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Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department (Review)

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[Intervention Review]

Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

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ABSTRACT

Background

Pediatric acute respiratory infections (ARIs) represent a significant burden on pediatric emergency departments (ED) and families. Most of these illnesses are due to viruses. However, investigations (radiography, blood and urine testing) to rule out bacterial infections and antibiotics are often ordered because of diagnostic uncertainties. This results in prolonged ED visits and unnecessary antibiotic use. The risk of concurrent bacterial infection has been reported to be negligible in children over three months of age with a confirmed viral infection. Rapid viral testing in the ED may alleviate the need for precautionary testing and antibiotic use.

Objectives

To determine the effect of rapid viral testing in the ED on the rate of precautionary testing, antibiotic use and ED length of visit.

Search strategy

We searched the Cochrane Central register of Controlled Trials (CENTRAL) (*The Cochrane Library*, 2009, issue 1) which contains the ARI Group's Specialized Register, MEDLINE (1950 to April Week 3 2009), EMBASE (1988 to Week 16, 2009), MEDLINE In-Process & Other Non-Indexed Citations (April 27, 2009), HealthStar (1966 to 2009), BIOSIS Previews (1969 to 2009), CAB Abstracts (1973 to 2007), CBCA Reference (1970 to 2007), and Proquest Dissertations and Theses (1861 to 2009).

Selection criteria

Randomized controlled trials (RCTs) of rapid viral testing for children with ARIs in the ED.

Data collection and analysis

Two review authors used the inclusion criteria to select trials, evaluate their quality and extract data. Missing data were obtained from trial authors. Differences in rate of investigations and antibiotics use were expressed as risk ratios (RR) and difference in ED length of visits was expressed as mean difference, with 95% confidence interval (CI).

Main results

Four trials were included, three RCTs and one quazi-RCT, with 759 children in the rapid viral testing and 829 in the control group. Rapid viral testing did not reduce antibiotic use in the ED significantly, neither clinically nor statistically. We found lower rates of chest radiography (RR 0.77, 95% CI 0.65 to 0.91) in the rapid viral testing group but no effect on length of ED visits, blood or urine testing in the ED.

Authors' conclusions

Current evidence is insufficient, although promising, to support routine rapid viral testing as a means to reduce antibiotic use in pediatric EDs. Results suggest that rapid viral testing may be beneficial but are not statistically significant due to lack of power. A large trial addressing these outcome measures is needed.

PLAIN LANGUAGE SUMMARY

Does rapid viral testing in the Emergency Department affect the treatment of children with fever and respiratory problems?

Children admitted to Emergency Departments (ED) with fever and respiratory symptoms represent a major burden to the health care system, as well as significant anxiety and expense to parents and caregivers. Physicians often order diagnostic tests and may prescribe antibiotics when they are unsure of the cause of the illness and are concerned about the possibility of serious bacterial infection. However, in most cases, fever and respiratory symptoms are caused by viruses. In addition, in children in whom a virus is found to be the cause of their illness, the risk of serious bacterial infection is very low. This review was conducted to assess whether a rapid viral test done in the ED changes what physicians do when treating these children. We found that in previously healthy children coming to the ED with fever and respiratory symptoms, a rapid viral test reduces the use of chest X-rays and that there is a trend toward less antibiotic usage, and blood and urine investigations. The true impact of this intervention on the latter three outcomes requires trials with larger enrollment numbers.

BACKGROUND

Description of the condition

Acute respiratory infections (ARIs) are a serious public health issue and rank among the top five causes of illness and hospitalization in children. During influenza seasons, fever and respiratory infection symptoms make up to 25% of all reasons for a visit to an Emergency Department (ED) (Silka 2003). Although ARIs can be caused by bacteria, they are most commonly caused by viral infections. A rapid diagnosis of a viral infection may lead to a decrease in the use of antibiotics, additional testing and possibly admissions. The most commonly implicated causal viruses are influenza (A and B), respiratory syncytial virus (RSV), human parainfluenza (1, 2 and 3), rhinovirus and adenovirus. These viruses account for 35 to 87% of children with an ARI. The variability in the range of positive viral diagnosis may be affected by the choice of viral tests used and their scope of viral detection (Jennings 2004; Weigl 2000). There is a risk of concurrent bacterial infection in children with a confirmed viral ARI. A study of children aged 3 to 36 months with recognizable viral infections showed a concurrent rate of bacteremia of 0.01 to 0.8% (Greens 1999). A prospective multicenter study of infants less than 60 days old with an ARI showed a significant difference in the rate of urinary tract infection between RSV positive (5.4%) and negative infants (10.1%), a non-significant difference rate of bacteremia (1.1% and 2.3%) and no cases of bacterial meningitis among the 251 RSV positive infants and 8 cases out of 938 RSV negative infants (not statistically significant) (Levine 2004).

However, symptoms of viral ARI overlap with those of bacterial infections (such as pneumonia, bacteremia and meningitis) and in some cases, are difficult to distinguish. Without a confirmed viral diagnosis, medical assessment and diagnostic tests are often used before a decision on patient management, parental advice, and/or hospital admission are made. These precautionary tests lead to intense use of human health resources (nursing, laboratory and radiology staff) and hospital facilities. Furthermore, these tests are often invasive, sometimes unnecessarily prolonging a child's visit to the ED, resulting in sub-optimal ED service provision and contributing to lengthy ED wait times and overcrowding.

ARIs impose large costs on the health system, from a high number of physician visits, ED visits, hospitalization and antibiotic prescriptions. Studies comparing health care utilization for ARIs in children 0 to 15 years old during influenza season and the rest of the year showed significant excess in physician visits (28,000 to 51,000/100,000 age specific population annually), ED visits (~1600/100,000 age specific population annually), hospital admission (300 to 9500/100,000 age specific population annually) and antibiotic prescription (31,000/100,000 age specific population annually). Most of this burden came from children below three years of age (Menec 2003; Neuzil 2000).

A study comparing the costs associated with a visit to the ED versus a primary care provider, showed that the average cost for assessing a patient for an ARI in the ED (excluding antibiotics cost) is $206 to $221 and in comparison is $101 to $106 in a primary care provider's office. Up to 60% of patients with a common cold are treated with antimicrobials, which costs $37.5 million annually (Rosenstein 1998), despite most ARIs being caused by viruses. The physician and nursing costs only contributed to 17.5% of ARI management costs (Martin 2000). This suggests that extra investigations and antibiotic prescribing in the ED may be responsible for much of any unnecessary costs.

During the SARS outbreak in 2003, there was access to rapid respiratory viral diagnosis in acute care settings; (that is, provision of same-day identification of influenza virus A and B, parainfluenza virus 1, 2 and 3), RSV and adenovirus. This enabled rapid, informed patient management decisions and helped with triaging. This suggests a role for rapid viral diagnosis in alleviating the burden on EDs and improving health service delivery and health resource allocation, in the situation of increased use of EDs for ARI symptoms. A prompt viral diagnosis might improve decision-making and reduces unnecessary hospital admittance, prescription of antibiotics, and further diagnostic investigations.

This is supported by observational data from retrospective chart reviews of children admitted to hospital, with subsequent confirmed diagnosis of adenovirus infection, which revealed a change in management for 36%, including revision of antibiotic treatment and use of antiviral therapy (Rocholl 2004). Similarly, chart reviews of children testing positive via a rapid influenza diagnostic test were less likely to be prescribed antibiotics in the ED (20% versus 53%; P = 0.04) and when admitted were on antibiotics for fewer days (3.5 versus 5.4 days; P = 0.03) (Noyola 2000). Children with an early diagnosis of influenza also had fewer blood tests (17% versus 44%; P = 0.02) and urine tests performed (2% versus 24%; P = 0.006), compared to those children with a late diagnosis (Sharma 2002).

Description of the intervention

Advances in virology testing now allow for viral detection within 30 to 120 minutes by direct immuno-fluorescent antibody detection. These have been reported to have high sensitivity (up to 90%) and specificity (up to 99%) (Vega 2005). Confirmation of specific diagnosis of viral respiratory infection is now accessible and reliable.

How the intervention might work

Better investigating the possible diagnosis of children presenting to the ED with fever and respiratory symptoms may improve their management by more rational decisions about other investigations and treatment.

Why it is important to do this review

This literature has yet to be systematically reviewed. There may evidence of substantial reductions in unnecessary investigation costs and antibiotic prescribing for children with ARI in the ED, by positively identifying a viral illness rather than attempting to exclude a more serious bacterial cause.

OBJECTIVES

To determine if the use of a rapid viral detection test for children with an ARI in EDs changes patient management and resource use in the ED, compared to not using a rapid viral detection test. We hypothesized that rapid viral testing reduces antibiotic use in the ED as well as reduces the rate of ancillary testing and length of ED visits.

METHODS

Criteria for considering studies for this review

Types of studies

- Randomized controlled trials (RCTs) evaluating the use of rapid viral diagnosis in children admitted to the ED with an ARI.

Types of participants

We included:

- studies of otherwise healthy children aged 0 to 18 years old; or
- studies which reported separately on subgroups of children under 18 years of age, admitted to an ED with a clinical presentation consistent with an ARI (fever and respiratory symptoms such as cough, runny nose, sore throat, or congested nose).

We did not consider:

- studies including participants who are immunocompromized;
- studies including participants who have underlying chronic severe respiratory conditions (cystic fibrosis, bronchopulmonary dysplasia); or
- studies including participants with chronic heart conditions (such as uncorrected cyanotic heart lesions, or prosthetic valves).

Types of interventions

Rapid viral diagnosis from nasal pharyngeal aspirates or swabs by direct or indirect immunofluorescent antibody test (IDF, IFA), enzyme immunoassays (EIA), optical immunoassay (OIA) or molecular testing (multiplex PCR). Rapid viral diagnosis implies that results are made available during the participants' stay in the ED. The intervention group will include participants who have rapid viral diagnostic testing; while participants in the control group will have had no rapid viral diagnostic test performed, or the treating physician will have had no knowledge about the test results.

Types of outcome measures

Primary outcomes

- Antimicrobial prescription rate in the ED. A reduction of antibiotic use by 25% (RR 0.75) was considered clinically important.

Secondary outcomes

- Length of hospital (ED) stay. A reduction of 30 minutes was considered clinically important.
- Rate of ancillary tests (any blood tests or chest imaging or urine investigations) requested. A reduction in ancillary testing of 25% (RR 0.75) was considered clinically important.
- Rate of physician visit (ED or office) within two weeks after discharge from ED. A relative increase in physician visit within two weeks of discharge from an ED of 10% (RR 1.10) was considered clinically important.
- Hospital admission rate. A reduction in admission rate of 25% (RR 0.75) was considered clinically important.
- Acceptability of nasal specimen collection sampling for rapid viral testing (discomfort level with invasiveness of the procedure).

