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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 (EDs) 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 if the use of a rapid viral detection test for children with an acute respiratory infection (ARI) in Emergency Departments (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.

Search methods

We searched CENTRAL (2014, Issue 6), MEDLINE (1950 to July week 1, 2014), MEDLINE In-Process & Other Non-Indexed Citations (15 July 2014), EMBASE.com (1988 to July 2014), HealthStar (1966 to 2009), BIOSIS Previews (1969 to July 2014), CAB Abstracts (1973 to July 2014), 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. We obtained missing data from trial authors. We expressed differences in rate of investigations and antibiotic use as risk ratios (RRs), and expressed difference in ED length of visits as mean differences (MDs), with 95% confidence intervals (CIs).

Main results

No new trials were identified in this 2014 update. We included four trials (three RCTs and one quazi-RCT), with 759 children in the rapid viral testing group and 829 in the control group. Three out of the four studies were comparable in terms of young age of participants, with one study increasing the age of inclusion up to five years of age. All studies included either fever or respiratory symptoms as inclusion criteria (two required both, one required fever or respiratory symptoms, and one required only fever). All studies were comparable in terms of exclusion criteria, intervention, and outcome data. In terms of risk of bias, one study failed to utilize a random sequence generator, one study did not comment on completeness of outcome data, and only one of four studies included allocation concealment as part of the study design. None of the studies definitively blinded participants.

Rapid viral testing resulted in a trend toward decreased antibiotic use in the ED, but this was not statistically significant. 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, or blood or urine testing in the ED. No study made mention of any adverse effects related to viral testing.

Authors' conclusions

There is insufficient evidence to support routine rapid viral testing to reduce antibiotic use in pediatric EDs. Rapid viral testing may or may not reduce rates of antibiotic use, and other investigations (urine and blood testing); these studies do not provide enough power to resolve this question. However, rapid viral testing does reduce the rate of chest X-rays in the ED. An adequately powered trial with antibiotic use as an outcome is needed.

PLAIN LANGUAGE SUMMARY

Rapid viral testing for children in the Emergency Department with fever and respiratory symptoms

Review question
Does rapid viral testing in the Emergency Department influence the treatment of children with fever and breathing symptoms?

Background
Otherwise healthy children, aged 0 to 18 years, admitted to Emergency Departments (EDs) with fever and respiratory symptoms represent a major burden to the healthcare 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. We conducted this review to assess whether a rapid viral test, done in the ED, changes what physicians do when treating these children.

Study characteristics
We reviewed studies retrievable as of July 2014. We included four prospective controlled studies of previously healthy children under 18 years of age who attended an ED of an urgent care clinic because of fever and respiratory symptoms.

Key results
Based on these four studies, involving 759 study participants, we found that in previously healthy children coming to the ED with fever and respiratory symptoms, a rapid viral test showed a trend towards fewer antibiotic prescriptions, but this finding was not statistically significant. However, we found that rapid viral testing reduces the use of chest X-rays. There are also blood and urine investigations that can be undertaken. The true impact of this intervention on the frequency of blood and urine testing, as well as the length of the ED visit, requires trials with larger numbers of children. None of the included studies reported harm or adverse events related to the intervention tested.

Quality of the evidence
The quality of the evidence was considered moderate with regard to risk of bias, indirectness, imprecision, publication bias and inconsistency. While none of the studies used blinding, the impact of the use of rapid viral testing is in its ability to provide diagnostic information. Blinding of this interventions to the clinician would be impossible and make the intervention useless.

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 reduction 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 in the rate of bacteremia (1.1% and 2.3%) and no cases of bacterial meningitis among the 251 RSV positive infants and eight 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 suboptimal 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 an 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 USD 206 to USD 221, and in comparison is USD 101 to USD 106 in a primary care provider's office. Up to 60% of patients with a common cold are treated with antimicrobials, which cost USD 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 severe acute respiratory syndrome (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, and 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 revealing a change in management for 36% of the children, 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 value = 0.04) and when admitted were on antibiotics for fewer days (3.5 days versus 5.4 days; P value = 0.03) (Noyola 2000). Children with an early diagnosis of influenza also had fewer blood tests (17% versus 44%; P value = 0.02) and urine tests performed (2% versus 24%; P value = 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 immunofluorescent 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

A better diagnosis of children presenting to the ED with fever and respiratory symptoms may improve their management by allowing 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 be evidence of substantial reductions in unnecessary investigation costs and antibiotic prescribing for children with ARIs 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 acute respiratory infection (ARI) in Emergency Departments (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

1. 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:

1. studies of otherwise healthy children aged 0 to 18 years old; or
2. 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:

1. studies including participants who are immunocompromised;
2. studies including participants who have underlying chronic severe respiratory conditions (cystic fibrosis or bronchopulmonary dysplasia); or
3. 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, enzyme immunoassays, optical immunoassay, or molecular testing such as multiplex polymerase chain reaction. 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

1. Antimicrobial prescription rate in the ED: we considered a reduction of antibiotic use by 25% (risk ratio (RR) 0.75) as clinically important.

Secondary outcomes

1. Length of hospital (ED) stay: we considered a reduction of 30 minutes as clinically important.
2. Rate of ancillary tests (any blood tests or chest imaging or urine investigations) requested: we considered a reduction in ancillary testing of 25% (RR 0.75) as clinically important.
3. Rate of physician visit (ED or office) within two weeks after discharge from ED: we considered a relative increase in physician visit within two weeks of discharge from an ED of 10% (RR 1.10) as clinically important.
4. Hospital admission rate: we considered a reduction in admission rate of 25% (RR 0.75) as clinically important.
5. 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

For this 2014 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 6), which contains the Cochrane ARI Group's Specialized Register, MEDLINE (December 2011 to July week 1, 2014), EMBASE, (December 2011 to July 2014), MEDLINE In-Process & Other Non-Indexed Citations (15 July 2014), BIOSIS Previews (December 2011 to July 2014) and CAB Abstracts (December 2011 to July 2014). Details of previous searches are in Appendix 1.

We used the search strategy in Appendix 2 to search MEDLINE and CENTRAL. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008) revision; Ovid format (Lefebvre 2011). We also used a filter to identify 'child' studies based on the work of Boluyt 2008. We adapted this search strategy to search EMBASE (see Appendix 3), MEDLINE In-Process & Other Non-Indexed Citations (see Appendix 4), BIOSIS (see Appendix 5), and CAB Abstracts (see Appendix 6). We did not apply any language or publication restrictions.

Searching other resources

We included articles derived from the original search, which 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. We searched ClinicalTrials.gov (www.clinicaltrials.gov) and WHO ICTRP (www.who.int/ictrp) for completed and ongoing trials (latest search 17 July 2014). We searched the Pediatric Academic Society and Society for Pediatric Research joint conference abstracts databases from 2000 to 2010 for identification of meeting abstracts.

Data collection and analysis

Two review authors (QD, PE) independently extracted and verified data entry for accuracy. We used the Review Manager statistical package to conduct the analyses (RevMan 2014).

Selection of studies

Two review authors (QD, PE) screened titles and abstracts of identified citations to exclude trials which were clearly not relevant or did not meet the inclusion criteria for the review. We retrieved the full article for further examination for all abstracts or titles deemed relevant or potentially meeting the criteria by either review author. The two review authors assessed these articles to confirm that they met the inclusion criteria for the review.

Data extraction and management

Two review authors (QD, PE) independently extracted data from the published studies using standardized data extraction forms. We contacted trial authors to obtain unpublished information, including outcome data that were not explicitly stated in the published papers. We resolved disagreements in data extraction by discussion and consensus.

