

# Infection Control

## Evidence Update

Spring 2018  
(Quarterly)



Respecting everyone  
Embracing change  
Recognising success  
Working together  
**Our hospitals.**



## Lunchtime Drop-in Sessions

*All sessions last one hour*

### April (12.00-13.00)

17th (Tue) **Statistics**

25th (Wed) **Literature Searching**

### May (13.00-14.00)

3rd (Thu) **Critical Appraisal**

11th (Fri) **Statistics**

14th (Mon) **Literature Searching**

22nd (Tue) **Critical Appraisal**

30th (Wed) **Statistics**

### June (12.00-13.00)

7<sup>th</sup> (Thu) **Literature Searching**

11<sup>th</sup> (Mon) **Critical Appraisal**

20<sup>th</sup> (Wed) **Statistics**

28<sup>th</sup> (Thu) **Literature Searching**

## Your Outreach Librarian – **Sarah Barrett**

Whatever your information needs, the library is here to help. Just email us at [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

**Outreach:** Your Outreach Librarian can help facilitate evidence-based practice for all in the team, as well as assisting with academic study and research. We also offer one-to-one or small group training in **literature searching, critical appraisal and medical statistics**. Get in touch: [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

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Please email requests to [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

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# Updates

**NICE** National Institute for  
Health and Care Excellence

## [Antimicrobial stewardship](#)

Everything NICE has said on effective antimicrobial medicine use and preventing the spread of resistant microbes in an interactive flowchart

NICE Pathway Published August 2015 Last updated April 2018

## [Bronchiolitis in children](#)

Everything NICE has said on diagnosing and managing bronchiolitis in children in an interactive flowchart

NICE Pathway Published June 2015 Last updated March 2018



Chandelia S, Yadav AK, Kumar D, Chadha N. [Magnesium sulphate for acute bronchiolitis in children under two years of age \(Protocol\)](#). Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012965. DOI: 10.1002/14651858.CD012965.

Liu Z, Dumville JC, Norman G, Westby MJ, Blazeby J, McFarlane E, Welton NJ, O'Connor L, Cawthorne J, George RP, Crosbie EJ, Rithalia AD, Cheng HY. [Intraoperative interventions for preventing surgical site infection: an overview of Cochrane Reviews](#). Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012653. DOI: 10.1002/14651858.CD012653.pub2.

Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V. [Vaccines for preventing influenza in healthy children](#). Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD004879. DOI: 10.1002/14651858.CD004879.pub5.

Demicheli V, Jefferson T, Ferroni E, Rivetti A, Di Pietrantonj C. [Vaccines for preventing influenza in healthy adults](#). Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD001269. DOI: 10.1002/14651858.CD001269.pub6.

**UpToDate**<sup>®</sup>

OpenAthens login required. Register here: <https://openathens.nice.org.uk/>

[Infection prevention: Precautions for preventing transmission of infection](#)

Author: [Deverick J Anderson, MD, MPH](#)

Section Editor: [Anthony Harris, MD, MPH](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Dec 01, 2017.

#### [Clostridium difficile infection: Prevention and control](#)

Authors: [L Clifford McDonald, MD](#); [Preeti K Kutty, MD, MPH](#)

Section Editors: [Stephen B Calderwood, MD](#); [Sheldon L Kaplan, MD](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 12, 2018.

#### [Clostridium difficile infection in adults: Treatment and prevention](#)

Authors: [Ciarán P Kelly, MD](#); [J Thomas Lamont, MD](#); [Johan S Bakken, MD, PhD](#)

Section Editor: [Stephen B Calderwood, MD](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 30, 2018.

#### [Society guideline links: Clostridium difficile infection](#)

[European Society of Clinical Microbiology and Infectious Diseases \(ESCMID\): Guidance document for prevention of Clostridium difficile infection in acute healthcare settings \(2018\)](#)

#### [Bronchiolitis in infants and children: Treatment, outcome, and prevention](#)

Authors: [Pedro A Piedra, MD](#); [Ann R Stark, MD](#)

Section Editors: [George B Mallory, MD](#); [Morven S Edwards, MD](#)

Deputy Editor: [Mary M Torchia, MD](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Jan 05, 2018.

#### [Respiratory syncytial virus infection: Prevention](#)

Authors: [Frederick E Barr, MD](#); [Barney S Graham, MD, PhD](#)

Section Editors: [Morven S Edwards, MD](#); [George B Mallory, MD](#)

Deputy Editor: [Mary M Torchia, MD](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 30, 2018.

#### [Antimicrobial prophylaxis for prevention of surgical site infection in adults](#)

Authors: [Deverick J Anderson, MD, MPH](#); [Daniel J Sexton, MD](#)

Section Editor: [Anthony Harris, MD, MPH](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 09, 2018.

#### [Seasonal influenza in children: Prevention and treatment with antiviral drugs](#)

Author: [Flor M Munoz, MD, MSc](#)

Section Editors: [George B Mallory, MD](#); [Morven S Edwards, MD](#)

Deputy Editor: [Mary M Torchia, MD](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 05, 2018.

### [Seasonal influenza in children: Prevention with vaccines](#)

Author: [Flor M Munoz, MD, MSc](#)

Section Editors: [George B Mallory, MD](#); [Morven S Edwards, MD](#)

Deputy Editor: [Mary M Torchia, MD](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 26, 2018.

### [Infection control measures to prevent seasonal influenza in healthcare settings](#)

Author: [Anna R Thorner, MD](#)

Section Editor: [Martin S Hirsch, MD](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Feb 06, 2018.

### [Norovirus](#)

Authors: [David O Matson, MD, PhD](#); [Miguel G O'Ryan, MD](#); [Neil R Blacklow, MD](#)

Section Editor: [Martin S Hirsch, MD](#)

Deputy Editor: [Elinor L Baron, MD, DTMH](#)

#### [Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

**Literature review current through:** Mar 2018. | **This topic last updated:** Mar 09, 2018.



## Library Clinic

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May 2<sup>nd</sup>: **Canteen (Level 9, BRI) 12.00-14.00**

June 6<sup>th</sup>: **Terrace (Level 4, Education Centre) 12.00-14.00**

June 19<sup>th</sup>: **Welcome Centre, BRI 10.00-16.00**

July 3<sup>rd</sup>: **Welcome Centre, BRI 10.00-16.00**

July 4<sup>th</sup>: **Canteen (Level 9, BRI) 12.00-14.00**

August 8<sup>th</sup>: **Foyer, Education Centre 12.00-14.00**

August 29<sup>th</sup>: **Foyer, St Michael's Hospital 12.00-14.00**

September 5<sup>th</sup>: **Canteen (Level 9, BRI) 12.00-14.00**

September 11<sup>th</sup>: **Welcome Centre, BRI 10.00-16.00**

October 3<sup>rd</sup>: **Terrace (Level 4, Education Centre) 12.00-14.00**

November 7<sup>th</sup>: **Canteen (Level 9, BRI) 12.00-14.00**

December 5<sup>th</sup>: **Foyer, Education Centre 12.00-14.00**

December 11<sup>th</sup>: **Welcome Centre, BRI 10.00-16.00**

## Recent Database Articles

Below is a selection of articles recently added to the healthcare databases, grouped in the following categories:

- **C Difficile**
- **Bronchiolitis**
- **RSV**
- **Surgical Site Infection**
- **Influenza**
- **Norovirus**

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: [library@uhbristol.nhs.uk](mailto:library@uhbristol.nhs.uk)

### C Difficile

#### 1. Microbiologic factors affecting Clostridium difficile recurrence

**Author(s):** Chilton C.H.; Pickering D.S.; Freeman J.

**Source:** Clinical Microbiology and Infection; 2018

**Publication Date:** 2018

**Publication Type(s):** Article In Press

**Abstract:**Background: Recurrent Clostridium difficile infection (rCDI) places a huge economic and practical burden on healthcare facilities. Furthermore, rCDI may affect quality of life, leaving patients in an rCDI cycle and dependant on antibiotic therapy. Aims: To discuss the importance of microbiologic factors in the development of rCDI. Sources: Literature was drawn from a search of PubMed from 2000 onwards with the search term 'recurrent Clostridium difficile infection' and further references cited within these articles. Content: Meta-analyses and systematic reviews have shown that CDI and rCDI risk factors are similar. Development of rCDI is attendant on many factors, including immune status or function, comorbidities and concomitant treatments. Studies suggest that poor bacterial diversity is correlated with clinical rCDI. Narrow-spectrum gut microflora-sparing antimicrobials (e.g. surotomycin, cadazolid, ridinilazole) are in development for CDI treatment, while microbiota therapeutics (faecal microbiota transplantation, nontoxigenic C. difficile, stool substitutes) are increasingly being explored. rCDI can only occur when viable C. difficile spores are present, either within the gut lumen after infection or when reacquired from the environment. C. difficile spore germination can be influenced by gut environmental factors resulting from dysbiosis, and spore outgrowth may be affected stage by some antimicrobials (e.g. fidaxomicin, ramoplanin, oritavancin). Implications: rCDI is a significant challenge for healthcare professionals, requiring a

multifaceted approach; optimized infection control to minimize reinfection; *C. difficile*-targeted antibiotics to minimize dysbiosis; and gut microflora restoration to promote colonization resistance. These elements should be informed by our understanding of the microbiologic factors involved in both *C. difficile* itself and the gut microbiome. Copyright © 2017 European Society of Clinical Microbiology and Infectious Diseases

**Database:** EMBASE

## **2. Clostridium difficile classification overestimates hospital-acquired infections**

**Author(s):** McLure A.; Clements A.C.A.; Kirk M.; Glass K.

**Source:** Journal of Hospital Infection; 2018

**Publication Date:** 2018

**Publication Type(s):** Article In Press

**Abstract:**Background: *Clostridium difficile* infections occur frequently among hospitalized patients, with some infections acquired in hospital and others in the community. International guidelines classify cases as hospital-acquired if symptom onset occurs more than two days after admission. This classification informs surveillance and infection control, but has not been verified by empirical or modelling studies. Aim: To assess current classification of *C. difficile* acquisition using a simulation model as a reference standard. Methods: *C. difficile* transmission was simulated in a range of hospital scenarios. The sensitivity, specificity and precision of classifications that use cut-offs ranging from 0.25 h to 40 days were calculated. The optimal cut-off that correctly estimated the proportion of cases that were hospital acquired and the balanced cut-off that had equal sensitivity and specificity were identified. Findings: The recommended two-day cut-off overestimated the incidence of hospital-acquired cases in all scenarios and by >100% in the base scenario. The two-day cut-off had good sensitivity (96%) but poor specificity (48%) and precision (52%) to identify cases acquired during the current hospitalization. A five-day cut-off was balanced, and a six-day cut-off was optimal in the base scenario. The optimal and balanced cut-offs were more than two days for nearly all scenarios considered (ranges: four to nine days and two to eight days, respectively). Conclusion: Current guidelines for classifying *C. difficile* infections overestimate the proportion of cases acquired in hospital in all model scenarios. To reduce misclassification bias, an infection should be classified as being acquired prior to admission if symptoms begin within five days of admission.

**Database:** EMBASE

## **3. Reducing length of stay to improve Clostridium difficile-related health outcomes**

**Author(s):** Brain D.C.; Barnett A.G.; Halton K.; Graves N.; Yakob L.; Clements A.; Riley T.V.

**Source:** Infection, Disease and Health; 2018

**Publication Date:** 2018

**Publication Type(s):** Article In Press

**Abstract:**Background: *Clostridium difficile* infection is a serious hospital-acquired infection, causing negative outcomes for those who are afflicted by it. Hospital length of stay is known to be a risk factor for transmission and significant reductions in infection numbers can be realised if transmission is reduced. Methods: A Markov model was constructed to compare the impact that five alternative healthcare scenarios had on total *C. difficile* infections, QALYs gained and total number of patients requiring treatment in ICU. A previously published stochastic transmission model for *C. difficile* informed scenario effectiveness, while other parameters were estimated from published literature, administrative datasets and expert opinion. Results: Reducing inpatient LOS disrupts transmission of *C. difficile* and results in a large reduction of total infections. In turn, an increase in

QALYs is expected when the number of infections is reduced. A reduction in infections reduces the number of ICU admissions, which is likely to have a large economic benefit in the Australian setting. Coupling a reduction in overall inpatient LOS with a 'traditional' infection control intervention, such as hand hygiene or antimicrobial stewardship, improves results further than reducing LOS on its own. Conclusion: Implementing a LOS-focused intervention would be a practical challenge, especially for clinicians who already juggle high demand. However, it is not unattainable with the right local endorsement and could have significant benefits for health services.

**Database:** EMBASE

#### **4. Evaluating the Sporicidal Activity of Disinfectants against *Clostridium difficile* and *Bacillus amyloliquefaciens* Spores by Using the Improved Methods Based on ASTM E2197-11.**

**Author(s):** Uwamahoro, Marie Christine; Massicotte, Richard; Hurtubise, Yves; Gagné-Bourque, François; Mafu, Akier Assanta; Yahia, L'Hocine

**Source:** *Frontiers in public health*; 2018; vol. 6 ; p. 18

**Publication Date:** 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29459891

Available at [Frontiers in Public Health](#) - from Europe PubMed Central - Open Access

Available at [Frontiers in Public Health](#) - from frontiersin.org

**Abstract:** Spore-forming pathogenic bacteria, such as *Clostridium difficile*, are associated with nosocomial infection, leading to the increased use of sporicidal disinfectants, which impacts socioeconomic costs. However, *C. difficile* can be prevented using microorganisms such as *Bacillus amyloliquefaciens*, a prophylactic agent that has been proven to be effective against it in recent tests or it can be controlled by sporicidal disinfectants. These disinfectants against spores should be evaluated according to a known and recommended standard. Unfortunately, some newly manufactured disinfectants like Bioxy products have not yet been tested. ASTM E2197-11 is a standard test that uses stainless steel disks (1 cm in diameter) as carriers, and the performance of the test formulation is calculated by comparing the number of viable test organisms to that on the control carriers. Surface tests are preferable for evaluating disinfectants with sporicidal effects on hard surfaces. This study applies improved methods, based on the ASTM E2197-11 standard, for evaluating and comparing the sporicidal efficacies of several disinfectants against spores of *C. difficile* and *B. amyloliquefaciens*, which are used as the test organisms. With the improved method, all spores were recovered through vortexing and membrane filtration. The results show that chlorine-based products are effective in 5 min and Bioxy products at 5% w/v are effective in 10 min. Although Bioxy products may take longer to prove their effectiveness, their non-harmful effects to hospital surfaces and people have been well established in the literature.