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central register of Controlled Trials (CENTRAL) (*The Cochrane Library*, 2009, issue 1) which contains the ARI Group's Specialized Register, MEDLINE (1950 to April Week 3 2009), EMBASE (1988 to Week 16, 2009), MEDLINE In-Process & Other Non-Indexed Citations (April 27, 2009), HealthStar (1966 to 2009), BIOSIS Previews (1969 to 2009), CAB Abstracts (1973 to 2007), CBCA Reference (1970 to 2007) and Proquest Dissertations and Theses - Full Text (1861 to 2009). Search terms were adapted to accommodate the controlled vocabulary and search language for each electronic resource. In MEDLINE, these search terms were combined with the highly sensitive search strategy for identifying RCTs (Lefebvre 2008). The filter was modified for use in MEDLINE In-Process & Other Non-Indexed Citations, Embase, and HealthStar. All search strategies included pediatric terms to restrict to pediatric studies. No language or date restrictions were applied to the search strategies. Detailed search strategies are available in Appendix 1, Appendix 2, Appendix 3, Appendix 4, Appendix 5, Appendix 6, Appendix 7, Appendix 8 and Appendix 9.

Searching other resources

Included articles derived from the original search were provided by the principal researcher and were tracked forward using the Cited Reference Search feature in Web of Science and the Scopus Citation Tracker. Clinical trials.gov was searched for additional unpublished trials. The Pediatric Academic Society and Society for Pediatric Research joint conference abstracts databases from 2003 to 2008 were searched for identification of meeting abstracts.
Two reviewers (QD, PE) searched the Pediatric Academic Society and Society for Pediatric Research joint meetings abstract archives from 2000 to 2007 for any other potential studies of rapid viral testing. All relevant abstracts were also found through the electronic databases.

Data collection and analysis

Two reviewers (QD, PE) independently extracted and verified data entry for accuracy. We used the Review Manager (RevMan) 5 statistical package to conduct the analyses. Pooled differences in rate of investigations and antibiotic use were analyzed using the Mantel-Hanzel test and expressed as risk ratio (RR) with 95% confidence interval (CI). Pooled difference in ED length of visits was analyzed using the inverse variance method and expressed as mean difference with 95% CI. The random-effects model was applied to all statistical analyses.

Selection of studies

Two reviewers (QD, PE) screened titles and abstracts of identified citations to exclude trials which are clearly not relevant or did not meet the inclusion criteria of the review. For all abstracts or titles

deemed relevant or potentially meeting the criteria by either review author, the full article was retrieved for further examination. The two review authors assessed these articles to confirm that they meet inclusion criteria for the review.

Data extraction and management

Two review authors independently extracted data from the published studies using standardized data extraction forms. Trial authors were contacted to obtain unpublished information, including outcome data that was not explicitly stated in the published papers. Disagreements in data extraction was resolved by discussion and consensus.

Assessment of risk of bias in included studies

The review authors evaluated the methodological quality of each trial. Review authors used the risk of bias tables Higgins 2008. Allocation concealment as described by Schulz was assessed as clearly adequate, clearly inadequate and unclear (Schulz 1995).

Unit of analysis issues

Dichotomous data such as antibiotic prescription in ED (primary objective), ancillary tests performed in ED, admission to the hospital and physician visits or re-visits to the ED within two weeks of discharge from original ED visit were expressed as RR. Continuous data such as mean length of stay in ED was expressed as mean difference (MD).

Assessment of heterogeneity

Heterogeneity was tested for using the Chi^2 statistic as provided by the RevMan 5 statistical package.

Assessment of reporting biases

We intended to use visual inspection of funnel plots to assess for publication bias and small study effects, but the small number of studies included in this review would make the interpretation of these plots difficult and of questionable meaning.

Subgroup analysis and investigation of heterogeneity

We did not perform subgroup analyses as data were not consistently available by age groups.

Sensitivity analysis

We performed a sensitivity analysis comparing studies where the risk of bias was deemed adequate for inclusion. Given the invasive nature of specimen acquisition for rapid respiratory virus testing, the intervention cannot be blinded and therefore, no study was deemed free of bias.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

We found seven prospective trials on the impact of rapid viral testing in children. Four studies were included in this review: three RCTs (Bonner 2003; Doan 2009; Poehling 2006) and one quazi-RCT (Iyer 2006). We excluded three studies (Abanses 2006; Cohen 2007; Esposito 2003). See 'Characteristics of excluded studies' table for descriptions and reasons for exclusion.

Results of the search

Electronic database searches resulted in 1180 references (after duplicates were eliminated), of which six were prospective randomized trials of rapid viral testing in children. Search from the PAS conference proceedings only yielded references which were already recovered from the electronic search. We found one additional potential study from the Clinical trials.gov registry but the many attempts at contacting the author to enquire about the status of this study were unsuccessful. Snowballing, using Scopus and Web of Sciences, and hand searching through references of included studies yielded one additional study of rapid viral testing in children (Cohen 2007). A total of seven studies were carefully reviewed with four meeting all the inclusion criteria.

Included studies

Bonner 2003 This was a single center RCT assessing participants presenting to a large American tertiary center pediatric ED with fever and symptoms of an acute respiratory illness for less than 72 hours. The goal of the study was to assess whether prior knowledge of a positive influenza test changed physician decision-making and management of these participants.

Results from this study found a statistically significant lower rate of antibiotic prescription (risk ratio (RR) 0.66 (95% CI 0.45 to 0.96)), shorter mean ED length of visit (-10.9 min (95% CI -19.56 to -2.24)) and lower rate of chest radiography (RR 0.61 (95% CI 0.40 to 0.92)) in participants who's rapid influenza test results were made available to the treating physician. A trend for lower rate of blood and urine investigations was also found but this was not statistically significant.

Details pertaining to participants, outcome measures and limitations are found in the 'Charateristics of included studies' tables.

Poehling 2006 This was a RCT assessing participants presenting to a pediatric ED or acute care clinic with signs and symptoms of respiratory tract infections. Data were analyzed and reported separately for these two populations. We only considered the study population enrolled from the ED. The goal of the study was to

assess whether a rapid diagnosis of influenza affects the evaluation and treatment of children with acute respiratory illnesses.

Approximately 20% of their study population were deemed high-risk medical participants, as defined in the publication *Red Book* (CID 2003), any patient for whom influenza vaccination is recommended (1. Children with chronic disorders of the pulmonary or cardiovascular systems, including asthma; 2. Children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases including diabetes mellitus, renal dysfunction, hemoglobinopathies, or immunosuppression including immunosuppression caused by medications or by human immunodeficiency (HIV) virus; 3. Children and adolescents who are receiving long-term aspirin therapy and, therefore, might be at risk for developing Reye's syndrome after an influenza infection). The primary trial author was contacted for further clarification.

Of these 20%, only five participants had a condition which may have met our exclusion criteria (congenital heart disease, bronchopulmonary dysplasia of unknown severity and possible immune defect reported by parents but unrelated to chemotherapy). The rest had asthma which is not an exclusion criteria for our review. Raw data excluding these five participants was obtained from the primary author and used for this meta-analysis.

Re-analyzed data showed a trend for lower rate of blood and urine investigations and chest radiography but a higher rate of antibiotic prescription in participants with rapid influenza results available to the treating physician, but none of these findings were statistically significant.

Details pertaining to participants, outcome measures and limitations are found in the 'Charateristics of included studies' tables.

Iyer 2006 This was a prospective, quazi-randomized, controlled trial assessing participants presenting to a large, urban, tertiary-care pediatric emergency department. The goal of this study was to assess the effect of rapid Influenza diagnosis on physician management of previously healthy febrile participants, aged two to 24 months, at risk for serious bacterial infection. Despite the fact that this study only mentioned fever as an inclusion criteria, close to 90% of the children enrolled in the study also had symptoms of an acute respiratory illness.

This study reported no significant differences in mean length of ED visit, laboratory testing, chest radiography or antibiotic use, and return to ED visit rates between the two study groups per original randomization.

Details pertaining to participants, outcome measures and limitations are found in the 'Charateristics of included studies' tables.

Doan 2009 This was a single center, open-label, randomized, controlled trial assessing participants presenting to a large Canadian tertiary center pediatric ED. The goal of the study was to measure the effect of a multi-viral rapid diagnostic test on the clinical management and resource utilization pertaining to healthy children who presented to the ED with signs and symptoms of a febrile acute respiratory infection.

With respect to the primary end-point, there was no statistically significant reduction in the length of the ED visits. As well, no statistically significant difference was found in ordering of chest radiographs, blood tests, urine analysis, or antibiotic prescription. Interestingly, though, there was a significant reduction in the rate of antibiotic prescription by primary care providers one week after discharge from the ED (RR = 0.36 (95% CI 0.14 to 0.95)).

Details pertaining to participants, outcome measures and limitations are found in the 'Charateristics of included studies' tables.

Excluded studies

Esposito 2003 This was a single center RCT assessing children presenting to a pediatric ED with fever and signs/symptoms of a respiratory illness. The goal of the study was to assess the effect of a rapid diagnosis of influenza on the management of children with influenza-like illnesses.

Children meeting the inclusion criteria were randomized to undergo tonsillar/pharyngeal swabs for rapid influenza testing or standard care. Results of influenza testing were made available to the treating physician within approximately 10 minutes, who then decided on further testing and management.

Endpoints analyzed in this study included: rates of routine blood examinations, chest X-rays, antibiotic prescription and days on antibiotics, admission to hospital, and antiviral drug use.

In this study, participants with a positive influenza diagnosis were significantly less likely to receive routine blood examinations or be prescribed antibiotics when compared with those not receiving rapid viral testing. No significant differences were found between the two groups with respect to rates of chest X-rays or admission to hospital. If children were prescribed antibiotics, there was no difference in length of antibiotic use. No children were prescribed antivirals.

This study was excluded due to the fact that children with underlying illnesses were included. The study included children with congenital heart disease, asthma, malignancy, neurological deficits, and cystic fibrosis.

Abanses 2006 This was a large single center RCT assessing healthy participants aged three to 36 months presenting to a large urban pediatric ED (64,000 patient visits per year) with fever. The goal of the study was to assess how rapid influenza testing of febrile infants and children affected physician decision-making with respect to diagnostic testing as well as ED charges and patient time in the ED. Although the inclusion criteria were based on fever, this paper was analyzed as a large proportion of children (> 60%) were found to have respiratory symptoms in the form of tachypnea.

Children meeting inclusion criteria were randomized into two groups. One group had rapid influenza test results available to the treating physician prior to assessment while the other group had influenza testing done only at the discretion of the treating physician after initial assessment. Study endpoints, as stated above, were: rates of diagnostic testing, ED charges, and length of ED

visit.

Although block randomization is mentioned, what is described is actually cluster randomization by 24 hour periods. Despite the initial intent to conduct an RCT, non-adherence to the protocol led to a significant number of participants not receiving the treatment they were randomly allocated to receive. A decision was made to analyze data as per actual treatment received, hence a convenience sample. Although there is mention of ITT analysis yielding no significant difference in the outcome measures between the two study groups, the results were not reported. Due to the failed randomization, this study did not meet this review's inclusion criteria. Cohen 2007 This was a multicenter cluster RCT of 30 community pediatric offices in France; 16 offices were randomized to use of Quickvue rapid Influenza test and 14 were not. A total of 602 participants aged one to 17 years old with influenza-like illnesses (chills, upper respiratory symptoms, headaches or myalgia) and without focal infections, were enrolled. The primary objective was to compare oseltamivir use and secondary objectives included comparisons of clinical presentation, ancillary testing and antibiotic use between the two study groups.