Assessment of risk of bias in included studies

The review authors evaluated the methodological quality of each trial using the 'Risk of bias' tool (Higgins 2011).

Measures of treatment effect

We expressed dichotomous data, such as antibiotic prescription in the ED (primary objective), ancillary tests performed in the ED, admission to the hospital and physician visits or re-visits to the ED within two weeks of discharge from the original ED visit, as risk ratios (RRs). We expressed continuous data, such as mean length of stay in the ED, as mean differences (MDs).

Unit of analysis issues

All included studies used individual participants as the unit of randomization and analysis.

Dealing with missing data

We still included studies with missing data, and included discussions of the implications of the missing data in the 'Risk of bias' tables. Where data were incomplete, we contacted the original investigators. We explored the context surrounding missing data with the study authors, but only performed analyses on available data.

Assessment of heterogeneity

We tested heterogeneity using the Chi^2 test as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

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.

Data synthesis

We analyzed pooled differences for the rate of investigations and antibiotic use using the Mantel-Haenszel test and expressed these as RRs with 95% confidence interval (CIs). We analyzed pooled difference in ED length of visits using the inverse variance method and expressed these as MDs with 95% CIs. We applied the random-effects model to all statistical analyses.

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 we deemed the risk of bias adequate for inclusion. Given the invasive nature of specimen acquisition for rapid respiratory viral testing, the intervention cannot be blinded and, therefore, we deemed no study free of bias.

RESULTS

Description of studies

In this 2014 update, in addition to the previous studies described in the review, we attempted to retrieve information on a trial reported as completed on ClinicalTrials.gov, which seemed to meet our inclusion criteria. However, we were unable to find a report of its results or to make contact with its principal investigator. In total, we are still left with nine prospective controlled trials on the impact of rapid viral testing in children in the ED. We included four studies in this review: three RCTs (Bonner 2003; Doan 2009; Poehling 2006) and one quazi-RCT (Iyer 2006). We excluded five studies (Abanses 2006; Cohen 2007; Esposito 2003; Ozkaya 2009; Ozkaya 2010). See Characteristics of excluded studies table for descriptions and reasons for exclusion.

Results of the search

Electronic database searches resulted in 1568 references (after we eliminated duplicates), of which eight were prospective studies of rapid viral testing in children. A search of the Pediatric Academic Society conference proceedings only yielded references which were already recovered from the electronic search. We found one additional potential study from the ClinicalTrials.gov registry, but many attempts at contacting the trial authors to enquire about the status of this study were unsuccessful. Snowballing, using Scopus and Web of Sciences, and handsearching through references of included studies yielded one additional study of rapid viral testing in children (Cohen 2007). We carefully reviewed a total of nine studies, of which four met all of the inclusion criteria.

Included studies

Bonner 2003 was a single-center RCT assessing participants presenting to a large United States 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. A total of 418 participants were enrolled with 391 completing the study.

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

Poehling 2006 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. A total of 468 participants were enrolled in the study.

Approximately 20% of their study population were deemed high-risk medical participants (as defined in the publication *Red Book* (CID 2003)) and influenza vaccination was recommended for these patients (i.e. 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; and 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). We contacted the primary trial author for further clarification.

Of these 20%, only five participants had a condition that 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. We obtained the raw data, excluding these five participants, from the primary author and used the data for this meta-analysis.

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

Iyer 2006 was a prospective, quazi-RCT assessing participants presenting to a large, urban, tertiary care pediatric ED. The goal of this study was to assess the effect of rapid influenza diagnosis on physician management of previously healthy febrile participants, aged 2 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. A total of 700 participants were included in the study.

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

Doan 2009 was a single-center, open-label, RCT 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 ARI. A total of 204 participants were enrolled with 200 completing the study.

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

Excluded studies

Esposito 2003 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.

We excluded this study 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 was a large, single-center RCT assessing healthy participants aged 3 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 was based on fever, we analyzed this paper as a large proportion of children (> 60%) were found to have respiratory symptoms in the form of tachypnea.

Children meeting the 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 randomizations are mentioned, what is described is actually cluster-randomization by 24-hour periods. Despite the initial intent to conduct a 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 intention-to-treat 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 was a multicenter, cluster-RCT of 30 community pediatric offices in France; 16 offices were randomized to use Quickvue rapid influenza test and 14 were not. A total of 602 participants, aged 1 to 17 years, 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 value < 0.0001). Antibiotics (9.5% versus 3.9%, P value = 0.008) and chest radiography (4.0% versus 1.2%, P value = 0.035) were 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 value = 0.0001), and a larger proportion of asthmatic participants (15.9% versus 10.2%, P value = 0.04).

This is the first RCT of rapid influenza testing in community pediatric practices. We did not include this study 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.

Ozkaya 2009 was a study of children aged between 3 and 14 years, treated at a pediatric ED with influenza-like illnesses, to evaluate the impact of rapid viral testing on the rate of antibiotic

prescription. The intervention group underwent rapid influenza testing and results were made available to the treating clinician prior to making a decision regarding antibiotic prescription. Not only did the control group undergo rapid influenza testing after the child had already been prescribed antibiotics, but children were only enrolled into the control group if an antibiotic had been prescribed. The rate of antibiotic prescription in the group of children with a known influenza status was not compared to the incidence of antibiotic prescription in a group of children with an unknown influenza status; it was compared to a pre-established rate of antibiotic prescription (100%), as dictated by the investigators, through their selection criteria. We excluded this study from this review as the significance of such a comparison and the interpretation of this study are arguable.

Ozkaya 2010 was a study involving children aged 8 months to 11 years, treated at a pediatric ED with signs and symptoms consistent with an influenza-like illness, to evaluate the impact of rapid influenza testing on the rate of ancillary testing, ED length of stay, and rate of admission to an observation unit. One hundred and fifty screened children were eligible to participate in the study, but only 75 were enrolled. The reason for this was not explained. The intervention group had nasopharyngeal swabs collected for testing with influenza A/B rapid test kits, and results were made available to the treating clinician prior to their initial clinical assessment. The other group was managed without knowledge of their influenza status. Rapid influenza testing was ordered by the investigator (not involved in the participants' clinical management) at the time of other ancillary testing being ordered by the treating clinician. The timing of patient selection and enrollment into this control group is not explicitly described. Allocation concealment and blindness to the outcome measures at the time of enrollment cannot be assured. Furthermore, treatment allocation was not randomized, nor described. We excluded this study from this review due to these significant methodological issues.

Risk of bias in included studies

The overall risk of bias is presented graphically in Figure 1 and summarized in Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

