70% Home 83%	81.1%	Mail 91.2% Home interview 85.9%
Hochstim 1967	Community sample, Alameda City, California	Household health and socio-demographic data	91%	Mail 88% Home 93%	99.1%	Mail 98.1% Home interview 99.0%
		Knowledge and use, Papanicolaou smear	94%	Mail 89% Home 96%	98.3%	Mail 98.0% Home interview 99.0%
Lam 1988	Community sample, Hong Kong	Doctor consultation in previous 7 days	92%	Home 97%		

TABLE 6.2.2 Literature survey: reliability of telephone questionnaires, and agreement with face-to-face questionnaires

Author	Participants	Questionaire content	Reliability (test-retest)	Agreement between modes
O'Toole 1986	Australian Vietnam war veterans	General, including medical	Agreement 79-100%.	No mode differences (Data not provided)
Stein 1995	Community sample, Massachusetts	Behavioural risk factors	Kappa 0.30-0.90. Median 0.75 Discordance symmetrical in distribution	
Korner-Bitensky 1995	Patients discharged form a physical rehabilitation facility, Montreal	Activities of daily living		Telephone *vs* home interview. Kappa 0.54-0.76. Median 0.72
Weinberger 1994	Patients over 65 prescribed 5 or more regular medications	Health related quality of life	Cronbachs alpha 0.50-0.86. Median 0.755	Telephone *vs* face-to-face. Correlation co-efficents for scores 0.33-0.77. Median 0.625

Test-retest agreement varied with individual questions. In most cases agreement was good, with median kappa or Cronbach's alpha statistics of 0.75. Agreement with face-to-face interviews again varied from question to question, but was reasonable for most questions. Median kappa and Cronbach's alpha statistics were 0.72 and 0.625. No systematic differences were found between telephone and face-to-face modes (Weinberger et al 1994).

6.2.2.3.3 Validity

The five studies of validity showed highly variable sensitivity, specificity, or agreement for different questions in all questionnaire modes (Hochstim 1967; O'Toole et al 1986; Shinar et al 1987; Weeks et al 1983; Yaffe, Shapiro and Fuchsberg 1978). The characteristics of these studies are summarised in Table 6.2.3. In two comparisons of telephone with mail questionnaires, agreement was similar (O'Toole et al 1986; Hochstim 1967). Two of four comparisons with home interviews also revealed very similar validity. The remaining two studies however revealed 10-20% superior agreement with references standards for home interview (Weeks et al 1983; Yaffe, Shapiro and Fuchsberg 1978). In one of these studies (Yaffe, Shapiro and Fuchsberg 1978) the superior validity of home interview in measuring health care utilisation and expenditure could be explained by the fact that the home interviewers checked actual records of health expenditure which were available in the home. In the other study (Weeks et al 1983) respondents signed consent forms to release health records to the researchers. Such forms were received less often from telephone respondents, presumably because of greater practical barriers to their return. This differential return rate could have resulted in a biased comparison of validity.

6.2.2.3.4 Costs

The characteristics of the four studies of comparisons of costs are summarised in Table 6.2.4. Three of four reports found similar costs for mail and telephone interviews, with face-to-face interviews costing approximately twice as much as either mail or telephone modes (Hochstim 1967; Siemiatycki 1979; Weeks et al 1983). In the remaining study (O'Toole et al 1986) telephone interview cost slightly more than home interview, and almost twice as much as mail. In this study telephone costs included the time and other costs of interviewer travel to a central telephone centre.

TABLE 6.2.3 Literature survey: validity of telephone interviews, and comparison with mail and home interview

Author	Participants	Questionaire content	Reference standard		Comparison mode	
O'Toole 1986	Australian Vietnam war veterans	General, including medical	Army records	Sensitivity 40-75% Specificity 20-96%	*Mail* Sensitivity Specificity *Home* Sensitivity Specificity	60-81% 0-57% 40-68% 21-80%
Weeks 1983	Community samples, Tampa Bay Florida	Household health data	Health records	Agreement 56%	*Home* Agreement	46%
Hochstim 1967	Community sample, Alameda City, California	Knowledge and use of Papanicolaou smear	Health records (confirmation only of positive reports of having had an examination)	Agreement 86%, 80%	*Mail* Agreement *Home* Agreement	87%, 79% 81%, 81%
Shinar 1987	Patients with stroke, Massachesetts	Activities of daily living	Directly observed performance	Correlation co-efficient Total scores > 0.97 Individual items >0.85 in most		
Yaffe 1978	Community samples, Baltimore City and Washington County, Maryland	Health care utilisation and expenditure	Health records	Agreement 1% higher to 11% lower for telephone than for home data with respect to utilisation, and 2% higher to 20% lower for expenditure.		

TABLE 6.2.4 Literature survey: costs of telephone interviews and of mail and face-to-face interviews.

Author	Participants	Questionaire content	Cost	Comparison mode
O'Toole 1986	Australian Vietnam war veterans	General, including medical	$74.33	Mail $42.75 Home $71.89
Weeks 1983	Community samples, Tampa Bay	Household health data	$34.63	Home $75.31
Siemiatycki 1979	Community sample, Montreal	Household health data	$7.10	Mail $ 6.08 Home $16.10
Hochstim 1967	Community sample, Alameda City, California	Household health and socio-demographic data	$4.49	Mail $4.05 Home $9.04
		Knowledge and use of Papanicolaou smear	$6.84	Mail $6.01 Home $10.35

The smaller sample size (n=600) in this case compared with other studies could also have resulted in less economy of scale than is usual for telephone surveys.

6.2.2.3.5 Socio-demographic effects

Five studies reported the association of socio-demographic factors with response rates or interview findings (Marcus and Telesky 1983; Nebot et al 1994; Siemiatycki 1979; Slade, Brennan and Spencer 1995; Stein et al 1996). The characteristics of these studies are summarised in Table 6.2.5. In most studies socio-demographic factors had little impact on response rates between questionnaire modes. In a single study, in a socially disadvantaged area in inner city Baltimore, telephone respondents were older, more educated, more frequently married and had had an HIV test more frequently than respondents to street interviews. Despite this, there were few differences in questionnaire findings. Those differences that were found occurred in younger women, the group less likely to have telephones (Nebot et al 1994). This suggests that the differences were an effect of sampling, rather than of the validity of the questionnaire itself.

6.2.2.4 Summary

1. No reports were found of the measurement of health related information by telephone in less developed countries.
2. In the studies identified, there were no consistent differences between telephone, mail and personal interviews with respect to response rate, reliability or validity, although some studies suggested superior validity of the face-to-face mode.
3. Costs of telephone and mail interviews were similar, and substantially lower than personal interviews.
4. Socio-demographic factors had little effect on response rates or on answers to health-related questions. The only effect of socio-demographic factors that was observed was in a socio-economically deprived area, and appeared to be an effect of sampling rather than of questionnaire validity.

TABLE 6.2.5 Literature survey: socio-demographic effects and inter-mode differences

Author	Participants	Questionaire content	Comparison mode		Effects
Nebot 1994	Women aged 17-35 years. Inner city Baltimore	Sexual and HIV risk behaviour	Face to face, street sample	*Response*	Telephone respondents older, more educated, more frequently married and had more frequently had an HIV test.
				Findings	Few differences between mode in reported sexual behaviour, except in younger women less likely to have telephones
Stein 1995	Community sample, Massachusetts	Behavioural risk factors	Test re-test	*Findings*	No consistent effect on reliability of gender, age, education, marital status, income, employment, ethnic origin.
Marcus 1983	Community sample, Los Angeles County	Household health data	Home	*Response*	Little effect on follow-up. Of 9 variables closest correlation was with total family income (R=0.23). The 9 variables together explained 7% of the variability of loss to follow-up .
Siemiatycki 1979	Community sample, Montreal	Household health data	Mail Home	Reponse	Response to mail lower with lower family income. Telephone and home visit responses unaffected by income.
Slade 1995	Community sample in 5 Australian states.	Oral health		*Response*	Correlation co-efficients between response rates and mean respondent characteristics in different postal code areas did not excede 0.18.

6.2.2.5 Implications for telephone follow-up in less developed countries

Socio-demographic factors had little impact on response rates in most studies identified (Siemiatycki 1979; Marcus and Telesky 1983; Slade, Brennan and Spencer 1995). However, in a socially disadvantaged area in inner city Baltimore the response rate differed between telephone and personal interview and answers to questions varied with socio-demographic factors (Nebot et al 1994). The relatively small differences in industrialised countries could be more marked in less developed countries, because of the greater contrasts in socio-economic status. This affects not only the validity of the questionnaire as a measurement instrument but also the applicability of the findings to members of the population not accessible by telephone.

6.2.3 Aims

1. To describe the effectiveness of the establishment and maintenance of telephone contact in the study population of the trial.
2. To determine the validity of answers to the telephone questionnaire in the trial.
3. To determine whether the telephone questionnaire findings are applicable to people in the same population who are not accessible by telephone.

6.2.4 Methods

This analysis overlaps elements of the report of the trial itself. Some information is repeated here, for convenience and coherence.

The methods of follow-up have been described in Section 3.5.5.1. The enrolment of patients offering a contact telephone number are described in Section 3.5.4.1.

For comparisons of the effect of radiography, only randomised participants described in the participant flow in the trial itself were included (Figure 4.1). For other analyses all enrolled subjects were included, whether included in the trial or not.

6.2.4.1 Feasibility

Reasons were recorded for failure to establish initial contact or to complete follow-up. The locations of the telephone access (home, employer's or neighbour's telephone)

were compared for differences in success at the establishment and maintenance of contact.

6.2.4.2 Validity of questionnaire

The validity of the questionnaire was assessed by means of three questions about the use of hospital facilities (subsequent visits and admissions to RXH and subsequent chest radiographs at RXH). The answers were validated by examination of the hospital records, without knowledge of the questionnaire findings.

6.2.4.3 Validity of the trial findings using telephone follow-up

In participants included in the trial who offered a telephone number, the effect of chest radiograph on the three hospital-based outcomes measured by telephone follow-up was compared with the effect as measured for the trial from hospital records (Section 3.5.5.3.1).

6.2.4.4 Applicability

The effect of chest radiography on the three hospital-based outcomes (measured from hospital records) in participants accessible by telephone was compared with the effect in those not accessible. (Section 3.5.5.3.2).

Accessible and non-accessible groups were also compared with respect to baseline characteristics, management and hospital based clinical outcome.

6.2.4.5 Data analysis

Differences in categorical data were compared using the uncorrected chi-squared test. The t-test was used to compare means of normally distributed continuous variables and the Kruskal-Wallis test to compare medians of variables not normally distributed. Agreement was expressed as a kappa statistic.

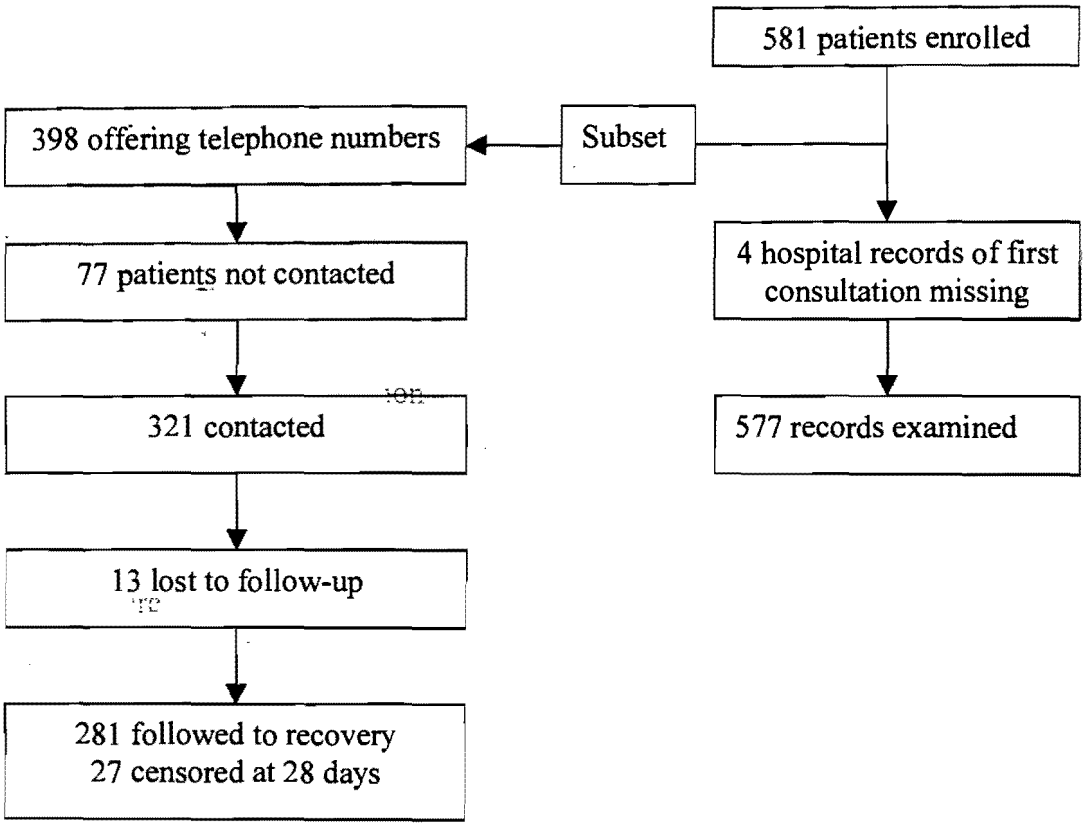
The effect of radiography in participants accessible and not accessible by telephone was compared using a chi-squared test (Rothman 1986) for categorical variables, and linear regression for the continuous variable. A two-tailed alpha level of 0.05 was regarded as significant.

6.2.5 Results

6.2.5.1 Enrolment

A profile of telephone follow-up is shown in Figure 6.2.1. Of 452 cases enrolled during the periods that subjects both with and without telephones were enrolled, 270 (59.7%) offered a contact number.

FIGURE 6.2.1 Profile of follow-up



6.2.5.2 Feasibility

Of 398 subjects who offered a telephone number 321 (80.7%) were contacted and 308 (77.4%) were followed to recovery or censored at 28 days. The reasons for failure to establish contact are shown in Table 6.2.6. Once contacted 308 (96.0%) of 321 subjects were followed to recovery or for 28 days. There was no difference in loss to follow-up between radiograph and control groups. The reasons for failure to maintain contact, once established, are shown in Table 6.2.7. Success of follow-up according to the location of the contact number is shown in Table 6.2.8.

There was a non-significant trend towards improved contacts rates if more than one telephone number was offered (Table 6.2.9).

TABLE 6.2.6 Reasons for failure to establish telephone contact (among participants offering a contact number).

	No.	%
Not living at or unknown at that number	31	40.2
No contact after 3 attempts	26	33.8
Access refused by telephone owner	10	13.0
Language problem	6	7.9
Discontinued telephone account	3	3.9
Unknown	1	1.3
TOTAL	77	

TABLE 6.2.7 Reasons for failure to maintain telephone contact (once contact established)

	No.	%
No subsequent reply	3	23.1
Refused further access by telephone owner	4	30.8
Moved, no further contact	2	15.4
Discontinued telephone account	2	15.4
Left employment, no home number	1	7.7
Unknown	1	7.7
TOTAL	13	

TABLE 6.2.8 Success at follow-up according to location of telephone (in participants offering a single number)[a].

	TOTAL	Home	Neighbour	Employer	p[b]
All participants[a]					
	n=317	n=236	n=21	n=60	
Overall follow-up (%)	242 (76.3)	191 (80.9)	15 (71.4)	36 (60.0)	0.003
Contactable (%)	253 (79.8)	197 (83.5)	17 (80.9)	39 (65.0)	0.006
	n=253	n=197	n=17	n=39	
Contact maintained (%)	(95.7)	191 (97.0)	15 (88.2)	36 (92.3)	0.13

a One cellular phone and 1 case of unknown location excluded.

b For difference between locations

TABLE 6.2.9 Success at establishing contact, according to the number of telephone numbers offered.

Number of contact numbers offered	n	Successful contact	%	95% CI
1	319	255	80.0	75.5 to 84.4
2	78	65	83.3	72.9 to 90.7
3	1	1	100	
Total	398	321		

Chi-square for linear trend 0.595, p=0.44

6.2.5.3 Validity

6.2.5.3.1 Questionnaire

Agreement between answers to telephonic questions and events recorded in the clinical records is shown in Table 6.2.10. Kappas for questions on a subsequent visit, hospital admission or chest radiograph were 0.88, 0.83 and 0.56 respectively. Using the clinical records as the reference standard, all three questions had a specificity above 98%. Sensitivity varied from 82% for a return visit to 56% for a radiograph.

TABLE 6.2.10 Validity of answers to telephonic questions, verified from hospital records (n=321)

	Agreement	Kappa	Sensitivity	Specificity
Outpatient visits (RXH)	0.96	0.87	81.8%	100%
Subsequent hospital admissions	0.99	0.83	71.4%	100%
Subsequent chest radiograph	0.95	0.56	55.6%	98.0%

6.2.5.3.2 Trial findings using telephone follow-up

The effect of chest radiography on the three hospital-based outcomes, measured by telephone interview, did not differ significantly from that measured from hospital records in patients offering a telephone number (See Section 4.2.11)

6.2.5.4 Applicability

The effect of chest radiography on clinical management and use of hospital facilities in participants accessible by telephone did not differ significantly from that in inaccessible participants (Section 4.2.9).

There were no significant differences in the baseline characteristics or clinical management of participants accessible and inaccessible by telephone (Table 6.2.11). Accessible participants however attended RXH more frequently for subsequent consultations (38.0% *vs.* 25.0%, p=0.001) but were not admitted to hospital nor did they receive subsequent radiographs more often.

TABLE 6.2.11 Comparison of participants accessible and not accessible by telephone.

	Accessible		Not		p
	(n=321)		(n=260)		
Baseline characteristics					
Median respiratory rate per minute (I-Q range)	58	(52-62)[a]	60	(52-62)[b]	0.15
Median age in months (I-Q range)	8.1	(5-15)	7.95	(4-15)	0.83
Mean Z-score for weight for age (SD)	0.0	(1.27)	-0.1	(1.48)	0.40
Median days duration of symptoms before enrolment (I-Q range)[c]	3	(1-14)[c]	3	(1-14)[b]	0.94
Clinicians' perceived need for radiography (%)	55	(19.7)[d]	43	(20.0)[e]	0.94
Management					
Additional tests ordered (%)	27	(8.7)[c,f]	27	(11.1)[c,g]	0.35
Mean number of drugs per prescription (SD)	3.2	(1.01)[b,f]	3.2	(0.98)[c,g]	0.90
Antibiotic use (%)	179	(57.7)[f]	136	(55.7)[g]	0.64
Admission at 1st consultation (%)	11	(3.5)[b]	16	(6.2)[c]	0.12
Follow up appointments within 28 days (%)	37	(12.1)[bf]	28	(11.6)[c,g]	0.86
Outcome					
Subsequent visits to RXH within 28 days (%)	122	(38.0)	65	(25.0)	<0.001
Subsequent admissions within 28 days (%)	9	(2.8)	11	(4.2)	0.35
Subsequent radiographs within 28 days (%)	27	(8.4)	25	(9.6)	0.47

a Missing data in 4 cases

b Missing data in 3 cases

c Missing data in 2 cases

d Missing data in 42 cases

e Missing data in 45 cases

f 11 patients admitted at first consultation excluded

g 16 patients admitted at first consultation excluded

6.2.5.5 Costs

In total, 945 calls were made. Time spent during telephone calls was 35 hours 58 minutes. Total time spent by the interviewer on follow-up (excluding coding and data entry) was 91 hours 56 minutes. The cost of telephonic data collection was R2 946 ($740.20, £486.54 on March 31 1996), or R9.18 ($2.31, £1.51 on March 31 1996) per subject successfully followed up.