**Database:** Medline

#### **5. *Clostridium difficile* infection in hospitalized patients with antibiotic-associated diarrhea: A systematic review and meta-analysis**

**Author(s):** Nasiri M.J.; Goudarzi M.; Hajikhani B.; Ghazi M.; Goudarzi H.; Pouriran R.

**Source:** *Anaerobe*; Apr 2018; vol. 50 ; p. 32-37

**Publication Date:** Apr 2018

**Publication Type(s):** Review

**Abstract:** Clostridium difficile is the main infectious cause of antibiotic associated diarrhea (AAD). The objective of this study was to determine the frequency of C. difficile AAD in hospitalized patients. We searched MEDLINE (Pubmed), Embase, Web of Science and Cochrane library for subject headings and text words related to C. difficile AAD. Studies that investigated the prevalence or frequency of C. difficile AAD in health care settings were considered eligible. Using a random-effects model, data obtained from the identified studies were combined. Of the 2464 citations identified, twenty studies (5496 patients) met the inclusion criteria of the present study. Pooling all studies, the frequency of C. difficile among AAD patients was 20.0% (95% CI 13.0-28.0). The most frequently used antibiotics in health care settings were the following: Clindamycin, fluoroquinolones and cephalosporins. The current systematic review demonstrated the significant presence of C. difficile among patients with AAD. The limited and rational use of broad spectrum antibiotics and implementation of standard infection control measures are recommended to reduce the risk of C. difficile associated infections in hospitalized patients.

**Database:** EMBASE

## **6. Cost-Effectiveness of Competing Treatment Strategies for Clostridium difficile Infection: A Systematic Review.**

**Author(s):** Le, Phuc; Nghiem, Van T; Mullen, Patricia Dolan; Deshpande, Abhishek

**Source:** Infection control and hospital epidemiology; Apr 2018; vol. 39 (no. 4); p. 412-424

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29463339

**Abstract:** BACKGROUND Clostridium difficile infection (CDI) presents a substantial economic burden and is associated with significant morbidity. While multiple treatment strategies have been evaluated, a cost-effective management strategy remains unclear. OBJECTIVE We conducted a systematic review to assess cost-effectiveness analyses of CDI treatment and to summarize key issues for clinicians and policy makers to consider. METHODS We searched PubMed and 5 other databases from inception to August 2016. These searches were not limited by study design or language of publication. Two reviewers independently screened the literature, abstracted data, and assessed methodological quality using the Drummond and Jefferson checklist. We extracted data on study characteristics, type of CDI, treatment characteristics, and model structure and inputs. RESULTS We included 14 studies, and 13 of these were from high-income countries. More than 90% of these studies were deemed moderate-to-high or high quality. Overall, 6 studies used a decision-tree model and 7 studies used a Markov model. Cost of therapy, time horizon, treatment cure rates, and recurrence rates were common influential factors in the study results. For initial CDI, fidaxomicin was a more cost-effective therapy than metronidazole or vancomycin in 2 of 3 studies. For severe initial CDI, 2 of 3 studies found fidaxomicin to be the most cost-effective therapy. For recurrent CDI, fidaxomicin was cost-effective in 3 of 5 studies, while fecal microbiota transplantation (FMT) by colonoscopy was consistently cost-effective in 4 of 4 studies. CONCLUSIONS The cost-effectiveness of fidaxomicin compared with other pharmacologic therapies was not definitive for either initial or recurrent CDI. Despite its high cost, FMT by colonoscopy may be a cost-effective therapy for recurrent CDI. A consensus on model design and assumptions are necessary for future comparison of CDI treatment.

**Database:** Medline

### **7. Reducing Clostridium difficile Colitis Rates Via Cost-Saving Diagnostic Stewardship.**

**Author(s):** Yen, Christina; Holtom, Paul; Butler-Wu, Susan M; Wald-Dickler, Noah; Shulman, Ira; Spellberg, Brad

**Source:** Infection control and hospital epidemiology; Apr 2018 ; p. 1-3

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29611494

**Abstract:**We conducted a quality improvement project at a large public tertiary-care academic hospital to reduce reported hospital-acquired Clostridium difficile infection (CDI) rates. We introduced diagnostic stewardship and provider education, resulting in a 2-fold reduction in C. difficile nucleic acid amplification test (NAAT) orders and markedly lower hospital CDI rate.

**Database:** Medline

### **8. Validation of Active Surveillance Testing for Clostridium difficile Colonization Using the cobas Cdiff Test.**

**Author(s):** Patel, Parul A; Schora, Donna M; Singh, Kamaljit; Peterson, Lance R

**Source:** Journal of clinical microbiology; Apr 2018; vol. 56 (no. 4)

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29367295

**Abstract:**Clostridium difficile infection (CDI) is not declining in the United States. Nucleic acid amplification tests (NAAT) are used as part of active surveillance testing programs to prevent health care-associated infection. The objective of this study was to validate the cobas Cdiff Test on the cobas 4800 System (cobas) within a four-hospital system using prospectively collected perirectal swabs from asymptomatic patients at admission and during monthly intensive care unit (ICU) screening in an infection control CDI reduction program. Performance of the cobas was compared to that of toxigenic culture. Each positive cobas sample and the next following negative patient swab were cultured. The study design gave 273 samples processed by both cobas (137 positive and 136 negative) and culture (one negative swab was not cultured). Discrepant analysis was performed using a second NAAT, the Xpert C. difficile Epi test (Xpert). This strategy was compared to a medical record review for antibiotic receipt that would inhibit growth of C. difficile in colonic stool. None of the cobas-negative samples were culture positive. The cobas positive predictive value was 75.2% (95% confidence interval [CI], 66.9% to 82%) and positive percent agreement was 100% (95% CI, 96.0% to 100%). Overall agreement between cobas and direct toxigenic culture was 87.6% (95% CI, 83.1% to 91%). For the cobas-positive/culture-negative (discrepant) samples, 7 Xpert-positive samples were from patients receiving inhibitory antimicrobials; only 4 of 23 Xpert-negative samples received these agents (P = 0.00006). Our results support use of the cobas as a reliable assay for an active surveillance testing program to detect asymptomatic carriers of toxigenic C. difficile.

**Database:** Medline

### **9. A Generalizable, Data-Driven Approach to Predict Daily Risk of Clostridium difficile Infection at Two Large Academic Health Centers.**

**Author(s):** Oh, Jeeheh; Makar, Maggie; Fusco, Christopher; McCaffrey, Robert; Rao, Krishna; Ryan, Erin E; Washer, Laraine; West, Lauren R; Young, Vincent B; Guttag, John; Hooper, David C; Shenoy, Erica S; Wiens, Jenna

**Source:** Infection control and hospital epidemiology; Apr 2018; vol. 39 (no. 4); p. 425-433

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29576042

**Abstract:**OBJECTIVE An estimated 293,300 healthcare-associated cases of Clostridium difficile infection (CDI) occur annually in the United States. To date, research has focused on developing risk prediction models for CDI that work well across institutions. However, this one-size-fits-all approach ignores important hospital-specific factors. We focus on a generalizable method for building facility-specific models. We demonstrate the applicability of the approach using electronic health records (EHR) from the University of Michigan Hospitals (UM) and the Massachusetts General Hospital (MGH). METHODS We utilized EHR data from 191,014 adult admissions to UM and 65,718 adult admissions to MGH. We extracted patient demographics, admission details, patient history, and daily hospitalization details, resulting in 4,836 features from patients at UM and 1,837 from patients at MGH. We used L2 regularized logistic regression to learn the models, and we measured the discriminative performance of the models on held-out data from each hospital. RESULTS Using the UM and MGH test data, the models achieved area under the receiver operating characteristic curve (AUROC) values of 0.82 (95% confidence interval [CI], 0.80-0.84) and 0.75 (95% CI, 0.73-0.78), respectively. Some predictive factors were shared between the 2 models, but many of the top predictive factors differed between facilities. CONCLUSION A data-driven approach to building models for estimating daily patient risk for CDI was used to build institution-specific models at 2 large hospitals with different patient populations and EHR systems. In contrast to traditional approaches that focus on developing models that apply across hospitals, our generalizable approach yields risk-stratification models tailored to an institution. These hospital-specific models allow for earlier and more accurate identification of high-risk patients and better targeting of infection prevention strategies.

**Database:** Medline

## 10. Guidance document for prevention of Clostridium difficile infection in acute healthcare settings.

**Author(s):** Tschudin-Sutter, Sarah; Kuijper, Ed J; Durovic, Ana; Vehreschild, Maria J G T; Barbut, Frédéric; Eckert, Catherine; Fitzpatrick, Fidelma; Hell, Markus; Norén, Torbjörn; O'Driscoll, Jean; Coia, John; Gastmeier, Petra; von Müller, Lutz; Wilcox, Mark H; Widmer, Andreas F; Committee

**Source:** Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29505879

**Abstract:**SCOPE Clostridium difficile infection (CDI) is the most important infective cause of healthcare-associated diarrhoea in high income countries and one of the most important healthcare-associated pathogens in both Europe and the United States. It is associated with high morbidity and mortality resulting in both societal and financial burden. A significant proportion of this burden is potentially preventable by a combination of targeted infection prevention and control measures and antimicrobial stewardship. The aim of this guidance document is to provide an update on recommendations for prevention of C. difficile infections in acute care settings to provide guidance to those responsible for institutional infection prevention and control programs. METHODS An expert group was set up by the European Study Group for C. difficile (ESGCD), which performed a systematic review of the literature on prevention of CDI in adults hospitalized in acute care settings

and derived respective recommendations according to the GRADE approach. Recommendations are stratified for both outbreak and endemic settings providing. QUESTIONS ADDRESSED BY THE GUIDELINE AND RECOMMENDATIONS This guidance document provides thirty-six statements on strategies to prevent *C. difficile* infection in acute care settings, including eighteen strong recommendations. No recommendation was provided for three questions.

**Database:** Medline

**11. Extended-pulsed fidaxomicin versus vancomycin for *Clostridium difficile* infection in patients 60 years and older (EXTEND): a randomised, controlled, open-label, phase 3b/4 trial.**

**Author(s):** Guery, Benoit; Menichetti, Francesco; Anttila, Veli-Jukka; Adomakoh, Nicholas; Aguado, Jose Maria; Bisnauthsing, Karen; Georgopali, Areti; Goldenberg, Simon D; Karas, Andreas; Kazeem, Gbenga; Longshaw, Chris; Palacios-Fabrega, Jose Alejandro; Cornely, Oliver A; Vehreschild, Maria J G T; EXTEND Clinical Study Group

**Source:** The Lancet. Infectious diseases; Mar 2018; vol. 18 (no. 3); p. 296-307

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29273269

Available at [The Lancet. Infectious diseases](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:** BACKGROUND *Clostridium difficile* infection causes severe complications and frequently recurs. An extended-pulsed fidaxomicin regimen might facilitate sustained clinical cure by prolonging *C difficile* suppression and supporting gut microbiota recovery. We aimed to compare clinical outcomes of extended-pulsed fidaxomicin with standard vancomycin. METHODS In this randomised, controlled, open-label, superiority study, we recruited hospitalised adults aged 60 years and older with confirmed *C difficile* infection at 86 European hospitals. Patients were randomly assigned (1:1) using an interactive web response system to receive extended-pulsed fidaxomicin (200 mg oral tablets, twice daily on days 1-5, then once daily on alternate days on days 7-25) or vancomycin (125 mg oral capsules, four times daily on days 1-10), stratified by baseline *C difficile* infection severity, cancer presence, age ( $\geq 75$  years vs  $< 75$  years), and number of previous *C difficile* infection occurrences. The primary endpoint was sustained clinical cure 30 days after end of treatment (day 55 for extended-pulsed fidaxomicin and day 40 for vancomycin), assessed in all randomised patients who met the inclusion criteria and received at least one dose of study medication (modified full analysis set). Adverse events were assessed in all patients who received at least one dose of study drug. The study is registered with ClinicalTrials.gov, number NCT02254967. FINDINGS Between Nov 6, 2014, and May 5, 2016, 364 patients were enrolled and randomly assigned to receive extended-pulsed fidaxomicin or vancomycin. 362 patients received at least one dose of study medication (181 in each group). 124 (70%) of 177 patients in the modified full analysis set receiving extended-pulsed fidaxomicin achieved sustained clinical cure 30 days after end of treatment, compared with 106 (59%) of 179 patients receiving vancomycin (difference 11% [95% CI 1.0-20.7],  $p=0.030$ ; odds ratio 1.62 [95% CI 1.04-2.54]). Incidence of treatment-emergent adverse events did not differ between extended-pulsed fidaxomicin (121 [67%] of 181) and vancomycin (128 [71%] of 181) treatment arms. One death in the vancomycin arm was considered by the investigator to be related to study drug. INTERPRETATION Extended-pulsed fidaxomicin was superior to standard-dose vancomycin for sustained cure of *C difficile* infection, and, to our knowledge, extended-pulsed fidaxomicin recurrence rates in this study are the lowest observed in a randomised clinical trial of antibiotic treatment for *C difficile* infection. FUNDING Astellas Pharma, Inc.

**Database:** Medline

**12. Clostridium difficile Exposures, Colonization, and the Microbiome: Implications for Prevention.**

**Author(s):** Revolinski, Sara L; Munoz-Price, L Silvia

**Source:** Infection control and hospital epidemiology; Mar 2018 ; p. 1-7

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29553000

**Abstract:**New studies have been published regarding the epidemiology of Clostridium difficile in topics such as asymptomatic C. difficile colonization, community-associated C. difficile infection, environmental contamination outside healthcare settings, animal colonization, and the interactions between C. difficile and the gut microbiome. In addition to summarizing these findings, this review offers a perspective on the potential impact of high-throughput sequencing and other potential techniques on the prevention of C. difficile.

**Database:** Medline

**13. Electronically Available Comorbid Conditions for Risk Prediction of Healthcare-Associated Clostridium difficile Infection.**

**Author(s):** Harris, Anthony D; Sbarra, Alyssa N; Leekha, Surbhi; Jackson, Sarah S; Johnson, J Kristie; Pineles, Lisa; Thom, Kerri A

**Source:** Infection control and hospital epidemiology; Mar 2018; vol. 39 (no. 3); p. 297-301

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29397800

**Abstract:**OBJECTIVE To analyze whether electronically available comorbid conditions are risk factors for Centers for Disease Control and Prevention (CDC)-defined, hospital-onset Clostridium difficile infection (CDI) after controlling for antibiotic and gastric acid suppression therapy use. PATIENTS Patients aged  $\geq 18$  years admitted to the University of Maryland Medical Center between November 7, 2015, and May 31, 2017. METHODS Comorbid conditions were assessed using the Elixhauser comorbidity index. The Elixhauser comorbidity index and the comorbid condition components were calculated using the International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) codes extracted from electronic medical records. Bivariate associations between CDI and potential covariates for multivariable regression, including antibiotic use, gastric acid suppression therapy use, as well as comorbid conditions, were estimated using log binomial multivariable regression. RESULTS After controlling for antibiotic use, age, proton-pump inhibitor use, and histamine-blocker use, the Elixhauser comorbidity index was a significant risk factor for predicting CDI. There was an increased risk of 1.26 (95% CI, 1.19-1.32) of having CDI for each additional Elixhauser point added to the total Elixhauser score. CONCLUSIONS An increase in Elixhauser score is associated with CDI. Our study and other studies have shown that comorbid conditions are important risk factors for CDI. Electronically available comorbid conditions and scores like the Elixhauser index should be considered for risk-adjustment of CDC CDI rates.