This study found that with participants enrolled in pediatric offices where rapid influenza testing was used, oseltamivir was used more frequently (37.9% versus 13.7% P < 0.0001). Antibiotics (9.5% versus 3.9% P = 0.008) and chest radiography (4.0% versus 1.2% P = 0.035) was also more frequently used in the rapid influenza testing group. Statistically and clinically significant differences in clinical features between the two study groups included a younger mean age (4.7 versus 5.7 years old P = 0.0001) and a larger proportion of asthmatic participants (15.9% versus 10.2% P = 0.04).

This is the first RCT of rapid influenza testing in community pediatric practices. This study was not included in this review because the setting was not in the ED. One particular concern with this study is the large number of analytical comparisons (well over 30) without corrections surrounding the statistical significance level.

Risk of bias in included studies

Allocation

Bonner 2003 and Doan 2009 used computer randomization programs to block randomize participants to their study groups. Poehling 2006 used a random number generator to randomize study days in blocks of four and six. Iyer 2006 allocated participants to study groups using alternating days.

Blinding

This intervention does not lend itself to blinding.

Incomplete outcome data

Incomplete outcome data were all successfully retrieved by contacting individual study authors.

Selective reporting

There was no selective reporting found in the included trials.

Other potential sources of bias

In the two trials where participants are individually randomized (Bonner 2003; Doan 2009), as opposed to randomizing days like for the Poehling 2006 trial, there is potential for contamination. If many children are rapidly diagnosed with influenza on a given day (in the intervention group), it is possible that children without rapid viral testing (in the control group) would be assumed by the treating physician to have influenza due to the commonality in their presentation with children in the intervention group. This would introduce a conservative bias, reducing the difference in effect between the two study groups and increasing a type II error.

Effects of interventions

Antibiotic use (prescribed) in ED

All four studies reported the proportion of participants receiving or being prescribed antibiotics in the ED by study groups. Three did not find a statistically significant effect despite a trend favoring rapid viral testing. Bonner 2003 was the only trial to report a statistically significant effect for rapid influenza testing on antibiotic prescription (RR = 0.66 (95% CI 0.45 to 0.96)). Pooled results showed a non-statistically significant trend for reduced antibiotic prescription in the ED favoring the treatment group (RR 0.89 (95% CI 0.71 to 1.12)). Sensitivity analysis using the three trials deemed adequate (higher quality) by the method of Higgins 2008 (Bonner 2003; Doan 2009; Poehling 2006) did not find a statistically significant effect either (RR 0.86 (95% CI 0.61 to 1.22)).

ED length of visit

Three studies reported on this outcome. Only Bonner 2003 showed a statistically significant effect, while Doan 2009 and Iyer 2006 only showed a trend favoring rapid viral testing. Pooled results showed no statistically significant reduction in mean ED length of visit (mean difference = -10.6 min (95% CI -22.5 to 1.25)). Sensitivity analysis using only the two trials deemed adequate by the method of Higgins 2008 (Doan 2009 and Bonner 2003), did not find a statistically significant effect either (mean difference: -19.47 (95% CI -51.38 to 12.44)).

Blood investigations

All four studies reported proportions of participants undergoing blood investigations. Bonner 2003 and Iyer 2006 reported complete blood count (CBC) and blood cultures separately. We anticipated substantial overlap between participants receiving CBC and blood cultures and have analyzed them as one outcome. Authors were contacted and data for this outcome was provided to analyze them as one outcome. All four showed a trend for reduced blood investigations in the treatment group, which is not statistically significant. Pooled results showed a lower rate of blood investigations in the treatment group, which was not statistically significant (RR 0.79 (95% CI 0.62 to 1.0)). Sensitivity analysis of the three trials deemed adequate by the method of Higgins 2008, however, we found a significant effect (RR 0.61 (95% CI 0.42 to 0.89)).

Urine investigations

All four studies reported the proportion of participants undergoing urine investigations. Bonner 2003 and Iyer 2006 reported urine analyses and urine cultures separately. We anticipated some overlap between participants undergoing urine analysis and urine cultures and have analyzed them as one outcome. Authors were contacted and data for this outcome was provided to analyze them as one outcome. None of the studies found a statistically significant difference in rate of urine investigations between the study groups. Pooled results showed no meaningful nor statistically significant effect of rapid viral testing on urine investigations in the ED (RR 0.97 (95% CI 0.79 to 1.19)). Sensitivity analysis using the three trials deemed adequate by the method of Higgins 2008 found similar results (RR 0.93 (95% CI 0.70 to 1.25)).

Chest radiography

All four studies reported on this outcome. Three did not find a statistically significant effect despite a trend favoring rapid viral testing. Bonner 2003 was the only one to report a statistically significant effect for rapid influenza testing on chest radiography (RR 0.61 (95% CI 0.40 to 0.92)). Pooled results showed a statistically significant effect of rapid viral testing on chest radiography in the ED favoring the treatment group (RR 0.77 (95% CI 0.65 to 0.91)). Sensitivity analysis of the three trials deemed adequate by the method of Higgins 2008 found a similar but stronger effect (RR 0.59 (95% CI 0.43 to 0.81)).

Return visits to a physician (or to ED) post discharge

Only two studies reported on this outcome (Doan 2009; Iyer 2006). Neither found a statistically significant effect and pooled results did not find a significant effect either (RR 1.00 (95% CI 0.77 to 1.29)). Only Doan 2009 was deemed adequate by the method of Higgins 2008, hence a sensitivity analysis was not performed for this outcome.

Hospital admission

Only one study reported this outcome (Iyer 2006).

Acceptability of nasal specimen collection sampling for rapid viral testing

None of the included studies provided data on this outcome.

Heterogeneity

Tests of heterogeneity were performed for all outcome measures. There was no suggestion of significant heterogeneity, but the small number of trials included in this review may have contributed to the lack of significance on these statistical tests.

DISCUSSION

Summary of main results

This meta-analysis demonstrated that the use of a rapid viral diagnostic test did not dramatically affect physician decision-making. The only exception to this was the fact that a rapid diagnosis of a viral infection decreased the rate of chest radiography use in the ED and then on sensitivity analysis for the rate of blood investigations. A weak trend toward reduction in antibiotics and ED length of visit was seen, but these were not statistically significant.

Overall completeness and applicability of evidence

The results of this meta-analysis suggest a benefit in using rapid respiratory viral testing mainly for reducing the rate of chest radiography and blood investigations, but the evidence surrounding antibiotics is still incomplete. Although a weak trend for a reduction in antibiotic prescription rate was shown, this was not statistically significant and the results of individual trials on this outcome were conflicting, making the current evidence not yet applicable.

Most studies of rapid viral testing have been aimed at detecting influenza virus only, except for one, which used a multi-respiratory viral panel. While a multi-viral panel can capture a larger number of viruses, the test used by Doan 2009 was laboratory bound and not as freely accessible to clinicians as the rapid influenza test, which can be performed at the bedside and therefore offers a much more rapid result to the treating physician. Although point of care testing for RSV is available and has been shown to have high sensitivity (90%) and specificity (92%) Mackie 2001 we have not found any trials using rapid RSV testing meeting the criteria for our review. Considering that RSV and influenza formed 73% to 95%

of the positive viral tests in the study by Doan 2009, perhaps using point of care testing for influenza and RSV in the ED through future studies would provide more evidence to support the practice of rapid viral testing in the ED.

The evidence we gathered through this review is still lacking information on key issues surrounding implementation of rapid viral testing in the ED. We have found no information on safety and side effects of this intervention, nor cost comparisons between the rapid viral test and the averted ancillary testing by using this intervention. It will be difficult to evaluate the value caregivers assign to averting blood sampling, radiography exposure and unnecessary antibiotics, as well as shortening their ED visit and may require a different approach from RCTs.

Quality of the evidence

Three out of four of the included studies are high quality RCTs. The one quazi-RCT(Iyer 2006) was clearly stated as such, and the methodology was well described. We have therefore presented the results for individual outcomes (where possible) with and without the contribution of the quazi-RCT.

The bias from contamination, which may have been introduced with the two trials of individual subject randomization (Bonner 2003; Doan 2009), would be a conservative one and strengthens the validity of the significant findings in this meta-analysis.

Potential biases in the review process

To the best of our knowledge, no bias was introduced during the review process.

Agreements and disagreements with other studies or reviews

Reasons for lack of effect on antibiotic prescription rates and urine investigations are unclear. Although Levine 2004 and Byington 2004 reported lower rates of bacterial infections in febrile infants less then three months old who tested positive for viral infection, the rate of bacterial urinary tract infection in that group was not negligible (up to 7%). It is possible that physicians may still be apprehensive in dismissing the potential for a concurrent urinary tract infection, despite the presence of a virus and persist in ordering urine tests and prescribing precautionary antibiotics. Urinary testing is dependant on obtaining a urine sample, which in young children may take a long time, hence prolong the ED length of visits.

However, Purcell 2002 reports rate of bacterial infection (all were urinary tract infections) in febrile RSV positive children up to two years old (1/3 were less then three months old) to be much lower at less than 1%, which puts into question this precautionary practice, at least in children over three months old.

A number of rapid viral testing studies report subgroup analyses of participants with positive rapid viral results versus those with negative results. These demonstrated that a positive rapid viral diagnosis decreased the number of ancillary tests, antibiotics prescribed, and ED length of visits. While it is interesting to see that a positive result can decrease the amount of additional tests, the question is whether the rapid viral test is worth doing before one knows its result. As rapid viral diagnosis requires an invasive and uncomfortable test for the children (either through nasopharyngeal swabs or washings), it is important to determine how it may affect the outcome of the tested population as a whole. In the four studies mentioned above, the rate of positive viral diagnosis ranged from as low as 19% to 66% (19% to 52% for influenza testing alone and 66% for multi-viral testing). Therefore, at least one-third of the children received an invasive test that may not have altered the course of their work-up or management. As one cannot definitively predict whether a child will have a positive test prior to doing it, this represents a large number of non-helpful tests, which will actually add to the burden presented by children with febrile respiratory illnesses.

AUTHORS' CONCLUSIONS

Implications for practice

Current evidence is insufficient, although promising, in supporting the widespread implementation of rapid viral diagnostic testing in the ED to reduce antibiotic prescription and ancillary investigations. The combined number of participants from the few available studies was not large enough to statistically detect a significant effect of rapid viral testing on our primary outcome and most of our secondary outcomes.

Implications for research

As pediatric ED physicians become more comfortable managing febrile children with a confirmed viral diagnosis without further ancillary testing and precautionary antibiotics, further trials of rapid viral testing may demonstrate a more sizable impact which would be detected upon ITT analyses, rather than just in subgroup analyses. A large RCT is still needed as findings from this meta-analysis found opposing effects on antibiotic use in the ED between studies. While they also suggest a positive effect of rapid viral testing on blood investigations and ED length of visit, they lacked the power to reach statistical significance.