6.2.6 Discussion

Inter-observer agreement in examination of hospital records was very high, the lowest of the kappa statistics for the three outcomes being 0.88 (Section 4.2.12). Follow-up of hospital records exceeded 99% (Section 4.1.3.2). These factors suggest that examination of hospital records was a suitable reference standard against which to measure the validity of telephone findings.

Data from hospital records were available for participants both accessible and not accessible by telephone. Comparison of these two groups of participants was thus possible with respect to clinical management, outcome and the effect of chest radiography.

6.2.6.1 Feasibility

In this study telephone follow-up was successfully conducted in members of a South African urban population who offered a telephone number. This study was conducted from a public sector hospital. Approximately half of the population of Cape Town use public sector health care and this half generally have the poorer socio-economic circumstances (Mohamed et al 1995).

Approximately 60% of participants offered a telephone number, and 77% of those were followed till recovery or for 28 days. Failure to make initial telephone contact was by far the most important factor in loss to follow-up. In future studies, more careful selection of participants offering telephone numbers could improve follow-up rates. A pilot study could be helpful in assessing the suitability of this method of follow-up in a specific setting, and inform inclusion criteria for any ensuing study.

6.2.6.2 Validity

6.2.6.2.1 Questionnaire

Validation of time to recovery was not possible because of the lack of a reference standard. The nature of the caregiver's assessment of recovery differs from that of recall of specific events such as hospital consultation. The validity of telephonic answers to categorical questions can thus not necessarily be generalised to assessment of time to recovery.

The validity of answers to the questions verifiable from hospital records was very good for subsequent hospital visits and admissions, and fair for subsequent chest radiographs. The relatively low sensitivity of the question about subsequent chest radiographs might be partially explained by confusion between radiographs performed at and after randomisation, and the less prominent nature of a radiograph compared with a hospital visit or admission.

6.2.6.2.2 Trial findings

Comparison of the effect of chest radiography measured by telephone interview with that measured from hospital records enabled an assessment of overall validity of telephone follow-up, including the impact of loss to telephone follow-up. There was little meaningful difference in the findings (Section 5.3.5).

6.2.6.3 Applicability

Patients with and without telephones were followed up in identical manner as regards clinical management and subsequent use of hospital facilities. This enabled comparison of the two groups with respect to the effect of chest radiography and also the frequency of management and hospital based clinical outcomes.

6.2.6.3.1 Questionnaire findings

Patients accessible and not accessible by telephone were very similar, except that accessible patients made more return visits to RXH. It is unlikely that this was due to greater severity of illness because the need for subsequent chest radiographs and admission to hospital was actually lower in accessible subjects than in the non-accessible group. The difference in visits could reflect greater access to the hospital

(especially after-hours) associated with higher socio-economic status. Another possibility is that the greater number of visits was an effect of the telephone call itself. A return visit could have been precipitated by an enquiry about the child's condition. Whatever the reason for the difference it did not alter the effect of radiography. Telephone questionnaire findings in subjects who were accessible by telephone thus appear to be applicable to those who were not accessible, except when the variable measured could be affected by the interview.

6.2.6.3.2 Trial findings

There was no significant difference between accessible and non-accessible groups in the effect of chest radiography on the eight hospital-based outcomes. (Section 4.2.9).

6.2.6.4 Advantages of telephone follow-up

Telephone interviews offer many obvious advantages over face to face interviews in the follow-up of people in a less developed country.

In this trial, telephone follow-up offered flexibility and convenience for both respondents and interviewer. Respondents were telephoned at times designated by them as convenient, including after working hours. The interviewer was based at home and was paid by the hour, greatly reducing costs. She did not need to travel to work and was able to fit interviews into the rest of her schedule. She had no contact with hospital or study personnel, other than the principal investigator, and could thus be blinded to the study hypothesis for the duration of the prolonged study.

The relatively frequent contact with participants that was possible enabled time to recovery to be used as the principal outcome. This outcome is both clinically meaningful and enabled the use of survival analysis, with consequent increased statistical efficiency. Frequent assessment increased the precision of measurement, not just by reducing the period between calls but also by the capacity to use the observer's recall to identify a specific day of recovery in the period between assessments.

The advantages of telephone follow-up with respect to feasibility become even clearer when compared with alternative forms of follow-up. A single return visit for assessment of recovery after 7, 10 or 14 days would have been inconvenient for

caregivers, who were either employed or had domestic responsibilities. This barrier, together with the fact that a significant proportion of the children would have recovered by the appointment date, was expected to result in an unacceptably low follow-up rate. Home visits would have avoided the above problems, provided that the caregiver was at home, and provided that the address was traceable. However both of the face-to-face interview options carried a high unit cost. For these reasons frequent face-to-face interviews to measure time to recovery were judged not to be feasible.

If a categorical outcome such as the proportion of cases recovered at a specified time had been used instead, approximately 500 cases would have been needed to achieve the same statistical power as the 295 cases in this study. The cost of telephonic data collection in 1996 was R9.18 ($2.31, £1.51 on March 31 1996) per subject successfully followed up. A conservative estimate of the cost of a single face-to-face interview is R43 ($10.81, £7.09) per case, assuming 10 minutes per interview, 1 hr travelling time (40 km at R0.40 per kilometre) to visit each of the average of 2 cases per day, and the same personnel cost per hour as for telephone interviews. A single visit to the 500 participants necessary to achieve equivalent power would thus have cost approximately R21 500 ($5400, £3550), compared with R2 946 ($740.20, £486.54) in the trial.

6.2.6.5 Generalisabaility to other settings

This study was conducted from a public sector urban hospital. During the period of unrestricted enrolment in the trial 60% of patients offered a contact telephone number. The study findings thus appear generalisable to settings where 60% or more of patients offer a telephone number, but may not be applicable to settings with lower telephone coverage.

6.2.7 Conclusions

1. Telephone follow-up in this trial resulted in a level of follow-up unlikely to have been achieved by other methods in this setting and was associated with great cost advantages.
2. The validity of the questionnaire findings for distinct events was high in the population studied. The validity of measurement of time to recovery, which differs in nature from distinct health services events, could not be assessed.
3. The answers to the telephone questionnaire were generalisable to patients in the same hospital population without telephones, except for outcomes that could be affected by the interview itself.
4. The estimate of the effect of chest radiography measured by telephone appears valid.
5. The trial findings measured by telephone follow-up appear generalisable to patients in the same hospital population without telephones.
6. The findings regarding the feasibility, validity and applicability of telephone follow-up may be generalisable to settings where 60% or more of patients offer a telephone number, but are unlikely to be applicable to settings with lower telephone coverage.

Chapter 6.3

Issues arising from the trial

Determinants of clinical management decisions in acute lower respiratory infections in children

6.3.1 Background

The study of clinical decisions in acute respiratory infections has concentrated mainly on antibiotic use. The reasons for this are the widespread inappropriate use of antibiotics for ARI and its implications for the development of bacterial resistance to antibiotics. Colds, upper respiratory tract infections, bronchitis and bronchiolitis, for which antibiotics are not usually indicated (Gadomski 1993; Welliver and Cherry 1992), account for 21% of all ambulatory antibiotic prescriptions for children in the USA (Nyquist et al 1998). Increasing bacterial resistance to antibiotics is a major and growing problem (Neu 1992; Kunin 1993; Wise et al 1998) and reducing community antibiotic use appears to limit or reduce the resistance to antibiotics (Seppälä et al 1997).

Studies of non-clinical determinants of management decisions in ARI have used several sources of information:

a) Large existing databases enable the study of a wide range of clinicians and patients (Mainous, Hueston and Clark 1996), but are retrospective and may provide little information on individual clinicians or on confounding variables.
b) Prospective records of individual consultations provide detailed information on individual clinicians and patients in actual practice (Gonzales, Steiner and Sande 1997; MacFarlane et al 1997; Kuyvenhoven, De Melker and Van der Velden 1993). Difficulties in conducting such studies include the need for clinicians to complete data capture forms, and the effect on clinical behaviour of an intrusive research process. Such studies usually take place at a large number of practice sites. Potential problems are the representativeness of clinicians willing to participate in such studies and the extent to which patient sampling procedures are followed in studies involving clinicians in many different settings. Many confounding factors related to practice site and patient population complicate the analysis and interpretation of the findings.
c) Self-reported clinician responses to case vignettes (De Melker and Kuyvenhoven 1991; Howie 1976; Stephenson, Henry and Norman 1988; Wagner et al 1976; Windak et al 1996) facilitate the study of non-clinical factors by minimising clinical confounding factors, but it is not clear whether hypothetical responses reflect actual practice. Good correlation was found between the assessment of disease activity in rheumatoid arthritis made on case vignettes and when seeing the real patients on which the vignettes were based (Kirwin et al 1983). There was however poor agreement between stated and actual

practice in the diagnosis and management of urinary tract infection (Goran, Williamson and Gonnella 1973) and between general practitioners' stated and actual referral rates (Morrell and Roland 1990). There were also major inconsistencies between responses of both medical students and pharmacists to case vignettes and to actors they believed to be real patients (Norman and Feightner 1981; Page and Fielding 1980).

The database of this trial provided an unusual opportunity to study the determinants of management decisions. Because of the need to preserve usual clinical behaviour, special efforts were made not to disrupt usual clinical practice. These efforts included identification of participants and measurement of baseline variables independently of the clinician, a minimally disruptive enrolment and randomisation process, use of usual clinical records for the recording of clinical information, and an assurance to the clinicians that individual clinical practice would not be examined. A single practice site and prospective identification of patients with a defined clinical presentation provided a relatively homogeneous clinical setting, while the participating clinicians represented a wide range of training and experience.

Two clinical decisions were initially examined to identify determinants of the decisions. These were the use of chest radiography and prescription of an antibiotic. The findings prompted an unplanned analysis of the remaining four decisions recorded during the trial. These four decisions were i) the performance of another diagnostic test or tests, ii) admission to hospital at the first consultation, iii) scheduling of a follow-up appointment and iv) the number of drugs prescribed (excluding antibiotics). All of these analyses are reported in this section.

6.3.2 Aims

1. To determine the clinical and clinician-related determinants of the clinicians' perception of the need for chest radiography in acute lower respiratory infections in children (*Analysis 1*).
2. To determine the clinical and clinician-related determinants of antibiotic use in acute lower respiratory infections in children (*Analysis 2*).
3. To examine the consistency of the direction of association of general medical and specific outpatient experience with management decisions in acute lower respiratory infection in children (*Analysis 3*, post hoc).

6.3.3 Methods

6.3.3.1 Study design

Cross-sectional analytic study

6.3.3.2 General

The enrolling nurse measured clinical variables before the patient consulted the clinician. Apart from weight, this information was not presented to the clinicians. The clinician's perception of the need for chest radiography was measured by the clinician recording (before randomisation) whether he or she would have requested a radiograph if the patient had not been part of the trial. This was done by ticking the appropriate box next to "Usually" in the stamp on the consultation sheet (Appendix 7).

The clinicians were the 52 medical practitioners working full-time or part-time in the general outpatients department. The median time (with 25^{th}–75^{th} centiles) spent in the outpatients department was 12 months (1-38 months) and time since qualification was 5 years (2-17.5 years). Five clinicians (10%) were registrable as specialist paediatricians in South Africa and 17 (33%) possessed a postgraduate paediatric qualification. Most such qualifications were the Diploma in Child Health (South Africa), which requires six months of approved paediatric experience and a written and clinical examination, but no course attendance. The following clinician characteristics were assessed:

i) general medical experience, measured as time since qualification
ii) specific outpatient experience, measured as time spent working in the Red Cross Children's Hospital outpatients department
iii) possession of a postgraduate paediatric qualification.

Data on clinician experience and qualifications were obtained directly from the clinicians. Measurement of management decisions, and of the reliability of the measurement is described in Sections 3.5.5.2 and 3.5.5.3.3.

Potential determinants of the perceived need for radiography, antibiotic use and other management decisions were assessed in multiple logistic regression models, except for the number of drugs prescribed, where multiple linear regression was used. Inter-observer

agreement was expressed as a kappa statistic (Fleiss 1981), and correlation as a Spearman rank order correlation coefficient. A two-tailed alpha level of 0.05 was regarded as significant.

6.3.3.3 Chest radiograph use

All cases enrolled by the nurse were included (whether entered into the trial or not) except for patients excluded from the trial for administrative or unknown reasons.

The following potential determinants were assessed: age, gender, z-score for weight for age, respiratory rate, duration of symptoms before presentation, clinicians' possession of a postgraduate paediatric qualification, clinicians' general medical and specific outpatient experience, and the patients' accessibility by telephone. Accessibility by telephone was used as a marker of socio-economic status. When the patient was seen by more than one doctor the characteristics of the doctor enrolling the patient were used in the analysis.

The best predictive logistic regression model of the perceived need for chest radiography was selected using forward stepwise regression, with a level of significance of 0.20 for entry into the model and a level of 0.10 for removal.

6.3.3.4 Antibiotic use

All cases not admitted to hospital were included in this analysis, whether or not they were entered into the trial.

The same determinants were assessed as for the perceived need for radiography, except that chest radiograph use was included in this analysis. When the patient was seen by more than one doctor, the characteristics of the doctor prescribing medication were used.

The best predictive logistic regression model of antibiotic use was selected using forward stepwise regression, with a level of significance of 0.20 for entry into the model and a level of 0.10 for removal.

6.3.3.5 Associations with general and specific clinical experience

The remaining four clinical decisions recorded during the trial were evaluated for their association with qualification and experience. The decisions were:

i) performance of another diagnostic test or tests

ii) admission to hospital at the first consultation

iii) scheduling of a follow-up appointment

iv) the number of drugs prescribed (excluding antibiotics).

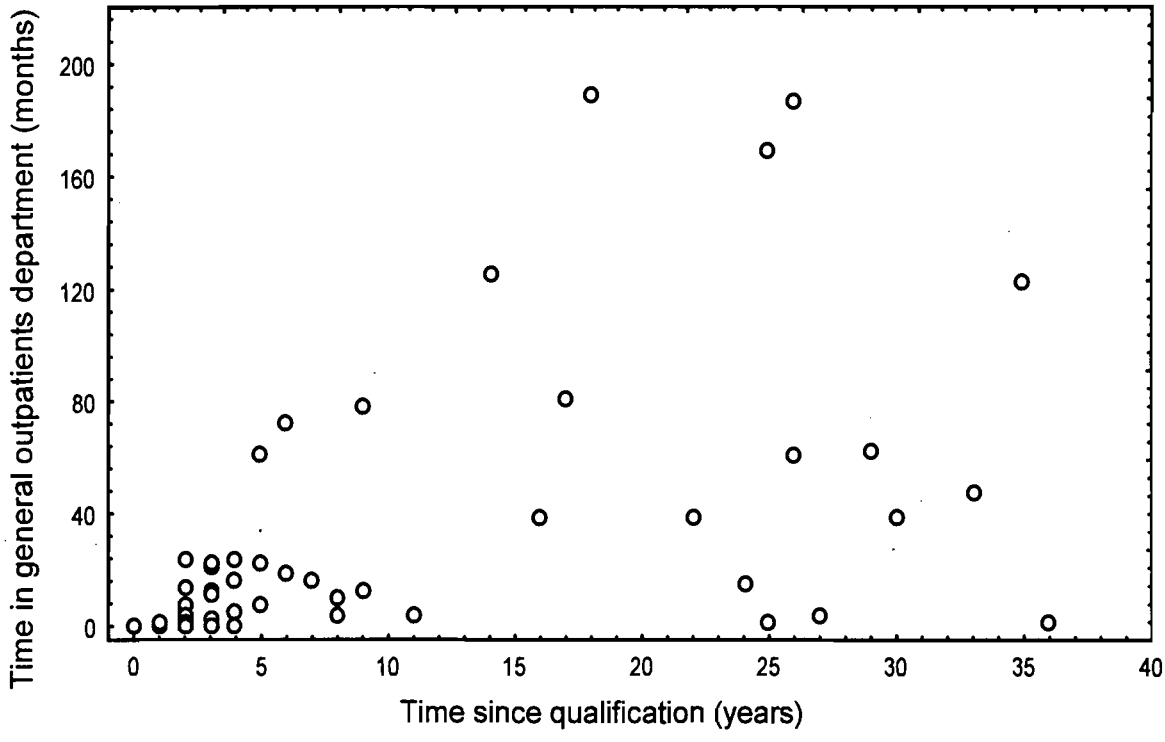
The direction of association of each of the six decisions with general medical and specific outpatient experience were estimated using the regression models.

The following potential confounding variables were adjusted for in the regression models; age, gender, z-score for weight for age, respiratory rate, duration of symptoms before presentation, chest radiograph use and accessibility by telephone.

6.3.4 Results

The association between duration of clinicians' general medical and specific outpatient experience is represented graphically in Figure 6.3.1. The correlation coefficient between years of specific outpatient and general medical experience was 0.64.

FIGURE 6.3.1 Clinicians' general medical and specific outpatient experience.



The kappa statistic for inter-observer agreement in the record review was 1.00 for all six management decisions, except for antibiotic use and the number of drugs per script where kappa was 0.93 and 0.99 (weighted kappa) respectively (Table 4.26).

6.3.4.1 General

Five hundred and eighty one patients were enrolled in this study. The clinical records of 576 (99.1%) were retrieved.

6.3.4.2 Chest radiograph use

Of 576 patients with clinical records, 11 were excluded by the clinicians for administrative or unknown reasons. There was no record of the clinicians' perception of the need for radiograph in a further 23 cases, and data on determinants were incomplete in 10 cases. The remaining 532 children were included in the analysis.

The parameter estimates for the logistic regression model are shown in Appendix 13. The perception of the need for chest radiography was associated with patient age, weight for age and clinician's time since graduation (Table 6.3.1).

TABLE 6.3.1 Determinants of the clinicians' perception of the need for chest radiography.

	Odds ratio (95% CI) n=532	**p**
Age[1]	1.34 (1.07 to 1.70)	0.01
Weight for age[2]	0.82 (0.69 to 0.96)	0.01
Clinicians' general experience (time since qualification)[3]	0.79 (0.65 to 0.96)	0.03

1 odds ratio for each 1 year increase in age
2 odds ratio for each unit increase in z-score
3 odds ratio for an increase of 10 years

The perceived need for chest radiography was not significantly associated with clinician's possession of a postgraduate qualification or time spent working in the outpatient department, nor with patient gender, duration of symptoms before presentation, respiratory rate or accessibility by telephone.

6.3.4.3 Antibiotic use

Of 576 patients with clinical records, 27 were admitted to hospital at the first consultation. Of 549 children not admitted to hospital 315 (57.4%) were prescribed an antibiotic.

The following diagnoses were made in patients not admitted to hospital: bronchiolitis in 265 (48.3%), upper respiratory infection in 86 (15.7%), pneumonia in 58 (10.6%), asthma in 37 (6.7%), non-specific diagnoses (such as "lower respiratory infection") in 65 (11.8%), no diagnosis or an undetermined diagnosis in 38 (8.0%).

Data on potential determinants were incomplete in a further 16 cases. The remaining 533 children were included in the analysis. The parameter estimates of the logistic regression model are shown in Appendix 13. Antibiotic use was significantly associated with patient age, use of chest radiography, and clinicians' general and outpatient experience (Table 6.3.2).

TABLE 6.3.2 Determinants of antibiotic use.

	Odds ratio (95% CI) n=533	p
Age[1]	2.37 (2.05 to 2.75)	0.0001
Clinicians' general experience (time since qualification)[2]	0.59 (0.53 to 0.66)	0.0001
Clinicians' specific outpatient experience[2]	2.53 (1.47 to 4.37)	0.001
Chest radiography	1.55 (1.08 to 2.25)	0.02

1 odds ratio for each 1 year increase in age
2 odds ratio for an increase of 10 years

Antibiotic use was not associated with possession of a postgraduate qualification. The association with clinicians' general experience was in the opposite direction to that with outpatient experience.

6.3.4.4 Associations with general and specific clinical experience

The parameter estimates of the regression models are shown in Appendix 13. The associations of experience with all six management decisions examined, including the perceived need for chest radiography and antibiotic use, are tabulated in Table 6.3.3.