**Database:** Medline

#### 14. Susceptibilities of clinical *Clostridium difficile* isolates to antimicrobials: a systematic review and meta-analysis of studies since 1970

**Author(s):** Khanafer N.; Vanhems P.; Daneman N.; Simor A.; Brown K.A.; Greene T.; Samore M.

**Source:** Clinical Microbiology and Infection; Feb 2018; vol. 24 (no. 2); p. 171-174

**Publication Date:** Feb 2018

**Publication Type(s):** Review

**Abstract:** Objectives: Although exposure to antibiotics can cause *Clostridium difficile* infection, certain antibiotics are used to treat *C. difficile*. Measurements of antimicrobial *C. difficile* activity could help to identify antibiotic risk and emergent resistance. Here, we describe publication patterns relating to *C. difficile* susceptibilities and estimate minimum inhibitory concentrations (MIC) for antibiotic classes in the published literature between January 1970 and June 2014. Methods: We queried PUBMED and EMBASE for studies reporting antibiotic *C. difficile* MIC in English or French. We used mixed-effects models to obtain pooled estimates of antibiotic class median MIC (MIC<sub>50</sub>), 90th percentile of MIC (MIC<sub>90</sub>), and MIC<sub>90</sub>:MIC<sub>50</sub> ratio. Results: Our search identified 182 articles that met our inclusion criteria, of which 27 were retained for meta-analysis. Aminoglycosides (MIC<sub>50</sub> 120 mg/L, 95% CI 62-250), 3rd (MIC<sub>50</sub> 75 mg/L, 95% CI 39-130) and 2nd generation cephalosporins (MIC<sub>50</sub> 64 mg/L, 95% CI 27-140) had the least *C. difficile* activity. Rifamycins (MIC<sub>50</sub> 0.034 mg/L, 95% CI 0.012-0.099) and tetracyclines (MIC<sub>50</sub> 0.29 mg/L, 95% CI 0.054-1.7) had the highest level of activity. The activity of 3rd generation cephalosporins was more than three times lower than that of 1st generation agents (MIC<sub>50</sub> 19 mg/L, 95% CI 7.0-54). Time-trends in MIC<sub>50</sub> were increasing for carbapenems (70% increase per 10 years) while decreasing for tetracyclines (51% decrease per 10 years). Conclusions: We found a 3500-fold variation in antibiotic *C. difficile* MIC<sub>50</sub>, with aminoglycosides as the least active agents and rifamycins as the most active. Further research is needed to determine how in vitro measures can help assess patient *C. difficile* risk and guide antimicrobial stewardship.

**Database:** EMBASE

#### 15. Selection and characterization of DNA aptamers for detection of glutamate dehydrogenase from *Clostridium difficile*

**Author(s):** Liu M.; Brennan J.D.; Li Y.; Yin Q.

**Source:** Biochimie; Feb 2018; vol. 145 ; p. 151-157

**Publication Date:** Feb 2018

**Publication Type(s):** Article

**Abstract:** Rapid and accurate diagnosis of *Clostridium difficile* infections (CDI) is crucial for patient treatment, infection control and epidemiological monitoring. As an important antigen, glutamate dehydrogenase (GDH) has been proposed as a preliminary screening test target for CDI. However, current assays based on GDH activity or GDH immunoassays have suboptimal sensitivity and specificity. Herein, we describe the selection and characterization of single-stranded DNA aptamers that specifically target GDH. After 10 rounds of selection, high-throughput sequencing was used to identify enriched aptamer candidates. Of 10 candidates, three aptamers for GDH were identified. Gel shift assays showed that these aptamers exhibited low nanomolar affinities. One aptamer was optimized based on structural analysis and further engineered into a structure-switching fluorescence signaling aptamer, wherein desorption from reduced graphene oxide (RGO) upon binding of GDH led to an increase in fluorescence emission. This method allowed for quantitative detection of GDH with a detection limit of 1 nM, providing great potential for its further application in CDI diagnosis.

**Database:** EMBASE

### **16. Impact of antimicrobial stewardship interventions on Clostridium difficile infection and clinical outcomes: segmented regression analyses.**

**Author(s):** Patton, Andrea; Davey, Peter; Harbarth, Stephan; Nathwani, Dilip; Sneddon, Jacqueline; Marwick, Charis A

**Source:** The Journal of antimicrobial chemotherapy; Feb 2018; vol. 73 (no. 2); p. 517-526

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29177477

**Abstract:**BackgroundAntimicrobial exposure is associated with increased risk of Clostridium difficile infection (CDI), but the impact of prescribing interventions on CDI and other outcomes is less clear.ObjectivesTo evaluate the effect of an antimicrobial stewardship intervention targeting high-risk antimicrobials (HRA), implemented in October 2008, and to compare the findings with similar studies from a systematic review.MethodsAll patients admitted to Medicine and Surgery in Ninewells Hospital from October 2006 to September 2010 were included. Intervention effects on HRA use (dispensed DDD), CDI cases and mortality rates, per 1000 admissions per month, were analysed separately in Medicine and Surgery using segmented regression of interrupted time series (ITS) data. Data from comparable published studies were reanalysed using the same method.ResultsSix months post-intervention, there were relative reductions in HRA use of 33% (95% CI 11-56) in Medicine and 32% (95% CI 19-46) in Surgery. At 12 months, there was an estimated reduction in CDI of 7.0 cases/1000 admissions [relative change -24% (95% CI - 55 to 6)] in Medicine, but no change in Surgery {estimated 0.1 fewer cases/1000 admissions [-2% (95% CI - 116 to 112)]}. Mortality reduced throughout the study period, unaffected by the intervention. In all six comparable studies, HRA use reduced significantly, but reductions in CDI rates were only statistically significant in two and none measured mortality. Pre-intervention CDI rates and trends influenced the intervention effect.ConclusionsDespite large reductions in HRA prescribing and reductions in CDI, demonstrating real-world impact of stewardship interventions remains challenging.

**Database:** Medline

### **17. Low Risk of Primary Clostridium difficile Infection With Tetracyclines: A Systematic Review and Metaanalysis.**

**Author(s):** Tariq, Raseen; Cho, Janice; Kapoor, Saloni; Orenstein, Robert; Singh, Siddharth; Pardi, Darrell S; Khanna, Sahil

**Source:** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Feb 2018; vol. 66 (no. 4); p. 514-522

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29401273

**Abstract:**BackgroundThe choice of antibiotics for systemic infections in patients with a high risk of Clostridium difficile infection (CDI) remains a clinical practice dilemma. Although some studies suggest that tetracyclines may be associated with a lower risk of CDI than other antibiotics, other results are conflicting. We conducted a systematic review and metaanalysis of studies that assessed the risk of CDI with tetracyclines compared to other antibiotics.MethodsWe conducted a systematic search of Medline, Embase, and Web of Science from January 1978 through December 2016 to include studies that assessed the association between tetracycline use and risk of CDI. Weighted summary estimates were calculated using generalized inverse variance with a random-effects model

using RevMan 5.3. Study quality was assessed using the Newcastle-Ottawa scale. Results Six studies (4 case control, 2 cohort) with patient recruitment between 1993 and 2012 were included.

Metaanalysis using a random-effects model, demonstrated that tetracyclines were associated with a decreased risk of CDI (odds ratio [OR], 0.62; 95% confidence interval [CI], 0.47-0.81;  $P < .001$ ). There was significant heterogeneity, with an  $I^2$  of 53% with no publication bias. Subgroup analysis of studies that evaluated the risk of CDI with doxycycline alone also demonstrated a decreased risk of CDI (OR, 0.55; 95% CI, 0.40-0.75;  $P < .001$ ). Conclusions Metaanalyses of existing studies suggest that tetracyclines may be associated with a decreased risk of CDI compared with other antimicrobials. It may be reasonable to use tetracyclines whenever appropriate to decrease CDI associated with antibiotic use.

**Database:** Medline

### **18. New insights into transmission of Clostridium difficile infection-narrative review.**

**Author(s):** Durovic, A; Widmer, A F; Tschudin-Sutter, S

**Source:** Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases; Feb 2018

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 29427800

**Abstract:**BACKGROUND Traditionally, Clostridium difficile has been considered a typical healthcare-associated pathogen—that is, one transmitted within healthcare facilities and thus prevented by implementation of standard infection control measures. Recently this concept has been challenged by studies suggesting a relevant role for community acquisition of C. difficile. AIMSTo discusses the current literature, compiled during the last decade, reporting on sources of acquisition of C. difficile and subsequent transmission. SOURCEThe databases PubMed, Medline, Embase and the Cochrane Database were searched for articles published from 1 January 2007 to 30 June 2017 reporting on possible transmission pathways of C. difficile and/or suggesting a source of acquisition of C. difficile. All study types reporting on adult populations were considered; case reports and series were excluded. The PRISMA guidelines for the reporting of systematic reviews were followed. CONTENTAmong 24 original articles included, 63% report on transmission of C. difficile in healthcare settings and 37% investigate sources and transmission of C. difficile in the community. Contact with symptomatic carriers (53.3%), the hospital environment (40.0%) and asymptomatic carriers (20%) were the most commonly reported transmission pathways within healthcare settings. The leading sources for acquisition of C. difficile in the community include direct contact with symptomatic and asymptomatic carriers in the community, including infants (30%) and residents of long-term non-acute care facilities (30%), followed by contact with contaminated environments in outpatient care settings (20%) and exposure to livestock or livestock farms (20%). IMPLICATIONSIn healthcare settings, future control efforts may need to focus on extending cleaning and disinfection procedures beyond the immediate surroundings of symptomatic carriers. Potential targets to prevent acquisition of C. difficile in the community include household settings, long-term care facilities and outpatient settings, while the role of livestock in entertaining transmission requires further investigation.

**Database:** Medline

### **19. Identification of target risk groups for population-based Clostridium difficile infection prevention strategies using a population attributable risk approach.**

**Author(s):** Oh, Sung-Hee; Kang, Hye-Young

**Source:** International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases; Jan 2018; vol. 66 ; p. 107-112

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29162405

Available at [International Journal of Infectious Diseases](#) - from ScienceDirect

**Abstract:**OBJECTIVESWe aimed to determine risk factors associated with Clostridium difficile infection (CDI) and assess the contributions of these factors on CDI burden.METHODSWe conducted a 1:4 matched case-control study using a national claims dataset. Cases were incident CDI without a history of CDI in the previous 84 days, and were age- and sex-matched with control patients. We ascertained exposure, defined as a history of morbidities and drug use within 90 days. The population attributable risk (PAR) percent for risk factors was estimated using odds ratios (ORs) obtained from the case-control study.RESULTSOverall, the strongest CDI-associated risk factors, which have significant contributions to the CDI burden as well, were the experience of gastroenteritis (OR=5.08, PAR%=17.09%) and use of antibiotics (OR=1.69, PAR%=19.00%), followed by the experiences of female pelvic infection, irritable bowel syndrome, inflammatory bowel disease, and pneumonia, and use of proton-pump inhibitors (OR=1.52-2.37, PAR%=1.95-2.90).CONCLUSIONSThe control of risk factors that had strong association with CDI and affected large proportions of total CDI cases would be beneficial for CDI prevention. We suggest performing CDI testing for symptomatic patients with gastroenteritis and implementing antibiotics stewardship.

**Database:** Medline

## 20. Assessing the burden of Clostridium difficile infections for hospitals.

**Author(s):** Hebbinckuys, E; Marissal, J-P; Preda, C; Leclercq, V

**Source:** The Journal of hospital infection; Jan 2018; vol. 98 (no. 1); p. 29-35

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28890287

**Abstract:**BACKGROUNDNosocomial infections place a heavy burden on the healthcare system. However, quantifying the burden raises many questions, ranging from the way to accurately estimate the extra length of stay at hospital to defining and costing the preventive methods among the different care providers.AIMTo estimate the cost of nosocomial infection by C. difficile to inform the hospital managers.METHODSMulti-state modelling based on Markov processes and bootstrapping was used to derive individual estimates of the prolongation of stay at hospital associated with Clostridium difficile infection (CDI). Indicators of cost for hospitals were then computed, including an estimation of the productivity losses derived from diagnosis-related group (DRG)-based payment systems. Patients were aged  $\geq 55$  years, admitted in two hospital facilities in Lille, with and without an episode of CDI from January 1st, 2013 to September 15th, 2014.FINDINGSA total of 52 episodes were screened during the study period. The estimated mean cost of CDI was approximately €23,909 (SD: 17,458) for an extended length of hospital stay (N = 27). In the case of a reduced length of hospital stay (N = 25), the mean cost was approximately €-14,697 (SD: 16,936), which represents net savings for the hospitals. The main cost/savings driver was the productivity losses/gains resulting from the nosocomial infection. A sensitivity analysis showed that the main factor explaining the amount of costs or savings due to nosocomial infections was the length of the hospital stay.CONCLUSIONThe notion of productivity gains in the case of deaths as a

factor revealing the incompleteness of the payment systems is discussed, followed by the methodological issues associated with the statistical method used to control for temporality bias.

**Database:** Medline

## Bronchiolitis

### 1. Medication use in infants admitted with bronchiolitis

**Author(s):** Oakley E.; Brys T.; Williams A.; Babl F.E.; Krieser D.; Davidson A.; Donath S.; Jachno K.; South M.; Borland M.; Neutze J.; Phillips N.; Dalziel S.R.