Future studies are also needed to assess the impact of this intervention on other secondary outcomes. These include adverse effects of the intervention, effects on hospital admissions, and the rate of other severe concurrent bacterial infections. In addition, it will be important to evaluate the cost effectiveness of this intervention before it is implemented more widely.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by year of study]*

Bonner 2003

Methods	Randomized controlled trial
Participants	Previously healthy participants age 2 months -21 years old presenting to the Alabama Children's Hospital Emergency Department with fever, respiratory symptoms, malaise or headaches of 72 hrs duration or less (N = 391).
Interventions	Treatment group: results of nasopharyngeal swab for rapid influenza testing using FluOIA test (turnaround time < 25 minutes) being revealed to treating physicians at initial patient assessment. Control group: Results of the rapid test were not available to the treating physician.
Outcomes	Proportion of participants undergoing laboratory testing, radiographs, antibiotics or antiviral use, length of ED stay. Proportion of participants who had visits to a physician or new prescriptions for same illness post discharge from ED. Length of school (daycare) or work time loss related to this illness.
Notes	Original published data was analyzed using participants with revealed negative rapid influenza test results as a control group. We obtained unpublished raw data to analyse participants into 2 study groups, those who had the rapid test results revealed to the treating physician (irrespective of test results) as the intervention group and those whose rapid inluenza test results were not revealed to the treating physician (control).

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computerized randomization program in blocks of 4 participants (2 to intervention and 2 to control)
Allocation concealment?	Unclear	Randomization list was produced prior to the study. It is not mentioned whether individual allocation was concealed prior to enrolment.
Blinding? All outcomes	No	The impact of knowing the results of viral testing was the intervention being tested, and as such, could not be blinded.
Incomplete outcome data addressed? All outcomes	Yes	22 enrolled participants left before they were seen by the treating physician or received any treatment, hence could not contribute to the outcomes.

Bonner 2003 (*Continued*)

Free of selective reporting?	Yes	All outcomes are reported. Although published data was reported only per sub-group (by rapid viral testing result) , when contacted, the author supplied complete data for this review.
Free of other bias?	Yes	No other significant bias was found.

Poehling 2006

Methods	Randomized controlled trial using days as the unit of randomization for treatment allocation
Participants	Children under the age of 5 years old with fever or acute respiratory symptoms during the 2002-2003 and 2003-2004 influenza season coming to Vanderbilt Pediatric Emergency Department (N = 305). This is a university-based pediatric ED in Nashville, Tennessee caring for approximately 30,000 children annually.
Interventions	Three days per week, participants were enrolled into the study. Study days were prospectively randomized in blocks of 4 and 6, using a random number generator, to the point-of-care rapid influenza testing and results made available to the treating physician prior to patient assessment versus standard testing with results made unavailable until the subject had been discharged form the ED. There were equal numbers of study days for each group.
Outcomes	Proportion of participants undergoing laboratory testing (urine and blood), chest radiographs, antibiotics and antiviral use.
Notes	Although this study enrolled 5 participants with chronic cardio-respiratory (bronchopulmonary dysplasia and congenital heart defect) or immune disorders of unknown severity (as reported by parents but not related to chemotherapy), which may meet our review exclusion criteria, the primary author was contacted and raw data excluding these 5 participants was obtained (N = 300). We used this data for the purpose of the meta-analysis.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Block of days randomization by random number generator
Allocation concealment?	Unclear	Although participants could not have known which treatment was going to be in effect when coming to the ED, it is not specified in the publication whether participants were unaware of the treatment allocation until after consent for study partici-

Poehling 2006 (*Continued*)

		pation was obtained.
Blinding? All outcomes	No	The impact of knowing the results of viral testing was the intervention being tested, and as such, could not be blinded.
Incomplete outcome data addressed? All outcomes	Unclear	During the study period, 60 eligible children were not enrolled in the study. No mention is made of why these children were not enrolled.
Free of selective reporting?	Yes	All outcomes are reported.
Free of other bias?	Yes	No other significant bias was found.

Iyer 2006

Methods	Quazi-randomized controlled trial, using alternating days for treatment allocation
Participants	Children 2 to 24 months of age coming to the Cincinnati Children's Hospital Medical Center ED with fever (N = 700).
Interventions	Treatment group: Nasal swab for rapid influenza testing using Quickvue providing a result within 30 minutes. Control group: nasal swab for rapid influenza testing using Quickvue, but these were performed only twice daily to simulate routine laboratory testing turnaround and results were not available to the treating physician until the patient had been discharged from the ED.
Outcomes	Proportion of participants having blood culture, complete blood count, urine analyses, chest radiography, antibiotics use, hospital admission and return visits to the ED within 14 days of discharge. ED length of visits, visit-associated costs.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	No	Alternate days used for treatment allocation
Allocation concealment?	Unclear	Although participants could not have known which treatment was going to be in effect when coming to the ED, it is not specified in the publication whether participants were unaware of the treatment allocation until after consent for study participation was obtained.

Iyer 2006 (*Continued*)

Blinding? All outcomes	No	The impact of knowing the results of viral testing was the intervention being tested, and as such, could not be blinded.
Incomplete outcome data addressed? All outcomes	Yes	During the study period, 67 eligible participants were not enrolled in the study. Thirty-six children were missed during the initial screening process (these were discovered during a retrospective review of daily patient logs). Informed consent was not obtained on 19 participants. Five participants left before evaluation by a physician and 7 were enrolled twice within one month. Information was documented on only 11 of these participants, therefore it is unclear how the remaining 56 participants might have affected the outcome.
Free of selective reporting?	Yes	All outcomes are reported.
Free of other bias?	Yes	No other significant bias was noted.

Doan 2009

Methods	Randomized controlled trial
Participants	Previously healthy children age 3-36 months old coming to the ED at British Columbia Children's Hospital with fever and any respiratory symptoms (N = 199).
Interventions	Treatment group: Naso-pharyngeal aspirate for rapid respiratory virus panel (Influenza A/B, Parainfluenza 1/2/3, RSV, Adenovirus) using direct immuno-fluorescence assay (Light Diagnostics Simul Fluor Respiratory Screening agent). Control group: Routine admission to ED. Any test done was requested after assessment by treating physician.
Outcomes	ED length of visit, proportion of participants undergoing laboratory testing (blood and or urine) radiographs and antibiotics use. These outcome measures were also assessed post ED discharge.
Notes	Two of the authors of this Cochrane review are also investigators on this trial.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Patients were randomized to either study groups using a computer randomization program in variable block size (2, 4, 6 or 8).

Doan 2009 (*Continued*)

Allocation concealment?	Yes	Computer program was only accessed at the time consent for study participation was obtained.
Blinding? All outcomes	Unclear	The impact of knowing the results of viral testing was the intervention being tested, and as such, could not be blinded.
Incomplete outcome data addressed? All outcomes	Yes	During the study period, 175 eligible children were not enrolled either because they were treated in the ED during hours when the virology laboratory was not open or consent was not obtained. A retrospective chart review of these patient's outcome measures showed no systematic or significant differences to enrolled participants.
Free of selective reporting?	Yes	All outcomes are reported.
Free of other bias?	Yes	No other significant bias was noted.

FluOIA: rapid test for detection of influenza
ED: Emergency Department

Characteristics of excluded studies *[ordered by study ID]*

Abanses 2006	Although set out to be an RCT, when the treatment was not provided as per randomized allocation, these participants were re-assigned to the control group and vice versa and were analyzed as such (convenience sample). This study was no longer analyzed as an RCT hence did not meet our inclusion criteria.
Cohen 2007	This trial is set in community pediatric clinics, not in the ED.
Esposito 2003	This trial included children with congenital heart diseases (without specification about correction status) and significant chronic respiratory diseases (cystic fibrosis).

DATA AND ANALYSES

Comparison 1. Antibiotics use

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Antibiotics prescribed in ED	4	1590	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.71, 1.12]
2 Sensitivity analysis per risk of bias	3	890	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.61, 1.22]

Comparison 2. ED length of visit

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean ED length of visit in minutes	3	1290	Mean Difference (IV, Random, 95% CI)	-10.61 [-22.47, 1.25]
2 Sensitivity analysis per risk of bias	2	590	Mean Difference (IV, Random, 95% CI)	-19.47 [-51.38, 12.44]

Comparison 3. Laboratory investigations

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Blood investigations (cell count and/or cultures)	4	1590	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.62, 1.00]
2 Urine testing	4	1588	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.79, 1.19]
3 Blood investigation: sensitivity analysis per risk of bias	3	888	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.42, 0.89]
4 Urine testing: sensitivity analysis per risk of bias	3	890	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.70, 1.25]

Comparison 4. Chest radiography

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Chest radiography	4	1590	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.65, 0.91]
2 Sensitivity analysis per risk of bias	3	890	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.43, 0.81]

Comparison 5. Visits to physician or ED post ED discharge

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post ED discharge visit to MD	2	899	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.77, 1.29]

Analysis 1.1. Comparison 1 Antibiotics use, Outcome 1 Antibiotics prescribed in ED.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 1 Antibiotics use

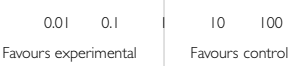
Outcome: 1 Antibiotics prescribed in ED

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	34/193	53/198		25.8 %	0.66 [0.45, 0.96]
Doan 2009	16/89	23/110		13.6 %	0.86 [0.48, 1.53]
Iyer 2006	54/345	59/355		30.6 %	0.94 [0.67, 1.32]
Poehling 2006	43/134	48/166		30.0 %	1.11 [0.79, 1.56]
Total (95% CI)	**761**	**829**		**100.0 %**	**0.89 [0.71, 1.12]**

Total events: 147 (Rapid viral testing), 183 (Control)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 4.11$, df = 3 (P = 0.25); $I^2 = 27\%$

Test for overall effect: Z = 0.99 (P = 0.32)

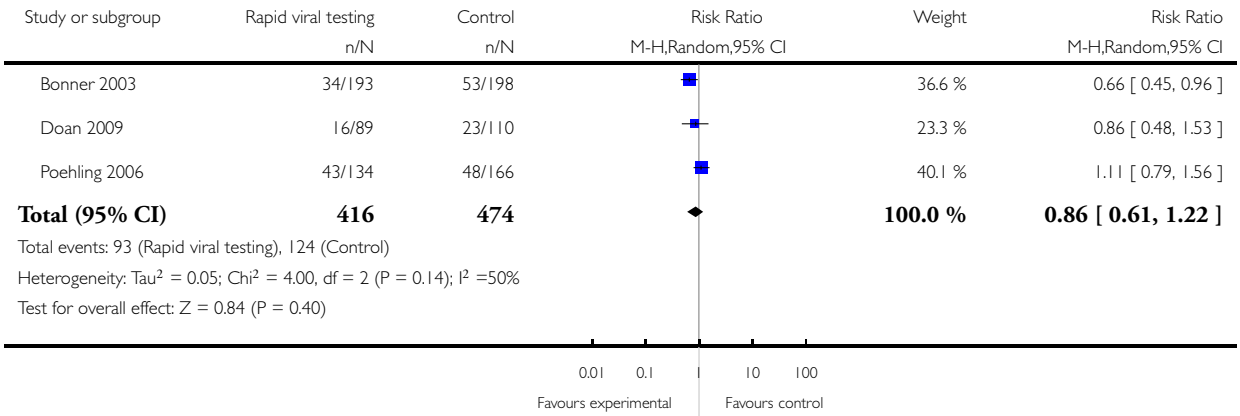


Analysis 1.2. Comparison 1 Antibiotics use, Outcome 2 Sensitivity analysis per risk of bias.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 1 Antibiotics use