TABLE 6.3.3 Associations of clinicians' general medical and specific outpatient experience with clinical management decisions.

	Time since qualification[a]		Time working in general outpatients[a]	
	Odds ratio[b]	p	Odds ratio[b]	p
Perceived need for radiography	0.72	0.02	1.60	0.12
Antibiotic use	0.59	0.0001	2.60	0.001
Additional test(s) ordered	0.69	0.08	1.90	0.14
Admission to hospital	0.72	0.41	0.06	0.05
Follow-up appointment	0.65	0.03	1.47	0.36
No. of drugs per script (excluding antibiotics)[b]	-0.10	0.05	0.01	0.90

a for each increase of 10 years
b the regression co-efficient, rather than the odds ratio is presented for the number of drugs per script

The association with clinician's general experience was in the direction of lesser intervention in all six decisions, while that with outpatient experience was in the direction of greater intervention in five of six decisions. The probability of the association with either characteristic being in the same direction in all six cases, and in the opposite direction with the other characteristic in five or more cases is 0.003.

6.3.5 Discussion

6.3.5.1 Chest radiograph use

The perception of the need for chest radiography increased with patient age. The direction of this association is perhaps surprising. Clinicians might be expected to be more inclined to radiograph younger infants, in whom signs of disease are subtler and less specific. The explanation for the association given by a group of the clinicians involved in the study was that caregivers' thresholds for seeking care were lower in younger infants, with the result that younger children presenting to the hospital were generally less ill than older children. This

explanation implies that the perceived need for chest radiography depends on severity of illness, rather than the potential discriminatory power of the investigation. Another explanation is that viral-appearing lower respiratory infections were commoner in the younger children, with a resultant lower perceived need for radiography in younger children. In this sample pneumonia became commoner relative to bronchiolitis as age increased (p=0.00004, chi squared test for trend, data not shown).

The association of perceived need for radiography with decreasing z-score for weight for age is expected. Children who weigh less for age are more likely to have a chronic illness, such as tuberculosis, the diagnosis of which relies heavily on chest radiography in children (Coulter 1992).

Accessibility by telephone was not a determinant of a perceived need for radiography. This is surprising. A reason regularly offered by local practitioners for the use of special investigations in the study setting is the need for greater diagnostic confidence before discharging children home to areas with poor access to the hospital. The elements of access to health services associated with accessibility by telephone were however not associated with a perceived need for chest radiography.

6.3.5.2 Antibiotic use

The strong association of antibiotic use with increasing age is probably because viral lower respiratory infections were commoner in the younger children. A contributory possibility is that the selection process noted by the clinicians in Section 6.3.5.1 above resulted in older children being more ill when brought to hospital.

The association of antibiotic use with chest radiography is consistent with the bivariate analysis of the trial itself (see Section 4.2.4.1).

According to WHO guidelines, all children in the sample should have received antibiotics. The WHO guidelines however do not distinguish between pneumonia and bronchiolitis, a viral illness for which antibiotics are not generally recommended (Welliver and Cherry 1992; Wohl 1990). The 57% overall antibiotic usage in this study thus reflects a relatively greater sophistication of the clinicians in distinguishing between pneumonia and bronchiolitis. Antibiotic use in 57% of children with bronchiolits in this study (data not shown) is lower than

the 72% usage for acute bronchitis and bronchiolitis (ICD-9 (1988) code 466) recorded in a large survey in the USA (Nyquist et al 1998), but appears very high for a viral illness. Standard textbooks however contain provisos that antibiotic use may be prudent when the diagnosis is uncertain (Welliver and Cherry 1992; Wohl 1990). The degree of appropriateness of the antibiotic use in this study is thus difficult to assess.

There was a striking difference in the direction of association of antibiotic use with specific outpatient and general medical experience. The odds ratios of 2.60 and 0,59 for antibiotic use with each 10-year increase of outpatient and general experience respectively appear to be clinically meaningful associations. The high inter-observer agreement in data extraction suggests that the information obtained is valid, and the findings are very unlikely to have arisen by chance. It is necessary to consider collinearity of clinician outpatient and general experience, leading to poor convergence of the regression model (Hosmer and Lemeshow 1989), as the reason for the surprising findings. This does not appear to be the case in this analysis. The correlation co-efficient between general and outpatient experience was only 0.64, and the standard errors of the parameter estimates (as reflected by the confidence intervals for the odds ratios) were not large. Collinearity produces large standard errors (Hosmer and Lemeshow 1989).

6.3.5.3 Association with general and specific clinical experience

The single practice site, the relative homogeneity of the patient population, the conditions of normal clinical practice and statistical adjustment for patient variables facilitated the assessment of clinician characteristics in this study by minimising confounding factors associated with practice site and patient population.

Although the pattern of association was strongest for antibiotic use, a similar pattern of opposing directions of association with general and specific medical experience was present for a range of other management decisions in this sample, with specific outpatient experience being associated with more active decisions. Such differences in decision-making between clinicians with different experience do not appear to be limited to our study setting. In a questionnaire study using case vignettes of children with acute upper and lower respiratory infections, family physicians were consistently more active than paediatricians in recording findings on history and examination, ordering diagnostic tests, prescribing medication, admission to hospital and

scheduling follow-up (Wagner et al 1976). Outpatient experience in our study represented predominantly ambulatory primary care exposure similar in some respects to family practice, but different in others. These findings suggest that patterns of association with experience extend across the immediate clinical setting.

The unexpected finding of opposing directions of association is difficult to explain. One possibility is that inherent personal characteristics that affect clinical decision-making also help determine the settings in which clinicians choose to spend most of their careers. Another is that different effects of general medical and specific outpatient experience themselves influence management decisions in opposite directions. The above-mentioned difference in practice patterns between family physicians and paediatricians increased with time from graduation (Wagner et al 1976), suggesting that at least part of the effect is due to the experience itself.

The difficulty in explaining the findings illustrates a complex and poorly understood relationship between experience and clinical behaviour, which should be taken into account in future research and practice. A fuller understanding of the association of different forms of experience with clinical decisions could improve the effectiveness of interventions to improve knowledge and practice in a range of management decisions, and especially antibiotic use.

6.3.6 Conclusions

1. The perceived need for chest radiography was associated with patient age, weight for age and clinician's general experience.
2. Antibiotic use was associated with patient age, chest radiography, and clinicians' general and outpatient experience
3. The associations of clinician's specific outpatient and general medical experience with antibiotic use were in opposing directions.
4. Associations of clinician characteristics with antibiotic use appear to be part of a pattern of less active management with increasing general medical experience, and more active decisions with increasing outpatient experience across different clinical decisions and practice settings.
5. A fuller understanding of the association of different forms of experience with clinical decisions could improve the effectiveness of interventions to improve knowledge and practice in a range of management decisions, and especially antibiotic use.

Chapter 6.4

Issues arising from the trial

Duration of illness in ambulatory children with a diagnosis of bronchiolitis

6.4.1 Background

The long-term prognosis of children with bronchiolitis has been studied (Kattan et al 1977; McConnachie and Rochmann 1985; Milner and Murray 1989) but little is known about the duration of the acute illness. Knowledge of the typical course of bronchiolitis is important for clinicians when considering the differential diagnosis of lower respiratory illness. Parents too need to know by when to expect their child to recover, as unfulfilled tacit expectations are likely to result in anxiety and discouragement.

Standard paediatric textbooks offer contradictory information on the issue: "Recovery is complete in a few days." (Orenstein 1996), ". . full recovery may take about 2 weeks." (Henderson 1996), "Wheezing and hypoxia may last for as long as 3 or 4 weeks." (McKenzie 1992). The duration of hospitalisation for bronchiolitis has been reported from clinical trials (Klassen et al 1997; Richter and Seddon 1998; Rodriguez et al 1997), but this information is of questionable generalisability because of the highly selected groups of hospitalised patients and variations between hospitals in management practices. Furthermore, hospital discharge does not imply full recovery. A MEDLINE search (Appendix 2) failed to identify any reports of duration of illness or time to recovery in bronchiolitis.

By following up a cohort of children at home, the trial provided an unusual opportunity to describe the duration of illness in ambulatory children with a diagnosis of bronchiolitis and a defined clinical presentation.

6.4.2 Aims and objectives

6.4.2.1 Aim

To describe the course of illness in ambulatory children with a diagnosis of bronchiolitis.

6.4.2.2 Objectives

1. To describe the duration of illness in ambulatory children with a diagnosis of bronchiolitis.
2. To determine the use of hospital services and admission to hospital during an episode of bronchiolitis in children who, according to WHO guidelines, should initially be treated at home.
3. To identify predictors of the duration of illness.

6.4.3 Methods

6.4.3.1 Study design

Prospective inception cohort study.

6.4.3.2 Study plan

Children meeting the case definition for the trial (whether or not they were eventually entered into the trial) were included in this analysis if they were aged under 24 months, received a diagnosis of bronchiolitis and offered a contact telephone number.

A diagnosis of bronchiolitis was regarded as the final diagnosis recorded by the clinician on the routine consultation sheet. The diagnosis was made on clinical grounds (with or without the use of chest radiography). Viral cultures and antigen detection to provide an aetiological diagnosis were not performed.

Time to recovery, use of health services and admission to hospital were measured as described in Section 3.5.5. The duration of the illness was taken as the reported duration of symptoms before presentation plus the time to recovery after presentation. The variables assessed as potential predictors of duration of illness were respiratory rate, age, gender and z score for weight for age.

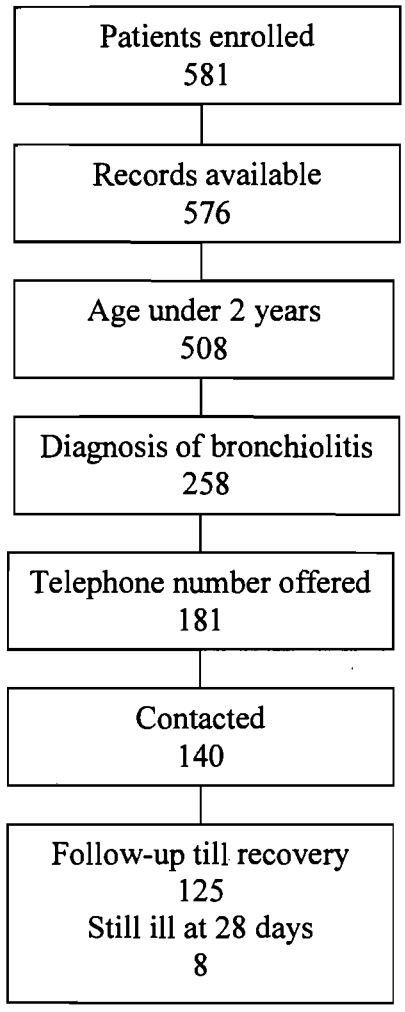
6.4.3.3 Analysis

Duration of illness was presented as a Kaplan-Meier survival curve. The difference between duration of illness in patients with and without chest radiography was tested using the log rank test. Predictors of duration of illness were assessed in a Cox proportional hazards regression model. A two-tailed alpha level of 0.05 was regarded as significant.

6.4.4 Results

Patient flow is shown in Figure 6.4.1. Of 181 patients offering a contact telephone number, 133 (73.5%) were followed till recovery or for 28 days.

FIGURE 6.4.1 Follow-up of children with a diagnosis of bronchiolitis.



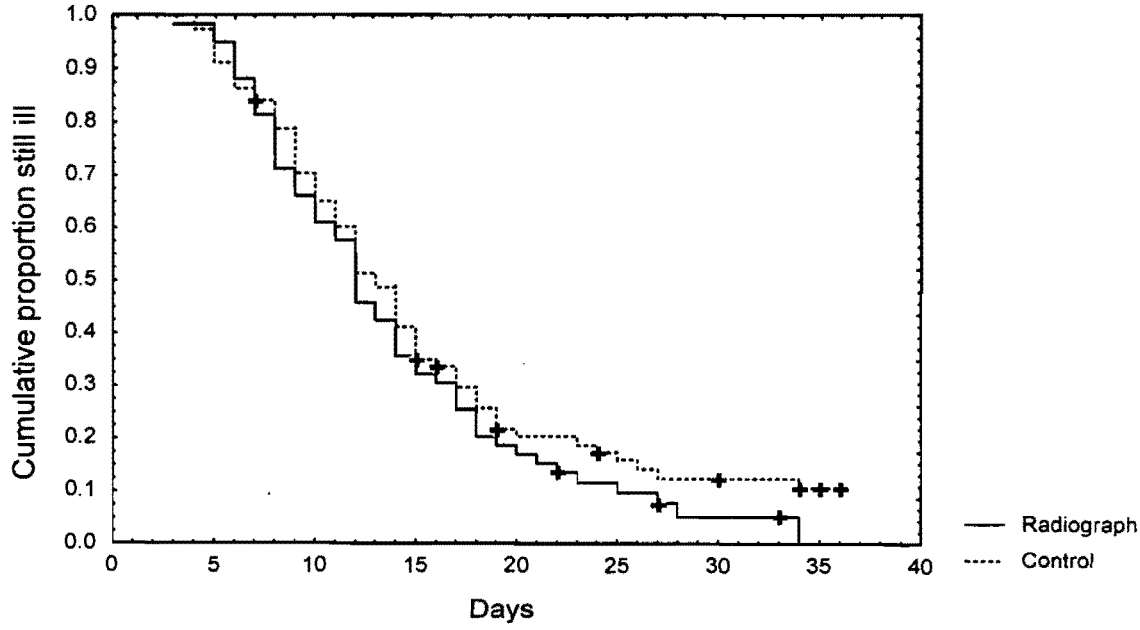
A summary of baseline characteristics is shown in Table 6.4.1. There was no significant difference in duration of illness in patients managed with and without chest radiography (p=0.25) (Figure 6.4.2). Both groups were thus analysed together.

TABLE 6.4.1 Baseline characteristics of patients with a diagnosis of bronchiolitis and accessible by telephone (n=140).

Median respiratory rate per minute (I-Q range)	60	(40-89)
Males (%)	71	(50.7)
Median age in months (I-Q range)	6.0	(4.1-9.5)
Mean Z score for weight for age (SD)	0.2	(1.14)
Median days duration of symptoms before enrolment (I-Q range)	4	(3-6)
Clinicians' perceived need for chest radiograph[1] (%)	18	(13.5)
Chest radiograph performed (%)	59	(42.1)

1 Data missing for 7 patients

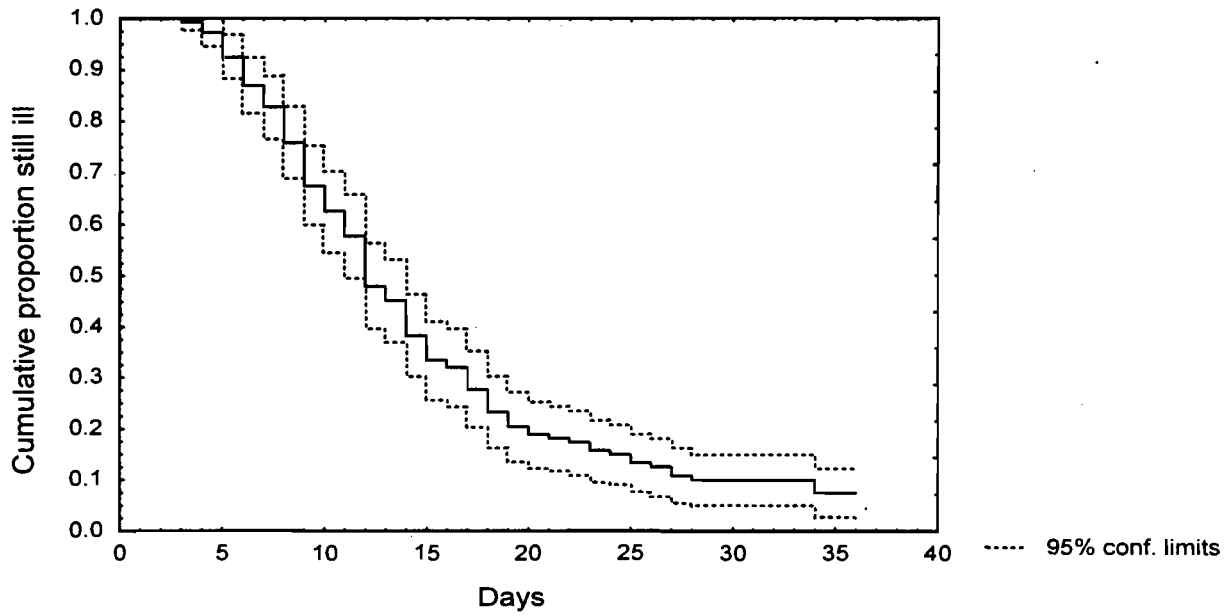
FIGURE 6.4.2 Comparison of duration of illness in patients managed with and without chest radiography.



No deaths were recorded. The 95% confidence interval for the estimate of any serious event not recorded in this sample is 0 to 2.6%.

The survival curve for time from onset of symptoms to recovery is shown in Figure 6.4.3. The median duration of illness was 12 days. Thirty nine percent were still ill after 14 days, 18% after 21 days and 9% after 28 days. There was no association between duration of illness and age, gender, z score for weight for age, or respiratory rate. Parameter estimates from the proportional hazards regression model are shown in Appendix 13.

FIGURE 6.4.3 Duration of illness in children with a diagnosis of bronchiolitis.



Three patients (2.1%) were admitted to hospital at the first consultation and seven children (5.0%) at a subsequent consultation within 28 days. Fifty-five patients (39.3%) had a total of 75 subsequent unscheduled consultations within 28 days; 43 patients visited the Children's Hospital (53 visits) and 18 (including 6 who also visited the hospital) visited other health facilities such as primary care clinics and private general practitioners (22 visits). The median time from the enrolment consultation to the first unscheduled visit was 13 days (16 days from the onset of symptoms).

There were no meaningful differences between study patients accessible by telephone and children meeting the case definition for the trial who were not accessible, with respect to baseline characteristics, management and subsequent use of the Children's Hospital (Table 6.4.2).

6.4.5 Discussion

This is the first report, to the investigator's knowledge, of duration of illness and parental health-seeking behaviour during bronchiolitis. The children in this ambulatory sample recovered with few complications, but resolution of symptoms took longer than 14 days in approximately 40% of patients. A large proportion of subjects thus took longer to recover than the "few days" or "about 2 weeks" described in standard paediatric textbooks (Orenstein 1996; Hendersen 1996). The sample is too small to provide precise information on serious rare outcomes.

A potential limitation of the study is that no diagnostic criteria for bronchiolitis were specified. Bronchiolitis is however a clinical diagnosis (Welliver and Cherry 1992) and this sample represents bronchiolitis as diagnosed by a large number of clinicians with a wide range of training and clinical experience, in children fitting a case definition for severity. No objective or explicit criteria were used to judge recovery, but recovery is appropriately a parent's assessment. These data relate to ambulatory children with a clinical diagnosis of bronchiolitis. This is not necessarily a description of duration of illness of respiratory syncitial virus infection, because causative viruses were not identified.

Although the study was performed at a teaching hospital the sample is likely to represent ambulatory children with bronchiolitis attending a primary health care facility, for the reasons discussed in Section 3.2.1.

Patients accessible by telephone were similar to those not accessible with respect to baseline characteristics, management and hospital-based outcome. The children in this study thus appear to be broadly representative of children with bronchiolitis who are ill enough to be brought for medical attention, but well enough to be treated at home thereafter.

TABLE 6.4.2 Comparison of children with a diagnosis of bronchiolitis and accessible or not accessible by telephone.