**Source:** EMA - Emergency Medicine Australasia; 2018

**Publication Date:** 2018

**Publication Type(s):** Article In Press

**Abstract:**Background: There are no medications known that improve the outcome of infants with bronchiolitis. Studies have shown the management of bronchiolitis to be varied. Objectives: To describe medication use at the seven study hospitals from a recent multi-centre randomised controlled trial on hydration in bronchiolitis (comparative rehydration in bronchiolitis [CRIB]). Methods: A retrospective analysis of extant data of infants between 2 months (corrected for prematurity) and 12 months of age admitted with bronchiolitis identified through the CRIB trial. CRIB study records, medical records, pathology and radiology databases were used to collect data using a standardised form and entered in a single site database. Medications investigated included salbutamol, adrenaline, steroids, ipratropium bromide, normal saline, hypertonic saline, steroids and antibiotics. Results: There were 3456 infants available for analysis, of which 42.0% received at least one medication during hospitalisation. Medication use varied by site between 27.0 and 48.7%. The most frequently used medication was salbutamol (25.5%). Medication use in general, and salbutamol use in particular, increased by 8.2 and 9.3%, respectively, per month after 4 months of age; from 22.9 and 3.6% at 4 months to 81.4 and 68.8% at 11 months. In infants admitted to the intensive care unit (ICU) compared with those not admitted to ICU 81.6 and 39.5%, respectively, received medication at one point during the hospital stay. Conclusions: Medication was used for infants with bronchiolitis frequently and variably in Australia and New Zealand. Medication use increased with age. Better strategies for translating evidence into practice are needed. Medicine.

**Database:** EMBASE

### 2. Hypertonic saline inhalations in bronchiolitis-A cumulative meta-analysis

**Author(s):** Heikkila P.; Renko M.; Korppi M.

**Source:** Pediatric Pulmonology; 2018; vol. 53 (no. 2); p. 233-242

**Publication Date:** 2018

**Publication Type(s):** Review

**Abstract:**We undertook a cumulative meta-analysis for the efficacy of hypertonic saline (HS) compared to normal saline (NS) inhalations or no inhalations as controls in bronchiolitis. We performed literature searches from PubMed, Scopus, and by hand search until 20 June 2017. We accepted published randomized controlled trials of HS inhalations in children with bronchiolitis aged <24 months. We evaluated the differences between treatment group with HS and control group without HS inhalations for the length-of-stay in hospital (LOS) by cumulative mean difference (MD) and in hospitalization rate by cumulative risk ratio (RR). We identified 18 studies including 2102 children treated in hospital, and the cumulative MD in LOS was -0.471 days (95% confidence interval [CI] -0.765 to -0.177, Higgins heterogeneity test [I<sup>2</sup>] 72.9%). The cumulative MD reduced in more

recently published papers. In studies with the upper age limit of 12 months, the cumulative MD was -0.408 days (95%CI -0.733 to -0.083) without any important heterogeneity (I<sup>2</sup> = 0%). If only studies with a very low risk of bias were included, the cumulative MD was 0.034 (95%CI -0.361 to 0.293) without any important heterogeneity (I<sup>2</sup> = 0%). We identified eight studies including 1834 children in the outpatient setting, and the cumulative risk ratio for hospitalization was 0.771 (95%CI 0.619-0.959, I<sup>2</sup> 55.8%). In conclusion, HS inhalations offered only limited clinical benefits, though the differences between HS and control groups were statistically significant. The heterogeneity between the studies was substantial. Further studies are warranted with consistent definitions of bronchiolitis and comparable research frames.

**Database:** EMBASE

### 3. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis

**Author(s):** Franklin D.; Schlapbach L.J.; Schibler A.; Fraser J.F.; Jones M.; Babl F.E.; Oakley E.; Craig S.; Neutze J.; Furyk J.; Dalziel S.R.; Whitty J.A.

**Source:** New England Journal of Medicine; Mar 2018; vol. 378 (no. 12); p. 1121-1131

**Publication Date:** Mar 2018

**Publication Type(s):** Article

Available at [New England Journal of Medicine](#) - from Ovid (Journals @ Ovid) - Remote Access

**Abstract:**BACKGROUND High-flow oxygen therapy through a nasal cannula has been increasingly used in infants with bronchiolitis, despite limited high-quality evidence of its efficacy. The efficacy of high-flow oxygen therapy through a nasal cannula in settings other than intensive care units (ICUs) is unclear. METHODS In this multicenter, randomized, controlled trial, we assigned infants younger than 12 months of age who had bronchiolitis and a need for supplemental oxygen therapy to receive either high-flow oxygen therapy (high-flow group) or standard oxygen therapy (standard-therapy group). Infants in the standard-therapy group could receive rescue high-flow oxygen therapy if their condition met criteria for treatment failure. The primary outcome was escalation of care due to treatment failure (defined as meeting ≥3 of 4 clinical criteria: persistent tachycardia, tachypnea, hypoxemia, and medical review triggered by a hospital early-warning tool). Secondary outcomes included duration of hospital stay, duration of oxygen therapy, and rates of transfer to a tertiary hospital, ICU admission, intubation, and adverse events. RESULTS The analyses included 1472 patients. The percentage of infants receiving escalation of care was 12% (87 of 739 infants) in the high-flow group, as compared with 23% (167 of 733) in the standard-therapy group (risk difference, -11 percentage points; 95% confidence interval, -15 to -7; P<0.001). No significant differences were observed in the duration of hospital stay or the duration of oxygen therapy. In each group, one case of pneumothorax (<1% of infants) occurred. Among the 167 infants in the standard-therapy group who had treatment failure, 102 (61%) had a response to high-flow rescue therapy. CONCLUSIONS Among infants with bronchiolitis who were treated outside an ICU, those who received high-flow oxygen therapy had significantly lower rates of escalation of care due to treatment failure than those in the group that received standard oxygen therapy.

**Database:** EMBASE

### 4. Nebulized hypertonic saline in infants hospitalized with moderately severe bronchiolitis due to RSV infection: A multicenter randomized controlled trial

**Author(s):** Morikawa Y.; Miura M.; Kaneko T.; Ishikura K.; Furuhata M.Y.; Morino S.; Omori T.; Otsuka M.; Chiga M.; Obonai T.; Hataya H.; Hasegawa Y.; Honda M.

**Source:** Pediatric Pulmonology; Mar 2018; vol. 53 (no. 3); p. 358-365

**Publication Date:** Mar 2018

**Publication Type(s):** Article

**Abstract:**Introduction: The efficacy of nebulized hypertonic saline (HS) therapy for shortening hospital length of stay (LOS) or improving bronchiolitic symptoms remains controversial. Most studies enrolled small numbers of subjects and did not consider the role of respiratory syncytial virus (RSV), the most common cause of acute bronchiolitis. Our aim was to evaluate the efficacy and safety of nebulized HS therapy for acute bronchiolitis due to RSV in moderately ill hospitalized infants. Materials and Methods: This was an open-label, multicenter, randomized controlled trial comparing a nebulized HS treatment group with a normal saline (NS) group. The subjects, 128 infants with bronchiolitis due to RSV, were admitted to five hospitals in Tokyo, Japan. Three-percent HS or NS was administered via bronchodilator four times daily post-admission. The primary outcome was LOS, defined as the time until the patients fulfilled the discharge criteria, namely, absence of fever, no need for supplemental oxygen, and adequate feeding. Survival analysis was conducted in accordance with the intention-to-treat principle. Results: The baseline characteristics were similar between the two groups. There was no significant overall difference in LOS between the groups (4.81 +/- 2.14 days in HS vs 4.61 +/- 2.18 days in NS; P = 0.60). Survival analysis by log-rank test also showed no significance (P = 0.62). Multivariate adjustment did not significantly alter the results. The treatment was well-tolerated, with no adverse effects attributable to the use of HS. Conclusions: Nebulized HS therapy did not significantly reduce LOS among infants with bronchiolitis due to RSV.

**Database:** EMBASE

## 5. Respiratory Syncytial Virus and Rhinovirus Bronchiolitis Are Associated with Distinct Metabolic Pathways

**Author(s):** Stewart C.J.; Wong M.C.; Ajami N.J.; Petrosino J.F.; Piedra P.A.; Hasegawa K.; Espinola J.A.; Tierney C.N.; Camargo C.A.; Mansbach J.M.

**Source:** Journal of Infectious Diseases; Mar 2018; vol. 217 (no. 7); p. 1160-1169

**Publication Date:** Mar 2018

**Publication Type(s):** Article

**Abstract:**Background Bronchiolitis, the leading cause of hospitalization among infants in the United States, is most commonly caused by respiratory syncytial virus (RSV), followed by rhinovirus (RV). Conventional perception is that bronchiolitis is a single entity, albeit with different viral etiologies and degrees of severity. Methods We conducted a cross-sectional study of nasopharyngeal aspirates from 106 infants hospitalized with bronchiolitis due to either RSV only (80 patients) or RV only (26 patients). We performed metabolomics analysis and 16S ribosomal RNA gene sequencing on all samples and metagenomic sequencing on 58 of 106 samples. Results Infants with RSV-only and RV-only infections had significantly different nasopharyngeal metabolome profiles (P <.001) and bacterial metagenome profiles (P <.05). RSV-only infection was associated with metabolites from a range of pathways and with a microbiome dominated by *Streptococcus pneumoniae*. By contrast, RV-only infection was associated with increased levels of essential and nonessential N-acetyl amino acids and with a high relative abundance of *Haemophilus influenzae*. These co-occurring species were associated with driving the bacterially derived metabolic pathways. Multi-omic analysis showed that both the virus and the microbiome were significantly associated with metabolic function in infants hospitalized with bronchiolitis. Conclusion Although replication of these findings is necessary, they highlight that bronchiolitis is not a uniform disease between RSV and RV infections, a result with future implications for prevention and treatment.

**Database:** EMBASE

## 6. The cost-effectiveness of hypertonic saline inhalations for infant bronchiolitis: a decision analysis.

**Author(s):** Heikkilä, Paula; Mecklin, Minna; Korppi, Matti

**Source:** World journal of pediatrics : WJP; Feb 2018; vol. 14 (no. 1); p. 26-34

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29476325

**Abstract:**BACKGROUND This study evaluated the cost-effectiveness of hypertonic saline (HS) inhalations for infant bronchiolitis, compared to normal saline inhalations or standard treatment without inhalations as controls. METHOD The decision tree in the decision analysis was used to calculate the expected costs. Actual cost data were obtained from our retrospective case-control study on bronchiolitis treatment. The effectiveness of treatment, based on the hospitalization rate of those admitted to the emergency department and the length of stay (LOS) of those who were hospitalized, was collected from previous studies. For the effectiveness estimations, we made a meta-analysis summarizing the results of the meta-analysis of the Cochrane review in 2013 and the results of 10 studies published after it. RESULT The mean hospitalization rate was 24.7% in the HS inhalation group and 32.6% in the control group [risk ratio: 0.80, 95% confidence interval (CI) 0.67-0.96] and the mean LOS was 3.736 (HS group) and 4.292 (controls) days (mean difference: -0.55 days, 95% CI -0.96 to -0.15), respectively. The expected costs per patient, when both inpatients and outpatients were included, were €816 (\$1111) in the HS inhalation group and €962 (\$1310) in the control group. The expected costs per hospitalization, when only inpatients were included, were €2600 (\$3540) in the HS inhalation group and €2890 (\$3935) in the control group. CONCLUSION HS inhalations slightly reduced the expected hospitalization costs of infant bronchiolitis. However, the low effectiveness, rather than the cost, is the factor that will limit the use of HS inhalations in infant bronchiolitis.

**Database:** Medline

## 7. The management of children with bronchiolitis in the Australasian hospital setting: development of a clinical practice guideline.

**Author(s):** O'Brien, Sharon; Wilson, Sally; Gill, Fenella J; Cotterell, Elizabeth; Borland, Meredith L; Oakley, Edward; Dalziel, Stuart R; Paediatric Research in Emergency Departments International Collaborative (PREDICT) network, Australasia

**Source:** BMC medical research methodology; Feb 2018; vol. 18 (no. 1); p. 22

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29433429

Available at [BMC Medical Research Methodology](#) - from BioMed Central

Available at [BMC Medical Research Methodology](#) - from Europe PubMed Central - Open Access

Available at [BMC Medical Research Methodology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

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**Abstract:**BACKGROUND Bronchiolitis is the commonest respiratory infection in children less than 12 months and cause of hospitalisation in infants under 6 months of age in Australasia. Unfortunately there is substantial variation in management, despite high levels of supporting

evidence. This paper reports on the process, strengths and challenges of the hybrid approach used to develop the first Australasian management guideline relevant to the local population. **METHOD** An adaptation of the nine steps recommended by the National Health and Medical Research Council (NHMRC) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology were utilised. Following establishment of the Guideline Development Committee (GDC), we identified the population, intervention, comparator, outcomes and time of interest (PICOT) questions, undertook a systematic literature search and graded the evidence and recommendations using the NHMRC and GRADE processes. Using Nominal Group Techniques (NGT), consensus was sought in formulating the clinical practice recommendations and practice points. Key health professional bodies were consulted to ensure relevance in the Australasian emergency and ward settings. **RESULTS** From 33 PICOT questions, clinical recommendations for practice that were deemed relevant to the Australasian population were identified. Specific considerations for the management of Australian and New Zealand indigenous infants in relation to the use of azithromycin and risk factors for more serious illness are included. Using NGT, consensus demonstrated by a median Likert score > 8 for all recommendations was achieved. The guideline presents clinical guidance, followed by the key recommendations and evidence review behind each recommendation. **CONCLUSION** Developing evidence-based clinical guidelines is a complex process with considerable challenges. Challenges included having committee members located over two countries and five time zones, large volume of literature and variation of member's knowledge of grading of evidence and recommendations. The GRADE and NHMRC processes provided a systematic and transparent approach ensuring a final structure including bedside interface, and a descriptive summary of the evidence base and tables for each key statement. Involvement of stakeholders who will ultimately be end-users as members of the GDC provided valuable knowledge. Lessons learnt during this guideline development process provide valuable insight for those planning development of evidence-based guidelines.

**Database:** Medline

## **8. Systematic review of instruments aimed at evaluating the severity of bronchiolitis**

**Author(s):** Rodriguez-Martinez C.E.; Sossa-Briceno M.P.; Nino G.

**Source:** Paediatric Respiratory Reviews; Jan 2018; vol. 25 ; p. 85-87

**Publication Date:** Jan 2018

**Publication Type(s):** Review

**Abstract:** Objective: No recent studies have performed a systematic review of all available instruments aimed at evaluating the severity of bronchiolitis. The objective of the present study was to perform a systematic review of instruments aimed at evaluating the severity of bronchiolitis and to evaluate their measurement properties. Methods: A systematic search of the literature was performed in order to identify studies in which an instrument for evaluating the severity of bronchiolitis was described. Instruments were evaluated based on their reliability, validity, utility, endorsement frequency, restrictions in range, comprehension, and lack of ambiguity. Results: A total of 77 articles, describing a total of 32 different instruments were included in the review. The number of items included in the instruments ranged from 2 to 26. Upon analyzing their content, respiratory rate turned out to be the most frequently used item (in 26/32, 81.3% of the instruments), followed by wheezing (in 25/32, 78.1% of the instruments). In 18 (56.3%) instruments, there was a report of at least one of their measurement properties, mainly reliability and utility. Taking into consideration the information contained in the instruments, as well as their measurement properties, one was considered to be the best one available. Conclusions: Among the 32 instruments aimed at evaluating the severity of bronchiolitis that were identified and systematically examined, one was considered to

be the best one available. However, there is an urgent need to develop better instruments and to validate them in a more comprehensive and proper way.