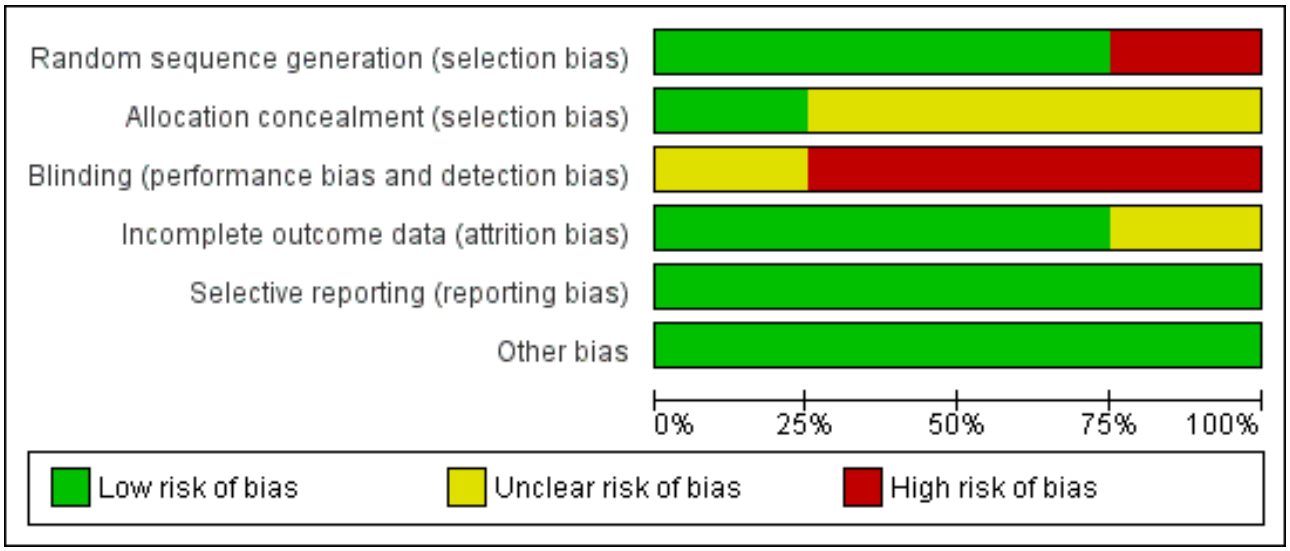
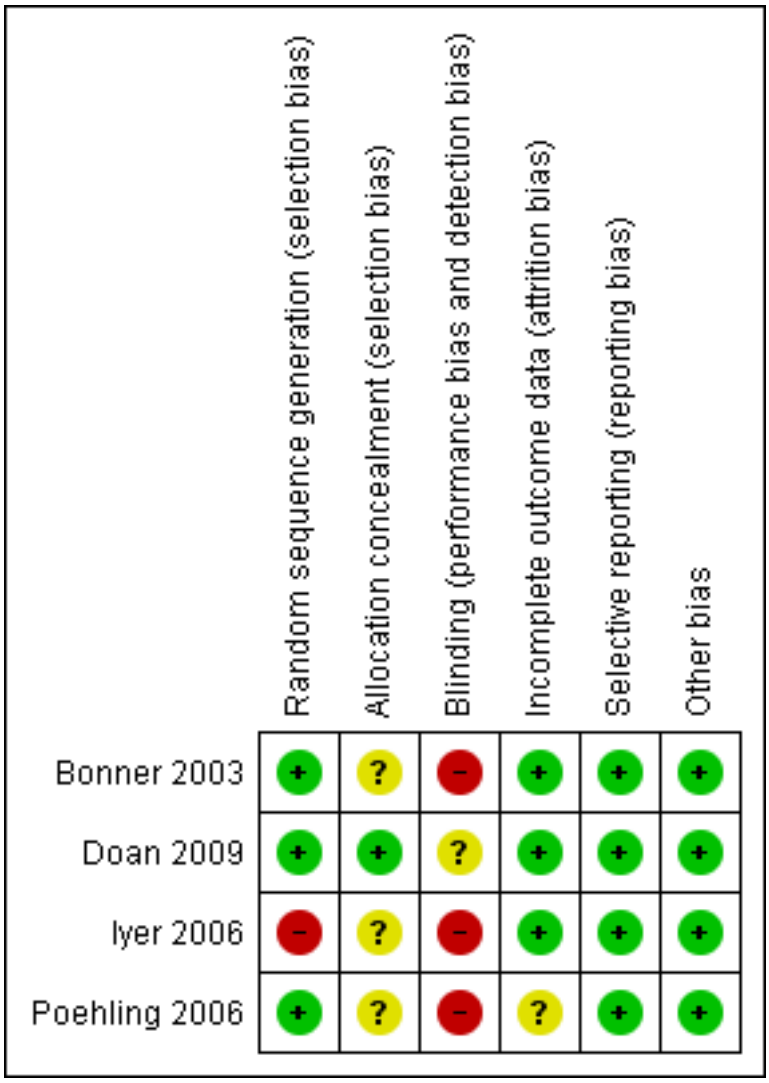


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



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

We successfully retrieved all incomplete outcome data by contacting the individual study authors.

Selective reporting

We found no selective reporting 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 using randomizing days, as in 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

Primary outcome

1. Antimicrobial prescription rate in the Emergency Department (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 (risk ratio (RR) 0.66, 95% confidence interval (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) (Analysis 1.1). Sensitivity analysis using the three trials deemed adequate (higher quality) by the method of Higgins 2011 (Bonner 2003; Doan 2009; Poehling 2006), did not find a statistically significant effect either (RR 0.86, 95% CI 0.61 to 1.22) (Analysis 1.2).

Secondary outcomes

1. Length of hospital (ED) stay: we considered a reduction of 30 minutes as clinically important

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 (MD) -10.6 minutes, 95% CI -22.47 to 1.25) (Analysis 2.1). Sensitivity analysis using only the two trials deemed adequate by the method of Higgins 2011 (Bonner 2003; Doan 2009), did not find a statistically significant effect either (MD -19.47, 95% CI -51.38 to 12.44) (Analysis 2.2).

2. Rate of ancillary tests (any blood tests, urine investigations or chest radiography) requested

Blood tests

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 so contacted study authors who provided the data for us to analyze them as one outcome. 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) (Analysis 3.1). Sensitivity analysis of the three trials deemed adequate by the method of Higgins 2011 (Bonner 2003; Doan 2009; Poehling 2006), however, found a significant effect (RR 0.61, 95% CI 0.42 to 0.89) (Analysis 3.3).

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 so contacted study authors, who provided the data for us 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) (Analysis 3.2). Sensitivity analysis using the three trials deemed adequate by the method of Higgins 2011 (Bonner 2003; Doan 2009; Poehling 2006), found similar results (RR 0.93, 95% CI 0.70 to 1.25) (Analysis 3.4).

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) (Analysis 4.1). Sensitivity analysis of the three trials deemed adequate by the method of Higgins 2011 found a similar but stronger effect (RR 0.59, 95% CI 0.43 to 0.81) (Analysis 4.2).

3. Rate of physician visit (ED or office) within two weeks after discharge from ED

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) (Analysis 5.1). Only Doan 2009 was deemed adequate by the method of Higgins 2011, hence we did not perform a sensitivity analysis for this outcome.

4. Hospital admission rate

Only one study reported this outcome (Iyer 2006). Point of care testing for influenza increased rates of admission compared with standard influenza testing, with an admission rate of 11.6% (95% CI 8.2 to 15.0) for point of care testing and an admission rate of 10.4% (95% CI 7.2 to 13.6) for standard influenza testing.

5. Acceptability of nasal specimen collection sampling for rapid viral testing

None of the included studies provided data on this outcome.

Heterogeneity

We performed tests of heterogeneity 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 reduced the rate of chest radiography use in the Emergency Department (ED). 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 for the treating physician. Although point-of-care testing for respiratory syncytial virus (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 the 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 randomized controlled trials (RCTs).