	Followed by telephone		Not accessible by telephone		p
	(n=140)		(n=118)		
Baseline characteristics					
Median respiratory rate/minute (I-Q range)	60	(54-63)	60	(54-70)	0.52
Males (%)	71	(50.7)	69	(58.5)	0.21
Median age in months (I-Q range)	6.0	(4.1-9.5)	5.9	(3.4-10.8)	0.80
Mean Z score for weight for age (SD)	0.2	(1.14)	0.0	(1.04)	0.25
Median days duration of symptoms before enrolment (I-Q range)	4	(3-6)	3	(2-7)	0.47
Perceived need for radiography[1] (%)	18	(13.5)	12	(11.3)	0.61
Chest radiograph performed (%)	59	(42.1)	57	(48.3)	0.32
Management					
Additional tests ordered[2] (%)	4	(2.9)	8	(6.8)	0.14
Mean no. of drugs per prescription (SD)[2]	3.2	(0.89)	3.1	(0.86)	0.86
Antibiotic use[2] (%)	68	(49.6)	49	(41.9)	0.22
Admission at 1st consultation (%)	3	(2.1)	1	(0.8)	0.63
Follow up appointments[2,3] (%)	5	(3.6)	8	(6.8)	0.25
Outcome					
Subsequent visits to hospital[3] (%)	48	(34.3)	31	(26.3)	0.16
Subsequent admissions[3] (%)	7	(5.0)	7	(5.9)	0.74
Subsequent chest radiographs[3] (%)	7	(5.0)	10	(8.5)	0.26

1 Data missing for 7 study patients and 12 non-accessible patients

2 Excluding 3 study subjects and 1 non-accessible patient admitted at first consultation.

3 Within 28 days

Almost 40% of children made subsequent unscheduled visits for health care within 28 days. The relatively long delay from initial consultation to return visit (median 13 days) and the low admission rate (9.3% of visits) suggests that the bulk of visits were because of slow recovery, rather than acute deterioration. Usual practice in the department at the time of the study was to inform parents that recovery could take up to two weeks. This advice was unduly optimistic. Counselling parents to expect a longer duration of illness, with gradual improvement, could reduce anxiety and the high rate of return visits.

6.4.6 Conclusions

1. Ambulatory children with a diagnosis of bronchiolitis recover with few complications, but resolution of symptoms may take several weeks.
2. The high rate of unscheduled return visits that was observed in this cohort probably reflects parental concern regarding slow recovery. Counselling parents to expect gradual improvement over a period of up to three or four weeks could reduce these concerns.
3. Age, weight for age, gender and respiratory rate are not clinically useful predictors of time to recovery.

Chapter 7

Summary of conclusions and recommendations

7.1 Literature review

7.1.1 Observer variation in radiological interpretation

Radiological assessment of the presence of, or features of, lower respiratory infection is made with moderate to good inter- and intra-observer agreement, when assessed by expert observers.

7.1.2 Radiological differentiation of bacterial from viral lower respiratory infection

The diagnostic value of chest radiography in distinguishing bacterial from viral pneumonia is unknown, principally because of the methodological limitations of the available studies.

7.1.3 Radiological assessment of severity of illness

The usefulness of chest radiography in the assessment of the severity of illness in viral respiratory infections is uncertain because of methodological limitations of the two available studies.

7.1.4 Effect of radiography on clinical management and outcome

In uncontrolled before-after studies, chest radiography had a small but meaningful effect in both directions on diagnosis, antibiotic use and possibly admission to hospital. These findings are probably overestimates, given the uncontrolled before-after study design.

No controlled trials of the effect of chest radiography on clinical management or outcome in children with acute lower respiratory infection were identified.

7.2 Effect of chest radiography on the clinical management and outcome of children with acute lower respiratory infection

7.2.1 Clinical outcome

Chest radiography had no effect on time to recovery, or subsequent visits for medical care, admissions to hospital or chest radiography.

7.2.2 Diagnosis and clinical management

Statistically significant effects of chest radiography were demonstrated on:

Diagnosis: Radiographs resulted in pneumonia being diagnosed more often (14.4% *vs.* 8.4%), and bronchiolitis less often (43.6% *vs.* 55.9%).

Antibiotic use: This was increased from 52.2% to 60.8%. Chest radiography was associated with an absolute reduction in antibiotic use of 15.8% in patients with a perceived need for radiography, and an increase of 11.1% in patients without a perceived need.

Chest radiography showed trends that approached, but did not reach, statistical significance with respect to an increase in follow-up appointments (from 8.6% to 13.5%) and admission to hospital at the first consultation (from 2.3% to 4.7%). No effect was found on test ordering or the number of drugs prescribed.

7.2.3 Consultation time

Chest radiograph increased consultation time by two minutes (22%) and greatly increased time from start to finish of the consultation. The difference in consultation time is probably an underestimate, but the applicability of these findings to usual clinical practice is questionable.

7.2.4 Effect of clinician's experience

The effect of chest radiography did not depend on the clinicians' paediatric outpatient experience and the possession of a post-graduate qualification in paediatrics. The trial findings appear to be applicable to less experienced doctors in other settings.

7.2.5 Clinical subgroups of patients who could benefit

The effect of chest radiography was independent of age, weight for age, duration of symptoms, respiratory rate or physicians' perception of the need for radiography. There are unlikely to be clinically easily identifiable sub-groups of children in the group studied who will benefit from chest radiography.

7.2.6 Applicability of findings

The trial findings appear broadly applicable to children who fit the World Health Organization case definition for pneumonia, although doubt persists about the applicability of the findings to areas with a low prevalence of wheeze.

7.2.7 Summary

Despite a net change in diagnosis and an increase in antibiotic usage, the use of chest radiography did not reduce time to recovery or subsequent health facility usage in children meeting the World Health Organization case definition for pneumonia. This lack of effect was not modified by clinicians' experience and there were no clinically identifiable sub-groups of children within this case definition likely to benefit from chest radiography.

7.2.8 Recommendations

Chest radiograph is not indicated in the management of children who fulfil the World Health Organization case definition for pneumonia, if they have been symptomatic for 14 days or less and do not have a household contact with active tuberculosis.

The findings of the trial need to be confirmed in areas with a lower prevalence of wheeze.

7.3 Tuberculosis case finding

Chest radiography in ambulatory children with acute lower respiratory infections lasting 14 days or less and without a contact with active tuberculosis did not yield a meaningful increase in the diagnosis or treatment of tuberculosis.

7.3.1 Applicability

Given the very high incidence of tuberculosis in the setting in which this study was performed, it is unlikely that chest radiography will be beneficial in children with the same case definition in other settings.

7.3.2 Recommendation

Routine chest radiography is not indicated for the detection of tuberculosis in children with acute lower respiratory infections.

7.4 Telephone follow-up

7.4.1 Feasibility

Telephone follow-up resulted in a level of follow-up unlikely to have been achieved by other methods in this setting, and was associated with great cost advantages.

7.4.2 Validity

The validity of the questionnaire findings for distinct events was high in the population studied. The validity of measurement of time to recovery, which differs in nature from distinct health services events, could not be assessed.

The estimate of the effect of chest radiography measured by telephone follow-up appears valid.

7.4.3 Applicability

The answers to the telephone questionnaire were generalisable to patients in the same hospital population without telephones, except for variables that could be affected by the interview itself.

The trial findings measured by telephone follow-up appear generalisable to patients in the same hospital population without telephones.

The findings regarding the feasibility, validity and applicability of telephone follow-up may be generalisable to settings where 60% or more of patients offer a telephone number, but are unlikely to be applicable to settings with lower telephone coverage.

7.4.4 Recommendation

Telephone interview may be considered as an option for follow-up in communities with some, but limited, access to telephones. A pilot study is recommended to confirm feasibility.

7.5 Determinants of clinical management decisions

7.5.1 Chest radiography

The perceived need for chest radiography was associated with increasing patient age, decreasing weight for age and decreasing clinician's general experience.

7.5.2 Antibiotic use

Antibiotic use was associated with increasing patient age, use of chest radiography, and clinicians' general and outpatient experience.

7.5.3 Associations with clinician experience

The associations of antibiotic use with clinician's specific outpatient and general medical experience were in opposing directions.

Associations of clinician characteristics with antibiotic use appear to be part of a pattern of association, across different clinical decisions and practice settings, of less active management with increasing general medical experience, and more active decisions with increasing outpatient experience.

7.5.4 Recommendation

A fuller understanding is needed of the association of different forms of experience with clinical decisions. This could improve the effectiveness of interventions to improve knowledge and practice in a range of management decisions, and especially antibiotic use.

7.6 Duration of illness in bronchiolitis

7.6.1 Duration of illness

Ambulatory children with bronchiolitis recover with few complications, but resolution of symptoms may take several weeks.

7.6.2 Clinical predictors

Age, weight for age, gender and respiratory rate are not clinically useful predictors of time to recovery.

7.6.3 Care-seeking behaviour

The high rate of unscheduled return visits that was observed in this cohort probably reflects parental concern regarding slow recovery.

7.6.4 Recommendation

Parental concern and unnecessary return visits for care could be reduced by counseling parents to expect gradual improvement over a period of up to three or four weeks.

References

Alario et al 1987

Alario AJ, McCarthy PL, Markowitz R, Kornguth P, Rosenfield N, Leventhal JM. Usefulness of chest radiographs with acute lower respiratory tract disease. J Pediatr 1987; 111:187-193

Altman 1991a

Altman DG. Practical statistics for medical research. London: Chapman & Hall, 1991

Altman 1991b

Altman DG. Randomisation. Essential for reducing bias [editorial]. BMJ 1991; 302:1481-1482

Altman 1998

Altman DG. Confidence intervals for the number needed to treat. BMJ 1998; 317:1309-1312

American College of Radiology 1995

American College of Radiology. ACR standard for the performance of pediatric and adult chest radiography. Reston VA: American College of Radiology, 1995

Aneshensel et al 1982

Aneshensel CS, Frerichs RR, Clark VA, Yokopenic PA. Telephone versus in-person surveys of community health status. Am J Public Health 1982; 72:1017-1021

Annals of Internal Medicine 1994

Purpose and procedure [editorial policy] Ann Intern Med 1994;120 Suppl 1: A-9-10

Arason et al 1996

Arason V, Kristinsson K, Sigurdsson J, Stefánsdóttir G, Mölstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children? Cross-sectional prevalence study. BMJ 1996; 313:387-391

Bailar and MacMahon 1997

Bailar JC, MacMahon B. Randomization in the Canadian National Breast Screening Study: a review for evidence of subversion. Can Med Assoc J 1997; 156: 193-199

Bang et al 1990

Bang AT, Bang RA, Tale O, Sontakke P, Solanki J, Wargantiwar R, Kelzarkar P. Reduction in pneumonia mortality and total childhood mortality by means of community-based intervention trial in Gadchiroli, India. Lancet 1990; 336:201-206

Béclère 1901

Béclère A. On the technique of the application of the Röntgen rays in the diagnosis of tuberculosis. In: Trans Br Cong Tuberc; London, 1901; 3:278 quoted by Posner (1971)

Beentjies and Timmermans 1990

Beentjies LB, Timmermans CWM. Age and sex specific radiographic examination frequency in the Netherlands. Br J Radiol 1990; 63:691-697

Bettenay, de Campo and McCrossin 1988

Bettenay FAL, de Campo JF, McCrossin DB. Differentiating bacterial from viral pneumonias in children. Pediatr Radiol 1988; 18:453-454

Birkelo et al 1947

Birkelo CC, Chamberlain WE, Phelps PS, Schools PE, Zacks D, Yerushalmy J. Tuberculosis case finding. A comparison of the effectiveness of various roentgenographic and photofluorometric methods. JAMA 1947; 133:359-366

BMJ 1896

The new photography [editorial]. BMJ 1896;1:289-290

Bourne, Bloom and Sayed 1991

Bourne DE, Bloom B, Sayed AR. 1991. The morbidity spectrum seen by general practitioners in South Africa. S Afr Med J 1991; 80:513-514

Boyd NF 1997

Boyd NF. The review of randomization in the Canadion National Breast Screening Study. Is the debate over? Can Med Assoc J 1997; 156: 207-9

Bradshaw, Laubsher and Schneider 1995

Bradshaw D, Laubsher R, Schneider M. Estimated cause of death profiles for the nine new provinces based on 1990 data. Parow: South African Medical Research Council, February 1995

Campbell 1958

Campbell EJM. The respiratory muscles and the mechanics of breathing. London: Lloyd-Luke, 1958

Campbell 1995

Campbell H. Acute respiratory infection: a global challenge [annotation]. Arch Dis Child 1995;73:281-286

Campbell et al 1989

Campbell H, Byass P, Lamont AC, Forgie IM, O'Neill KP, Lloyd-Evans N, Greenwood BM. Assessment of clinical criteria for identification of severe acute lower respiratory tract infections in children. Lancet 1989;1:297-299

Carleton, Sanders and Burack 1960

Carleton RA, Sanders CA, Burack WR. Heparin administration after acute myocardial infarction. N Eng J Med 1960;263:1002-1005

Cassiani, Zanetti and Pela 1992

Cassiani SHdeB, Zanetti ML, Pelá NTR. The telephone survey: a methodoligical strategy for obtaining information. Journal of Advanced Nursing 1992;17:576-81

Chalmers et al 1983

Chalmers TC, Celano P, Sacks HS, Smith H. Bias in treatment assignment in controlled clinical trials. N Eng J Med 1983;309:1358-1361

Cherian et al 1988

Cherian T, John TJ, Simoes E, Steinhoff MC, John M. Evaluation of simple clinical signs for the diagnosis of acute lower respiratory tract infection. Lancet 1988; 2:125-128

Cherian et al 1997

Cherian T, Steinhoff MC, Simoes EA, John TJ. Clinical signs of acute lower respiratory tract infections in malnourished infants and children. Pediatr Infect Dis J 1997;16:490-494

Cherry 1992

Cherry J. Mycoplasma and ureaplasma infections. In: Feigin RD, Cherry JD, eds. Textbook of pediatric infectious diseases. 3rd ed. Philadelphia: Saunders, 1992

Chirgwin and Hammerschlag 1992

Chirgwin K, Hammerschlag MR. Chlamydia pneumonia. In: Feigin RD, Cherry JD, eds. Textbook of pediatric infectious diseases. 3rd ed. Philadelphia: Saunders, 1992

Coblenz et al 1991

Coblenz CL, Babcook CJ, Alton D, Riley BJ, Norman G. Observer variation in detecting the radiologic features associated with bronchiolitis. Investig Radiol 1991;26:115-118

Cochrane Library 1998

Cochrane Library. Issue 2, 1998. Oxford: Update Software

Cohen 1992

Cohen ML. Epidemiology of drug resistance: implications for a post-antibiotic era. Science 1992;257:1050-1055

Com-Nougue, Rodary and Patte 1993

Com-Nougue C, Rodary C, Patte C. How to establish equivalence when data are censored: a randomised trial of treatments for B cell non-Hodgkin lymphoma. Stat Med 1993;12:1353-1364

Congeni and Nankeris 1978

Congeni BL, Nankeris GA. Diagnosis of pneumonia by counterimmuno-electrophoresis of respiratory secretions. Am J Dis Child 1978;132:684-687

Coolidge 1913

Coolidge WD. A powerful Roentgen ray tube with a pure electron discharge. Phys Rev 1913;2:450 quoted by Posner (1971)

Coulter 1992

Coulter JBS. Tuberculosis. In: Campbell AGM, McIntosh N, eds. Forfar and Arneil's textbook of paediatrics. 4th ed. Edinburgh: Churchill Livingstone, 1992

Courtoy, Lande and Turner 1989

Courtoy I, Lande AE, Turner RB. Accuracy of radiographic differentiation of bacterial from nonbacterial pneumonia. Clin Pediatr 1989;28:261-264

Dai et al 1995

Dai Y, Foy HM, Zhu Z, Chen B, Tong F. Respiratory rate and signs in roentgenographically confirmed pneumonia among children in China. Pediatr Infect Dis J 1995;14:48-50

Dally 1903

Dally JFH. On the use of Roentgen rays in the diagnosis of pulmonary disease. Lancet 1903;1:1800-1806

Datta et al 1987

Datta N, Kumar V, Kumar L, Singhi S. Application of case management to the control of acute lower respiratory infections in low-birth-weight infants: a feasibility study. Bull WHO 1987;65:77-82

Davies et al 1996

Davies HD, Wang EE, Manson D, Babyn P, Shuckett B. Reliability of the chest radiograph in the diagnosis of lower respiratory infections in young children. Pediatr Infect Dis J 1996;15: 600-604

Dawson et al 1990

Dawson KP, Long A, Kennedy J, Mogridge N. The chest radiograph in acute bronchiolitis. J Pediatr Child Health 1990;26:209-11

De Abreu 1939

De Abreu M. Collective fluorography. Radiology 1939;33:363-371

De Melker and Kuyvenhoven 1991

De Melker RA, Kuyvenhoven MM. Management of upper respiratory tract infection in Dutch general practice. Br J Gen Pract 1991;41:504-507

Department of Health 1995

Department of Health. Tuberculosis update. Epidemiological Comments 1995;22:13-17

Department of Health 1996a

Department of Health. Sixth national HIV survey of women attending antenatal clinics of the public health services in the Republic of South Africa, October 1996. Epidemiological Comments 1996;23:3-17

Department of Health 1996b

Department of Health. The South African tuberculosis control programme. Practical guidelines. Pretoria: Department of Health,1996

Detsky and Sackett 1985

Detsky AS, Sackett DL. When was a "negative" clinical trial big enough? How many patients you needed depends on what you found. Arch Int Med 1985;145:709-712

Eriksson et al 1986

Eriksson J, Nordshus T, Carlsen K-H, Ørstadvik I, Westvik J, Eng J. Radiological findings in children with respiratory syncitial virus infection: relationship to clinical and bacteriological findings. Pediatr Radiol 1986;16:120-122

Evidence-Based Medicine 1998

Purpose and procedure [editorial policy]. Evidence-Based Medicine 1998;3:66

Falade et al 1995

Falade AG, Tschäppeler H, Greenwood BM, Mulholland EK. Use of simple clinical signs to predict pneumonia in young Gambian children: the influence of malnutrition. Bull WHO 1995;73:299-304

Fauveau et al 1992

Fauveau V, Stewart MK, Chakraborty J, Khan SA. Impact on mortality of a community-based programme to control acute respiratory tract infections. Bull WHO 1992;70:109-16

Fisk 1928

Fisk EL. Roentgenology: the hand-maid of diagnosis. Radiology 1928;11:153-155

Fleisher, Ludwid and McSorley 1983

Fleisher G, Ludwid S, McSorley M. Interpretation of pediatric x-ray films by emergency department pediatricians. Ann Emerg Med 1983;12:153-158

Fleiss 1981

Fleiss JL. Statistical Methods for Rates and Proportions, 2nd ed. New York: John Wiley & Sons, 1981:212-225

Forgie et al 1991

Forgie IM, O'Neill KP, Lloyd-Evans N, Leinonen M, Campbell H, Whittle HC, Greenwood BM. Etiology of acute lower respiratory tract infections in Gambian children: II. Acute lower respiratory tract infection in children ages one to nine years presenting at the hospital. Pediatr Infect Dis J 1991;10:42-47

Fosarelli and DeAngelis 1987

Fosarelli PD, DeAngelis C. Outpatient radiographic exposure in the first five years of life. Clin Pediatr 1987;26:296-301

Franken et al 1995

Franken EA, Bergus GR, Koch TJ, Barbaum KS, Smith WL. Added value of radiologist consultation to family practitioners in the outpatient setting. Radiology 1995;197:759-762.