**Database:** EMBASE

### **9. A Randomized Controlled Trial of a Single Dose Furosemide to Improve Respiratory Distress in Moderate to Severe Bronchiolitis**

**Author(s):** Williamson K.; Avarello J.; Bredin G.; Gangadharan S.

**Source:** Journal of Emergency Medicine; Jan 2018; vol. 54 (no. 1); p. 40-46

**Publication Date:** Jan 2018

**Publication Type(s):** Article

**Abstract:**Background Bronchiolitis is one of the most common disorders of the lower respiratory tract in infants. While historically diuretics have been used in severe bronchiolitis, no studies have looked directly at their early use in children in the emergency department. Objective The primary objective of this study was to determine whether a single early dose of a diuretic in infants with moderate to severe bronchiolitis would improve respiratory distress. Secondary objectives examined whether it reduced the use of noninvasive ventilation and hospital length of stay. Methods Patients diagnosed with clinical bronchiolitis were enrolled at a tertiary care, academic children's hospital over a 3-year period. This was a double-blind, randomized controlled trial in which subjects were randomly assigned to either furosemide or placebo. Respiratory rate and oxygen saturation at the time of medication delivery and at 2 and 4 h post-intervention were recorded, as well as other data. Exact logistic regression was used to examine associations. Results There were 46 subjects enrolled and randomized. There was no difference in respiratory rates, measured as a decrease of  $\geq 25\%$ , at both 2 and 4 h after intervention between furosemide and placebo groups (odds ratios 1.13 and 1.13, respectively). There was also no difference in oxygen saturation, intensive care unit admission rate, or hospital length of stay between groups. Conclusions While theoretically a single dose of a diuretic to reduce lung fluid would improve respiratory distress in children with bronchiolitis, our randomized controlled medication trial showed no difference in outcomes. ClinicalTrials.gov ID: NCT02469597.

**Database:** EMBASE

### **10. Clinical definition of respiratory viral infections in young children and potential bronchiolitis misclassification**

**Author(s):** Megalaa R.; Perez G.F.; Kilaikode-Cheruveettara S.; Kotwal N.; Nino G.; Rodriguez-Martinez C.E.

**Source:** Journal of Investigative Medicine; Jan 2018; vol. 66 (no. 1); p. 46-51

**Publication Date:** Jan 2018

**Publication Type(s):** Article

**Abstract:**Viral respiratory infections are often grouped as a single respiratory syndrome named 'viral bronchiolitis', independently of the viral etiology or individual risk factors. Clinical trials and guidelines have used a more stringent definition of viral bronchiolitis, including only the first episode of wheezing in children less than 12 months of age without concomitant respiratory comorbidities. There is increasing evidence suggesting that this definition is not being followed by pediatric care providers, but it is unclear to what extent viral respiratory infections are currently misclassified as viral bronchiolitis using standard definitions. We conducted a retrospective analysis of hospitalized young children ( $\leq 3$  years) due to viral respiratory infections. Bronchiolitis was defined as the first wheezing episode less than 12 months of age. Demographic variables and comorbidities were

obtained by electronic medical record review. The study comprised a total of 513 hospitalizations (n=453). Viral bronchiolitis was diagnosed in 144 admissions (28.1%). Notably, we identified that the majority of children diagnosed with bronchiolitis (63%) were misclassified as they had prior episodes of wheezing. Many children with bronchiolitis misclassification had significant comorbidities, including prematurity (51%), neuromuscular conditions (9.8%), and congenital heart disease (9.8%). Misclassification of bronchiolitis is a common problem that may lead to inappropriate management of viral respiratory infections in young children. A comprehensive approach that takes into consideration viral etiology and individual risk factors may lead to a more accurate clinical assessment of this condition and would potentially prevent bronchiolitis misclassification.

**Database:** EMBASE

### **11. Network Meta-Analysis Comparing the Efficacy of Therapeutic Treatments for Bronchiolitis in Children.**

**Author(s):** Guo, Caili; Sun, Xiaomin; Wang, Xiaowen; Guo, Qing; Chen, Dan

**Source:** JPEN. Journal of parenteral and enteral nutrition; Jan 2018; vol. 42 (no. 1); p. 186-195

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29388676

**Abstract:**BACKGROUND This study aims to compare placebo (PBO) and 7 therapeutic regimens—namely, bronchodilator agents (BAs), hypertonic saline (HS), BA ± HS, corticosteroids (CS), epinephrine (EP), EP ± CS, and EP ± HS—to determine the optimal bronchiolitis treatment. METHODS We plotted networks using the curative outcome of several studies and specified the relations among the experiments by using mean difference, standardized mean difference, and corresponding 95% credible interval. The surface under the cumulative ranking curve (SUCRA) was used to separately rank each therapy on clinical severity score (CSS) and length of hospital stay (LHS). RESULT This network meta-analysis included 40 articles from 1995 to 2016 concerning the treatment of bronchiolitis in children. All 7 therapeutic regimens displayed no significant difference to PBO with regard to CSS in our study. Among the 7 therapies, BA performed better than CS. As for LHS, EP and EP ± HS had an advantage over PBO. Moreover, EP and EP ± HS were also more efficient than BA. The SUCRA results showed that EP ± CS is most effective, and EP ± HS is second most effective with regard to CSS. With regard to LHS, EP ± HS ranked first, EP ± CS ranked second, and EP ranked third. CONCLUSION We recommend EP ± CS and EP ± HS as the first choice for bronchiolitis treatment in children because of their outstanding performance with regard to CSS and LHS.

**Database:** Medline

## **RSV**

### **1. Safety of Palivizumab Stewardship in Conjunction with Infection Prevention and Control Strategies for Healthcare-Associated Respiratory Syncytial Virus Infections**

**Author(s):** Patel R.M.; Kociolek L.K.; Merrick E.; Reuter C.; Kronforst K.; Patel S.J.; Zheng X.

**Source:** Infection Control and Hospital Epidemiology; Apr 2018; vol. 39 (no. 4); p. 485-487

**Publication Date:** Apr 2018

**Publication Type(s):** Article

**Abstract:** Transitioning from administration of monthly palivizumab to a single dose at discharge was associated with substantial pharmacy cost savings. With the concurrent adoption of private hospital rooms and visitor restriction policies, hospital-wide and neonatal intensive care unit healthcare-associated respiratory syncytial virus infections decreased following these changes.

**Database:** EMBASE

## **2. Respiratory syncytial virus prevention and asthma in healthy preterm infants: a randomised controlled trial**

**Author(s):** Scheltema N.M.; Nibbelke E.E.; Blanken M.O.; Mazur N.I.; Wildenbeest J.G.; Bont L.J.; van der Ent C.K.; Pouw J.; Rovers M.M.; Naaktgeboren C.A.

**Source:** The Lancet Respiratory Medicine; Apr 2018; vol. 6 (no. 4); p. 257-264

**Publication Date:** Apr 2018

**Publication Type(s):** Article

**Abstract:** Background: Respiratory syncytial virus (RSV) infection is associated with subsequent wheeze and asthma. We previously reported on the causal relationship between prevention of RSV infection during infancy and reduced frequency of subsequent wheeze using a double-blind, randomised, placebo-controlled trial (MAKI). We continued follow-up and analysed the effect of RSV prevention during infancy on asthma and lung function at age 6 years. Methods: We studied 429 infants born at 32-35 weeks of gestation between 2008-10 who had randomly received either palivizumab for RSV immunoprophylaxis or placebo during the RSV season of their first year of life. After the first year of follow-up, single, assessor-blind follow-up of children continued until they were aged 6 years. Primary outcomes were parent-reported current asthma and forced expiratory volume in 0.5 s (FEV<sub>0.5</sub>). The trial is registered in the ISRCTN registry, number ISRCTN73641710. Findings: 395 (92%) of 429 participants completed this 6-year follow-up study. Parent-reported current asthma was reported in 28 (14.1%) of 199 children in the RSV prevention group and 47 (24.0%) of 196 children in the placebo group (absolute risk reduction [ARR] 9.9%, 95% CI 2.2 to 17.6). The difference in current asthma, which was a composite endpoint, was due to a difference in infrequent wheeze (one to three episodes in the past year; 12 [6.0%] of 199 vs 26 [13.4%] of 194, ARR 7.4%, 95% CI 1.5 to 13.2). FEV<sub>0.5</sub> percentage predicted values were similar between the RSV prevention group (89.1% [SD 10.6]) and placebo group (90.1% [11.1]), with a mean difference of 1.0 (95% CI -1.3 to 3.3). The proportion of children with current physician-diagnosed asthma was similar between the RSV prevention group (19 [10.3%] of 185) and placebo group (18 [9.9%] of 182), with an ARR of -0.4 (95% CI -6.5 to 5.8). Interpretation: In otherwise healthy preterm infants, this single-blind, randomised, placebo-controlled trial showed that RSV prevention did not have a major effect on current asthma or lung function at age 6 years. Future research will inform on the effect of RSV prevention on asthma at school age in the general population. Funding: AbbVie. Copyright

**Database:** EMBASE

## **3. Use of palivizumab in the immunoprophylaxis of respiratory syncytial virus**

**Author(s):** Marin M.; Alzueta N.; Molins E.; Pio M.; Gascon A.

**Source:** European Journal of Hospital Pharmacy; Mar 2018; vol. 25

**Publication Date:** Mar 2018

**Publication Type(s):** Conference Abstract

**Abstract:** Background Palivizumab is a monoclonal antibody that provides passive immunity against respiratory syncytial virus (RSV). Purpose To evaluate the use of palivizumab as immunoprophylaxis against RSV in the 2016 to 2017 campaign in a tertiary hospital. Material and methods Retrospective

observational study (October 2016 to March 2017) that included patients in follow-up by the paediatric service who received palivizumab as immunoprophylaxis against RSV in a tertiary hospital. The variables collected were: sex, gestational age, age at the beginning of the vaccination campaign, number of doses, prescription criteria established by the Spanish Society of Neonatology (SEN) (A: children <2 years of age with bronchopulmonary disease; B: gestational age <28 weeks and age <12 months; C: gestational age between 29 and 32 weeks and age <6 months; and D: gestational age between 32 and 35 weeks, age <10 weeks and brother/sister of school age), number of hospitalisations for bronchiolitis and result of the immunochromatographic test for the qualitative detection of RSV antigens in nasopharyngeal samples. Data were obtained from the clinical history, laboratory data and FarHo (pharmacy software). Results Twenty patients (55% males) were included, with a mean age of 6.8+/-5.12 months at the beginning of the campaign. Its use was justified according to the prescription criteria established by the SEN; A: six patients (30%); B: six patients (30%); C: two patients (10%); and D: six patients (30%). All patients received the recommended dose, with the mean dose administered being 93.1+/-31.1 mg. Patients received an average of 2.1+/-0.75 administrations. The total cost was 42,528.9. Only one patient (0.05%) was hospitalised for acute bronchiolitis, and the RSV test was positive. The patient had received only one dose of palivizumab, which had been given the day before hospital admission. Conclusion Palivizumab has been effective in the prevention of RSV bronchiolitis in high-risk patients. In all cases it has been used under the criteria established by the SEN. More studies are needed to assess the effectiveness with these criteria. According to the results obtained we shall proceed to the establishment of an action protocol for the next vaccination campaign in the hospital.

**Database:** EMBASE

#### **4. Palivizumab prophylaxis for respiratory syncytial virus: Examining the evidence around value**

**Author(s):** Olchanski N.; Pope E.; D'Cruz B.; Neumann P.J.; Hansen R.N.; Sullivan S.D.; Fergie J.; Goldstein M.; Krilov L.R.; McLaurin K.K.; Nabrit-Stephens B.; Oster G.; Schaecher K.; Shaya F.T.

**Source:** Open Forum Infectious Diseases; Mar 2018; vol. 5 (no. 3)

**Publication Date:** Mar 2018

**Publication Type(s):** Article

Available at [Open forum infectious diseases](#) - from Oxford Journals - Open Access

Available at [Open forum infectious diseases](#) - from Europe PubMed Central - Open Access

Available at [Open forum infectious diseases](#) - from PubMed Central

**Abstract:** Respiratory syncytial virus (RSV) infection is the most common cause of lower respiratory tract infection and the leading cause of hospitalization among young children, incurring high annual costs among US children under the age of 5 years. Palivizumab has been found to be effective in reducing hospitalization and preventing serious lower respiratory tract infections in high-risk infants. This paper presents a systematic review of the cost-effectiveness studies of palivizumab and describes the main highlights of a round table discussion with clinical, payer, economic, research method, and other experts. The objectives of the discussion were to (1) review the current state of clinical, epidemiology, and economic data related to severe RSV disease; (2) review new cost-effectiveness estimates of RSV immunoprophylaxis in US preterm infants, including a review of the field's areas of agreement and disagreement; and (3) identify needs for further research.

**Database:** EMBASE

## 5. Induction and subversion of human protective immunity: Contrasting influenza and respiratory syncytial virus

**Author(s):** Ascough S.; Paterson S.; Chiu C.

**Source:** *Frontiers in Immunology*; Mar 2018; vol. 9

**Publication Date:** Mar 2018

**Publication Type(s):** Review

Available at [Frontiers in immunology](#) - from Europe PubMed Central - Open Access

Available at [Frontiers in immunology](#) - from frontiersin.org

**Abstract:** Respiratory syncytial virus (RSV) and influenza are among the most important causes of severe respiratory disease worldwide. Despite the clinical need, barriers to developing reliably effective vaccines against these viruses have remained firmly in place for decades. Overcoming these hurdles requires better understanding of human immunity and the strategies by which these pathogens evade it. Although superficially similar, the virology and host response to RSV and influenza are strikingly distinct. Influenza induces robust strain-specific immunity following natural infection, although protection by current vaccines is short-lived. In contrast, even strain-specific protection is incomplete after RSV and there are currently no licensed RSV vaccines. Although animal models have been critical for developing a fundamental understanding of antiviral immunity, extrapolating to human disease has been problematic. It is only with recent translational advances (such as controlled human infection models and high-dimensional technologies) that the mechanisms responsible for differences in protection against RSV compared to influenza have begun to be elucidated in the human context. Influenza infection elicits high-affinity IgA in the respiratory tract and virus-specific IgG, which correlates with protection. Long-lived influenza-specific T cells have also been shown to ameliorate disease. This robust immunity promotes rapid emergence of antigenic variants leading to immune escape. RSV differs markedly, as reinfection with similar strains occurs despite natural infection inducing high levels of antibody against conserved antigens. The immunomodulatory mechanisms of RSV are thus highly effective in inhibiting long-term protection, with disturbance of type I interferon signaling, antigen presentation and chemokine-induced inflammation possibly all contributing. These lead to widespread effects on adaptive immunity with impaired B cell memory and reduced T cell generation and functionality. Here, we discuss the differences in clinical outcome and immune response following influenza and RSV. Specifically, we focus on differences in their recognition by innate immunity; the strategies used by each virus to evade these early immune responses; and effects across the innate-adaptive interface that may prevent long-lived memory generation. Thus, by comparing these globally important pathogens, we highlight mechanisms by which optimal antiviral immunity may be better induced and discuss the potential for these insights to inform novel vaccines.