Outcome: 2 Sensitivity analysis per risk of bias

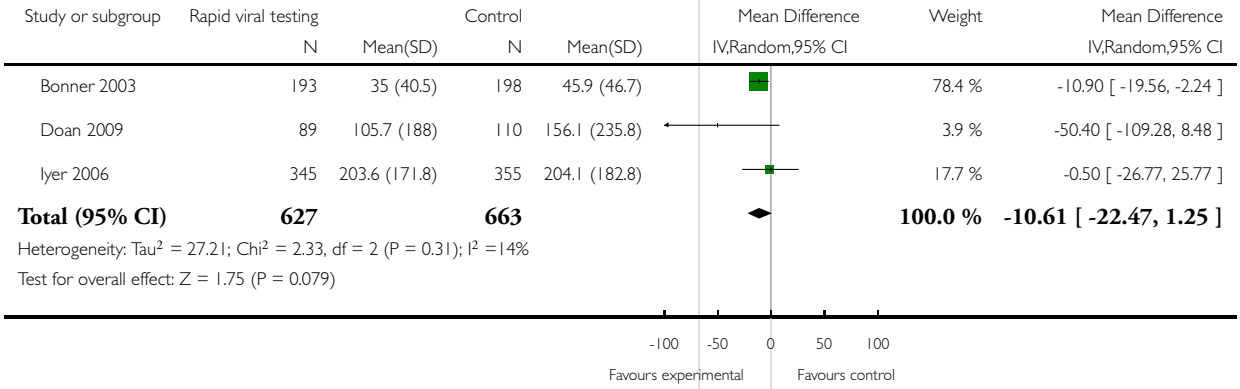


Analysis 2.1. Comparison 2 ED length of visit, Outcome 1 Mean ED length of visit in minutes.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 2 ED length of visit

Outcome: 1 Mean ED length of visit in minutes



Analysis 2.2. Comparison 2 ED length of visit, Outcome 2 Sensitivity analysis per risk of bias.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

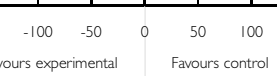
Comparison: 2 ED length of visit

Outcome: 2 Sensitivity analysis per risk of bias

Study or subgroup	Rapid viral testing N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Bonner 2003	193	35 (40.5)	198	45.9 (46.7)		78.3 %	-10.90 [-19.56, -2.24]
Doan 2009	89	105.7 (188)	110	156.1 (235.8)		21.7 %	-50.40 [-109.28, 8.48]
Total (95% CI)	**282**		**308**			**100.0 %**	**-19.47 [-51.38, 12.44]**

Heterogeneity: Tau² = 319.07; Chi² = 1.69, df = 1 (P = 0.19); I² =41%

Test for overall effect: Z = 1.20 (P = 0.23)



Analysis 3.1. Comparison 3 Laboratory investigations, Outcome 1 Blood investigations (cell count and/or cultures).

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 3 Laboratory investigations

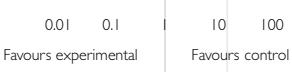
Outcome: 1 Blood investigations (cell count and/or cultures)

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	13/193	21/198		12.2 %	0.64 [0.33, 1.23]
Doan 2009	9/89	19/110		9.9 %	0.59 [0.28, 1.23]
Iyer 2006	93/345	104/355		63.1 %	0.92 [0.73, 1.17]
Poehling 2006	14/134	29/166		14.8 %	0.60 [0.33, 1.09]
Total (95% CI)	**761**	**829**		**100.0 %**	**0.79 [0.62, 1.00]**

Total events: 129 (Rapid viral testing), 173 (Control)

Heterogeneity: Tau² = 0.01; Chi² = 3.40, df = 3 (P = 0.33); I² =12%

Test for overall effect: Z = 1.93 (P = 0.054)



Analysis 3.2. Comparison 3 Laboratory investigations, Outcome 2 Urine testing.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 3 Laboratory investigations

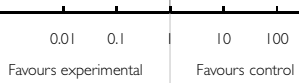
Outcome: 2 Urine testing

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	19/191	26/198		13.4 %	0.76 [0.43, 1.32]
Doan 2009	28/89	31/110		22.6 %	1.12 [0.73, 1.71]
Iyer 2006	73/345	75/355		50.6 %	1.00 [0.75, 1.33]
Poehling 2006	18/134	26/166		13.4 %	0.86 [0.49, 1.50]
Total (95% CI)	**759**	**829**		**100.0 %**	**0.97 [0.79, 1.19]**

Total events: 138 (Rapid viral testing), 158 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.42$, df = 3 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 0.31 (P = 0.76)



Analysis 3.3. Comparison 3 Laboratory investigations, Outcome 3 Blood investigation: sensitivity analysis per risk of bias.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 3 Laboratory investigations

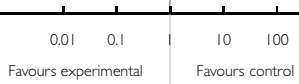
Outcome: 3 Blood investigation: sensitivity analysis per risk of bias

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	13/191	21/198		33.0 %	0.64 [0.33, 1.24]
Doan 2009	9/89	19/110		26.3 %	0.59 [0.28, 1.23]
Poehling 2006	14/134	29/166		40.8 %	0.60 [0.33, 1.09]
Total (95% CI)	**414**	**474**		**100.0 %**	**0.61 [0.42, 0.89]**

Total events: 36 (Rapid viral testing), 69 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.04$, df = 2 (P = 0.98); $I^2 = 0.0\%$

Test for overall effect: Z = 2.56 (P = 0.011)



Analysis 3.4. Comparison 3 Laboratory investigations, Outcome 4 Urine testing: sensitivity analysis per risk of bias.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 3 Laboratory investigations

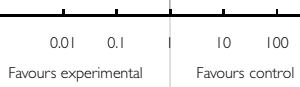
Outcome: 4 Urine testing: sensitivity analysis per risk of bias

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	19/193	26/198		27.0 %	0.75 [0.43, 1.31]
Doan 2009	28/89	31/110		45.9 %	1.12 [0.73, 1.71]
Poehling 2006	18/134	26/166		27.1 %	0.86 [0.49, 1.50]
Total (95% CI)	**416**	**474**		**100.0 %**	**0.93 [0.70, 1.25]**

Total events: 65 (Rapid viral testing), 83 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.37$, df = 2 (P = 0.50); $I^2 = 0.0\%$

Test for overall effect: Z = 0.47 (P = 0.64)



Analysis 4.1. Comparison 4 Chest radiography, Outcome 1 Chest radiography.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 4 Chest radiography

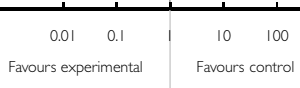
Outcome: 1 Chest radiography

Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bonner 2003	29/193	49/198		17.2 %	0.61 [0.40, 0.92]
Doan 2009	21/89	37/110		14.1 %	0.70 [0.44, 1.11]
Iyer 2006	86/345	100/355		48.3 %	0.88 [0.69, 1.13]
Poehling 2006	31/134	53/166		20.4 %	0.72 [0.50, 1.06]
Total (95% CI)	**761**	**829**		**100.0 %**	**0.77 [0.65, 0.91]**

Total events: 167 (Rapid viral testing), 239 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.74$, df = 3 (P = 0.43); $I^2 = 0.0\%$

Test for overall effect: Z = 2.97 (P = 0.0029)



Analysis 4.2. Comparison 4 Chest radiography, Outcome 2 Sensitivity analysis per risk of bias.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 4 Chest radiography

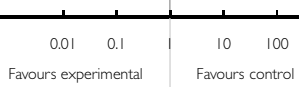
Outcome: 2 Sensitivity analysis per risk of bias

Study or subgroup	Rapid viral testing n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bonner 2003	29/193	49/198		38.0 %	0.54 [0.32, 0.90]
Doan 2009	21/89	37/110		25.0 %	0.61 [0.32, 1.14]
Poehling 2006	31/134	53/166		37.0 %	0.64 [0.38, 1.08]
Total (95% CI)	**416**	**474**		**100.0 %**	**0.59 [0.43, 0.81]**

Total events: 81 (Rapid viral testing), 139 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.24$, df = 2 (P = 0.89); $I^2 = 0.0\%$

Test for overall effect: Z = 3.26 (P = 0.0011)



Analysis 5.1. Comparison 5 Visits to physician or ED post ED discharge, Outcome 1 Post ED discharge visit to MD.

Review: Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department

Comparison: 5 Visits to physician or ED post ED discharge

Outcome: 1 Post ED discharge visit to MD

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Doan 2009	30/89	43/110		44.5 %	0.86 [0.59, 1.25]
Iyer 2006	61/345	56/355		55.5 %	1.12 [0.80, 1.56]
Total (95% CI)	**434**	**465**		**100.0 %**	**1.00 [0.77, 1.29]**

Total events: 91 (Experimental), 99 (Control)

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.08$, df = 1 (P = 0.30); $I^2 = 7\%$

Test for overall effect: Z = 0.02 (P = 0.98)

APPENDICES

Appendix 1. CENTRAL search strategy

EBM Reviews - Cochrane Central Register of Controlled Trials (1st Quarter 2009)

1. exp Respiratory Tract Infections/
2. exp Orthomyxoviridae/
3. Orthomyxoviridae Infections/
4. Influenza, Human/
5. exp Picornaviridae/
6. exp Picornaviridae Infections/
7. exp Adenoviridae/
8. Adenovirus Infections, Human/
9. exp Paramyxoviridae/
10. exp Paramyxoviridae Infections/
11. exp Coronaviridae/
12. exp Coronaviridae Infections/
13. (influenza adj3 (A or B)).mp.
14. (human adj2 influenz$).mp.
15. (metapneumovirus$ or meta-pneumovirus$ or "meta pneumovirus$").mp.
16. hMPV$.mp.
17. pneumovirus$.mp.
18. (rhinovirus$ or rhino-virus$ or "rhino virus$").mp.
19. (orthomyxovirus$ or ortho-myxovirus$ or "ortho myxovirus$").mp.
20. (adenovirus$ or adeno-virus$ or "adeno virus$").mp.
21. (parainfluenza$ or para-influenza$ or "para influenza$").mp.
22. (coronavirus$ or corona-virus$ or "corona virus$").mp.
23. (enterovirus$ or entero-virus$ or "entero virus$").mp.
24. picornavir$.mp.
25. respiratory syncytial virus.mp.
26. RSV.mp.
27. (acute adj3 respiratory).mp.
28. (respiratory adj2 virus$).mp.
29. ARI$.mp.
30. exp fever/
31. (febrile adj3 respiratory).mp.
32. pyrogens/
33. pyrogen$.mp.
34. nasal aspirate$.mp.
35. exp Antigens, Viral/
36. or/1-35
37. exp "sensitivity and specificity"/
38. (sensitiv$ or specificity).mp.
39. exp likelihood functions/
40. (likelihood adj3 ratio$).mp.
41. (ROC-curve or ROC curve or receiver operating characteristic curve).sh,mp.
42. diagnos$.mp.
43. exp Diagnosis/
44. (diagnost$ adj (accura$ or sensitiv$ or reliab$ or reliance or value)).af.
45. di.fs.
46. (routine adj5 test$).mp.
47. (false adj (positiv$ or negativ$)).mp.
48. ((observer adj variation$) or (predictive adj3 value)).mp.