Friedman, Furberg and DeMets 1985

Friedman LM, Furberg CD, DeMets DL. Fundamentals of Clinical Trials. 2nd ed. Massachusetts: PSG Publishing Company, 1985:63

Friis et al 1990

Friis B, Eiken M, Hornsleth A, Jensen A. Chest X-ray appearances in pneumonia and bronchiolitis. Correlation to virological diagnosis and secretory bacterial findings. Acta Paediatr Scand 1990;79:219-25

Gadomski 1993

Gadomski AM. Potential interventions for preventing pneumonia among young children: lack of effect of antibiotic treatment for upper respiratory infections. Pediatr Infect Dis J 1993;12:115-120

Garenne, Ronsmans and Campbell 1992

Garenne M, Ronsmans C, Campbell H. The magnitude of mortality from acute respiratory infections in children under 5 years in developing countries. Wld Hlth Statist Quart 1992; 45:180-191

Garland 1949

Garland LH. On the scientific evaluation of diagnostic procedures. Radiology 1949;52:309-327

Garland 1959

Garland LH. Studies on the accuracy of diagnostic procedures. AJR 1959;82:25-38

Gleckman and Borrega 1997

Gleckman RA, Borrega F. Adverse reactions to antibiotics. Postgraduate Medicine 1997;101:97-108

Godlee 1992

Godlee F. Environmental radiation: a cause for concern? BMJ 1992;304:299-304

Gonzales, Steiner and Sande 1997

Gonzales R, Steiner JF, Sande MA. Antibitotic prescribing for adults with colds, upper respriatory tract infections, and bronchitis by ambulatory care physicians. JAMA 1997;278:901-904

Goran, Williamson and Gonnella 1973

Goran MJ, Williamson JW, Gonnella JS. The validity of patient management problems. Journal of Medical Education 1973; 48:171-177

Greene 1992

Greene R. Imaging the respiratory system in the first few years after the discovery of the x-ray: contributions of Francis H Williams, MD. AJR 1992;159:1-7

Grossman and Caplan 1988

Grossman LK, Caplan SE. Clinical, laboratory and radiological information in the diagnosis of pneumonia in children. Ann Emerg Med 1988; 17:43-46

Gurney 1995

Gurney JW. Why chest radiography became routine. Radiology 1995;195:245-246

Guyatt et al 1986

Guyatt GH, Tugwell PX, Feeny DH, Drummond MF, Haynes RB. The role of before-after studies of therapeutic impact in the evaluation of diagnostic technologies. J Chron Dis 1986;39:295-304

Guyatt, Sackett and Cook 1993

Guyatt GH, Sackett DL, Cook DJ for the Evidence-Based Medicine Working Group. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? JAMA 1993; 270: 2598-2601

Harari et al 1991

Harari M, Shann F, Spooner V, Meisner S, Carney M, De Campo J. Clinical signs of pneumonia in children. Lancet 1991;338:928-930

Haygood and Briggs 1992

Haygood TM, Briggs JE. World War II military led the way in screening chest radiography. Mil Med 1992;157:113-116

Health Systems Trust 1995

Health Systems Trust. South African Health Review 1995. Durban: Health Systems Trust, 1995

Health Systems Trust 1996

Health Systems Trust. South African Health Review 1996. Durban: Health Systems Trust, 1996

Health Systems Trust 1997

Health Systems Trust. South African Health Review 1997. Durban: Health Systems Trust, 1997

Henderson 1996

Henderson FW. Viral Respiratory Infections. In: Rudolph AM, Hoffman JIE, Rudolph CD, editors. Rudolph's Pediatrics. 20th ed. Stamford Appleton & Lange, 1996; 671-679

Hochstim 1967

Hochstim JR. A critical comparison of three strategies of collecting data from households. Journal of the American Statistical Association 1967;62:976-989

Hodges 1945

Hodges PC. Development of diagnostic X-ray apparatus during the first fifty years. Radiology 1945;45:438-448

Hoffman et al 1988

Hoffman M, Pick W, Joubert G, Yach D, Thomas T, Klopper JML. 1988. Morbidity profile of the Mamre community. S Afr Med J 1988;74:358-361

Hosmer and Lemeshow 1989

Hosmer DW, Lemeshow S. Applied logistic regression. New York; John Wiley & Sons, 1989

Howie 1976

Howie JGR. Clinical judgement and antibiotic use in general practice. BMJ 1976; 2:1061-1064

Hubbell et al 1985

Hubbell FA, Greenfield S, Tyler JL, Chetty K, Wyle FA. The impact of routine admission chest x-ray films on patient care. N Eng J Med 1985; 312:209-213

ICD-9 1988

International classification of diseases, ninth revision, clinical modification. Washington, DC; Public Health Service, US Dept of Health and Human Services, 1988

Irwig et al 1995

Irwig L, Macaskill P, Glasziou P, Fahey M. 1995. Meta-analytic methods for diagnostic test accuracy. J Clin Epidemiol 1995;48:119-130

Isaacs 1989

Isaacs D. 1989. Problems in determining the etiology of community-acquired childhood pneumonia. Pediatr Infect Dis J 1989;8:143-148

Jaeschke, Guyatt and Sackett 1994

Jaeschke R, Guyatt GH, Sackett DL for the Evidence-Based Medicine Working Group. Users' guides to the medical literature III How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? JAMA 1994;271:703-707

Jegathesan 1985

Jegathesan M. Practical issues in the determination of the aetiology of acute respiratory infections. In: Douglas RM, Kerby-Eaton E, eds. Acute respiratory infections in children. Proceedings of an international workshop, Sydney, Australia 1984. Adelaide: University of Adelaide, 1985

Johnson and Lilford 1990

Johnson N, Lilford RJ. Computerized automation of clinical trials. Baillière's Clin Obstet and Gynaecol 1990; 4:771-786

Kashland 1992

Kashland DE. The microbial wars. Science 1992;257:1021

Kattan et al 1977

Kattan M, Keens TG, Lappierre J-G, Levison H, Bryan C, Reilly BJ. Pulmonary function abnormalities in symptom-free children after bronchiolitis. Pediatrics 1977;59: 683-688

Khan et al 1990

Khan AJ, Khan, JA, Akbar M, Addiss DG. Acute respiratory infections in children: a case management intervention in Abbottabad District, Pakistan. Bull WHO 1990;68:577-585

Kiekara et al 1996

Kiekara O, Korppi M, Tanska S, Soimakallio S. Radiological diagnosis of pneumonia in children. Ann Med 1996;28:69-72

Kirwan et al 1983

Kirwan JR, Bellamy N, Condon H, Buchanan WW, Barnes CG. Judging "current disease activity" in rheumatoid arthritis – an international comparison. J Rheumatol 1983;10:901-905

Klassen et al 1997

Klassen TP, Sutcliffe T, Watters LK, Wells GA, Allen UD, Li MM. Dexamethasone in salbutamol-treated inpatients with acute bronchiolitis: a randomised controlled trial. J Pediatr 1997;130:191-196

Klein 1992

Klein JO. Bacterial pneumonias. In: Feigin RD, Cherry JD, eds. Textbook of pediatric infectious diseases. 3rd ed. Philadelphia: Saunders, 1992

Korner-Bitensky and Wood-Dauphinee 1995

Korner-Bitensky N, Wood-Dauphinee S. Barthel index information elicited over the telephone. Is it reliable? Am J Phys Rehabil 1995; 74:9-18

Korppi et al 1991

Korppi M, Leinonen M, Koskela M, Mäkelä PH, Saikku P, Launiala K. Bacterial infection in under school age children with expiratory difficulty. Pediatr Pulmonol 1991;10:254-259

Korppi et al 1993

Korppi M, Kiekara O, Heiskanen-Kosma T, Soimakallio S. Comparison of radiological findings and microbial aetiology of childhood pneumonia. Acta Paediatr 1993;82:360-363

Kramer, Roberts-Brauer and Williams 1992

Kramer MM, Roberts-Brauer R, Williams RL. Bias and "overcall" in interpreting chest radiographs in young febrile children. Pediatrics 1992;90:11-13

Kuhn 1990a

Kuhn JP. Pulmonary infection. In: Silverman FN, Kuhn JP, eds. Essentials of Caffey's pediatric x-ray diagnosis. Chicago: Year Book Medical Publishers, 1990

Kuhn 1990b

Kuhn JP. 1990a. Disorders of the peripheral airways and disturbances of pulmonary aeration. In: Silverman FN, Kuhn JP, eds. Essentials of Caffey's pediatric x-ray diagnosis. Chicago: Year Book Medical Publishers, 1990

Kunin 1993

Kunin CM. Resistance to antimicrobial drugs – a worldwide calamity. Ann Intern Med 1993;118:557-561

Kuyvenhoven et al 1984

Kuyvenhoven MM, Jacobs HM, Touw-Otten FWMM, Van Es JC. Written simulation of patient-doctor encounters. 3. Comparison of the performance in the simulation with prescription and referral data in reality. Fam Pract 1984;1:25-29

Kuyvenhoven, De Melker and Van der Velden 1993

Kuyvenhoven M, De Melker R, Van der Velden K. Prescriptions of antibiotics and prescribers' characteristics. A study into prescription of antibiotics in upper respiratory tract infections in general practice. Fam Pract 1993;10:366-370

Lam, Kleevans and Wong 1988

Lam TH, Kleevans JWL, Wong CM. Doctor-consultation in Hong Kong: a comparison between findings of a telephone interview with the general household survey. Community Medicine 1988;10:175-179

Lancet 1896

The new photography [annotation]. Lancet 1896;1:432-433

Lancet 1988

Pneumonia in chilhood [editorial]. Lancet 1988;1:741-743

Last 1988

Last JM, edited for the International Epidemiological Association. A dictionary of epidemiology. 2nd ed. New York: Oxford University Press, 1988

Leonidas 1987

Leonadas JC. Viral vs. bacterial pulmonary infections - radiographic differentiation. Pediatr Radiol 1987;17:174

Leowski 1986

Leowski J. Mortality from acute respiratory infections in children under 5 years of age: global estimates. World Hlth Statist Quart 1986;39:138-144

Leventhal 1979

Leventhal JM. Clinical decision-making of pediatric residents. Presented at the 19th meeting of the Ambulatory Pediatric Association, Atlanta, May 1,1979

MacFarlane et al 1997

MacFarlane J, Lewis SA, MacFarlane R, Holmes W. Contemporary use of antibiotics in 1089 adults with acute lower respiratory tract illness in general practice in the U.K.: implications for developing management guidelines. Respir Med 1997;91:427-434

Mainous, Hueston and Clark 1996

Mainous AG, Hueston WJ, Clark JR. Antibiotics and upper respiratory infection. Do some folks think there is a cure for the common cold? J Fam Pract 1996;42:357-361

Marcus and Telesky 1983

Marcus AC, Telesky CW. Non-participation in telephone follow-up interviews. Am J Public Health 1983;73:72-77.

Margolis and Gadomski 1998

Margolis P, Gadomski A. Does this infant have pneumonia? JAMA 1998;279:308-313

Martin, Moskowitz and Milbrath 1979

Martin JE, Moskowitz M, Milbrath JR. Breast cancer missed by mammography. AJR 1979;132:737-739

McCaig and Hughes 1995

McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. JAMA 1995;273:214-219

McCarthy et al 1981

McCarthy PL, Spiesel SZ, Stashwick CA, Ablow RC, Masters SJ, Dolan TF. Radiographic findings and etiologic diagnosis in ambulatory childhood pneumonias. Clin Paediatr 1981;20:686-691.

McConnachie and Roghmann 1985

McConnachie KM, Roghmann KJ. Predicting clinically significant lower respiratory tract illness in childhood following mild bronchiolitis. Am J Dis Child 1985;139:625-631

McKenzie 1992

McKenzie S. Respiratory infections. In: Campbell AGM, McIntosh N, editors. Forfar and Arneil's Textbook of Paediatrics. 4th ed. Edinburgh Churchill Livingstone, 1992; 565-656

Medical Association of South Africa 1996

Medical Association of South Africa. 1996 Guide to fees for medical services. Cape Town: The Association, 1996

Melbye and Dale 1992

Malbye H, Dale K. Interobserver variability in the radiographic diagnosis of adult outpatient pneumonia. Acta Radiol 1992;33;79-81

Members of the Early Cancer Cooperative Study 1984

Members of the Early Cancer Cooperative Study. Early lung cancer detection: summary and conclusions. Am Rev Respir Dis 1984;130:565-570

Milner and Murray 1989

Milner AD, Murray M. Acute bronchiolitis in infancy: treatment and prognosis [editorial]. Thorax 1989;44:1-5

Mohamed et al 1995

Mohamed H, Valentine N, Khosa S, McIntyre D. Health utilisation in a spectrum of suburbs in the Cape metropole. Cape Town: Health Economics Unit, Department of Community Health, University of Cape Town; Nov, 1995. Working Paper No 14

Moher et al 1998

Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, Tugwell P, Klassen TP. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? Lancet 1998;352:609-613

Morell and Roland 1990

Morell DC, Roland MO. Analysis of referral behaviour: responses to simulated case histories may not reflect real clinical behaviour. Br J Gen Pract 1990; 40: 182-185

Mtango and Neuvians 1986

Mtango FDE, Neuvians D. Acute respiratory infections in children under 5 years: control project in Bagamoyo District, Tanzania. Trans R Soc Trop Med Hyg 1986;80:851-8

Mulholland et al 1992

Mulholland EK, Simoes EAF, Costales MOD, McGrath EJ, Manalac EM, Gove S. Standardised diagnosis of pneumonia in developing countries. Pediatr Inf Dis J 1992;11:77-81

Nebot et al 1994

Nebot M, Celentano DD, Burtwell L, Davis A, Davis M, Polacsek M, Santelli J. AIDS and behavioural risk factors in women in inner city Baltimore: a comparison of telephone and face to face surveys. J Epidemiol Community Health 1994; 48:412-418

Neu 1992

Neu HC. The crisis in antibiotic resistance. Science 1992;257:1064-1073

Neue Freie Presse 1896

Neue Freie Presse 1896 Jan 5; Vienna

Njalsson et al 1995

Njalsson T, Sigurdsson JA, Sverrisson G, Brekkan A. Use of X-rays in family practice. A multicentre study. Fam Pract 1995;12:143-148

Norman and Feightner 1981

Norman GR, Feightner JW. A comparison of behaviour on simulated patients and patient management problems. Medical Education 1981;15:26-32

Norman et al 1992

Norman GR, Brooks LR, Coblenz CL, Babcook CJ. The correlation of feature identification and category judgements in diagnostic radiology. Memory and Cognition 1992;20:344-355

Nyquist et al 1998

Nyquist A-C, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. JAMA 1998;279:875-877

Orenstein 1996

Orenstein DM. Bronchiolitis. In: Behrman RE, Kliegman RM, Arvin AM, editors. Nelson Textbook of Pediatrics. 15th ed. Philadelphia: Saunders, 1996; 1211-1213

O'Toole et al 1986

O'Toole BI, Battistutta AL, Long A, Crouch K. A comparison of costs and data quality of three health survey methods: mail, telephone and personal home interview. Am J Epidemiol 1986;124:317-328

Page and Fielding 1980

Page GG, Fielding DW. Performance on PMPs and performance in practice: are they related? Journal of Medical Education 1980;55:529-537

Panday et al 1991

Panday MR, Daulaire NMP, Starbuck ES, Houston RM, McPherson K. Reduction in total under-five mortality in western Nepal through community-based antimicrobial treatment of pneumonia. Lancet 1991;338:993-997

Parmar and Machin 1995

Parmar MKB, Machin D. Survival analysis: a practical approach. New York: Wiley, 1995: 87-88

Peto and Peto 1972

Peto R, Peto J. Asymptotically efficient rank invariant test procedures. Journal of the Royal Statistical Society 1972;Series A 135:185-207

Pio, Loewski and Ten Dam 1985

Pio A, Loewski J, Ten Dam HG. The magnitude of the problem of acute respiratory infections. In: Douglas RM, Kerby-Eaton E, eds. Acute respiratory infections in children. Proceedings of an international workshop, Sydney, Australia 1984. Adelaide: University of Adelaide, 1985

Pocock 1982

Pocock SJ. Statistical aspects of clinical trial design. The Statistician 1982;31:1-18

Posner 1971

Posner E. The early years of chest radiology in Britain. Thorax 1971;26:233-239

Power et al 1997

Power M, Els R, Zwarenstein M, Lewin S, Vundule C, Mostert J. Most patients attending a "walk-in" clinic at Red Cross War Memorial Children's Hospital could safely be managed at primary care level. S Afr Med J 1997;87:36-41

Prescott 1938

Prescott SC. 1938. Frances Henry Williams. Proc Am Acad of Arts Sci 1938;134:399-402 quoted by Greene (1992)

Prober 1996

Prober CG. Pneumonia. In: Behrman RE, Kliegman RM, Arvin AM, eds. Nelson textbook of pediatrics. 15th ed. Philadelphia: Saunders, 1996

Provincial Administration of the Western Cape 1995

Provincial Administration of the Western Cape. Draft Provincial Health Plan. Cape Town: Provincial Administration of the Western Cape, 1995

Provincial Reference Group 1997

Provincial Reference Group: Maternal, Child and Women's Health. Acute Respiratory Infections. Cape Town: Provincial Administration of the Western Cape, 1997

Redd et al 1994

Redd SC, Vreus R, Metsing M, Mohobane PH, Patrick E, Moteetee M. Clinical signs of pneumonia in children attending a hospital outpatient department in Lesotho. Bull WHO 1994;72:113-118.

Reichman 1975

Reichman LB. Tuberculosis screening and chest x-ray films. Chest 1975;68:448-451

Richter and Seddon 1998

Richter H, Seddon P. Early nebulised budesonide in the treatment of bronchiolitis and the prevention of postbronchiolitic wheezing. J Pediatr 1998;132:849-853

Rodriguez et al 1997

Rodriguez WJ, Gruber WC, Groothuis JR, Simoes EAF, Rosas AJ, Lepow M, Kramer A, Hemming V; and the RSV-IGIV Study Group. Respiratory syncitial virus immune globulin treatment of RSV lower respiratory tract infection in previously healthy children. Pediatrics 1997;100:937-942

Roesin et al 1990

Roesin R, Sutanto A, Sastra K, Winarti. ARI intervention study in Kediri, Indonesia. (A summary of study results). Bull Int Union Tuberculosis Lung Disease 1990;65:23

Röntgen 1895

Röntgen WC. Über eine neue Art von Stralen. Vorläufige Mitteilung. Sitzungberichte der Wurzburger Physik-mediz Gesellschaft. 1895;29:132 quoted by Posner (1971)

Rothman 1986

Rothman KJ. 1986. Modern Epidemiology. Boston: Little, Brown and Co, 1986

Royal College of Radiologists 1993

Royal College of Radiologists. Making the best use of a department of clinical radiology. Guidelines for doctors. 2nd ed. London: Royal College of Radiologists, 1993

Sackett et al 1991

Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. A basic science for clinical medicine. 2nd ed. Boston; Little Brown and Company, 1991

Sackett et al 1997

Sackett DL, Richardson WS, Rosenberg W, Haynes RB (eds). Evidence-based medicine. How to practice and teach EBM. New York: Churchill Livingstone, 1997

Sazawel and Black 1992

Sazawel S, Black RE. Meta-analysis of intervention trials on case-management of pneumonia in community settings. Lancet 1992;340:528-533

Schulz 1995

Schulz KF. Subverting randomization in controlled trials. JAMA 1995;274:1456-1458

Schulz 1996

Schulz KF. Randomised trials, human nature, and reporting guidelines. Lancet 1996;348:596-598

Schulz et al 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodical quality associated with estimates of treatment effects in controlled trials. JAMA 1995;273:408-412

Seppälä et al 1997

Seppälä H, Klaukka T, Vuopio-Varkila J, Muotiala A, Helenius H, Lager K Huovinen P and the Finnish Study Group for Antimibrobial Resistance. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. N Eng J Med 1997;337: 441-446

Shann et al 1984

Shann F, Gratten M, Germer S, Linneman V, Hazlet D, Payne R. Aetiology of pneumonia in Goroka Hospital, Papua New Guinea. Lancet 1984;2:537-541

Shinar et al 1987

Shinar D, Gross CR, Bronstein KS, Licata-Gehr EE, Eden DI, Cabrera AR. Reliability of the activities of daily living scale and its use in telephone interview. Arch Phys Rehabil 1987;67:723-728.

Siemiatycki 1979

Siemiatycki J. A comparison of mail, telephone and home interview strategies for household health surveys. Am J Public Health 1979;69:238-245.