**Database:** EMBASE

## 6. Past, Present and Future Approaches to the Prevention and Treatment of Respiratory Syncytial Virus Infection in Children

**Author(s):** Simoes E.A.F.; Bont L.; Manzoni P.; Fauroux B.; Paes B.; Figueras-Aloy J.; Checchia P.A.; Carbonell-Estrany X.

**Source:** *Infectious Diseases and Therapy*; Mar 2018; vol. 7 (no. 1); p. 87-120

**Publication Date:** Mar 2018

**Publication Type(s):** Review

Available at [Infectious diseases and therapy](#) - from Europe PubMed Central - Open Access

Available at [Infectious diseases and therapy](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Available at [Infectious diseases and therapy](#) - from International DOI Foundation

**Abstract:** Introduction: The REGAL (RSV Evidence - A Geographical Archive of the Literature) series has provided a comprehensive review of the published evidence in the field of respiratory syncytial virus (RSV) in Western countries over the last 20 years. This seventh and final publication covers the past, present and future approaches to the prevention and treatment of RSV infection among infants and children. Methods: A systematic review was undertaken of publications between January 1, 1995 and December 31, 2017 across PubMed, Embase and The Cochrane Library. Studies reporting data on the effectiveness and tolerability of prophylactic and therapeutic agents for RSV infection were included. Study quality and strength of evidence (SOE) were graded using recognized criteria. A further nonsystematic search of the published literature and Clinicaltrials.gov on antiviral therapies and RSV vaccines currently in development was also undertaken. Results: The systematic review identified 1441 studies of which 161 were included. Management of RSV remains centered around prophylaxis with the monoclonal antibody palivizumab, which has proven effective in reducing RSV hospitalization (RSVH) in preterm infants OpenSPiltSPi 36 weeks' gestational age (72% reduction), children with bronchopulmonary dysplasia (65% reduction), and infants with hemodynamically significant congenital heart disease (53% reduction) (high SOE). Palivizumab has also shown to be effective in reducing recurrent wheezing following RSVH (high SOE). Treatment of RSV with ribavirin has conflicting success (moderate SOE). Antibodies with increased potency and extended half-life are currently entering phase 3 trials. There are approximately 15 RSV vaccines in clinical development targeting the infant directly or indirectly via the mother. Conclusion: Palivizumab remains the only product licensed for RSV prophylaxis, and only available for high-risk infants. For the general population, there are several promising vaccines and monoclonal antibodies in various stages of clinical development, with the aim to significantly reduce the global healthcare impact of this common viral infection. Funding: AbbVie.

**Database:** EMBASE

## 7. Multicenter clinical evaluation of the Alere i respiratory syncytial virus isothermal nucleic acid amplification assay

**Author(s):** Hassan F.; Hays L.M.; Moffatt M.E.; Selvarangan R.; Bonner A.; Bradford B.J.; Franklin R.; Hendry P.; Kaminetsky J.; Vaughn M.; Cieslak K.

**Source:** Journal of Clinical Microbiology; Mar 2018; vol. 56 (no. 3)

**Publication Date:** Mar 2018

**Publication Type(s):** Article

**Abstract:** The Alere i respiratory syncytial virus (RSV) assay is an isothermal nucleic acid amplification test capable of detecting RSV directly from respiratory specimens, with results being available in 13 min after test initiation. The objective of this study was to evaluate the performance characteristics of the Alere i RSV assay in a point-of-care setting by using direct nasopharyngeal (NP) swab specimens (direct NP) and nasopharyngeal swab specimens eluted and transported in viral transport medium (VTM NP). The study was a prospective, multicenter, clinical trial conducted at 9 sites across the United States to evaluate the clinical performance of the Alere i RSV assay with respiratory specimens obtained from both children (age, 18 years) and older adults (age, 60 years). The performance of the Alere i RSV assay was compared with that of the reference method, the Prodesse ProFlu real-time reverse transcriptase PCR (RT-PCR) assay. All specimens with discrepant test results were tested further by a second FDA-cleared PCR assay (the Verigene respiratory virus plus nucleic acid test; Luminex Inc., TX). A total of 554 subjects with signs and symptoms of respiratory infections were enrolled, and respiratory samples were collected in this study. In

comparison with the ProFlu real-time RT-PCR, the overall sensitivity and specificity of Alere i RSV assay for the detection of RSV were 98.6% (95% confidence interval [CI], 94.4 to 99.7%) and 98.0% (95% CI, 95.8 to 99.1%), respectively, for direct NP and 98.6% (95% CI, 94.4 to 99.7%) and 97.8% (95% CI, 95.5 to 98.9%), respectively, for VTM NP. The Alere i RSV is a highly sensitive and specific molecular assay ideal for rapid RSV detection in patients in the point-of-care setting due to its minimal hands-on time and rapid result availability.

**Database:** EMBASE

## **8. Respiratory syncytial virus infection in elderly adults.**

**Author(s):** Haber, N

**Source:** Medecine et maladies infectieuses; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 29548714

**Abstract:**Respiratory syncytial virus (RSV) is a major cause of severe lower respiratory tract infections in infants and young children. Reinfections are common throughout adult life with more severe presentations occurring in immunocompromised individuals, subjects with underlying high-risk cardiopulmonary diseases, and in the elderly. There is now a significant body of literature indicating that the impact of RSV in elderly adults is similar to that of non-pandemic influenza, both in the community and in nursing homes. Clinical manifestations of RSV infections are similar to those caused by other viral respiratory pathogens, including influenza viruses. Molecular tests (reverse transcription-PCR) now provide a rapid diagnosis. The sputum sample combined with nasopharyngeal swab increases the diagnostic yield. At the present time, treatment is mainly symptomatic. The prevention of RSV consists in various infection control strategies, such as standard precautions, especially hand washing and droplet precautions to limit the nosocomial spread. Vaccines and antiviral agents for the prevention and treatment of RSV infections in elderly adults are currently not available, but they are being developed.

**Database:** Medline

## **9. Implementation of a rapid influenza A/B and RSV direct molecular assay improves emergency department oseltamivir use in paediatric patients.**

**Author(s):** Mitchell, Stephanie L; Chang, Yeh-Chung; Feemster, Kristen; Cárdenas, Ana María

**Source:** Journal of medical microbiology; Mar 2018; vol. 67 (no. 3); p. 358-363

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29458688

**Abstract:**PURPOSEInfluenza A virus (FluA), influenza B virus (FluB) and respiratory syncytial virus (RSV) illnesses increase hospitalizations during seasonal epidemics.METHODLOGYTo determine the utility of the Simplexa FluA/B & RSV Direct Assay (Direct Flu/RSV) and its impact on oseltamivir use, we offered this assay to emergency department (ED) patients with influenza-like illness.RESULTSUtilization of the Direct Flu/RSV provided a turnaround time (TAT) of 2 hours. Compared to the flu season prior to implementation of the Direct Flu/RSV, clinicians were more likely to prescribe 5 days of oseltamivir therapy for Direct Flu/RSV-positive patients in comparison to those with a negative test.CONCLUSIONSUse of Direct Flu/RSV provides results rapidly, which leads to more appropriate use of oseltamivir. The ease of use of this assay and quick TAT allows for

prompt decision-making, which is essential for patient care and effective disease control during the influenza season.

**Database:** Medline

#### **10. Risk scoring tool to predict respiratory syncytial virus hospitalisation in premature infants.**

**Author(s):** Blanken, Maarten O; Paes, Bosco; Anderson, Evan J; Lanari, Marcello; Sheridan-Pereira, Margaret; Buchan, Scot; Fullarton, John R; Grubb, ElizaBeth; Notario, Gerard; Rodgers-Gray, Barry S; Carbonell-Estrany, Xavier

**Source:** Pediatric pulmonology; Feb 2018

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29405612

**Abstract:**BACKGROUNDThe objective was to develop a risk scoring tool which predicts respiratory syncytial virus hospitalisation (RSVH) in moderate-late preterm infants (32-35 weeks' gestational age) in the Northern Hemisphere.METHODSRisk factors for RSVH were pooled from six observational studies of infants born 32 weeks and 0 days to 35 weeks and 6 days without comorbidity from 2000 to 2014. Of 13 475 infants, 484 had RSVH in the first year of life. Logistic regression was used to identify the most predictive risk factors, based on area under the receiver operating characteristic curve (AUROC). The model was validated internally by 100-fold bootstrapping and externally with data from a seventh observational study. The model coefficients were converted into rounded multipliers, stratified into risk groups, and number needed to treat (NNT) calculated.RESULTSThe risk factors identified in the model included (i) proximity of birth to the RSV season; (ii) second-hand smoke exposure; and (iii) siblings and/or daycare. The AUROC was 0.773 (sensitivity: 68.9%; specificity: 73.0%). The mean AUROC from internal bootstrapping was 0.773. For external validation with data from Ireland, the AUROC was 0.707 using Irish coefficients and 0.681 using source model coefficients. Cut-off scores for RSVH were  $\leq 19$  for low- (1.0%), 20-45 for moderate- (3.3%), and 50-56 (9.5%) for high-risk infants. The high-risk group captured 62.0% of RSVHs within 23.6% of the total population (NNT 15.3).CONCLUSIONSThis risk scoring tool has good predictive accuracy and can improve targeting for RSVH prevention in moderate-late preterm infants.

**Database:** Medline

#### **11. Safety and immunogenicity of 3 formulations of an investigational respiratory syncytial virus vaccine in non-pregnant women: results from two phase II trials.**

**Author(s):** Beran, Jiri; Lickliter, Jason D; Schwarz, Tino F; Johnson, Casey; Chu, Laurence; Domachowske, Joseph B; Van Damme, Pierre; Withanage, Kanchanamala; Fissette, Laurence A; David, Marie-Pierre; Maleux, Koen; Schmidt, Alexander C; Picciolato, Marta; Dieussaert, Ilse

**Source:** The Journal of infectious diseases; Feb 2018

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29401325

**Abstract:**BackgroundRespiratory syncytial virus (RSV) causes bronchiolitis and pneumonia in neonates and infants. RSV vaccination during pregnancy could boost pre-existing neutralizing antibody titers, providing passive protection to newborns.MethodsTwo observer-blind, controlled studies (RSV F-020 [NCT02360475], RSV F-024 [NCT02753413]) evaluated immunogenicity and safety of an investigational RSV vaccine in healthy, non-pregnant 18-45-year-old women. Both studies used

licensed Tdap vaccine as control. RSV F-020 evaluated immunogenicity and safety: participants were randomized (1:1:1:1) to receive one dose of RSV-PreF vaccine containing 30µg or 60µg non-adjuvanted RSV-PreF, or 60µg aluminum-adjuvanted RSV-PreF, or Tdap. RSV F-024 evaluated safety: participants were randomized 1:1 to receive one dose of 60µg non-adjuvanted RSV-PreF or Tdap. Results Both studies showed similar reactogenicity profiles for RSV-PreF and Tdap. No serious adverse events were considered vaccine-related. In RSV F-020, geometric means of the ratios of RSV-A neutralizing antibody at Day 30 compared to pre-vaccination were 3.1-3.9 in RSV-PreF-vaccinees and 0.9 in controls. Palivizumab-competing antibody concentrations increased >14-fold in RSV-PreF-vaccinees at Day 30. RSV antibody titers waned after Day 30 but remained well-above baseline through Day 90. Conclusions All formulations of RSV-PreF boosted pre-existing immune responses in 18-45-year old women with comparable immunogenicity. The RSV-PreF safety profile was similar to Tdap.

**Database:** Medline

## 12. Respiratory syncytial virus seasonality and its implications on prevention strategies

**Author(s):** Janet S.; Broad J.; Snape M.D.

**Source:** Human Vaccines and Immunotherapeutics; Jan 2018; vol. 14 (no. 1); p. 234-244

**Publication Date:** Jan 2018

**Publication Type(s):** Review

**Abstract:** With maternal and infant vaccines against respiratory syncytial virus (RSV) in development, it is timely to consider how the deployment of these vaccines might vary according to local RSV disease seasonality. In temperate regions RSV infection is predictably limited to a period of 3 to 5 months, while in tropical regions disease seasonality is often both more variable and more prolonged. Accordingly, in tropical regions a year-round immunisation schedule for both maternal and infant immunisation might be appropriate. In contrast, in temperate regions the benefit of year-round maternal immunisation would be heavily dependent on the duration of protection this provided, potentially necessitating a strategy directed at children due to be born in the months immediately prior to the RSV season. This review will consider the impact of seasonality on maternal and infant immunisation strategies against RSV, and the potential of an alternative approach of passive immunisation for all infants immediately prior to the RSV season.

**Database:** EMBASE

## 13. Cost-effectiveness of rule-based immunoprophylaxis against respiratory syncytial virus infections in preterm infants

**Author(s):** Blanken M.O.; Nibbelke E.E.; Sanders E.A.M.; Bont L.; Frederix G.W.; Koffijberg H.; Rovers M.M.

**Source:** European Journal of Pediatrics; Jan 2018; vol. 177 (no. 1); p. 133-144

**Publication Date:** Jan 2018

**Publication Type(s):** Article

Available at [European journal of pediatrics](#) - from International DOI Foundation

**Abstract:** The objective of the paper is to assess the cost-effectiveness of targeted respiratory syncytial virus (RSV) prophylaxis based on a validated prediction rule with 1-year time horizon in moderately preterm infants compared to no prophylaxis. Data on health care consumption were derived from a randomised clinical trial on wheeze reduction following RSV prophylaxis and a large birth cohort study on risk prediction of RSV hospitalisation. We calculated the incremental cost-

effectiveness ratio (ICER) of targeted RSV prophylaxis vs. no prophylaxis per quality-adjusted life year (QALYs) using a societal perspective, including medical and parental costs and effects. Costs and health outcomes were modelled in a decision tree analysis with sensitivity analyses. Targeted RSV prophylaxis in infants with a first-year RSV hospitalisation risk of > 10% resulted in a QALY gain of 0.02 (0.931 vs. 0.929) per patient against additional cost of 472 compared to no prophylaxis (ICER 214,748/QALY). The ICER falls below a threshold of 80,000 per QALY when RSV prophylaxis cost would be lowered from 928 (baseline) to 406 per unit. At a unit cost of 97, RSV prophylaxis would be cost saving. Conclusions: Targeted RSV prophylaxis is not cost-effective in reducing RSV burden of disease in moderately preterm infants, but it can become cost-effective if lower priced biosimilar palivizumab or a vaccine would be available.