Quality of the evidence

Three out of four of the included studies are high-quality RCTs. The one quazi-RCT was clearly stated as such and the methodology was well described (Iyer 2006). 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 dependent 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 the rate of bacterial infection (all were urinary tract infections) in febrile RSV positive children up to two years old (one-third were less than three months old), to be much lower, at less than 1%, which calls 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 reduced the number of ancillary tests, antibiotics prescribed, and ED length of visits. While it is interesting to see that a positive result can reduce the number 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 unhelpful tests, which will actually add to the burden presented by children with acute 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 Emergency Department (ED) to reduce antibiotic prescription and ancillary investigations. The combined number of participants from the few available studies was not large enough to detect a statistically 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 an intention-to-treat analyses, rather than just in subgroup analyses. A large randomized controlled trial (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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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by year of study]

Bonner 2003

Methods	RCT
Participants	Previously healthy participants, age 2 months to 21 years old, presenting to the Alabama Children's Hospital Emergency Department with fever, respiratory symptoms, malaise or headaches of 72 hours duration or less (N = 391)
Interventions	Treatment group: results of nasopharyngeal swab for rapid influenza testing using FluOIA test (turn-around 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

Bonner 2003 *(Continued)*

	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 were analyzed using participants with revealed negative rapid influenza test results as a control group. We obtained unpublished raw data to analyze participants in 2 study groups, those who had the rapid test results revealed to the treating physician (irrespective of test results) (the intervention group) and those whose rapid influenza test results were not revealed to the treating physician (control group)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerized randomization program in blocks of 4 participants (2 to intervention and 2 to control)
Allocation concealment (selection bias)	Unclear risk	Randomization list was produced prior to the study. It is not mentioned whether individual allocation was concealed prior to enrollment
Blinding (performance bias and detection bias) All outcomes	High risk	The impact of knowing the results of viral testing was the intervention being tested and, as such, could not be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	22 enrolled participants left before they were seen by the treating physician or received any treatment, hence could not contribute to the outcomes
Selective reporting (reporting bias)	Low risk	All outcomes are reported. Although published data were reported only per subgroup (by rapid viral testing result), when contacted the author supplied complete data for this review
Other bias	Low risk	No other significant bias was found

Poehling 2006

Methods	RCT 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 to 2003 and 2003 to 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	3 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 were made available to the treating physician prior to patient assessment, versus standard testing with results made unavailable until the participant had been discharged from 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	This study enrolled 5 participants with chronic cardiorespiratory (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. We contacted the primary au-

Poehling 2006 *(Continued)*

	thor and obtained the raw data excluding these 5 participants (N = 300). We used these data for the purpose of the meta-analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block of days randomization by random number generator
Allocation concealment (selection bias)	Unclear risk	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
Blinding (performance bias and detection bias) All outcomes	High risk	The impact of knowing the results of viral testing was the intervention being tested and, as such, could not be blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	During the study period, 60 eligible children were not enrolled in the study. No mention is made of why these children were not enrolled
Selective reporting (reporting bias)	Low risk	All outcomes are reported
Other bias	Low risk	No other significant bias was found

Iyer 2006

Methods	Quazi-RCT, 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

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Alternate days used for treatment allocation

Iyer 2006 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	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
Blinding (performance bias and detection bias) All outcomes	High risk	The impact of knowing the results of viral testing was the intervention being tested and, as such, could not be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	During the study period, 67 eligible participants were not enrolled in the study. 36 children were missed during the initial screening process (these were discovered during a retrospective review of daily patient logs). Informed consent was not obtained for 19 participants. 5 participants left before evaluation by a physician and 7 were enrolled twice within 1 month. Information was documented on only 11 of these participants, therefore it is unclear how the remaining 56 participants might have affected the outcome
Selective reporting (reporting bias)	Low risk	All outcomes are reported
Other bias	Low risk	No other significant bias was noted

Doan 2009

Methods	RCT
Participants	Previously healthy children age 3 to 36 months old coming to the ED at British Columbia Children's Hospital with fever and any respiratory symptoms (N = 199)
Interventions	Treatment group: nasopharyngeal aspirate for rapid respiratory virus panel (influenza A/B, parainfluenza 1/2/3, RSV, adenovirus) using direct immunofluorescence assay (Light Diagnostics SimulFluor 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	2 of the authors of this Cochrane review are also investigators on this trial

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomized to either study groups using a computer randomization program in variable block size (2, 4, 6 or 8)
Allocation concealment (selection bias)	Low risk	Computer program was only accessed at the time consent for study participation was obtained
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The impact of knowing the results of viral testing was the intervention being tested and, as such, could not be blinded

Doan 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	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
Selective reporting (reporting bias)	Low risk	All outcomes are reported
Other bias	Low risk	No other significant bias was noted

FluOIA: rapid test for detection of influenza
ED: Emergency Department
N: number of children in the study
RCT: randomized controlled trial
RSV: respiratory syncytial virus

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

Study	Reason for exclusion
Abanses 2006	Although set out to be a RCT, when the treatment was not provided as per randomized allocation, these participants were reassigned to the control group and vice versa and were analyzed as such (convenience sample). This study was no longer analyzed as a RCT and 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)
Ozkaya 2009	There are methodological concerns with this study. The outcome measure, antibiotic prescription rate, was compared between children with known influenza status and a group of children with a predetermined rate of antibiotic prescription (100%), as dictated by the investigators through their selection criteria, rather than to the incidence of antibiotic prescription rate among children with unknown influenza status
Ozkaya 2010	There are methodological concerns with this study. It is unclear when participants were enrolled during their ED visit, hence allocation concealment and blindness to the outcome measures status at the time of participants' enrollment cannot be assured. Furthermore, treatment allocation was not randomized, nor described

ED: Emergency Department
RCT: randomized controlled trial

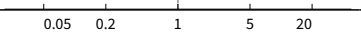
DATA AND ANALYSES

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]

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

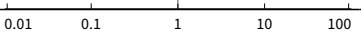
Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bonner 2003	34/193	53/198		25.8%	0.66[0.45,0.96]
Doan 2009	16/89	23/110		13.57%	0.86[0.48,1.53]
Iyer 2006	54/345	59/355		30.6%	0.94[0.67,1.32]
Poehling 2006	43/134	48/166		30.03%	1.11[0.79,1.56]
Total (95% CI)	**761**	**829**		**100%**	**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=27.02%					
Test for overall effect: Z=0.99(P=0.32)					



Favors rapid testing — Favors control

Analysis 1.2. Comparison 1 Antibiotics use, Outcome 2 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	34/193	53/198		36.56%	0.66[0.45,0.96]
Doan 2009	16/89	23/110		23.31%	0.86[0.48,1.53]
Poehling 2006	43/134	48/166		40.13%	1.11[0.79,1.56]
Total (95% CI)	**416**	**474**		**100%**	**0.86[0.61,1.22]**
Total events: 93 (Rapid viral testing), 124 (Control)					
Heterogeneity: Tau^2=0.05; Chi^2=4, df=2(P=0.14); I^2=50.02%					
Test for overall effect: Z=0.84(P=0.4)					