Simpson et al 1974

Simpson W, Hacking PM, Court SDM, Gardner PS. The radiological findings in respiratory syncitial virus infection in children. Part I. Definitions and interobserver variation in assessment of abnormalities on the chest x-ray. Pediatr Radiol 1974;2:97-100

Singhi et al 1994

Singhi S, Dhawan A, Kataria S, Walia BNS. Validity of clinical signs for the identification of pneumonia in children. Ann Trop Paediatr 1994;14:53-58

Slade, Brennan and Spencer 1995

Slade GD, Brennan D, Spencer AJ. Methodological aspects of a computer-assisted telephone interview survey of oral health. Aust Dent J 1995;40:306-310

South Africa 1996

South Africa. Central Statistical Services. RSA statistics in brief 1996. Pretoria: Central Statistical Services, 1996

South Africa 1997

South Africa. Central Statistical Services. Recorded deaths 1994. Pretoria: Central Statistical Services, 1997. CSS report no 03-09-01 (1994)

Stein et al 1996

Stein AD, Courval JM, Lederman RI, Shea S. Reproducibility of responses to telephone interviews: demographic predictors of discordance in risk factor status. Am J Epidemiol 1995;141:1097-1105.

Stephenson, Henry and Norman 1988

Stephenson MJ, Henry N, Norman GR. Factors influencing antibiotic use in acute respiratory tract infections in family practice. Can Fam Physician 1988;34:2149-2152

Stickler, Hoffman and Taylor 1984

Stickler GB, Hoffman AD, Taylor WF. Problems in the clinical and roentgenographic diagnosis of pneumonia in young children. Clin Paediatr 1984;23:398-399

Swischuk and Hayden 1986

Swischuk LE, Hayden CK. Viral vs. bacterial pulmonary infections in children. (Is roentgenographic differentiation possible?). Pediatr Radiol 1986;16:278-284

Taylor et al 1995

Taylor JA, Del Beccaro M, Done S, Winters W. Establishing clinically relevant standards for tachypnoea in febrile children younger than 2 years. Arch Pediatr Adolesc Med 1995;149:283-287

Telkom SA Limited 1998

Telkom SA Limited. Annual report 1997/8. Pretoria: Telkom, 1998

Turner et al 1987

Turner RB, Lande AE, Chase P, Hilton N, Weinberg D. Pneumonia in pediatric outpatients: cause and clinical manifestations. J Pediatr 1987;111:194-200

United Nations 1988

United Nations. Sources, effects and risks of ionizing radiation. United Nations Scientific Committee on the Effects of Atomic Radiation 1988 report to the General Assembly, with annexes. New York: United Nations, 1988

United Nations 1993

United Nations. Sources and effects of ionizing radiation. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1993 report to the General Assembly, with scientific annexes. New York: United Nations, 1993

Usha, Katariya and Walia 1990

Usha N, Katariya S, Walia BNS. Simple clinical signs of lower respiratory infection. Trop Doct 1990;20:158-160

Vetter et al 1996

Vetter KM, Djomand G, Zadi F, Diaby L, Brattegaard K, Timité M, Andoh J, Adou JA, De Cock KM and Project Retro-CI. Clinical spectrum of human immunodeficiency virus disease in children in a West African city. Pediatr Infect Dis J 1996;15:438-442

Von Schirnding, Yach and Klein 1991

Von Schirnding YER, Yach D, Klein M. Acute respiratory infections as an important cause of childhood deaths in South Africa. S Afr Med J 1991;80:79-82

Wade W 1896

Wade W. The new kind of radiation [letter] BMJ 1896;1:362

Wagner et al 1976

Wagner EH, Greenberg RA, Imrey PB, Williams CA, Wolf SH, Ibraham MA. Influence of training and experience on selecting criteria to evaluate medical care. N Eng J Med 1976;294:871-876

Wahlgren et al 1984

Wahlgren H, Eriksson M, Mortensson W, Forsgren M, Melén B. Isolation of pathogenic bacteria from the nasopharynx of children with respiratory syncitial virus infection. Scand J Infect Dis 1984;16:139-143

Walsham 1901

Walsham H. Discussion on the use of the Röntgen rays in the diagnosis of pulmonary tuberculosis. In Trans Br Congr Tuberc 1901;3:267 quoted by Posner (1971)

Ward 1896

Ward HS. Practical radiography. A hand book of the applications of the X rays. London: Photogram, 1896 quoted by Posner (1971)

Weeks et al 1983

Weeks MF, Kulka RA, Lessler JT, Whitmore RW. Personal versus telephone surveys for collecting household health data at the local level. Am J Public Health 1983;73:1389-1394

Weinberger et al 1994

Weinberger M, Nagle B, Hanlon JT, Samsa GP, Schmader K, Landsman PB, Uttech KM, Cowper PA, Cohen HJ, Feussner JR. Assessing health-related quality of life in elderly outpatients: telephone versus face-to-face administration. J Am Geriatr Soc 1994;42:1295-1299

Welliver and Cherry 1992

Welliver RC, Cherry JD. Bronchiolitis and infectious asthma. In: Feigen RD, Cherry JD, eds. Textbook of pediatric infectious diseases. 3rd ed. Philadelphia: Saunders, 1992

WHO Expert Committee 1974

WHO Expert Committee on Tuberculosis. Ninth report. Geneva: World Health Organisation, 1974. WHO Technical Report Series No. 552

WHO Scientific Group 1983

WHO Scientific Group on the Indications for and Limitations of Major X-ray Diagnostic Investigations. A rational approach to radiodiagnostic investigations. Geneva: World Health Organization, 1983. WHO Technical Report Series No. 689

Wildin, Chonmaitree and Swischuk 1988

Wildin SR, Chonmaitree T, Swischuk LE. Roentgenographic features of common pediatric viral respiratory tract infections. AJDC 1988;142:43-46

Williams 1901

Williams FH. The Roentgen rays in medicine and surgery. New York: Macmillan, 1901 quoted by Greene (1992)

Windak et al 1996

Windak A, Tomasik T, Jacobs HM, de Melker RA. Are antibiotics over-prescribed in Poland? Management of upper respiratory tract infections in primary health care region of Warszawa, Wola. Fam Pract 1996;13:445-449

Wise et al 1998

Wise R, Hart A, Cars O, Streulens M, Helmuth R, Huovinen P, Sprenger M. Antimicrobial resistance. BMJ 1998;317:609-610

Wohl 1990

Wohl ME. Bronchiolitis. In:Chernick V, Kendig EL, eds. Kendig's disorders of the respiratory tract in children. 5th ed. Philadelphia; Saunders, 1990

Woolcock and Peat 1985

Woolcock AJ, Peat JK. The relationship between acute respiratory infections and chronic respiratory disease. In: Douglas RM, Kerby-Eaton E, eds; Acute respiratory infections in childhood. Proceedings of an international workshop, Sydney, Australia 1984. Adelaide: University of Adelaide, 1985

World Bank 1993

World Bank. World development report 1993. Investing in health. Oxford: Oxford University Press, 1993

World Bank 1997

World Bank. World development report. New York: Oxford University Press, 1997:214-215

World Health Organisation 1990

World Health Organisation. Acute respiratory infections in children: Case management in small hospitals in developing countries. A manual for doctors and other senior health workers. Geneva: World Health Organization, 1990 WHO/ARI/90.5

World Health Organisation 1991

World Health Organisation. Technical bases for the WHO recommendations on the management of pneumonia in children at first-level health facilities. Geneva: World Health Organization, 1991. WHO/ARI/91.20

World Health Organisation 1995

World Health Organisation. The management of acute respiratory infections in children. Practical guidelines for outpatient care. Geneva: World Health Organization, 1995

Yaffe, Shapiro and Fuchsberg 1978

Yaffe R, Shapiro S, Fuchsberg RR, Rohde CA. Medical economics survey-methods study: cost-effectiveness of alternative survey strategies. Med Care 1978;16:641-659

Appendices

Appendix 1

The financial cost of chest radiography to Red Cross Children's Hospital

A.1.1 Aim

To determine the financial cost to the hospital of chest radiography performed at Red Cross Children's Hospital

A.1.2 Methods

Only financial costs to the hospital were measured. Direct costs to the patients and social costs such as the loss of earnings of those caring for sick children were not considered

Unless otherwise stated, costs were for the hospital financial year April 1996 to March 1997. Costs measured were for both antero-posterior and lateral films.

The hospital did not keep specific records of the number of chest radiographs performed. Their number was thus calculated using the estimated proportion of all investigations performed which were chest radiographs (estimated by the chief radiographer and the senior radiologist to be 70%).

A.1.2.1 Capital costs

A.1.2.1.1 Equipment

The average replacement costs per year were calculated. The current replacement costs and the expected useful life of the equipment were obtained from the suppliers. For shared equipment, costs attributable to chest radiography were apportioned proportionally according to the number of films processed.

A.1.2.1.2 Buildings

The average annual replacement cost of building space used for chest radiography was calculated. For shared space, costs attributable to chest radiography were apportioned proportionally, according to the estimated proportion of time spent on chest radiography by shared staff (estimated by the chief radiographer at 50%). The current replacement cost per square metre was obtained from a current building project at the hospital. A twenty-year useful life of the buildings was assumed.

A.1.2.2 Recurrent costs

A.1.2.2.1 Personnel

Actual salaries, including all benefits, were used for radiology staff other than radiologists. Detailed information was available only from July 1996, so the period July 1996 to June 1997 was studied. For staff performing functions in addition to chest radiography, costs attributable to chest radiography were calculated according to the proportion of time spent on chest radiography by shared staff (estimated by the chief radiographer at 50%).

The diverse nature of radiologists' duties complicated the estimation of the proportion of their time spent on chest radiography. Radiologist time was thus determined using the senior radiologist's estimates of the average time taken to report on a chest radiograph by specialists and registrars (three and five minutes respectively). The time spent by specialists relative to registrars on such reporting was assumed to be in proportion to the number of posts (two specialists and three registrars). The cost of radiologist time was calculated using a 40-hour week, with overtime allowances excluded. (Chest radiographs are seldom reported on after-hours.)

Clinical consultations with chest radiography took two minutes longer, on average, than those without (Section 4.2.6). The cost of the additional two minutes of clinician time was thus included in the costing. Actual salaries were used, with overtime allowances included, where applicable. The calculation was based on a 56-hour week for full time staff receiving an overtime allowance and a 40-hour week for full-time staff not receiving an overtime allowance. No attempt was made to estimate other outpatient expenditure.

A.1.2.2.2 Supplies

Actual costs for the financial year were used. For supplies used for purposes in addition to chest radiography, the costs attributable to chest radiography were apportioned pro rata.

A.1.2.2.3 Maintenance

Mean actual expenditure over a two-year period from August 1995 to July 1997 was taken. The two-year period was used to reduce the effect of any unusual maintenance

expenditure. The period measured was chosen because the records for this period were conveniently available.

A.1.2.3 Administration

Administrative expenses were calculated for the hospital as a whole, and assigned proportionally to radiology. Assignment was performed according to salary costs of radiology relative to the hospital as a whole. (Relative surface area could not be used because information on the total surface area of hospital buildings was not available.)

A.1.2.3.1 Personnel

Actual expenditure on administrative salaries, including all benefits, was used.

A.1.2.3.2 Consumables

Actual expenditure on consumables was used, after specific radiological supplies had been deducted. Records were available for five months only. Annual expenditure was calculated pro rata.

A.1.2.3.3 Utilities

Actual expenditure on telephones, electricity and water was used.

A.1.2.4 Sensitivity analysis

The calculation of salaries was based on imprecise estimations of the proportion of time spent by staff on chest radiography and the rate at which radiologists reported on radiographs. In order to assess the effect of different assumptions on estimated personnel costs, the calculations were repeated using assumptions that were judged to be the highest and lowest reasonable estimates. The estimates used in the combinations that would result in the highest and lowest overall personnel costs are shown in Table A.1.1.

TABLE A.1.1 Estimates used in the sensitivity analysis

	Best estimate	Highest reasonable estimate	Lowest reasonable estimate
Proportion of time spent on chest radiographs (non-radiologists)	50%	60%	40%
Chest radiographs reported per hour	Specialist 20 Registrar 12	Specialist 24 Registrar 14	Specialist 16 Registrar 10

A.1.3 Results

The average and marginal unit costs of chest radiography are summarised in Table A.1.2.

TABLE A.1.2 Average and marginal unit costs of chest radiography (antero-posterior and lateral views).

	Total annual cost	Average unit cost	Marginal unit cost
Point estimate	R 1 613 737	R 58.75	R 8.47
Sensitivity analyses			
High	R 1 877 212	R 68.34	R 9.69
Low	R 1 348 413	R 49.08	R 7.23

The average unit cost of an antero-posterior and lateral chest radiograph was R58.75 ($12.95, £8.29 on 30 September 1996) and the marginal unit cost R8.47 ($1.87, £1.20)

A breakdown of the costs are shown in Table A.1.3. A breakdown of sensitivity analyses is shown in Tables A.1.4 and A.1.5.

TABLE A.1.3 The estimated financial cost to the hospital of chest radiography at Red Cross Children's Hospital

			Annual cost	Average unit cost	Marginal unit cost
Capital costs					
	Equipment		75 582	2.75	
	X-ray machine	30 000			
	Film processors	45 582			
	Buildings		44 082	1.60	
Recurrent costs					
	Personnel		1 047 139	38.12	
	Radiologists	144 487			
	Radiographers	516 655			
	Other radiological	341 904			
	Clinicians	44 093			
	Supplies		63 012	2.29	2.29
	Maintenance		83 446	3.04	
	Administration		300 476	10.94	
	Personnel	130 932			
	Utilities	5 102			0.19
	Consumables	164 442			5.99
TOTAL			**R 1 613 737**	**R 58.75**	**R 8.47**

TABLE A.1.4 Sensitivity analysis of the cost of chest radiography: lower estimates.

			Annual cost	Average unit cost	Marginal unit cost
Capital costs					
	Equipment		75 582	2.75	
	X-ray machine	30 000			
	Film processors	45 582			
	Buildings		32 266	1.28	
Recurrent costs					
	Personnel		853 726	31.07	
	Radiologists	122 786			
	Radiographers	413 324			
	Other radiological	273 523			
	Clinicians	44 093			
	Supplies		63 012	2.29	2.29
	Maintenance		83 446	3.04	
	Administration		240 381	8.75	
	Personnel	104 746			
	Utilities	4 082			0.15
	Consumables	131 554			4.79
TOTAL			**R 1 348 413**	**R 49.08**	**R 7.23**

TABLE A.1.5 Sensitivity analysis of the cost of radiography: higher estimates.

			Annual cost	Average unit cost	Marginal unit cost
Capital costs					
	Equipment		75 582	2.75	
	X-ray machine	30 000			
	Film processors	45 582			
	Buildings		52 889	1.93	
Recurrent costs					
	Personnel		1 241 713	45.20	
	Radiologists	176 351			
	Radiographers	619 985			
	Other radiological	401 284			
	Clinicians	44 093			
	Supplies		63 012	2.29	2.29
	Maintenance		83 446	3.04	
	Administration		360 570	13.13	
	Personnel	157 118			
	Utilities	6 122			0.22
	Consumables	197 330			7.18
TOTAL			**R 1 877 212**	**R 68.34**	**R 9.69**

Sensitivity analyses using higher and lower estimates produced a highest reasonable estimate of R68.34 ($15.07, £9.65) with a marginal cost of R 9.69 ($2.14, £1.37). The lowest reasonable estimate was R49.08 ($10.82, £6.93) with a marginal cost of R7.23 ($1.59, £1.02).

A.1.4 Discussion

Only direct costs to the hospital were calculated. Indirect costs to patients and caregivers of time spent waiting for the radiograph to be taken and to see the clinician for radiograph review were not included.

The estimated cost probably represents a lower than average cost to the health services, given the economies of scale in a large busy hospital dealing exclusively with children. The Scale of Benefits paid by the Representative Association of Medical Schemes (RAMS) in South Africa for a chest radiograph in 1996 was R59.20. The fee recommended by the Medical Association of South Africa was R144.70 (Medical Association of South Africa 1996).

Costs will vary widely according to the setting. If radiological facilities are not available at the point of service and referral to another facility for the examination is necessary, the costs to the health services, the patient and society increase markedly. Transport to the referral facility becomes necessary, as does a repeat consultation by a doctor at the referral facility.

The costing of the performance of a chest radiograph was planned as part of the trial, to enable an estimation of the cost effectiveness of the procedure. The finding of no effect of radiography in the trial makes the issue of cost effectiveness superfluous, except that the estimated cost will give health managers and clinicians an indication of savings that are potentially achievable by avoiding radiography.

Appendix 2

Electronic literature search strategies

A.2.1 Literature review

A.2.1.1 Observer variation

A.2.1.1.1 MEDLINE

1 observer variation/
2 radiography, thoracic/
3 radiography/
4 2 or 3
5 intraobserver.tw
6 interobserver.tw
7 5 or 6
8 1 or 7
9 bronchiolitis/ra
10 pneumonia/ra
11 respiratory tract infections/ra
12 9 or 10 or 11
13 4 and 8
14 12 or 13
15 limit 14 to age 0-18 years

A.2.1.1.2 HealthSTAR (URL: http://www.nlm.nih.gov/databases/freemedl.html)

1 exp pneumonia
2 exp respiratory tract infections
3 exp bronchiolitis
4 1 or 2 or 3
5 radiography
6 4 and 5
7 limit 6 to age 0-18 years

A.2.1.2 Differentiation of bacterial from viral pneumonia

A.2.1.2.1 MEDLINE

1 predictive value of tests/
2 "sensitivity and specificity"/
3 sensitivity.tw
4 specificity.tw
5 exp probability
6 1 or 2 or 3 or 4 or 5
7 pneumonia/ra
8 pneumonia, viral/ra
9 pneumonia, bacterial/ra
10 respiratory tract infections/ra
11 bacterial infections/ra
12 7 or 8 or 9 or 10 or 11
13 6 and 12
14 limit 13 to age 0-18 years

A.2.1.2.2 HealthSTAR

As for "observer variation"

A.2.1.3 Severity of lower respiratory infection

A.2.1.3.1 MEDLINE

1. severity.tw
2. pneumonia/di,ra
3. respiratory tract infections/di,ra
4. bronchiolitis/di,ra
5. 2 or 3 or 4
6. limit 4 to age 0-18 years
7. 1 and 6

A.2.1.3.2 HealthSTAR

As for "observer variation"

A.2.1.4 Impact on clinical management and outcome

A.2.1.4.1 MEDLINE (Ovid)

1 pneumonia/di,ra,th
2 respiratory tract infections/di,ra,th
3 bronchiolitis/di,ra,th
4 1 or 2 or 3
5 limit 4 to age 0-18 years

A.2.1.4.2 MEDLINE (using Silver Platter)

This is the search strategy used in assembling the specialised trials register of the Cochrane Acute Respiratory Infections Group.