**Database:** EMBASE

#### **14. Establishing Correlates of Protection for Vaccine Development: Considerations for the Respiratory Syncytial Virus Vaccine Field.**

**Author(s):** Kulkarni, Prasad S; Hurwitz, Julia L; Simões, Eric A F; Piedra, Pedro A

**Source:** Viral immunology; Jan 2018

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29336703

**Abstract:**Correlates of protection (CoPs) can play a significant role in vaccine development by assisting the selection of vaccine candidates for clinical trials, supporting clinical trial design and implementation, and simplifying tests of vaccine modifications. Because of this important role in vaccine development, it is essential that CoPs be defined by well-designed immunogenicity and efficacy studies, with attention paid to benefits and limitations. The respiratory syncytial virus (RSV) field is unique in that a great deal of information about the humoral response is available from basic research and clinical studies. Polyclonal and monoclonal antibodies have been used routinely in the clinic to protect vulnerable infants from infection, providing a wealth of information about correlations between neutralizing antibodies and disease prevention. Considerations for the establishment of future CoPs to support RSV vaccine development in different populations are therefore discussed.

**Database:** Medline

#### **15. Respiratory Syncytial Virus Seasonality: A Global Overview.**

**Author(s):** Obando-Pacheco, Pablo; Justicia-Grande, Antonio José; Rivero-Calle, Irene; Rodríguez-Tenreiro, Carmen; Sly, Peter; Ramilo, Octavio; Mejías, Asunción; Baraldi, Eugenio; Papadopoulos, Nikolaos G; Nair, Harish; Nunes, Marta C; Kragten-Tabatabaie, Leyla; Heikkinen, Terho; Greenough, Anne; Stein, Renato T; Manzoni, Paolo; Bont, Louis; Martín-Torres, Federico

**Source:** The Journal of infectious diseases; Jan 2018

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29390105

**Abstract:**Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory infections (ALRI) in children. By the age of 1 year, 60-70% of children have been infected by RSV. In addition, early-life RSV infection is associated with the development of recurrent wheezing and asthma in infancy and childhood. The need for precise epidemiologic data regarding RSV as a worldwide

pathogen has been growing steadily as novel RSV therapeutics are reaching the final stages of development. To optimize the prevention, diagnosis and treatment of RSV infection in a timely manner, knowledge about the differences in the timing of the RSV epidemics worldwide is needed. Previous analyses, based on literature reviews of individual reports obtained from medical databases, have fail to provide global country seasonality patterns. Until recently, only certain countries have been recording RSV incidence through their own surveillance systems. This analysis was based on national RSV surveillance reports and medical databases from 27 countries worldwide. This is the first study using original source high-quality surveillance data to establish a global, robust and homogeneous report on global country-specific RSV seasonality.

**Database:** Medline

### **16. Determining the outcomes of interventions to prevent respiratory syncytial virus disease in children: what to measure?**

**Author(s):** Karron, Ruth A; Zar, Heather J

**Source:** The Lancet. Respiratory medicine; Jan 2018; vol. 6 (no. 1); p. 65-74

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 28865676

**Abstract:**Respiratory syncytial virus (RSV) is the most common cause of viral acute lower respiratory tract illness (LRTI) in young children, and a major cause of hospital admissions and health-care utilisation globally. Substantial efforts have been made to develop RSV vaccines and vaccine-like monoclonal antibodies to prevent acute RSV LRTI. Prevention of acute disease could improve long-term lung health, with potential effects on wheezing, asthma, and chronic lung disease. This Personal View describes assessments that should be initiated during clinical trials and continued after licensure to fully evaluate the effect of RSV preventive interventions. These assessments include recording the incidence of RSV-specific LRTI and all-cause LRTI through two RSV seasons, and assessment of the prevalence and severity of recurrent wheezing or asthma in children aged up to 6 years. Standardised assessments in diverse settings are needed to fully determine the effect of interventions for the prevention of RSV disease.

**Database:** Medline

## **Surgical Site Infection**

### **1. Viable adhered Staphylococcus aureus highly reduced on novel antimicrobial sutures using chlorhexidine and octenidine to avoid surgical site infection (SSI).**

**Author(s):** Obermeier, Andreas; Schneider, Jochen; Harrasser, Norbert; Tübel, Jutta; Mühlhofer, Heinrich; Pförringer, Dominik; Deimling, Constantin von; Foehr, Peter; Kiefel, Barbara; Krämer, Christina; Stemberger, Axel; Schieker, Matthias; Burgkart, Rainer; von Eisenhart-Rothe, Rüdiger

**Source:** PloS one; 2018; vol. 13 (no. 1); p. e0190912

**Publication Date:** 2018

**Publication Type(s):** Research Support, Non-u.s. Gov't Journal Article

**PubMedID:** 29315313

Available at [PLOS ONE](#) - from Public Library of Science (PLoS)

Available at [PLOS ONE](#) - from Europe PubMed Central - Open Access

Available at [PLOS ONE](#) - from EBSCO (MEDLINE Complete)

Available at [PLOS ONE](#) - from PubMed Central

**Abstract:**BACKGROUND Surgical sutures can promote migration of bacteria and thus start infections. Antiseptic coating of sutures may inhibit proliferation of adhered bacteria and avoid such complications. OBJECTIVE This study investigated the inhibition of viable adhering bacteria on novel antimicrobially coated surgical sutures using chlorhexidine or octenidine, a critical factor for proliferation at the onset of local infections. The medical need, a rapid eradication of bacteria in wounds, can be fulfilled by a high antimicrobial efficacy during the first days after wound closure. METHODS As a pretesting on antibacterial efficacy against relevant bacterial pathogens a zone of inhibition assay was conducted with middle ranged concentrated suture coatings (22 µg/cm). For further investigation of adhering bacteria in detail the most clinically relevant *Staphylococcus aureus* (ATCC®49230™) was used. Absorbable braided sutures were coated with chlorhexidine-laurate, chlorhexidine-palmitate, octenidine-laurate, and octenidine-palmitate. Each coating type resulted in 11, 22, or 33 µg/cm drug content on sutures. Scanning electron microscopy (SEM) was performed once to inspect the coating quality and twice to investigate if bacteria have colonized on sutures. Adhesion experiments were assessed by exposing coated sutures to *S. aureus* suspensions for 3 h at 37°C. Subsequently, sutures were sonicated and the number of viable bacteria released from the suture surface was determined. Furthermore, the number of viable planktonic bacteria was measured in suspensions containing antimicrobial sutures. Commercially available sutures without drugs (Vicryl®, PGA Resorba®, and Gunze PGA), as well as triclosan-containing Vicryl® Plus were used as control groups. RESULTS Zone of inhibition assay documented a multispecies efficacy of novel coated sutures against tested bacterial strains, comparable to most relevant *S. aureus* over 48 hours. SEM pictures demonstrated uniform layers on coated sutures with higher roughness for palmitate coatings and sustaining integrity of coated sutures. Adherent *S. aureus* were found via SEM on all types of investigated sutures. The novel antimicrobial sutures showed significantly less viable adhered *S. aureus* bacteria (up to 6.1 log) compared to Vicryl® Plus (0.5 log). Within 11 µg/cm drug-containing sutures, octenidine-palmitate (OL11) showed the highest number of viable adhered *S. aureus* (0.5 log), similar to Vicryl® Plus. Chlorhexidine-laurate (CL11) showed the lowest number of *S. aureus* on sutures (1.7 log), a 1.2 log greater reduction. In addition, planktonic *S. aureus* in suspensions were highly inhibited by CL11 (0.9 log) represents a 0.6 log greater reduction compared to Vicryl® Plus (0.3 log). CONCLUSIONS Novel antimicrobial sutures can potentially limit surgical site infections caused by multiple pathogenic bacterial species. Therefore, a potential inhibition of multispecies biofilm formation is assumed. In detail tested with *S. aureus*, the chlorhexidine-laurate coating (CL11) best meets the medical requirements for a fast bacterial eradication. This suture coating shows the lowest survival rate of adhering as well as planktonic bacteria, a high drug release during the first-clinically most relevant- 48 hours, as well as biocompatibility. Thus, CL11 coatings should be recommended for prophylactic antimicrobial sutures as an optimal surgical supplement to reduce wound infections. However, animal and clinical investigations are important to prove safety and efficacy for future applications.

**Database:** Medline

## 2. Impact of the Antibiotic Stewardship Program on Prevention and Control of Surgical Site Infection during Peri-Operative Clean Surgery.

**Author(s):** Liu, Juyuan; Li, Na; Hao, Jinjuan; Li, Yanming; Liu, Anlei; Wu, Yinghong; Cai, Meng

**Source:** Surgical infections; Apr 2018; vol. 19 (no. 3); p. 326-333

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29461929

**Abstract:**BACKGROUND Surgical site infections (SSIs) are the leading cause of hospital-acquired infections and are associated with substantial healthcare costs, with increased morbidity and mortality. To investigate the effects of the antibiotic stewardship program on prevention and control of SSI during clean surgery, we investigated this situation in our institution. PATIENTS AND METHODS We performed a quasi-experimental study to compare the effect before and after the antibiotic stewardship program intervention. During the pre-intervention stage (January 1, 2010 through December 31, 2011), comprehensive surveillance was performed to determine the SSI baseline data. In the second stage (January 1, 2012 through December 31, 2016), an infectious diseases physician and an infection control practitioner identified the surgical patients daily and followed up on the duration of antimicrobial prophylaxis. RESULTS From January 1, 2010 to December 31, 2016, 41,426 patients underwent clean surgeries in a grade III, class A hospital. The rate of prophylactic antibiotic use in the 41,426 clean surgeries was reduced from 82.9% to 28.0% after the interventions. The rate of antibiotic agents administered within 120 minutes of the first incision increased from 20.8% to 85.1%. The rate at which prophylactic antimicrobial agents were discontinued in the first 24 hours after surgery increased from 22.1% to 60.4%. Appropriate antibiotic selection increased from 37.0% to 93.6%. Prophylactic antibiotic re-dosing increased from 3.8% to 64.8%. The SSI rate decreased from 0.7% to 0.5% ( $p < 0.05$ ). The pathogen detection rate increased from 16.7% up to 41.8% after intervention. The intensity of antibiotic consumption reduced from 74.9 defined daily doses (DDDs) per 100 bed-days to 34.2 DDDs per 100 bed-days after the interventions. CONCLUSION Long-term and continuous antibiotic stewardship programs have important effects on the prevention and control of SSI during clean surgery.

**Database:** Medline

### 3. Effectiveness of Preoperative Antibiotics in Preventing Surgical Site Infection After Common Soft Tissue Procedures of the Hand.

**Author(s):** Li, Kevin; Sambare, Tanmaya D; Jiang, Sam Y; Shearer, Emily J; Douglass, Nathan P; Kamal, Robin N

**Source:** Clinical orthopaedics and related research; Apr 2018; vol. 476 (no. 4); p. 664-673

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29432267

**Abstract:**BACKGROUND Antibiotic prophylaxis is a common but controversial practice for clean soft tissue procedures of the hand, such as carpal tunnel release or trigger finger release. Previous studies report no substantial reduction in the risk of surgical site infection (SSI) after antibiotic prophylaxis, yet are limited in power by low sample sizes and low overall rates of postoperative infection. QUESTIONS/PURPOSES Is there evidence that antibiotic prophylaxis decreases the risk of SSI after soft tissue hand surgery when using propensity score matching to control for potential confounding variables such as demographics, procedure type, medication use, existing comorbidities, and postoperative events? METHODS This retrospective analysis used the Truven Health MarketScan databases, large, multistate commercial insurance claims databases corresponding to inpatient and outpatient services and outpatient drug claims made between January 2007 and December 2014. The database includes records for patients enrolled in health insurance plans from self-insured employers and other private payers. Current Procedural Terminology codes were used to identify patients who underwent carpal tunnel release, trigger finger release, ganglion and retinacular cyst excision, de Quervain's release, or soft tissue mass excision, and to assign patients to one of two cohorts based on whether they had received preoperative antibiotic prophylaxis. We identified 943,741 patients, of whom 426,755 (45%) were excluded after meeting one or more exclusion criteria: 357,500 (38%) did not have 12 months of

consecutive insurance enrollment before surgery or 1 month of enrollment after surgery; 60,693 (6%) had concomitant bony, implant, or incision and drainage or débridement procedures; and 94,141 (10%) did not have complete data. In all, our initial cohort consisted of 516,986 patients, among whom 58,201 (11%) received antibiotic prophylaxis. Propensity scores were calculated and used to create cohorts matched on potential risk factors for SSI, including age, procedure type, recent use of steroids and immunosuppressive agents, diabetes, HIV/AIDs, tobacco use, obesity, rheumatoid arthritis, alcohol abuse, malnutrition, history of prior SSI, and local procedure volume. Multivariable logistic regression before and after propensity score matching was used to test whether antibiotic prophylaxis was associated with a decrease in the risk of SSI within 30 days after surgery. **RESULTS** After controlling for patient demographics, hand procedure type, medication use, existing comorbidities (eg, diabetes, HIV/AIDs, tobacco use, obesity), and postoperative events through propensity score matching, we found that the risk of postoperative SSI was no different between patients who had received antibiotic prophylaxis and those who had not (odds ratio, 1.03; 95% CI, 0.93-1.13;  $p = 0.585$ ). **CONCLUSIONS** Antibiotic prophylaxis for common soft tissue procedures of the hand is not associated with reduction in postoperative infection risk. While our analysis cannot account for factors that are not captured in the billing process, this study nevertheless provides strong evidence against unnecessary use of antibiotics before these procedures, especially given the difficulty of conducting a randomized prospective study with a sample size large enough to detect the effect of prophylaxis on the low baseline risk of infection. **LEVEL OF EVIDENCE** Level III, therapeutic study.