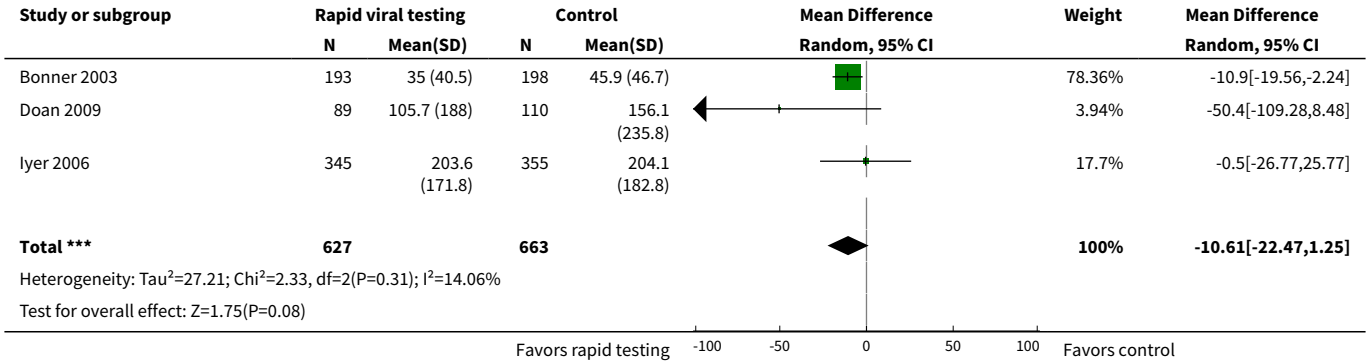
Favors rapid testing — Favors control

Comparison 2. ED length of visit

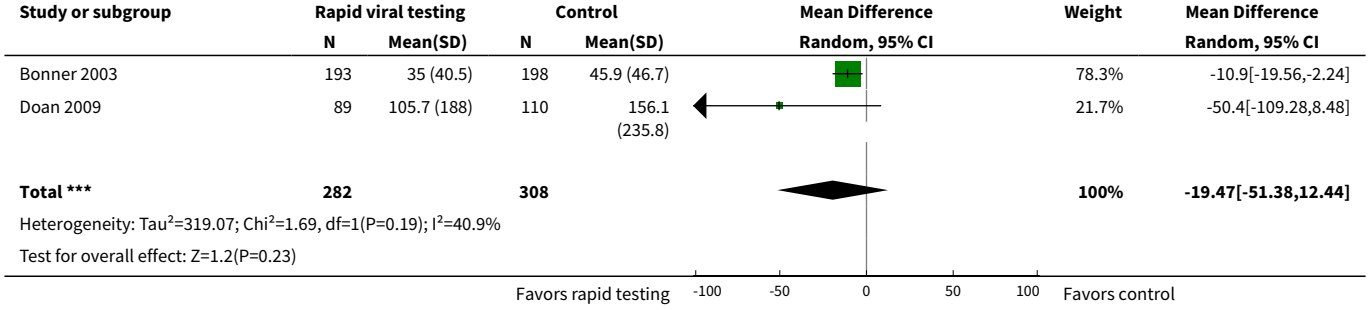
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean ED length of visit in minutes	3	1290	Mean Difference (IV, Random, 95% CI)	-10.61 [-22.47, 1.25]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Sensitivity analysis per risk of bias	2	590	Mean Difference (IV, Random, 95% CI)	-19.47 [-51.38, 12.44]

Analysis 2.1. 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.



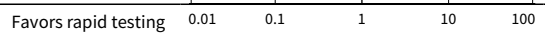
Comparison 3. Laboratory investigations

Outcome or subgroup title	No. of studies	No. of partici-pants	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]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Urine testing: sensitivity analysis per risk of bias	3	890	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.70, 1.25]

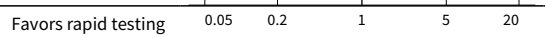
Analysis 3.1. Comparison 3 Laboratory investigations, Outcome 1 Blood investigations (cell count and/or cultures).

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		9.87%	0.59[0.28,1.23]
Iyer 2006	93/345	104/355		63.11%	0.92[0.73,1.17]
Poehling 2006	14/134	29/166		14.82%	0.6[0.33,1.09]
Total (95% CI)	**761**	**829**		**100%**	**0.79[0.62,1]**
Total events: 129 (Rapid viral testing), 173 (Control)					
Heterogeneity: Tau^2=0.01; Chi^2=3.4, df=3(P=0.33); I^2=11.7%					
Test for overall effect: Z=1.93(P=0.05)					



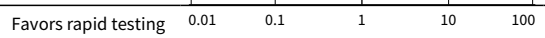
Analysis 3.2. Comparison 3 Laboratory investigations, Outcome 2 Urine testing.

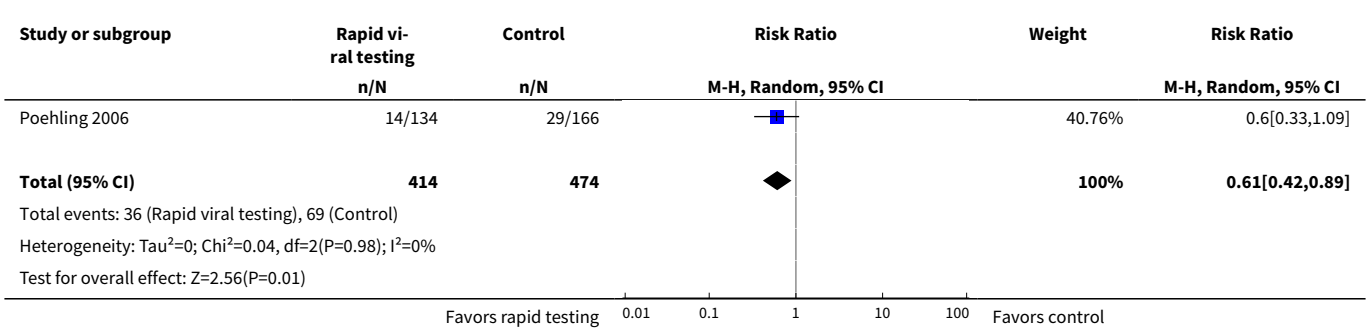
Study or subgroup	Rapid viral testing n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bonner 2003	19/191	26/198		13.35%	0.76[0.43,1.32]
Doan 2009	28/89	31/110		22.64%	1.12[0.73,1.71]
Iyer 2006	73/345	75/355		50.61%	1[0.75,1.33]
Poehling 2006	18/134	26/166		13.4%	0.86[0.49,1.5]
Total (95% CI)	**759**	**829**		**100%**	**0.97[0.79,1.19]**
Total events: 138 (Rapid viral testing), 158 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.42, df=3(P=0.7); I^2=0%					
Test for overall effect: Z=0.31(P=0.76)					



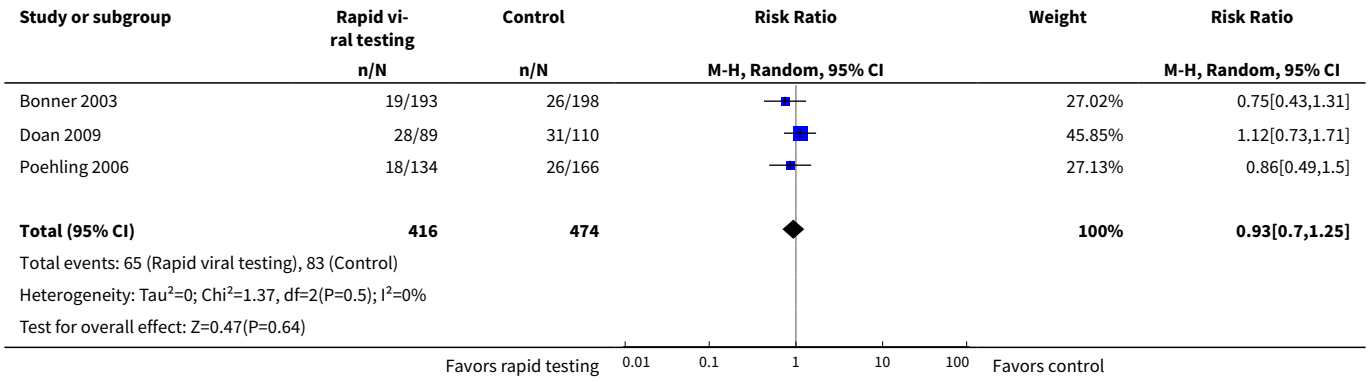
Analysis 3.3. Comparison 3 Laboratory investigations, Outcome 3 Blood investigation: sensitivity analysis per risk of bias.