1 PT=RANDOMIZED-CONTROLLED-TRIAL
2 PT=CONTROLLED-CLINICAL-TRIAL
3 RANDOMIZED-CONTROLLED-TRIALS
4 RANDOM-ALLOCATION
5 DOUBLE-BLIND-METHOD
6 SINGLE-BLIND-METHOD
7 #1 or #2 or #3 or #4 or #5 or #6
8 TG=ANIMAL not (TG=HUMAN and TG=ANIMAL)
9 #7 not #8
10 PT=CLINICAL-TRIAL
11 explode CLINICAL-TRIALS / ALL
12 (CLIN* near TRIAL*) in TI
13 (CLIN* near TRIAL*) in AB
14 (singl* or doubl* or trebl* or tripl*) near (blind* or mask*)
15 (#14 in ti) or (#14 in ab)
16 PLACEBOS
17 PLACEBO* in TI
18 PLACEBO* in AB
19 RANDOM* in TI
20 RANDOM* in AB
21 RESEARCH-DESIGN
22 volunteer*
23 #10 or #11 or #12 or #13 or #15 or #16 or #17 or #18 or #19 or #20
24 or #21 or #22
25 #23 not #8
26 #24 not #9
27 #9 or #25
28 explode "RESPIRATORY-TRACT-INFECTIONS"/ all subheadings
29 #27 not (TUBERCULOSIS* in MESH)

30 explode "OTITIS-MEDIA"/ all subheadings
31 #28 or #29
32 explode "NEOPLASMS"/ all subheadings
33 #30 not #31
34 explode "ASTHMA"/ all subheadings
35 #32 not #33
36 explode "CYSTIC-FIBROSIS"/ all subheadings
37 #34 not #35
38 explode "MENINGITIS-BACTERIAL"/ all subheadings
39 explode "MENINGOCOCCAL-INFECTIONS"/ all subheadings
40 #36 or #37 or #38
41 #26 and #39

A.2.1.4.3 HealthSTAR (URL: http://www.nlm.nih.gov/databases/freemedl.html)

1 exp pneumonia
2 exp respiratory tract infections
3 exp bronchiolitis
4 1 or 2 or 3
5 radiography
6 4 and 5
7 limit 6 to age 0-18 years
8 clinical trial
9 randomized clinical trial
10 controlled clinical trial
11 8 or 9 or 10
12 6 and 11

A.2.2 Telephone questionnaires

1 *telephone/
2 *questionnaires/
3 *interviews/
4 2 or 3
5 1 and 4

A.2.3 Duration of illness in bronchiolitis

1 prognosis/
2 treatment outcome/
3 1 or 2
4 bronchiolitis/
5 bronchiolitis, viral/
6 4 or 5
7 3 and 6

Appendix 3

Experts contacted during the literature searches

1. Observer variation

Dr W Simpson, Department of Radiology, Newcastle General Hospital, Newcastle upon Tyne, United Kingdom

Gunnar B Stickler, MD, Mayo Clinic, Rochester, United States of America

Dr Elaine Wang, Clinical Epidemiology Unit, The Hospital for Sick Children, University of Toronto, Toronto, Canada

Unsuccessful attempts were made (by letter or facsimile to the last available address) to contact the following:

Catherine J Babcook, MD, Department of Radiology, McMaster University Medical Centre, Hamilton, Ontario, Canada

Michael S Kramer, MD, Department of Paediatrics, McGill University Faculty of Medicine, Montreal, Quebec, Canada

Geoffrey R Norman, Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

2. Differentiation between bacterial and other infection

Dr JF de Campo, Department of Radiology, Royal Children's Hospital, Melbourne, Australia

Dr J Eriksson, Department of Radiology, Ullevål Hospital, Oslo, Norway

Dr Matti Korppi, Department of Paediatrics, Kuopio University Hospital, Kuopio, Finland

Dr P McCarthy, Department of Paediatrics, Yale University School of Medicine, New Haven, Connecticut, United States of America

Ronald B Turner, MD, Department of Paediatrics, Medical University of South Carolina, Charleston, South Carolina, United States of America

H Wahlgren, MD, Department of Radiology, St Goran's Hospital, Stockholm, Sweden

Unsuccessful attempts were made (by letter, email or facsimile to the last available address) to contact the following:

Dr D Isaacs, Department of Immunology and Infectious Diseases, New Children's Hospital, Westmead, New South Wales, Australia

3. Impact on clinical management and outcome

Dr Andrew Bush, Consultant Paediatric Chest Physician, Royal Brompton Hospital, London, United Kingdom

Dr John M Leventhal, Paediatrician and author of a key article, Department of Paediatrics, Yale School of Medicine, New Haven, United States of America

Dr Paul M McCarthy, author of a key article and Head: Section of General Pediatrics, Yale University School of Medicine, New Haven, United States of America

Dr K Mulholland, Division of Child Health and Development, World Health Organization, Geneva, Switzerland

Professor P Palmer, Professor of Radiology, University of California, Davis, Sacramento, California, United States of America and Member, Radiology Working Group, Programme for the Control of Acute Respiratory Infections, World Health Organization

Dr A Pio, Programme Manager, Division of Child Health and Development, World Health Organization, Geneva, Switzerland

Dr Frank Shann, Respiratory Paediatrician and key author, Royal Children's Hospital, Parkville, Victoria, Australia

Unsuccessful attempts were made (by letter or facsimile to the last available address) to contact the following:

Dr H Campbell, Medical Research Council Laboratories, Fajara, Banjul, The Gambia and Division of Child Health and Development, World Health Organization

Dr S Gove, Research Coordinator, Division of Child Health and Development, World Health Organization, Geneva, Switzerland

Dr Lindsay K Grossman, Paediatrician and author of a key article, Ohio State University College of Medicine, Columbus, Ohio, United States of America

Dr M Hendry, Pediatric Radiologist, Royal Hospital for Sick Children, Edinburgh, United Kingdom and Member, Radiology Working Group, Division of Child Health and Development, World Health Organization

Dr AC Lamont, Consultant Paediatric Radiologist, Leicester Royal Infirmary, Leicester, United Kingdom and Chairperson, Radiology Working Group, Division of Child Health and Development, World Health Organization

Appendix 4

CXR STUDY - ENROLMENT DATA

Study no. | | | |

[Patient sticker]

Date / /

Age	yrs mths	
Age 2mth - 4yr 11mth?	Yes / No	
Cough	Yes / No	
Duration of illness	days	
Duration less than 14d	Yes / No	
First visit	Yes / No	
Referred	No / Yes	
Drinking well	Yes / No	
TB contact	No / Yes	
Cyanosis	No / Yes	
Abnormally sleepy	No / Yes	
Stridor	No / Yes	
Chest indrawing	No / Yes	
Resp rate	/min	

If eligible so far, enter into book.

Weight	. kg	
Telephone	Yes / No	
Consent	Yes / No	

Phone number (W) (H) Preferred W H

Times to phone | Morning | Afternoon | Evening |

Contact person s name . . . . . .

If consent given:

i. stamp record sheet

ii. attach the randomisation envelope with the same number as the study number.

Appendix 5

CXR STUDY

PROCEDURE FOR DOCTORS

Consult with the patient just as you normally would, until the decision on whether to do an x-ray or not. Then:

1. **"Exclude if":** Check if any exclusion criteria listed are present (e.g. CCF. possible FB). If present, tick the appropriate block on the clinical record, forget about the trial, and place the numbered envelope **unopened** in the plastic sleeve on the wall.

   If you judge that failure to do a CXR would be dangerous to the patient, tick the "other" block among the exclusion criteria, note down the reason for exclusion, and exclude the patient as above. In other words, if you are not prepared to abide by a "No" allocation the patient should be excluded from the trial **before** opening the envelope.

2. **"CXR usually?":** Tick "Y" if you would normally have done a CXR (if the patient were not part of the trial), and "N" if not.

3. **Open the sealed envelope.**

   If it contains a *"CXR" sticker*, stick this in the appropriate place on the clinical record and order a CXR (even if you would not normally have done a CXR). Thereafter manage the patient as you judge best, with the help of the CXR

   If it contains a *"No" sticker*, stick this in the appropriate place on the clinical record, and manage the patient as you judge best, without the help of a CXR (even if you would normally have done a CXR).

4. At the end of the consultation (i.e. when writing up meds, if any), tick the appropriate "Diagnosis" block.

5. Apart from the decision regarding CXR, please manage the patient as you normally would.

6. Apart from filling in the box on the consultation sheet, no additional records are necessary.

George Swingler 12 February 1996

Appendix 6

RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL
MEDICAL OUTPATIENTS DEPARTMENT

Use sticker when available NAME: .....BIRTH DATE...../...../..... Folder Numer Race/Sex	Date...../...../.....	Last visit...../...../..... Temp o C
First doctor's stamp:	Weight kg centile	RTH card seen? Yes/No Up to date? Yes/No TB contact?

HISTORY, EXAMINATION, INVESTIGATIONS, INTERIM MANAGEMENT:

Interim plan

Diagnosis and problems (p.t.o. for more clinical notes)

1. ..... 2. .....

3. ..... 4. .....

Management and Treatment: .....

.....

.....

.....

.....

.....

.....

or equivalent

Immunisation needs	: given
measles	:
DWT	:
polio	:
Hep B	:

Follow-up Appointment on ..../..../.... to see .....

Referral Appointment on ..../..../.... to see .....

Last doctor's Stamp (if different)..... and signature .....

Red Cross War Memorial Children's Hospital

medical outpatients department

use sticker when available name ..... birth date / / folder number race / sex	date / /	last visit / /
	time	temp °C
first doctor's stamp:	weight kg	RTH card seen? *Yes/No* up to date? *Yes/No*
history, examination, investigations, interim management	centile	TB contact?

CXR STUDY

Exclude if:
- **Focal wheeze** ☐
- **History FB** ☐
- **CCF** ☐
- **Other.....** ☐

CXR usually? ☐ Y ☐ N

Diagnosis
- **Bronchiolitis** ☐
- **Pneumonia** ☐
- **Recurr wheeze** ☐
- **Other** ☐

interim plan

diagnoses and problems (pto for more clinical notes)

1 ..... 2 .....

3 ..... 4 .....

management and treatment

.....

.....

.....

.....

.....

Immunisation	
needs	*given*
measles	
DWT	
polio	
Hep B	

or equivalent

follow-up appointment on ___/___/___ to see .....

referal appointment on ___/___/___ to see .....

last doctor's stamp (if different) ..... and signature .....

JNIVERSITY OF CAPE TOWN

Department of Paediatrics & Child Health

Institute of Child Health

Red Cross War Memorial Children's Hospital
Rondebosch 7700, Cape
Republic of South Africa
Telephone: 0027-21-658-5111
0027-21-685-6529
Fax: 0027-21-689-1287

/ /96

attended Red Cross Children's Hospital today with her child. The child has been enrolled in a research study which involves telephoning the mother to find out how long the child takes to recover from the illness. In most cases, either 1 or 2 calls are necessary. Each interview should last 2-3 minutes.

We would be greatly appreciate it if your employee could be called to the telephone for this.

Thanking you

Yours sincerley,

DR GH Swingler

Paediatrician

Appendix 9

CXR STUDY - FOLLOW-UP QUESTIONAIRE

Study no. Patient name [M|F] Date enrolled / /

Phone no: (W) (H) Best [W|H] Times [Morn|Aft|Eve]

Contact person: Relationship:

Interview 1 Date / / Time

Good morning/afternoon/evening, I am XX phoning from Red Cross Hospital.

Are you <contact person>?
If not, *Is she available?*

Respondent **Relationship with patient**

As you will remember we agreed that someone would phone you to find out how <patient's name> is doing. This is a routine call and there is no reason to worry.

1. *Is <name> completely well yet?*

[No] → *What is still wrong?*
- Cough ☐
- Fever ☐
- Noisy breathing ☐
- Other _ _ _ _ _ _ ☐

_ _ _ _ _ _ _ _ _ _

[Yes] → *On what day was he/she last sick?* / /

2. *Since the visit to Red Cross Hospital have you needed to take <name> back to Red Cross Hospital for more treatment?*

[No] →

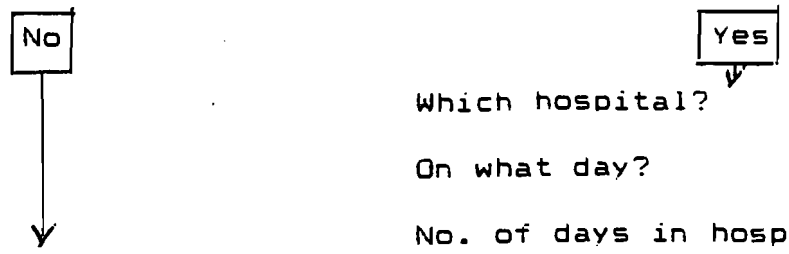
[Yes] →
- On what day? / /
- Did you have an appointment? [Yes|No]
- What type of transport did you use?
- How much did the transport cost?

3. *Since the visit to Red Cross Hospital have you needed to take <name> anywhere else for more treatment?*

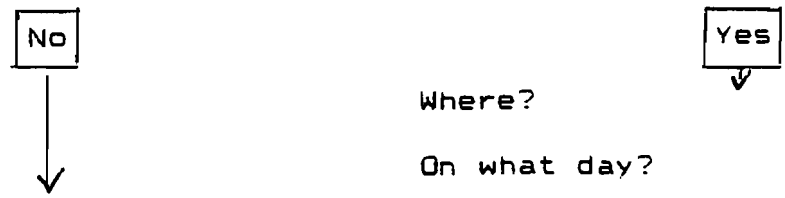
[No] →

[Yes] →
- Who?
- Where?
- On what day / /
- What type of transport did you use?
- How much did the transport cost?

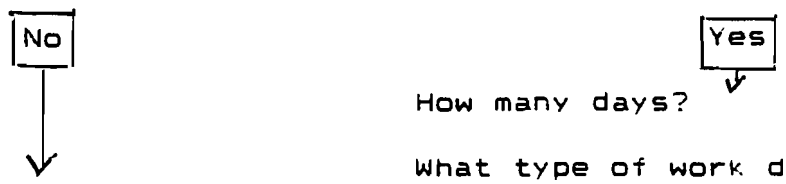
4. *Since the visit to Red Cross Hospital has <name> needed to be admitted to hospital?*



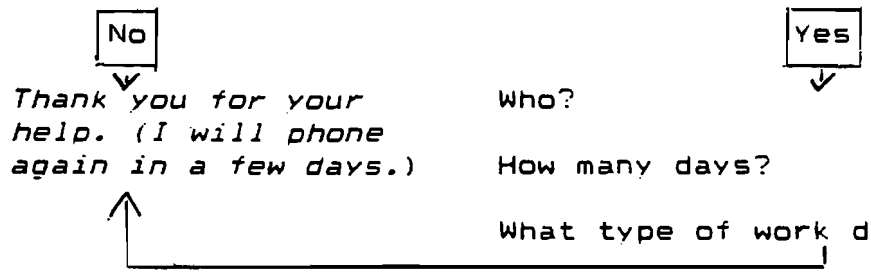
5. *Since the visit to Red Cross Hospital has <name> had a chest X-ray?*



6. *Since the visit to Red Cross Hospital have you needed to take time work because of <name>'s ilness?*



7. *Has anyone else needed to take time off work?*



Interview 2

Date / / Time

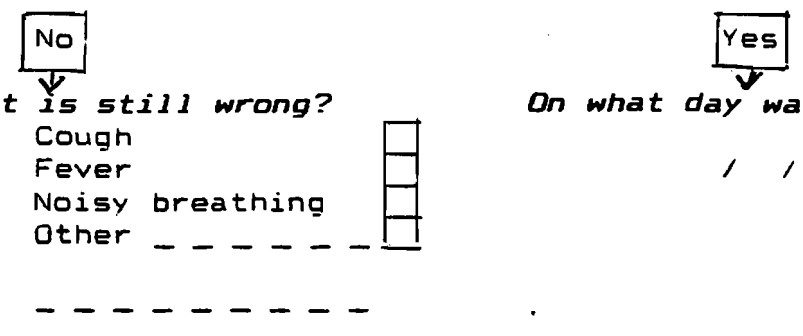
Good morning/afternoon/evening, I am XX phoning again from Red Cross Hospital.

Are you <contact person>?
If not, *Is she available?*

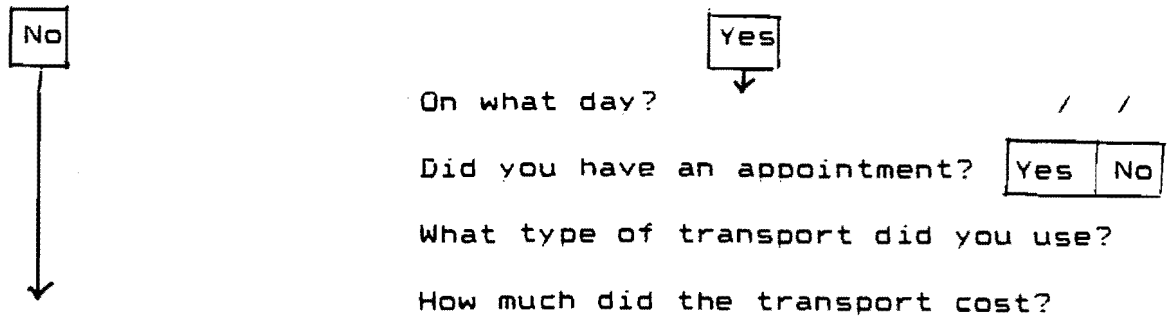
Respondent **Relationship with patient**

As you will remember I phoned a few days ago to find out how <patient's name> was doing.

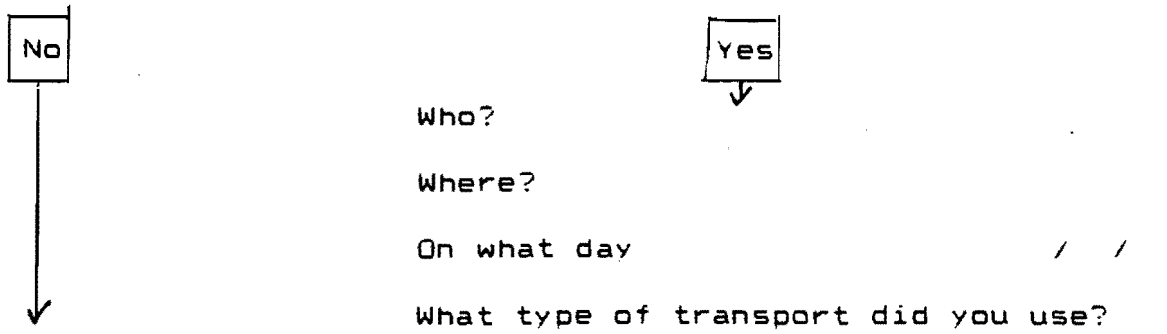
1. *Is <name> completely well yet?*



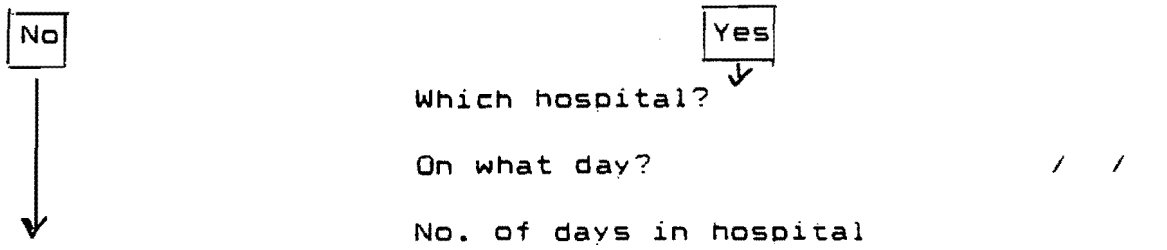
2. *Since my last call have you needed to take <name> back to Red Cross Hospital for more treatment?*



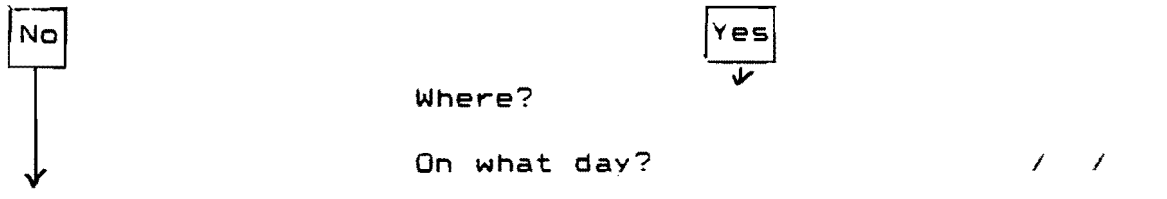
3. *Since my last call have you needed to take <name> anywhere else for more treatment?*



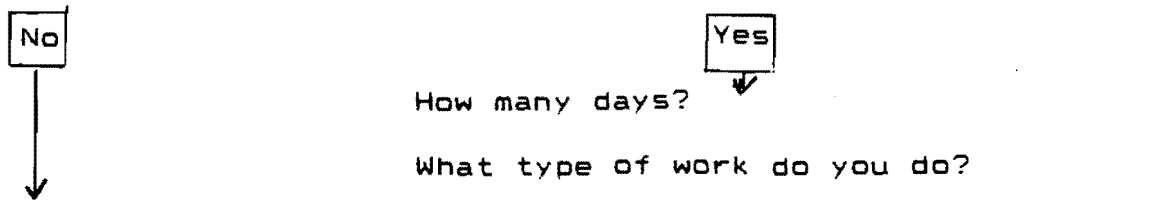
4. *Since my last call has <name> needed to be admitted to hospital?*



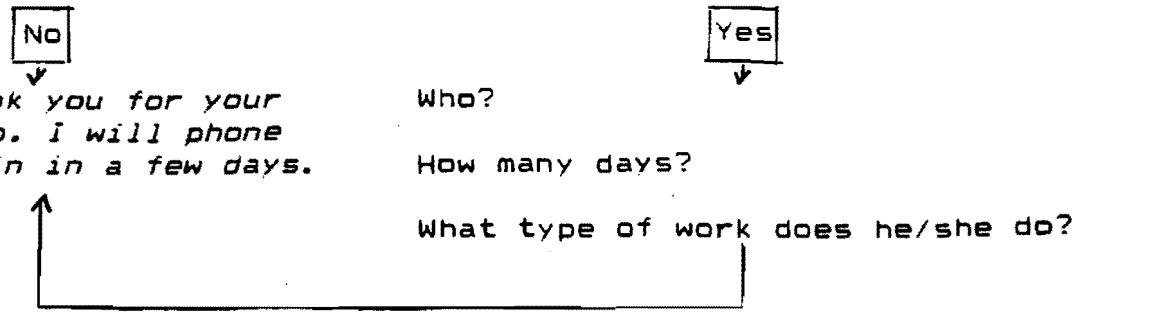
5. *Since my last call has <name> had a chest X-ray?*



6. *Since my last call have you needed to take time off work because of <name>'s ilness?*



7. *Has anyone else needed to take time off work?*



Appendix 10

CXR TRIAL - CLINICAL RECORDS

captured / /
complete ☐
captured / /

Study No. Patient's name Folder No.