49. du.fs.
50. Nasopharynx/
51. ((virus$ or viral) adj3 (detect$ or antigen?)).mp.
52. (antigen adj2 (test$ or detection)).mp.
53. or/37-52
54. exp Emergency medicine/
55. exp Emergencies/
56. exp Emergency service, hospital/
57. emergency medical services/
58. "hospital emergency service?".mp.
59. ED?.mp.
60. ER?.mp.
61. (emergenc$ adj5 (departmen$ or ward$ or service$ or unit$ or room$ or hospital$ or care or patient$ or physician$ or doctor$ or medicine or treatment$ or diagnos$ or resident$)).mp.
62. (emergency or emergencies).jn.
63. Point-of-Care Systems/
64. ("point of care" or point-of-care or POC).mp.
65. or/54-64
66. exp Infant/
67. exp Child/
68. Adolescent/
69. Minors/
70. exp Puberty/
71. exp Pediatrics/
72. infant$.mp.
73. infancy.mp.
74. newborn$.mp.
75. baby.mp.
76. babies.mp.
77. neonat$.mp.
78. preterm$.mp.
79. prematur$.mp.
80. postmatur$.mp.
81. kid.mp.
82. kids.mp.
83. toddler$.mp.
84. adolescen$.mp.
85. teen$.mp.
86. boy$.mp.
87. girl.mp.
88. minor$.mp.
89. pubert$.mp.
90. pubescen$.mp.
91. prepubescen$.mp.
92. pediatric$.mp.
93. paediatric$.mp.
94. peadiatric$.mp.
95. infan$.jw.
96. child$.jw.
97. pediatric$.jw.
98. paediatric$.jw.
99. adolescen$.jw.
100. youth$.jw.

101. school$.jw.
102. or/66-101
103. and/36,53,65,10

Appendix 2. MEDLINE search strategy

MEDLINE (1950 to April Week 3 2009)

1. exp Respiratory Tract Infections/
2. exp Orthomyxoviridae/
3. Orthomyxoviridae Infections/
4. Influenza, Human/
5. exp Picornaviridae/
6. exp Picornaviridae Infections/
7. exp Adenoviridae/
8. Adenovirus Infections, Human/
9. exp Paramyxoviridae/
10. exp Paramyxoviridae Infections/
11. exp Coronaviridae/
12. exp Coronaviridae Infections/
13. (influenza adj3 (A or B)).mp.
14. (human adj2 influenz$).mp.
15. (metapneumovirus$ or meta-pneumovirus$ or "meta pneumovirus$").mp.
16. hMPV$.mp.
17. pneumovirus$.mp.
18. (rhinovirus$ or rhino-virus$ or "rhino virus$").mp.
19. (orthomyxovirus$ or ortho-myxovirus$ or "ortho myxovirus$").mp.
20. (adenovirus$ or adeno-virus$ or "adeno virus$").mp.
21. (parainfluenza$ or para-influenza$ or "para influenza$").mp.
22. (coronavirus$ or corona-virus$ or "corona virus$").mp.
23. (enterovirus$ or entero-virus$ or "entero virus$").mp.
24. picornavir$.mp.
25. respiratory syncytial virus.mp.
26. RSV.mp.
27. (acute adj3 respiratory).mp.
28. (respiratory adj2 virus$).mp.
29. ARI$.mp.
30. exp fever/
31. (febrile adj3 respiratory).mp.
32. pyrogens/
33. pyrogen$.mp.
34. nasal aspirate$.mp.
35. exp Antigens, Viral/
36. or/1-35
37. exp "sensitivity and specificity"/
38. (sensitiv$ or specificity).mp.
39. exp likelihood functions/
40. (likelihood adj3 ratio$).mp.
41. (ROC-curve or ROC curve or receiver operating characteristic curve).sh,mp.
42. diagnos$.mp.
43. exp Diagnosis/
44. (diagnost$ adj (accura$ or sensitiv$ or reliab$ or reliance or value)).af.
45. di.fs.

46. (routine adj5 test$).mp.
47. (false adj (positiv$ or negativ$)).mp.
48. ((observer adj variation$) or (predictive adj3 value)).mp.
49. du.fs.
50. Nasopharynx/
51. ((virus$ or viral) adj3 (detect$ or antigen?)).mp.
52. (antigen adj2 (test$ or detection)).mp.
53. or/37-52
54. exp Emergency medicine/
55. exp Emergencies/
56. exp Emergency service, hospital/
57. emergency medical services/
58. "hospital emergency service?".mp.
59. ED?.mp.
60. ER?.mp.
61. (emergenc$ adj5 (departmen$ or ward$ or service$ or unit$ or room$ or hospital$ or care or patient$ or physician$ or doctor$ or medicine or treatment$ or diagnos$ or resident$)).mp.
62. (emergency or emergencies).jn.
63. Point-of-Care Systems/
64. ("point of care" or point-of-care or POC).mp.
65. or/54-64
66. exp Infant/
67. exp Child/
68. Adolescent/
69. Minors/
70. exp Puberty/
71. exp Pediatrics/
72. infant$.mp.
73. infancy.mp.
74. newborn$.mp.
75. baby.mp.
76. babies.mp.
77. neonat$.mp.
78. preterm$.mp.
79. prematur$.mp.
80. postmatur$.mp.
81. kid.mp.
82. kids.mp.
83. toddler$.mp.
84. adolescen$.mp.
85. teen$.mp.
86. boy$.mp.
87. girl.mp.
88. minor$.mp.
89. pubert$.mp.
90. pubescen$.mp.
91. prepubescen$.mp.
92. pediatric$.mp.
93. paediatric$.mp.
94. peadiatric$.mp.
95. infan$.jw.
96. child$.jw.
97. pediatric$.jw.

98. paediatric$.jw.
99. adolescen$.jw.
100. youth$.jw.
101. school$.jw.
102. or/66-101
103. and/36,53,65,102
104. clinical trial.pt.
105. randomi?ed.ti,ab.
106. placebo.ti,ab.
107. dt.fs.
108. randomly.ti,ab.
109. trial.ti,ab.
110. groups.ti,ab.
111. or/104-110
112. animals/
113. humans/
114. 112 not (112 and 113)
115. 111 not 114
116. and/103,115

Appendix 3. EMBASE search strategy

1. exp Respiratory Tract Infection/
2. exp orthomyxovirus/
3. exp picornavirus/
4. exp adenovirus/
5. exp paramyxovirus/
6. exp coronavirus/
7. exp Virus Infection/
8. (influenza adj3 (A or B)).mp.
9. (human adj2 influenz$).mp.
10. (metapneumovirus$ or meta-pneumovirus$ or "meta pneumovirus$").mp.
11. hMPV$.mp.
12. pneumovirus$.mp.
13. (rhinovirus$ or rhino-virus$ or "rhino virus$").mp.
14. (orthomyxovirus$ or ortho-myxovirus$ or "ortho myxovirus$").mp.
15. (adenovirus$ or adeno-virus$ or "adeno virus$").mp.
16. (parainfluenza$ or para-influenza$ or "para influenza$").mp.
17. (coronavirus$ or corona-virus$ or "corona virus$").mp.
18. (enterovirus$ or entero-virus$ or "entero virus$").mp.
19. picornavir$.mp.
20. respiratory syncytial virus.mp.
21. RSV.mp.
22. (acute adj3 respiratory).mp.
23. (respiratory adj2 virus$).mp.
24. ARI$.mp.
25. fever/
26. pyrexia idiopathica/
27. (febrile adj3 respiratory).mp.
28. pyrogen/
29. pyrogen$.mp.
30. nasal aspirate$.mp.

31. exp Virus Antigen/
32. or/1-31
33. exp "sensitivity and specificity"/
34. (sensitiv$ or specificity).mp.
35. statistical model/
36. (likelihood adj3 (function$ or ratio$)).mp.
37. (ROC-curve or ROC curve or receiver operating characteristic curve).sh,mp.
38. diagnos$.mp.
39. exp Diagnosis/
40. (diagnost$ adj (accura$ or sensitiv$ or reliab$ or reliance or value)).af.
41. di.fs.
42. (routine adj5 test$).mp.
43. (false adj (positiv$ or negativ$)).mp.
44. ((observer adj variation$) or (predictive adj3 value)).mp.
45. du.fs.
46. exp nasopharynx/
47. exp oropharynx/
48. ((virus$ or viral) adj3 (detect$ or antigen?)).mp.
49. (antigen adj2 (test$ or detection)).mp.
50. or/33-49
51. emergency medicine/
52. emergency/
53. emergency health service/
54. "hospital emergency service?".mp.
55. ED?.mp.
56. ER?.mp.
57. (emergenc$ adj5 (departmen$ or ward$ or service$ or unit$ or room$ or hospital$ or care or patient$ or physician$ or doctor$ or medicine or treatment$ or diagnos$ or resident$)).mp.
58. (emergency $ or emergencies $).jn.
59. hospital information system/
60. medical information system/
61. ("point of care" or point-of-care or POC).mp.
62. or/51-61
63. exp newborn/
64. exp child/
65. exp adolescent/
66. exp adolescence/
67. exp pediatrics/
68. infant$.mp.
69. infancy.mp.
70. newborn$.mp.
71. baby.mp.
72. babies.mp.
73. neonat$.mp.
74. preterm$.mp.
75. prematur$.mp.
76. postmatur$.mp.
77. kid.mp.
78. kids.mp.
79. child$.mp.
80. toddler$.mp.
81. adolescen$.mp.
82. teen$.mp.