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		32.97%	0.64[0.33,1.24]
Doan 2009	9/89	19/110		26.27%	0.59[0.28,1.23]





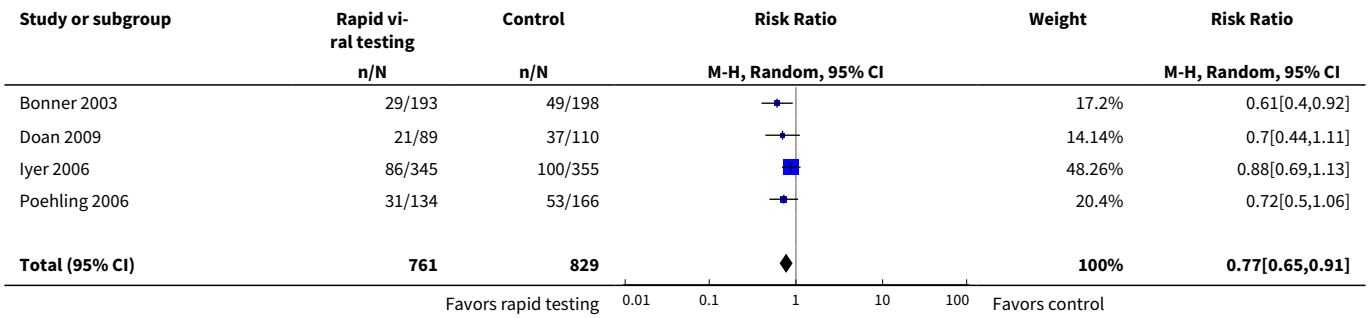
Analysis 3.4. Comparison 3 Laboratory investigations, Outcome 4 Urine testing: sensitivity analysis per risk of bias.

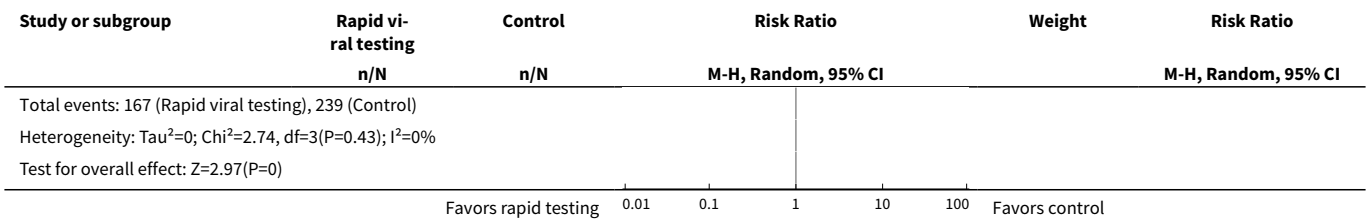


Comparison 4. Chest radiography

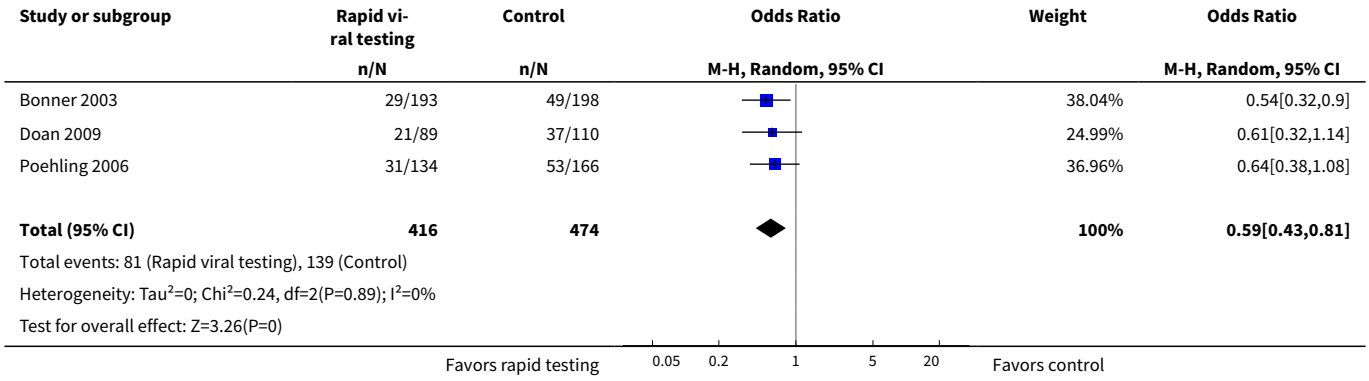
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Chest radiography	4	1590	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.65, 0.91]
2 Sensitivity analysis per risk of bias	3	890	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.43, 0.81]

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





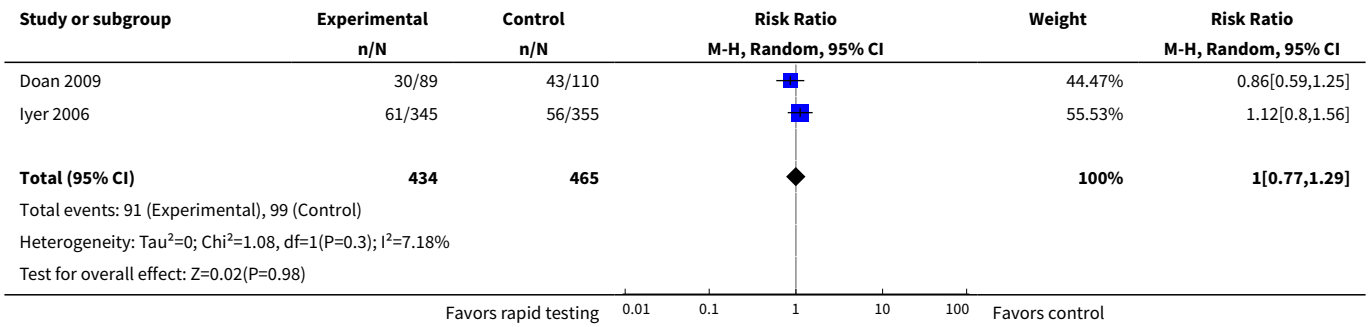
Analysis 4.2. Comparison 4 Chest radiography, Outcome 2 Sensitivity analysis per risk of bias.



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



APPENDICES

Appendix 1. Previous search strategy

For the original 2009 review we searched the Cochrane Central register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 1); 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. See search details below.

We updated the review in 2011 using an updated search of the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 4; www.thecochranelibrary.com, accessed 9 December 2011), which contains the Cochrane ARI Group's Specialized Register; MEDLINE (March 2009 to November week 3, 2011); EMBASE (January 2010 to December 2011); MEDLINE In-Process & Other Non-Indexed Citations (December 8, 2011); BIOSIS Previews (2009 to December 2011); and CAB Abstracts (2009 to December 2011).

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

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

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
100and/32,50,62,99
101exp clinical trial/
102randomi?ed.ti,ab.
103placebo.ti,ab.
104(ae or dt or to).fs.
105randomly.ti,ab.
106trial.ti,ab.
107groups.ti,ab.
108or/101-107
109animal/
110human/
111109 not (109 and 110)
112108 not 111
113and/100,112

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

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

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 parainfluenza* 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=(respiratory 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

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
#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((dou-	105526

(Continued)

	ble-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)	
#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
#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

(Continued)

#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
#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
#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

(Continued)

#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

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

ProQuest Dissertations and Theses - full text (1861 to 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.