Date consultation / /95

Weight

Excluded (0=No 1=Yes)

Reason (1=Unilat wheeze 2=FB 3=CCF 4=Too sick 5=Unexpl 6=Oth)

7=Not sick 8=Admin)

Reason "other" . . . . . .

CXR usually (0=No 1=Yes)

Randomisation group (C=CXR, N=No)

Doctor

No. of tests

Tine ☐
FBC ☐
ESR ☐
Other ☐ . . . . . .

No. drugs during consultation

Nebs (1=b-stim+ipr 2=b-stim 3=Ipr 4=Oth)

Steroids (1=Pred 2=Oth)

Paracetamol (1=Yes)

ORS (1=Yes)

Decongestant Drops (1=Sal 2=NaB 3=Oxy 4=Oth)

Oth . . . . . (1=Yes)

No. of drugs prescribed (to take home)

Antibiotic - oral (1=Am 2=Er 3=CoT 4=Oth)

Antibiotic - parenteral (1=IM Amp 2=Penilente)

Bronchodilator (1=Sal 2=Fen 3=Theoph 4=Oth)

Paracetamol (1=Yes)

Decongestant Drops (1=Sal 2=NaB 3=Oxy 4=Oth)

Oral (1=Dem 2=Oth)

Cough mixture (1=Mist tussi 2=Oth)

Eye oint (1=Chloro 2=Tetra)

ORS (1=Yes)

Other. . . . . (1=Yes)

Skins. . . . . (1=Yes)

Other management . . . . . (0=No 1=Yes) _ _ _ _ _

CXR report (0=N/A 1=Norm 2=B'itis 3=Pn 4=LRTI 5=Non-spec 6=Oth) _ _ _
7= Done, no report.

Second doctor? (0=No 1=Yes) _ _ _ _ _ _ _ _ _ _ _ _

Name . . . . . .

Final diagnosis (1=URTI 2=B'itis 3=Pn 4=LAO 5=Pert 6=Asth _ _ _ _
7=LRTI 8=Recurr wheeze 9=Oth) 0= No diag

Admitted same day (0=No 1=Yes) _ _ _ _ _ _ _ _

AB (1= Yes)
Duration (days)

Other (1=Yes)
Duration (days)

Booked follow-up, in 28 dys (# appts) _ _ _ _ _ _ _

MOPD (# appts)
Date / /

Other (# appts)
Date / / . . . . . .

Visits to RXH MOPD, in 28 dys (# visits) _ _ _ _ _ _

Related visits (#)

Booked 1. Date / /
Related Yes No

. . . . . Booked #

2. Date / /
Related Yes No Related #

. . . . . .

Unbooked 1. Date / /
Related Yes No Unbooked #

. . . . . Related #

2. Date / /
Related Yes No

. . . . . .

Subsequent admission, within 28 days (0=No 1=Yes) _ _ _ _ _

AB (1=Yes)
Duration

Other (1=Yes)
Duration

Subsequent CXRs at RXH within 28 days _ _ _ _ _

Date / /

Date / /

Comment . . . . . .

Appendix 11

Red Cross War Memorial Children's Hospital

medical outpatients department

use sticker when available name ..... birth date / /	date / /	last visit / /
folder number race / sex	time	temp °C
first doctor's stamp:	weight kg	RTH card seen? *Yes/No* up to date? *Yes/No*
history, examination, investigations, interim management	centile	TB contact?

CXR STUDY

Exclude if:
- **Focal wheeze** ☐
- **History FB** ☐
- **CCF** ☐
- **Other.....** ☐

CXR usually? ☐Y ☐N

Diagnosis
- **Bronchiolitis** ☐
- **Pneumonia** ☐
- **Recurr wheeze** ☐
- **Other** ☐

interim plan

	TIME In	TIME Out
Consultation	:	:
After neb 1	:	:
After neb 2	:	:
After CXR	:	:

diagnoses and problems

1 ..... 2 .....

3 ..... 4 .....

management and treatment

.....

.....

.....

.....

.....

or equivalent

Immunisation	
needs	*given*
measles	
DWT	
polio	
Hep B	

follow-up appointment on ___/___/___ to see .....

referal appointment on ___/___/___ to see .....

last doctor's stamp (if different) ..... and signature .....

Appendix 12

RESEARCH PROJECT ON THE USE OF CHEST X-RAYS IN LOWER RESPIRATORY INFECTIONS (CHEST INFECTIONS)

I understand the following, and give consent for

. . . . . .

to take part in research to find out when a child with a cough needs a chest X-ray.

1. In this research my child may or may not receive an X-ray.

2. If the doctor thinks an X-ray is essential it will definitely be done.

3. My child will be treated well even if he/she does not take part.

4*. I will be telephoned to ask how my child is recovering. This is a routine part of the research and will not mean that there is any special reason to worry.

Name Relationship to child

Signed

Witness Date

* Delete if not applicable

Appendix 13

Parameter estimates of regression models

A.13.1 Effect of chest radiography

A.13.1.1 Effect of chest radiography on time to recovery

A.13.1.1.1 Proportional hazards regression.

n=295	Beta	Std error	t-value	Hazard ratio	Wald statistic	p
Chest radiography	0.076443	0.126853	0.60261	1.079440	0.363134	0.546775
Age (months)	0.012082	0.007216	1.67421	1.012155	2.802986	0.094099
Weight for age (Z score)	-0.061342	0.051123	-1.19989	0.940501	1.439737	0.230191
Respiratory rate per minute	-0.004544	0.006954	-0.65342	0.995466	0.426957	0.513491
Duration of symptoms before presentation (days)	-0.032344	0.025932	-1.24725	0.968174	1.555631	0.212315
Clinicians' experience in GOPD (months)	0.000019	0.001320	0.01402	1.000018	0.000196	0.988816
Clinicians' possession of a postgraduate qualification	-0.065578	0.131091	-0.50025	0.936526	0.250252	0.616901
Clinicians' perception of the need for chest radiography	0.262924	0.164252	1.60074	1.300728	2.562365	0.109445

Chi-square = 12.50, df = 8, p =0 .13

A.13.1.1.2 Proportional hazards regression, including interactions with chest radiography

n=295	Beta	Std Error	t-value	Hazard ratio	Wald Statistic	p
Chest radiography	0.378870	0.900320	0.42082	1.460634	0.177087	0.673891
Age (months)	0.014778	0.009917	1.49022	1.014887	2.220741	0.136178
Weight for age (Z score)	-0.067484	0.072688	-0.92840	0.934743	0.861919	0.353209
Respiratory rate per minute	-0.002249	0.010269	-0.21903	0.997753	0.047974	0.826629
Duration of symptoms before presentation (days)	-0.042107	0.030253	-1.39184	0.958767	1.937230	0.163979
Clinicians' experience in GOPD (months)	-0.000350	0.001785	-0.19615	0.999650	0.038473	0.844497
Clinicians' possession of a postgraduate qualification	-0.015501	0.183743	-0.08436	0.984619	0.007117	0.932770
Clinicians' perception of the need for chest radiography	0.360126	0.229966	1.56599	1.433509	2.452331	0.117360
Age * chest radiography	-0.004704	0.011924	-0.39454	0.995307	0.155664	0.693183
Weght for age * radiography	0.023367	0.106142	0.22015	1.023642	0.048465	0.825757
Respiratory rate * radiography	-0.006291	0.013861	-0.45385	0.993729	0.205979	0.649941
Duration of symptoms * radiography	0.042602	0.048555	0.87740	1.043523	0.769835	0.380275
Clinicians' experience in GOPD * radiography	0.000411	0.002555	0.16096	1.000411	0.025908	0.872127
Clinicians' postgraduate qualifications * radiography	-0.097901	0.265583	-0.36863	0.906739	0.135886	0.712408
Clinicians' perception of need for radiograph * radiography	-0.143037	0.323532	-0.44211	0.866722	0.195463	0.658411

$Chi^2 = 14.7937$, df = 15, p = 0.4664 * denotes interaction

A.13.1.2 Effect of chest radiography on antibiotic use

A.13.1.2.1 Interaction with the perceived need for chest radiography

n=500	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate
Intercept	1	-0.9695	0.6733	2.0733	0.1499	
Chest radiography	1	0.6388	0.2128	9.0155	0.0027	0.176237
Age (months)	1	0.0733	0.0146	25.2922	0.0001	0.390360
Weight for age (Z score)	1	-0.0313	0.0838	0.1396	0.7087	-0.021547
Respiratory rate per minute	1	0.0036	0.0090	0.1603	0.6889	0.023601
Duration of symptoms before presentation (days)	1	-0.0116	0.0378	0.0942	0.7589	-0.017541
Clinicians' experience in GOPD (months)	1	0.0077	0.0026	8.9603	0.0028	0.214823
Clinicians' experience since qualification (years)	1	-0.0479	0.0124	14.9614	0.0001	-0.283079
Clinicians' possession of a postgraduate qualification	1	-0.0575	0.2146	0.0718	0.7887	-0.015849
Clinicians' perception of the need for CXR	1	3.1844	0.7464	18.2020	0.0001	0.666256
Chest radiography* perceived need for radiography	1	-2.2883	0.8559	7.1488	0.0075	-0.357767

* Denotes interaction

A.13.2 Determinants of clinical decisions

A.13.2.1 Perceived need for chest radiography

A.13.2.1.1 Selected model

n=532	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-1.170	0.190	37.979	0.000		
Age (months)	1	0.0248	0.00982	6.3814	0.0115	0.134025	1.025
Weight for age (Z score)	1	-0.2031	0.0824	6.0821	0.0137	-0.144149	0.816
Clinicians' experience since qualification (years)	1	-0.0231	0.0105	4.8738	0.0273	-0.132756	0.977

A.13.2.1.2 Model including all variables

n=532	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-2.2009	0.8313	7.0086	0.0081		
Age (months)	1	0.0326	0.0110	8.8151	0.0030	0.176367	1.033
Gender (male)	1	0.0234	0.2092	0.0125	0.9108	0.006453	1.024
Weight for age (Z score)	1	-0.2014	0.0841	5.7319	0.0167	-0.142907	0.818
Respiratory rate per minute	1	0.0136	0.0111	1.4972	0.2211	0.074231	1.014
Duration of symptoms before presentation (days)	1	0.0570	0.0359	2.5255	0.1120	0.089986	1.059
Clinicians' experience in GOPD (months)	1	0.0039	0.0025	2.4051	0.1209	0.109211	1.004
Clinicians experience since qualification (years)	1	-0.0323	0.0134	5.7627	0.0164	-0.185687	0.968
Clinicians' possession of a postgraduate qualification	1	-0.1776	0.2235	0.6319	0.4267	-0.048561	0.837
Accessibility by telephone	1	-0.2134	0.2101	1.0317	0.3098	-0.058528	0.808

A.13.2.2 Antibiotic use

A.13.2.2.1 Selected model

n=533	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-0.4089	0.2035	4.0379	0.0445		
Chest radiography	1	0.4413	0.1878	5.5187	0.0188	0.121642	1.555
Age (months)	1	0.0720	0.0123	34.3160	0.0001	0.408660	1.075
Clinicians' experience in GOPD (months)	1	0.0077	0.0023	11.1575	0.0008	0.221180	1.008
Clinicians' experience since qualification (years)	1	-0.0521	0.0112	21.7923	0.0001	-0.307173	0.949

A.13.2.2.2 Model including all variables

n=533	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-0.9839	0.7990	1.5163	0.2182		
Chest radiography	1	0.4497	0.1889	5.6681	0.0173	0.123953	1.568
Age (months)	1	0.0730	0.0135	29.2020	0.0001	0.414227	1.076
Gender (male)	1	0.1054	0.1885	0.3123	0.5763	0.029026	1.111
Weight for age (Z score)	1	-0.0906	0.0766	1.3987	0.2369	-0.062815	0.913
Respiratory rate per minute	1	0.0084	0.0107	0.6158	0.4326	0.044796	1.008
Duration of symptoms before presentation (days)	1	-0.0170	0.0343	0.2475	0.6189	-0.025961	0.983
Clinicians' experience in GOPD (months)	1	0.0080	0.0023	11.5154	0.0007	0.227556	1.008
Clinicians experience since qualification (years)	1	-0.0521	0.0117	19.6426	0.0001	-0.307085	0.949
Clinicians' possession of a postgraduate qualification	1	0.0159	0.2000	0.0064	0.9365	0.004389	1.016
Accessibility by telephone	1	0.1059	0.1915	0.3059	0.5802	0.029012	1.112

A.13.2.3 Associations of clinician experience with management decisions

A.13.2.3.1 Admission to hospital

n=560	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-6.4326	1.5869	16.4304	0.0001		
Chest radiograph use	1	0.7639	0.4371	3.0551	0.0805	0.210710	2.147
Age (months)	1	0.0061	0.0247	0.0602	0.8061	0.033933	1.006
Gender (male)	1	-0.1197	0.4198	0.0813	0.7755	-0.032963	0.887
Weight for age (Z score)	1	-0.3330	0.1671	3.9700	0.0463	-0.235863	0.717
Respiratory rate per minute	1	0.0555	0.0189	8.5875	0.0034	0.302528	1.057
Duration of symptoms before presentation (days)	1	0.0957	0.0677	2.0002	0.1573	0.151138	1.100
Clinicians' experience in GOPD (months)	1	-0.0228	0.0118	3.7321	0.0534	-0.643407	0.977
Clinicians experience since qualification (years)	1	-0.0327	0.0395	0.6825	0.4087	-0.190645	0.968
Clinicians' possession of a postgraduate qualification	1	0.2637	0.5008	0.2772	0.5985	0.072543	1.302
Accessibility by telephone	1	-0.4596	0.4279	1.1540	0.2827	-0.126091	0.632

A.13.2.3.2 Performance of one or more diagnostic tests

n=533	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-1.6828	1.3082	1.6548	0.1983		
Chest radiograph use	1	-0.1444	0.3018	0.2288	0.6324	-0.039795	0.866
Age (months)	1	0.0231	0.0138	2.8184	0.0932	0.131209	1.023
Gender (male)	1	0.2987	0.3077	0.9422	0.3317	0.082283	1.348
Weight for age (Z score)	1	-0.1476	0.1249	1.3959	0.2374	-0.102373	0.863
Respiratory rate per minute	1	-0.0181	0.0186	0.9523	0.3291	-0.096470	0.982
Duration of symptoms before presentation (days)	1	0.0653	0.0512	1.6286	0.2019	0.099429	1.067
Clinicians' experience in GOPD (months)	1	0.00533	0.00363	2.1496	0.1426	0.152144	1.005
Clinicians experience since qualification (years)	1	-0.0366	0.0210	3.0452	0.0810	-0.216003	0.964
Clinicians' possession of a postgraduate qualification	1	0.0319	0.3190	0.0100	0.9203	0.008786	1.032
Accessibility by telephone	1	-0.1152	0.3051	0.1426	0.7057	-0.031558	0.891

A.13.2.3.3 Scheduling of a follow-up appointment

n=533	df	Parameter Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Standardized Estimate	Odds Ratio
Intercept	1	-3.4174	1.1563	8.7342	0.0031		
Chest radiograph use	1	0.2486	0.2781	0.7991	0.3714	0.068528	1.282
Age (months)	1	0.0333	0.0126	6.9194	0.0085	0.188802	1.034
Gender (male)	1	0.1417	0.2813	0.2537	0.6145	0.039030	1.152
Weight for age (Z score)	1	-0.2060	0.1168	3.1139	0.0776	-0.142887	0.814
Respiratory rate per minute	1	0.00985	0.0156	0.3991	0.5276	0.052473	1.010
Duration of symptoms before presentation (days)	1	0.0439	0.0503	0.7624	0.3826	0.066836	1.045
Clinicians' experience in GOPD (months)	1	0.00323	0.00352	0.8380	0.3600	0.092111	1.003
Clinicians experience since qualification (years)	1	-0.0432	0.0200	4.6482	0.0311	-0.254650	0.958
Clinicians' possession of a postgraduate qualification	1	0.2854	0.2974	0.9209	0.3372	0.078571	1.330
Accessibility by telephone	1	0.2440	0.2853	0.7312	0.3925	0.066809	1.276

A.13.2.3.4 Number of drugs per prescription (other than antibiotics)

n=533	df	Parameter Estimate	Standard Error	T for H0: Parameter=0	Prob > |T|
Intercept	1	2.899465	0.33998187	8.528	0.0001
Chest radiograph use	1	-0.090351	0.08131980	-1.111	0.2671
Age (months)	1	-0.005444	0.00440001	-1.237	0.2166
Gender (male)	1	0.141113	0.08177155	1.726	0.0850
Weight for age (Z score)	1	-0.002076	0.03300384	-0.063	0.9499
Respiratory rate per minute	1	-0.001992	0.00461691	-0.431	0.6663
Duration of symptoms before presentation (days)	1	-0.009740	0.01511019	-0.645	0.5195
Clinicians' experience in GOPD (months)	1	0.000121	0.00098670	0.123	0.9025
Clinicians experience since qualification (years)	1	-0.009723	0.00494864	-1.965	0.0500
Clinicians' possession of a postgraduate qualification	1	0.136733	0.08616470	1.587	0.1131
Accessibility by telephone	1	-0.049451	0.08281961	-0.597	0.5507

A.13.3 Duration of illness in bronchiolitis

A.13.3.1.1 Predictors of duration of illness (proportional hazards regression)

n=140	Beta	Standard Error	t-value	Hazard ratio	Wald Statist	p
Gender (male)	-0.016750	0.182526	-0.09177	0.983389	0.008421	0.926883
Age (months)	0.022230	0.020130	1.10432	1.022478	1.219523	0.269463
Respiratory rate per minute	0.004892	0.012109	0.40402	1.004904	0.163233	0.686200
Weight for age (Z score)	-0.112297	0.085767	-1.30933	0.893778	1.714339	0.190433

$Chi^2 = 2.92857$, df = 4, p = .56986