83. boy$.mp.
84. girl$.mp.
85. minor$.mp.
86. pubert$.mp.
87. pubescen$.mp.
88. prepubescen$.mp.
89. pediatric$.mp.
90. paediatric$.mp.
91. peadiatric$.mp.
92. infan$.jw.
93. child$.jw.
94. pediatric$.jw.
95. paediatric$.jw.
96. adolescen$.jw.
97. youth$.jw.
98. school$.jw.
99. or/63-98
100. and/32,50,62,99
101. exp clinical trial/
102. randomi?ed.ti,ab.
103. placebo.ti,ab.
104. (ae or dt or to).fs.
105. randomly.ti,ab.
106. trial.ti,ab.
107. groups.ti,ab.
108. or/101-107
109. animal/
110. human/
111. 109 not (109 and 110)
112. 108 not 111
113. and/100,112

Appendix 4. HEALTHSTAR search strategy

HealthStar (1966 to March 2009)

1. exp Respiratory Tract Infections/
2. exp Orthomyxoviridae/
3. Orthomyxoviridae Infections/
4. Influenza, Human/
5. exp Picornaviridae/
6. exp Picornaviridae Infections/
7. exp Adenoviridae/
8. Adenovirus Infections, Human/
9. exp Paramyxoviridae/
10. exp Paramyxoviridae Infections/
11. exp Coronaviridae/
12. exp Coronaviridae Infections/
13. (influenza adj3 (A or B)).mp.
14. (human adj2 influenz$).mp.
15. (metapneumovirus$ or meta-pneumovirus$ or "meta pneumovirus$").mp.
16. hMPV$.mp.
17. pneumovirus$.mp.

18. (rhinovirus$ or rhino-virus$ or "rhino virus$").mp.
19. (orthomyxovirus$ or ortho-myxovirus$ or "ortho myxovirus$").mp.
20. (adenovirus$ or adeno-virus$ or "adeno virus$").mp.
21. (parainfluenza$ or para-influenza$ or "para influenza$").mp.
22. (coronavirus$ or corona-virus$ or "corona virus$").mp.
23. (enterovirus$ or entero-virus$ or "entero virus$").mp.
24. picornavir$.mp.
25. respiratory syncytial virus.mp.
26. RSV.mp.
27. (acute adj3 respiratory).mp.
28. (respiratory adj2 virus$).mp.
29. ARI$.mp.
30. exp fever/
31. (febrile adj3 respiratory).mp.
32. pyrogens/
33. pyrogen$.mp.
34. nasal aspirate$.mp.
35. exp Antigens, Viral/
36. or/1-35
37. exp "sensitivity and specificity"/
38. (sensitiv$ or specificity).mp.
39. exp likelihood functions/
40. (likelihood adj3 ratio$).mp.
41. (ROC-curve or ROC curve or receiver operating characteristic curve).sh,mp.
42. diagnos$.mp.
43. exp Diagnosis/
44. (diagnost$ adj (accura$ or sensitiv$ or reliab$ or reliance or value)).af.
45. di.fs.
46. (routine adj5 test$).mp.
47. (false adj (positiv$ or negativ$)).mp.
48. ((observer adj variation$) or (predictive adj3 value)).mp.
49. du.fs.
50. Nasopharynx/
51. ((virus$ or viral) adj3 (detect$ or antigen?)).mp.
52. (antigen adj2 (test$ or detection)).mp.
53. or/37-52
54. exp Emergency medicine/
55. exp Emergencies/
56. exp Emergency service, hospital/
57. emergency medical services/
58. "hospital emergency service?".mp.
59. ED?.mp.
60. ER?.mp.
61. (emergenc$ adj5 (departmen$ or ward$ or service$ or unit$ or room$ or hospital$ or care or patient$ or physician$ or doctor$ or medicine or treatment$ or diagnos$ or resident$)).mp.
62. (emergency $ or emergencies $).jn.
63. Point-of-Care Systems/
64. ("point of care" or point-of-care or POC).mp.
65. or/54-64
66. exp Infant/
67. exp Child/
68. Adolescent/
69. Minors/

70. exp Puberty/
71. exp Pediatrics/
72. infant$.mp.
73. infancy.mp.
74. newborn$.mp.
75. baby.mp.
76. babies.mp.
77. neonat$.mp.
78. preterm$.mp.
79. prematur$.mp.
80. postmatur$.mp.
81. kid.mp.
82. kids.mp.
83. toddler$.mp.
84. adolescen$.mp.
85. teen$.mp.
86. boy$.mp.
87. girl.mp.
88. minor$.mp.
89. pubert$.mp.
90. pubescen$.mp.
91. prepubescen$.mp.
92. pediatric$.mp.
93. paediatric$.mp.
94. peadiatric$.mp.
95. infan$.jw.
96. child$.jw.
97. pediatric$.jw.
98. paediatric$.jw.
99. adolescen$.jw.
100. youth$.jw.
101. school$.jw.
102. or/66-101
103. and/36,53,65,102
104. clinical trial.pt.
105. randomi?ed.ti,ab.
106. placebo.ti,ab.
107. dt.fs.
108. randomly.ti,ab.
109. trial.ti,ab.
110. groups.ti,ab.
111. or/104-110
112. limit 111 to humans
113. and/103,112

Appendix 5. MEDLINE In-Process search strategy

Ovid MEDLINE In-Process & Other
Non-Indexed Citations (April 27, 2009)

1. (influenza adj3 (A or B)).mp.
2. (human adj2 influenz$).mp.
3. (metapneumovirus$ or meta-pneumovirus$ or "meta pneumovirus$").mp.
4. hMPV$.mp.
5. pneumovirus$.mp.
6. (rhinovirus$ or rhino-virus$ or "rhino virus$").mp.
7. (orthomyxovir$ or ortho-myxovir$ or "ortho myxovir$").mp.
8. (adenovir$ or adeno-vir$ or "adeno vir$").mp.
9. (parainfluenza$ or para-influenza$ or "para influenza$").mp.
10. (paramyxovir$ or para-myxovir$ or "para myxovir$").mp.
11. (coronavirus$ or corona-virus$ or "corona virus$").mp.
12. (enterovirus$ or entero-virus$ or "entero virus$").mp.
13. picornavir$.mp.
14. respiratory syncytial virus.mp.
15. RSV.mp.
16. (acute adj3 respiratory).mp.
17. (respiratory adj2 (virus$ or infection?)).mp.
18. ARI$.mp.
19. fever.mp.
20. (febrile adj3 respiratory).mp.
21. pyrogen$.mp.
22. nasal aspirate$.mp.
23. (viral adj3 antigen$).mp.
24. or/1-23
25. (sensitiv$ or specificity).mp.
26. (likelihood adj3 (function$ or ratio$)).mp.
27. (ROC-curve or ROC curve or receiver operating characteristic curve).mp.
28. diagnos$.mp.
29. (diagnost$ adj (accura$ or sensitiv$ or reliab$ or reliance or value)).af.
30. (routine adj5 test$).mp.
31. (false adj (positiv$ or negativ$)).mp.
32. ((observer adj variation$) or (predictive adj3 value)).mp.
33. nasopharynx.mp.
34. ((virus$ or viral) adj3 (detect$ or antigen?)).mp.
35. (antigen adj2 (test$ or detection)).mp.
36. or/25-35
37. "hospital emergency service?".mp.
38. ED?.mp.
39. ER?.mp.
40. (emergenc$ adj5 (departmen$ or ward$ or service$ or unit$ or room$ or hospital$ or care or patient$ or physician$ or doctor$ or medicine or treatment$ or diagnos$ or resident$)).mp.
41. (emergency or emergencies).jn,mp.
42. ("point of care" or point-of-care or POC).mp.
43. or/37-42
44. infant$.mp.
45. infancy.mp.
46. newborn$.mp.
47. baby.mp.
48. babies.mp.

49. neonat$.mp.
50. preterm$.mp.
51. prematur$.mp.
52. postmatur$.mp.
53. kid.mp.
54. kids.mp.
55. toddler$.mp.
56. adolescen$.mp.
57. teen$.mp.
58. boy$.mp.
59. girl.mp.
60. minor$.mp.
61. pubert$.mp.
62. pubescen$.mp.
63. prepubescen$.mp.
64. pediatric$.mp.
65. paediatric$.mp.
66. peadiatric$.mp.
67. infan$.jw.
68. child$.jw.
69. pediatric$.jw.
70. paediatric$.jw.
71. adolescen$.jw.
72. youth$.jw.
73. school$.jw.
74. or/44-73
75. and/24,36,43,74
76. clinical trial.pt.
77. randomi?ed.ti,ab.
78. placebo.ti,ab.
79. dt.fs.
80. randomly.ti,ab.
81. trial.ti,ab.
82. groups.ti,ab.
83. or/76-82
84. and/76,83

Appendix 6. BIOSIS Previews search strategy

BIOSIS Previews ISI Web of Knowledge^{SM} v3.0 (1969 to April 2009)

Set	Search
#9	#8 AND #7
#8	TS=clinical trial* OR TS=research design OR TS=comparative stud* OR TS=evaluation stud* OR TS=controlled trial* OR TS=follow-up stud* OR TS=prospective stud* OR TS=random* OR TS=placebo* OR TS=(single blind*) OR TS=(double blind*)
#7	#6 AND #5

(*Continued*)

#6	TS=(hospital SAME emergency SAME service*) OR TS=(ED or EDS) OR TS=(ER or ERs) OR TS=(emergenc* SAME departmen*) OR TS=(emergenc* SAME ward*) OR TS=(emergenc* SAME service*) OR TS=(emergenc* SAME unit*) OR TS=(emergenc* SAME room*) OR TS=(emergenc* SAME hospital*) OR TS=(emergenc* SAME care) OR TS=(emergenc* SAME patient*) OR TS=(emergenc* SAME physician*) OR TS=(emergenc* SAME doctor*) OR TS=(emergenc* SAME medicine) OR TS=(emergenc* SAME treatment*) OR TS=(emergenc* SAME diagnos*) OR TS=(emergenc* SAME resident*) OR TS=(emergency OR emergencies) OR TS=("point of care" OR point-of-care OR POC)
#5	#4 AND #3
#4	TS=(sensitiv* OR specificity) OR TS=(likelihood SAME function*) OR TS=(likelihood SAME ratio*) OR TS=(ROC-curve OR "ROC curve") OR TS=(receiver SAME operating SAME characteristic SAME curve) OR TS=diagnos* OR TS=(diagnost* SAME accura*) OR TS=(diagnost* SAME sensitiv*) OR TS=(diagnost* SAME reliab*) OR TS=(diagnost* SAME reliance) OR TS=(diagnost* SAME value) OR TS=(routine SAME test*) OR TS=(false SAME positiv*) OR TS=(false SAME negativ*) OR TS=(observer SAME variation*) OR TS=(predictive SAME value) OR TS=nasopharynx OR TS=(vir* SAME detect*) OR TS=(vir* SAME antigen*) OR TS=(antigen SAME test*) OR TS=(antigen SAME detection)
#3	#2 AND #1
#2	TS=(influenza SAME A) OR TS=(influenza SAME B) OR TS=(human SAME influenz*) OR TS=(metapneumovirus* OR meta-pneumovirus* OR "meta pneumovirus*" OR hMPV* OR pneumovirus* OR rhinovirus* OR rhino-virus* OR "rhino virus*" OR orthomyxovir* OR ortho-myxovir* OR "ortho myxovir*" OR adenovir* or adeno-vir* or "adeno vir*" OR parain-fluenza* OR para-influenza* OR "para influenza*" OR paramyxovir* OR para-myxovir* OR "para myxovir*" OR coronavirus* OR corona-virus* OR "corona virus*" OR enterovirus* OR entero-virus* OR "entero virus*" OR picornavir*) OR TS=(respi-ratory SAME syncytial SAME virus) OR TS=RSV OR TS=(acute SAME respiratory) OR TS=(respiratory SAME infection*) OR TS=ARI* OR TS=fever OR TS=(febrile SAME respiratory) OR TS=pyrogen* OR TS=(nasal SAME aspirate*) OR TS=(viral SAME antigen*)
#1	TS=(infant* OR infancy OR newborn* OR baby OR babies OR neonat* OR preterm* OR prematur* OR postmatur* OR kid OR kids OR toddler* OR adolescen* OR teen* OR boy* OR girl OR minor* OR pubert* OR pubescen* OR prepubescen* OR pediatric* OR paediatric* OR peadiatric*) DocType=All document types; LitType=All literature types; Language=All languages; Taxa Notes=All Taxa Notes; Database=BIOSIS Previews; Timespan=1969-2009