Appendix 2. MEDLINE and CENTRAL search strategy

MEDLINE (Ovid)

1 exp Respiratory Tract Infections/ (290367)
2 (acute adj3 respiratory).tw. (26567)
3 (respiratory adj3 virus*).tw. (13969)
4 ari*.tw. (183543)
5 exp Orthomyxoviridae/ (43377)
6 Orthomyxoviridae Infections/ (7451)
7 (orthomyxovir* or ortho myxovirus* or ortho-myxovirus*).tw. (370)
8 Influenza, Human/ (35678)
9 (influenza* or flu).tw. (85736)
10 exp Picornaviridae/ (32222)
11 exp Picornaviridae Infections/ (50584)
12 picornavir*.tw. (2623)
13 (rhinovir* or rhino virus* or rhino-virus*).tw. (3542)
14 exp Adenoviridae/ (31925)
15 Adenovirus Infections, Human/ (1948)
16 (adenovir* or adeno virus* or adeno-virus*).tw. (42465)
17 exp Paramyxoviridae/ (28456)
18 exp Paramyxoviridae Infections/ (29849)
19 exp Coronaviridae/ (9326)
20 (coronavir* or corona-virus* or corona virus*).tw. (7191)
21 exp Coronaviridae Infections/ (7725)
22 (metapneumovir* or meta-pneumovir* or meta pneumovir*).tw. (1197)
23 hmpv*.tw. (691)
24 pneumovir*.tw. (316)
25 (parainfluenza* or para influenza* or para-influenza*).tw. (5142)
26 (enterovirus* or entero-virus* or entero virus*).tw. (6601)
27 (respiratory syncytial virus* or rsv).tw. (11646)
28 fever/ or "fever of unknown origin"/ (34398)
29 (febrile adj3 respiratory).tw. (390)
30 Pyrogens/ (2711)
31 pyrogen*.tw. (4947)
32 exp Antigens, Viral/ (93160)
33 ((viral or virus) adj2 antigen*).tw. (17026)
34 nasal aspirat*.tw. (126)
35 or/1-34 (803679)
36 exp "Sensitivity and Specificity"/ (419518)

37 (sensitiv* or specific*).tw. (2663003)
38 likelihood functions/ (17250)
39 (likelihood* adj3 ratio*).tw. (8429)
40 ((roc* or receiver operating characteristic) adj2 curve*).tw. (25089)
41 exp Diagnosis/ (6526369)
42 diagnos*.tw. (1553648)
43 di.fs. (2002607)
44 (routine adj5 test*).tw. (13308)
45 (false adj2 (positiv* or negativ*)).tw. (53674)
46 (observer adj2 variation*).tw. (958)
47 (predictive adj3 value).tw. (54963)
48 du.fs. (331591)
49 Nasopharynx/ (7064)
50 ((viral* or virus* or virol* or antigen* or antibod*) adj3 (test* or detect* or diagnos*)).tw. (120218)
51 ((viral or virus*) adj3 antigen?).tw. (20386)
52 or/36-51 (9445888)
53 Emergency Medicine/ (9841)
54 Emergencies/ (34355)
55 exp Emergency Service, Hospital/ (49741)
56 Emergency Medical Services/ (32117)
57 (ed? or er?).tw. (197478)
58 (emergenc* adj5 (department* 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*)).tw. (103070)
59 (emergency or emergencies).jn. (128)
60 Point-of-Care Systems/ (7215)
61 ("point of care" or point-of-care or poc).tw. (7100)
62 or/53-61 (358623)
63 exp Infant/ (937498)
64 (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).tw. (613296)
65 exp Child/ (1549368)
66 (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*).tw. (953267)
67 Adolescent/ (1618145)
68 (adoles* or teen* or boy* or girl*).tw. (313883)
69 Minors/ (2320)
70 Puberty/ (11193)
71 (minor* or pubert* or pubescen*).tw. (227288)
72 exp Pediatrics/ (43680)
73 (pediatric* or paediatric*).tw. (206748)
74 exp Schools/ (81470)
75 (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*).tw. (39946)
76 or/63-75 (3504613)
77 randomized controlled trial.pt. (378135)
78 controlled clinical trial.pt. (88788)
79 randomized.ab. (276180)
80 placebo.ab. (147508)
81 clinical trials as topic.sh. (170979)
82 randomly.ab. (195598)
83 trial.ti. (119243)
84 77 or 78 or 79 or 80 or 81 or 82 or 83 (866547)
85 exp animals/ not humans.sh. (3966430)
86 84 not 85 (795983)
87 35 and 52 and 62 and 76 and 86 (204)

Appendix 3. EMBASE.com search strategy

#64. #60 AND #63
#63. #61 OR #62
#62. random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR 'cross-over':ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR ((singl* OR doubl*) NEAR/1 blind*):ab,ti AND [embase]/lim
#61. 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp AND [embase]/lim 241,796 12 May 2011

#60. #56 AND #59
#59. #57 OR #58
#58. infant*:ab,ti OR infancy:ab,ti OR newborn*:ab,ti OR baby*:ab,ti OR babies:ab,ti OR neonat*:ab,ti OR preterm*:ab,ti OR prematur*:ab,ti OR child*:ab,ti OR schoolchild*:ab,ti OR 'school age':ab,ti OR 'school aged':ab,ti OR 'school ages':ab,ti OR preschool*:ab,ti OR kid:ab,ti OR kids:ab,ti OR toddler*:ab,ti OR adoles*:ab,ti OR teen*:ab,ti OR boy*:ab,ti OR girl*:ab,ti OR minor*:ab,ti OR juvenile*:ab,ti OR pubert*:ab,ti OR pubescen*:ab,ti OR pediatric*:ab,ti OR paediatric*:ab,ti OR kindergar*:ab,ti OR (school* NEAR/1 (primary OR nursery OR secondary OR elementary OR high)):ab,ti OR highschool*:ab,ti AND [embase]/lim
#57. 'infant'/exp OR 'child'/exp OR 'adolescent'/exp OR 'pediatrics'/exp AND [embase]/lim
#56. #35 AND #48 AND #55
#55. #49 OR #50 OR #51 OR #52 OR #53 OR #54
#54. 'point of care':ab,ti OR 'point-of-care':ab,ti OR poc:ab,ti AND [embase]/lim
#53. 'hospital information system'/de AND [embase]/lim
#52. emergency:jt OR emergencies:jt AND [embase]/lim
#51. ed?:ab,ti OR er?:ab,ti AND [embase]/lim
#50. (emergenc* NEAR/5 (department* 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*)):ab,ti AND [embase]/lim
#49. 'emergency medicine'/de OR 'emergency'/de OR 'emergency health service'/de AND [embase]/lim
#48. #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47
#47. ((viral* OR virus*) NEAR/3 antigen*):ab,ti AND [embase]/lim
#46. ((viral* OR virus* OR virol* OR antigen* OR antibod*) NEAR/3 (test* OR detect* OR diagnos*)):ab,ti AND [embase]/lim
#45. 'nasopharynx'/de AND [embase]/lim
#44. (routine NEAR/5 test*):ab,ti OR (false NEAR/2 positiv*):ab,ti OR (false NEAR/2 negative*):ab,ti OR (observer NEAR/2 variation*):ab,ti OR (predictive NEAR/2 value*):ab,ti AND [embase]/lim
#43. diagnos*:ab,ti AND [embase]/lim
#42. 'diagnosis'/exp AND [embase]/lim
#41. ('receiver operating characteristic' NEAR/2 curve*):ab,ti OR (roc NEAR/2 curve*):ab,ti AND [embase]/lim
#40. 'receiver operating characteristic'/de AND [embase]/lim
#39. (likelihood NEAR/3 ratio*):ab,ti AND [embase]/lim
#38. 'statistical model'/de AND [embase]/lim 25,607
#37. sensitivit*:ab,ti OR specific*:ab,ti AND [embase]/lim
#36. 'sensitivity and specificity'/de AND [embase]/lim
#35. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
#34. (nasal NEAR/1 aspirat*):ab,ti AND [embase]/lim
#33. ((viral OR virus) NEAR/2 antigen*):ab,ti AND [embase]/lim
#32. 'virus antigen'/exp AND [embase]/lim
#31. pyrogen*:ab,ti AND [embase]/lim
#30. 'pyrogen'/de AND [embase]/lim
#29. (febrile NEAR/3 respiratory):ab,ti AND [embase]/lim
#28. 'fever'/de OR 'pyrexia idiopathica'/de AND [embase]/lim
#27. 'respiratory syncytial virus':ab,ti OR 'respiratory syncytial viruses':ab,ti OR rsv:ab,ti AND [embase]/lim
#26. enterovir*:ab,ti OR 'entero virus':ab,ti OR 'entero viruses':ab,ti OR 'entero-virus':ab,ti OR 'entero-viruses':ab,ti AND [embase]/lim
#25. parainfluenza*:ab,ti OR 'para influenza':ab,ti OR 'para-influenza':ab,ti AND [embase]/lim
#24. pneumovir*:ab,ti AND [embase]/lim
#23. hmpv:ab,ti AND [embase]/lim
#22. metapneumovir*:ab,ti OR 'meta pneumovirus':ab,ti OR 'meta pneumoviruses':ab,ti OR 'meta-pneumovirus':ab,ti OR 'meta-pneumoviruses':ab,ti AND [embase]/lim 882 12 May 2011
#21. coronavir*:ab,ti OR 'corona virus':ab,ti OR 'corona-virus':ab,ti OR 'corona viruses':ab,ti AND [embase]/lim
#20. 'coronavirus infection'/de AND [embase]/lim
#19. 'coronavirus'/exp AND [embase]/lim
#18. 'paramyxovirus infection'/exp AND [embase]/lim
#17. 'paramyxovirus'/exp AND [embase]/lim
#16. adenovir*:ab,ti OR 'adeno-virus':ab,ti OR 'adeno-viruses':ab,ti OR 'adeno virus':ab,ti OR 'adeno viruses':ab,ti AND [embase]/lim
#15. 'human adenovirus infection'/de AND [embase]/lim
#14. 'adenovirus'/exp AND [embase]/lim
#13. rhinovir*:ab,ti OR 'rhino virus':ab,ti OR 'rhino viruses':ab,ti OR 'rhino-virus':ab,ti OR 'rhino-viruses':ab,ti AND [embase]/lim
#12. picornavir*:ab,ti AND [embase]/lim
#11. 'picornavirus infection'/exp AND [embase]/lim
#10. 'picornavirus'/exp AND [embase]/lim
#9. influenza*:ab,ti AND [embase]/lim
#8. 'influenza'/exp AND [embase]/lim

#7. orthomyxovirus*:ab,ti OR 'ortho myxovirus':ab,ti OR 'ortho myxoviruses':ab,ti OR 'ortho-myxovirus':ab,ti OR 'ortho-myxoviruses':ab,ti AND [embase]/lim
#6. 'orthomyxovirus infection'/de AND [embase]/lim
#5. 'orthomyxovirus'/exp AND [embase]/lim
#4. ari:ab,ti AND [embase]/lim
#3. (respiratory NEAR/3 virus*):ab,ti AND [embase]/lim
#2. (acute NEAR/3 respiratory):ab,ti AND [embase]/lim
#1. 'respiratory tract infection'/exp AND [embase]/lim

Appendix 4. MEDLINE (Ovid) In-Process and Other Non-Indexed Citations

1 (respiratory adj3 (infection* or acute or virus*)).tw.
2 (ari* or orthomyxovir* or influenz* or picornavir* or rhinovir* or coronavir* or metapneumovir* or hmpv or pneumovir* or parainfluenz* or enterovir* or respiratory syncytial vir* or rsv or fever* or pyrogen*).tw.
3 (febrile adj3 respiratory).tw.
4 ((viral or virus*) adj2 antigen*).tw.
5 nasal aspirat*.tw.
6 or/1-5
7 (sensitive* or specific* or likelihood* or roc or receiver operating characteristic* or diagnos*).tw.
8 (routine adj5 test*).tw.
9 (false adj2 (positive* or negative*)).tw.
10 (observer adj2 variation*).tw.
11 (predictiv* adj3 value*).tw.
12 nasopharynx.tw.
13 ((viral* or virus* or virol* or antigen* or antibod*) adj3 (test* or detect* or diagnos*)).tw.
14 ((viral* or virus*) adj3 antigen*).tw.
15 or/7-14
16 6 and 15
17 emergenc*.tw.
18 (point-of-care or point of care or poc).tw.
19 (ed? or er?).tw.
20 or/17-19
21 16 and 20
22 (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*).tw.
23 (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*).tw.
24 (adoles* or teen* or boy* or girl*).tw.
25 (minor* or juvenile* or pubert* or pubescen*).tw.
26 (pediatric* or paediatric*).tw.
27 (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*).tw.
28 or/22-27
29 21 and 28
30 (random* or placebo* or trial* or doubl* blind* or singl* blind*).tw.
31 29 and 30

Appendix 5. Biosis Previews (Thomson Reuters)

# 9	**158**
# 8	**2,200,348**
# 7	**1,353**
# 6	**2,018,594**

# 5	**4,514**
# 4	**629,384**
# 3	**139,662**
# 2	**5,503,526**
# 1	**374,180**

Appendix 6. CAB Abstracts (Thomson Reuters)

# 7	**14**
# 6	**308,391**
# 5	**235**
# 4	**506,114**
# 3	**142,175**
# 2	**1,227,918**
# 1	**155,699**

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FEEDBACK

Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department, 19 November 2009

Summary

The meta-analysis by Doan, et. al. is excellent. This is a comment related to the finding of a lack of significant reduction in the prescribing of antibiotics despite the use of rapid viral testing in EDs. The management of the first patient treated with penicillin for streptococcal sepsis included the continuation of a sulfa drug because of uncertainty regarding the effectiveness of penicillin. Old habits are hard to break. Also, in Doan (2009), physicians examining patients a week after they were known to have a positive rapid viral test may not have felt antibiotics were necessary if the patients had improved by that point.

Submitter agrees with default conflict of interest statement:
I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Reply

We'd like to thank Dr Zedd for the comments. Readers might note that in the Doan (2009) paper, children who underwent rapid viral testing received outpatient antibiotics within 1 week of ED discharge less frequently than those who did not get tested. Although Dr Zedd is right that with symptoms improvement over a week, the temptation to give antibiotics is reduced, there is no reason to suspect that these two groups would differ in the rate of symptoms improvement post-ED discharge.
Quynh Doan (31/07/2010)

Contributors

Arnold Zedd (18/11/2009)

WHAT'S NEW

Date	Event	Description
17 July 2014	New citation required but conclusions have not changed	No new trials were identified in this update.
17 July 2014	New search has been performed	Our conclusions remain unchanged.

HISTORY

Protocol first published: Issue 2, 2007
Review first published: Issue 4, 2009

Date	Event	Description
9 December 2011	New search has been performed	Searches conducted.
9 December 2011	New citation required but conclusions have not changed	We excluded two new trials (Ozkaya 2009; Ozkaya 2010). Our conclusions remain unchanged.
26 July 2010	Feedback has been incorporated	Feedback comment and reply added.
21 January 2010	Amended	Contact details updated.
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 (PE) 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

Quynh Doan: none known.
Terry Klassen: none known.
Paul Enarson: none known.
Niranjan Kissoon: 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.

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, we felt that an overtly complicated adapted Kappa for ordinal categorical inter-rater assessment was 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 determine definitively the effect of rapid viral testing. We concluded that further subgrouping of participants would be unlikely to yield significant information and so we did not run such analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

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

MeSH check words

Adolescent; Child; Humans; Infant