Appendix 7. CAB Abstracts search strategy

CAB Abstracts via ERL™ WebSPIRS™ 5.12 (1973 to 2007)

Search			Results
	#54	#53 and #52	1
	#53	#6 and #23 and #34 and #42	26
	#52	(#50)not(#51)	92642
	#51	((human) in DE)not((nonhuman) in DE)	202376

(*Continued*)

	#50	(explode "randomized-controlled-trials" in BT,DE,GE,OD) or (((controlled clinical trial*) in TI)or((controlled clinical trial*) in AB)) or (((random* or placebo* or double-blind) in TI)or((random* or placebo* or double-blind) in AB)) or (((randomi?ed controlled trial) in TI)or((randomi?ed controlled trial) in AB)) or (((single-blind-procedure) in SU)or((double-blind-procedure) in SU) or((crossover-procedure) in SU)) or (explode "clinical-trials" in BT,DE,GE,OD) or (explode "randomized-controlled-trials" in BT,DE,GE,OD)	105526
	#49	((controlled clinical trial*) in TI)or((controlled clinical trial*) in AB)	771
	#48	((random* or placebo* or double-blind) in TI)or((random* or placebo* or double-blind) in AB)	103451
	#47	((randomi?ed controlled trial) in TI)or((randomi?ed controlled trial) in AB)	2608
	#46	((single-blind-procedure) in SU)or((double-blind-procedure) in SU)or((crossover-procedure) in SU)	0
	#45	explode "clinical-trials" in BT,DE,GE,OD	6239
	#44	explode "randomized-controlled-trials" in BT,DE,GE,OD	3452
	#43	explode "randomized-controlled-trials" in BT,DE,GE,OD	3452
	#42	((emergenc* medicine)or(emergenc* treatment*)or(emergenc* diagnos*)) or ((emergenc* patient*)or(emergenc* physician*)or(emergenc* doctor*)) or ((emergenc* room*)or(emergenc* hospital*)or(emergenc*care)) or ((emergenc* departmen*)or(emergenc* ward*)or(emergenc* unit*)) or (((hospital emergency service*) in AB)or((ER*) in AB)or((ED*) in AB)) or (((hospital emergency service*) in TI)or((ER*) in TI)or((ED*) in TI)) or ((emergenc* resident)or(point of care)or(POC))	335359
	#41	(emergenc* resident)or(point of care)or(POC)	312
	#40	(emergenc* medicine)or(emergenc* treatment*)or(emergenc* diagnos*)	1251

(*Continued*)

	#39	(emergenc* patient*)or(emergenc* physician*)or(emergenc* doctor*)	62
	#38	(emergenc* room*)or(emergenc* hospital*)or(emergenc*care)	315
	#37	(emergenc* departmen*)or(emergenc* ward*)or(emergenc* unit*)	582
	#36	((hospital emergency service*) in AB)or((ER*) in AB) or((ED*) in AB)	305566
	#35	((hospital emergency service*) in TI)or((ER*) in TI) or((ED*) in TI)	79346
	#34	(explode "statistical-analysis" in BT,DE,GE,OD) or (explode "nasopharynx-" in BT,DE,GE,OD) or ((antigen test*)or(antigen detection)) or ((vir* detection)or(vir* antigen)) or ((observer variation)or(predictive value)) or ((ROC-curve)or(receiver operating characteristic curve)) or ((("false-negative-results" in BT,DE,GE,OD) or ("false-positive-results" in BT,DE,GE,OD)) or (explode "diagnosis-" in BT,DE,GE,OD) or (((likelihood ratio) in AB)or((likelihood function) in AB)) or (((sensitiv*) in AB)or((specificity) in AB))	297894
	#33	explode "nasopharynx-" in BT,DE,GE,OD	246
	#32	(antigen test*)or(antigen detection)	1839
	#31	(vir* detection)or(vir* antigen)	3248
	#30	(observer variation)or(predictive value)	2341
	#29	(ROC-curve)or(receiver operating characteristic curve)	138
	#28	("false-negative-results" in BT,DE,GE,OD) or ("false-positive-results" in BT,DE,GE,OD)	338
	#27	explode "diagnosis-" in BT,DE,GE,OD	108639
	#26	((likelihood ratio) in AB)or((likelihood function) in AB)	653
	#25	((sensitiv*) in AB)or((specificity) in AB)	166410

(*Continued*)

	#24	explode "statistical-analysis" in BT,DE,GE,OD	34711
	#23	(nasal aspirate*) or (("fever-" in BT,DE,GE,OD) or ("pyrogens-" in BT,DE,GE,OD)) or (explode "Paramyxoviridae-" in BT,DE,GE,OD) or (((influenza) in TI) or((influenza) in AB)) or (explode "influenza-" in BT,DE,GE,OD) or ((explode "human-respiratory-syncytial-virus" in BT,DE,GE,OD) or (explode "lower-respiratory-tract-infections" in BT,DE,GE,OD)) or (((ARI*) in TI)or((ARI*) in AB)) or (((respiratory infection*) in TI)or((respiratory infection*) in AB)) or (((respiratory virus*) in TI)or((respiratory virus*) in AB)) or (((acute respiratory) in TI)or((acute respiratory) in AB)) or (explode "Enterovirus-" in BT,DE,GE,OD) or (explode "Coronavirus-" in BT,DE,GE,OD) or (explode "parainfluenza-virus" in BT,DE,GE,OD) or (explode "human-adenovirus" in BT,DE,GE,OD) or (explode "Orthomyxoviridae-" in BT,DE,GE,OD) or (explode "Rhinovirus-" in BT,DE,GE,OD)	100764
	#22	nasal aspirate*	12
	#21	("fever-" in BT,DE,GE,OD) or ("pyrogens-" in BT,DE,GE,OD)	2017
	#20	((ARI*) in TI)or((ARI*) in AB)	71333
	#19	((respiratory infection*) in TI)or((respiratory infection*) in AB)	1585
	#18	((respiratory virus*) in TI)or((respiratory virus*) in AB)	315
	#17	((acute respiratory) in TI)or((acute respiratory) in AB)	1515
	#16	explode "Enterovirus-" in BT,DE,GE,OD	2861
	#15	explode "Coronavirus-" in BT,DE,GE,OD	5393
	#14	explode "parainfluenza-virus" in BT,DE,GE,OD	463
	#13	explode "human-adenovirus" in BT,DE,GE,OD	137
	#12	explode "Orthomyxoviridae-" in BT,DE,GE,OD	5908
	#11	explode "Rhinovirus-" in BT,DE,GE,OD	270

(*Continued)*

	#10	explode "Paramyxoviridae-" in BT,DE,GE,OD	10783
	#9	((influenza) in TI)or((influenza) in AB)	6414
	#8	explode "influenza-" in BT,DE,GE,OD	1953
	#7	(explode "human-respiratory-syncytial-virus" in BT,DE,GE,OD) or (explode "lower-respiratory-tract-infections" in BT,DE,GE,OD)	364
	#6	(((paediatric*) in AB)or((pediatric*) in AB)or((pediatric*) in AB)) or (((paediatric*) in TI)or((pediatric*) in TI)or((peadtric*) in TI)) or (explode "adolescents-" in BT,DE,GE,OD) or (explode "children-" in BT,DE,GE,OD) or (explode "infants-" in BT,DE,GE,OD)	70047
	#5	((paediatric*) in AB)or((pediatric*) in AB)or((pediatric*) in AB)	4679
	#4	((paediatric*) in TI)or((pediatric*) in TI)or((peadtric*) in TI)	1898
	#3	explode "adolescents-" in BT,DE,GE,OD	7452
	#2	explode "children-" in BT,DE,GE,OD	48050
	#1	explode "infants-" in BT,DE,GE,OD	23356

Appendix 8. CBCA search strategy

CBCA ProQuest (1970 to 2007)
("acute respiratory" OR ARI OR influenza) AND (diagnos*) AND (emergenc* or ED* or ER* OR "point of care" OR POC) AND (infant* or child* or adolescen* OR pediatric*) Limit: Scholarly documents

Appendix 9. Proquest Dissertations and Theses search strategy

Proquest Dissertations and Theses - Full Text (1861-2009)
("acute respiratory" OR ARI OR influenza) AND (diagnos*) AND (emergenc* or ED* or ER* OR "point of care" OR POC) AND (infant* or child* or adolescen* OR pediatric*) Limit: Scholarly documents.

Evid.-Based Child Health **5**: 709–751 (2010)

WHAT'S NEW

Last assessed as up-to-date: 26 April 2009.

21 January 2010	Amended	Contact details updated.

HISTORY

Protocol first published: Issue 2, 2007

Review first published: Issue 4, 2009

16 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Quynh Doan (QD) designed and wrote the protocol.

Terry Klassen (TK) and QD prepared the quality assessment forms and data extraction forms.

Paul Enarson and QD selected and reviewed relevant studies, assessed the quality of studies, extracted and analyzed the data and wrote the review draft.

Niranjan Kissoon (NK), David Johnson (DJ) and TK provided advice, reviewed, edited and approved the draft.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of British Columbia, Canada.

Electronic database search engines and reference manager programs were accessible from the University Library.

- Albert Research Center for Child Health Evidence, Canada.

Librarian expertise and support was provided by this organization.

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External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1) At the protocol stage, we had intended to assess inter-rater agreement for quality of trial assessment, but as there was no disagreement between the two review authors (QD, PE) regarding the quality assessment of the included trials, an overtly complicated adapted Kappa for ordinal categorical inter-rater assessment was felt to be unwarranted.

2) At the protocol stage, we were going to see if subgroup analyses by child age categories would yield important differences in outcomes. As so few studies were included in this review, pooled results still lacked power to definitively determine the effect of rapid viral testing. We concluded that further sub-grouping of participants would unlikely yield significant information and did not run such analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

*Emergency Service, Hospital; Adolescent; Anti-Bacterial Agents [*therapeutic use]; Bacterial Infections [diagnosis]; Fever [*virology]; Length of Stay; Radiography, Thoracic [utilization]; Randomized Controlled Trials as Topic; Respiratory Tract Infections [*virology]; Virus Diseases [*diagnosis]

MeSH check words

Child; Humans; Infant