**Database:** Medline

#### **4. Comparison of chlorhexidine-isopropanol with isopropanol skin antisepsis for prevention of surgical-site infection after abdominal surgery.**

**Author(s):** Harnoss, J C; Assadian, O; Kramer, A; Probst, P; Müller-Lantzsch, C; Scheerer, L; Bruckner, T; Diener, M K; Büchler, M W; Ulrich, A B

**Source:** The British journal of surgery; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29600816

**Abstract:** **BACKGROUND** Prevention of surgical-site infection (SSI) has received increasing attention. Clinical trials have focused on the role of skin antisepsis in preventing SSI. The benefit of combining antiseptic chlorhexidine with alcohol has not been compared with alcohol-based skin preparation alone in a prospective controlled clinical trial. **METHODS** Between August and October 2014, patients undergoing abdominal surgery received preoperative skin antisepsis with 70 per cent isopropanol (PA). Those treated between November 2014 and January 2015 received 2 per cent chlorhexidine with 70 per cent isopropanol (CA). The primary endpoint was SSI on postoperative day (POD) 10, which was evaluated using univariable analysis, and a multivariable logistic regression model correcting for known independent risk factors for SSI. The study protocol was published in the German Registry of Clinical Studies (DRKS00011174). **RESULTS** In total, 500 patients undergoing elective midline laparotomy were included (CA 221, PA 279). The incidence of superficial and deep SSIs was significantly different on POD 10: 14 of 212 (6.6 per cent) among those treated with CA and 32 of 260 (12.3 per cent) in those who received PA ( $P = 0.038$ ). In the multivariable analysis, skin antisepsis with CA was an independent factor for reduced incidence of SSI on POD 10 ( $P = 0.034$ ). **CONCLUSION** This study showed a benefit of adding chlorhexidine to alcohol for skin antisepsis in reducing early SSI compared with alcohol alone.

**Database:** Medline

**5. A survey of practice and opinions on the use of topical antibiotics to prevent surgical site infection: more confusion than consensus.**

**Author(s):** Cooper, Charlotte; Horner, Carlyne; Barlow, Gavin; Stryja, Jan; Sandy-Hodgetts, Kylie; Guise, Tracey; Humphreys, Hilary

**Source:** The Journal of antimicrobial chemotherapy; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29596598

**Abstract:**BackgroundSurgical site infection (SSI) is one of the most common causes of healthcare-associated infection. Although the use of topical antibiotics to prevent SSI is not recommended by current guidelines, published studies document conflicting results and conclusions.ObjectivesThe objectives of this survey were to: (i) determine the extent of the use of topical antibiotics to prevent SSI in clinical practice; and (ii) gather the opinions of healthcare professionals most likely to be involved in their use.MethodsA questionnaire was circulated to members of BSAC and the European Wound Management Association (EWMA).ResultsThe questionnaire received 160 responses from a variety of healthcare professionals around the world. Most respondents (70%) did not have guidelines for the use of topical antibiotics for the prevention of SSI in their institution; if present, local guidance was based on national guidelines (20/31, 65%). Most respondents did not use or recommend topical antibiotics to prevent SSI; of those that did, gentamicin collagen sponges were most commonly used (24/96 responses, 25%). Over half of the surgeons (18/33, 55%) who responded to the survey did not use topical antibiotics for the prevention of SSI but, when used, contaminated surgery (8/33, 24%) was the most commonly stated indication.ConclusionsThere are diverse opinions and practices among healthcare professionals about the use of topical antibiotics for the prevention of SSI. This considerable, and possibly inappropriate, variation in clinical practice needs to be addressed as part of antibiotic stewardship.

**Database:** Medline

**6. Update to the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Guideline for the Prevention of Surgical Site Infection (2017): A summary, review, and strategies for implementation.**

**Author(s):** O'Hara, Lyndsay M; Thom, Kerri A; Preas, Michael Anne

**Source:** American journal of infection control; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29525367

**Abstract:**Surgical site infections remain a common cause of morbidity, mortality, and increased length of stay and cost amongst hospitalized patients in the United States. This article summarizes the evidence used to inform the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Guideline for the Prevention of Surgical Site Infection (2017), and highlights key updates and new recommendations. We also present specific suggestions for how infection preventionists can play a central role in guideline implementation by translating these recommendations into evidence-based policies and practices in their facility.

**Database:** Medline

### **7. The effect of triclosan-coated sutures on the rate of surgical site infection after hip and knee arthroplasty: a double-blind randomized controlled trial of 2546 patients.**

**Author(s):** Sprowson, A P; Jensen, C; Parsons, N; Partington, P; Emmerson, K; Carluke, I; Asaad, S; Pratt, R; Muller, S; Ahmed, I; Reed, M R

**Source:** The bone & joint journal; Mar 2018; vol. 100

**Publication Date:** Mar 2018

**Publication Type(s):** Randomized Controlled Trial Multicenter Study Journal Article

**PubMedID:** 29589500

**Abstract:**Aims Surgical site infection (SSI) is a common complication of surgery with an incidence of about 1% in the United Kingdom. Sutures can lead to the development of a SSI, as micro-organisms can colonize the suture as it is implanted. Triclosan-coated sutures, being antimicrobial, were developed to reduce the rate of SSI. Our aim was to assess whether triclosan-coated sutures cause a reduction in SSIs following arthroplasty of the hip and knee. Patients and Methods This two-arm, parallel, double-blinded study involved 2546 patients undergoing elective total hip (THA) and total knee arthroplasty (TKA) at three hospitals. A total of 1323 were quasi-randomized to a standard suture group, and 1223 being quasi-randomized to the triclosan-coated suture group. The primary endpoint was the rate of SSI at 30 days postoperatively. Results The baseline characteristics of age, gender and comorbidities were well matched in the two groups. The rates of superficial SSI were 0.8% in the control group and 0.7% in the intervention group ( $p = 0.651$ ), and when deep and superficial SSIs were combined the rates were 2.5% and 1.8 ( $p = 0.266$ ). The length of stay in hospital and the rates of medical complications did not differ significantly between the groups ( $p = 1.000$ ). Conclusion This trial provided no evidence that the use of triclosan-coated sutures at THA and TKA leads to a reduction in the rate of SSI.

**Database:** Medline

### **8. Timing of surgical site infection and pulmonary complications after laparotomy.**

**Author(s):** Gundel, Ossian; Gundersen, Sofie Kirchhoff; Dahl, Rikke Maria; Jørgensen, Lars Nannestad; Rasmussen, Lars S; Wetterslev, Jørn; Sæbye, Ditte; Meyhoff, Christian S

**Source:** International journal of surgery (London, England); Feb 2018; vol. 52 ; p. 56-60

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29455044

**Abstract:**BACKGROUND Surgical site infection (SSI) and other postoperative complications are associated with high costs, morbidity, secondary surgery, and mortality. Many studies have identified factors that may prevent SSI and pulmonary complications, but it is important to know when they in fact occur. The aim of this study was to investigate the diagnostic timing of surgical site infections and pulmonary complications after laparotomy. MATERIAL AND METHOD This is a secondary analysis of the PROXI trial which was a randomized clinical trial conducted in 1400 patients undergoing elective or emergent laparotomy. Patients were randomly allocated to either 80% or 30% perioperative inspiratory oxygen fraction. RESULT SSI or pulmonary complications were diagnosed in 24.2% (95% CI: 22.0%-26.5%) of the patients at a median of 9 days [IQR: 5-15] after surgery. Most common was surgical site infection (19.6%); median time 10 days after surgery [IQR: 7-18]. The corresponding figures for anastomotic leakage was 5.7%, 8 days [IQR: 6-10]; pneumonia 3.5%, 5 days [IQR: 3-9]; and respiratory failure 2.3%, 3 days [IQR: 1-8]. The oxygen allocation was not significantly related to time of diagnosis for postoperative surgical site infections or pulmonary complications. CONCLUSION A high percentage of patients undergoing laparotomy develop a

postoperative complication. This study adds new knowledge by identifying time intervals within which medical professionals should be aware of surgical site infections and pulmonary complications in order to initiate appropriate treatment of the patients.

**Database:** Medline

**9. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study.**

**Author(s):** GlobalSurg Collaborative

**Source:** The Lancet. Infectious diseases; Feb 2018

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29452941

**Abstract:**BACKGROUND Surgical site infection (SSI) is one of the most common infections associated with health care, but its importance as a global health priority is not fully understood. We quantified the burden of SSI after gastrointestinal surgery in countries in all parts of the world. METHODSThis international, prospective, multicentre cohort study included consecutive patients undergoing elective or emergency gastrointestinal resection within 2-week time periods at any health-care facility in any country. Countries with participating centres were stratified into high-income, middle-income, and low-income groups according to the UN's Human Development Index (HDI). Data variables from the GlobalSurg 1 study and other studies that have been found to affect the likelihood of SSI were entered into risk adjustment models. The primary outcome measure was the 30-day SSI incidence (defined by US Centers for Disease Control and Prevention criteria for superficial and deep incisional SSI). Relationships with explanatory variables were examined using Bayesian multilevel logistic regression models. This trial is registered with ClinicalTrials.gov, number NCT02662231. FINDINGS Between Jan 4, 2016, and July 31, 2016, 13 265 records were submitted for analysis. 12 539 patients from 343 hospitals in 66 countries were included. 7339 (58.5%) patients were from high-HDI countries (193 hospitals in 30 countries), 3918 (31.2%) patients were from middle-HDI countries (82 hospitals in 18 countries), and 1282 (10.2%) patients were from low-HDI countries (68 hospitals in 18 countries). In total, 1538 (12.3%) patients had SSI within 30 days of surgery. The incidence of SSI varied between countries with high (691 [9.4%] of 7339 patients), middle (549 [14.0%] of 3918 patients), and low (298 [23.2%] of 1282) HDI ( $p < 0.001$ ). The highest SSI incidence in each HDI group was after dirty surgery (102 [17.8%] of 574 patients in high-HDI countries; 74 [31.4%] of 236 patients in middle-HDI countries; 72 [39.8%] of 181 patients in low-HDI countries). Following risk factor adjustment, patients in low-HDI countries were at greatest risk of SSI (adjusted odds ratio 1.60, 95% credible interval 1.05-2.37;  $p = 0.030$ ). 132 (21.6%) of 610 patients with an SSI and a microbiology culture result had an infection that was resistant to the prophylactic antibiotic used. Resistant infections were detected in 49 (16.6%) of 295 patients in high-HDI countries, in 37 (19.8%) of 187 patients in middle-HDI countries, and in 46 (35.9%) of 128 patients in low-HDI countries ( $p < 0.001$ ). INTERPRETATION Countries with a low HDI carry a disproportionately greater burden of SSI than countries with a middle or high HDI and might have higher rates of antibiotic resistance. In view of WHO recommendations on SSI prevention that highlight the absence of high-quality interventional research, urgent, pragmatic, randomised trials based in LMICs are needed to assess measures aiming to reduce this preventable complication. FUNDING DFID-MRC-Wellcome Trust Joint Global Health Trial Development Grant, National Institute of Health Research Global Health Research Unit Grant.

**Database:** Medline

## 10. Intraoperative interventions for preventing surgical site infection: an overview of Cochrane Reviews.

**Author(s):** Liu, Zhenmi; Dumville, Jo C; Norman, Gill; Westby, Maggie J; Blazeby, Jane; McFarlane, Emma; Welton, Nicky J; O'Connor, Louise; Cawthorne, Julie; George, Ryan P; Crosbie, Emma J; Rithalia, Amber D; Cheng, Hung-Yuan

**Source:** The Cochrane database of systematic reviews; Feb 2018; vol. 2 ; p. CD012653

**Publication Date:** Feb 2018

**Publication Type(s):** Research Support, Non-u.s. Gov't Journal Article Review

**PubMedID:** 29406579

Available at [Cochrane Database of Systematic Reviews](http://www.cochrane.org) - from Cochrane Collaboration (Wiley)

**Abstract:** **BACKGROUND** Surgical site infection (SSI) rates vary from 1% to 5% in the month following surgery. Due to the large number of surgical procedures conducted annually, the costs of these SSIs can be considerable in financial and social terms. Many interventions are used with the aim of reducing the risk of SSI in people undergoing surgery. These interventions can be broadly delivered at three stages: preoperatively, intraoperatively and postoperatively. The intraoperative interventions are largely focused on decontamination of skin using soap and antiseptics; the use of barriers to prevent movement of micro-organisms into incisions; and optimising the patient's own bodily functions to promote best recovery. Both decontamination and barrier methods can be aimed at people undergoing surgery and operating staff. Other interventions focused on SSI prevention may be aimed at the surgical environment and include methods of theatre cleansing and approaches to managing theatre traffic. **OBJECTIVES** To present an overview of Cochrane Reviews of the effectiveness and safety of interventions, delivered during the intraoperative period, aimed at preventing SSIs in all populations undergoing surgery in an operating theatre. **METHODS** Published Cochrane systematic reviews reporting the effectiveness of interventions delivered during the intraoperative period in terms of SSI prevention were eligible for inclusion in this overview. We also identified Cochrane protocols and title registrations for future inclusion into the overview. We searched the Cochrane Library on 01 July 2017. Two review authors independently screened search results and undertook data extraction and 'Risk of bias' and certainty assessment. We used the ROBIS (risk of bias in systematic reviews) tool to assess the quality of included reviews, and we used GRADE methods to assess the certainty of the evidence for each outcome. We summarised the characteristics of included reviews in the text and in additional tables. **MAIN RESULTS** We included 32 Cochrane Reviews in this overview: we judged 30 reviews as being at low risk of bias and two at unclear risk of bias. Thirteen reviews had not been updated in the past three years. Two reviews had no relevant data to extract. We extracted data from 30 reviews with 349 included trials, totaling 73,053 participants. Interventions assessed included gloving, use of disposable face masks, patient oxygenation protocols, use of skin antiseptics for hand washing and patient skin preparation, vaginal preparation, microbial sealants, methods of surgical incision, antibiotic prophylaxis and methods of skin closure. Overall, the GRADE certainty of evidence for outcomes was low or very low. Of the 77 comparisons providing evidence for the outcome of SSI, seven provided high- or moderate-certainty evidence, 39 provided low-certainty evidence and 31 very low-certainty evidence. Of the nine comparisons that provided evidence for the outcome of mortality, five provided low-certainty evidence and four very low-certainty evidence. There is high- or moderate-certainty evidence for the following outcomes for these intraoperative interventions. (1) Prophylactic intravenous antibiotics administered before caesarean incision reduce SSI risk compared with administration after cord clamping (10 trials, 5041 participants; risk ratio (RR) 0.59, 95% confidence interval (CI) 0.44 to 0.81; high-certainty evidence - assessed by review authors). (2) Preoperative antibiotics reduce SSI risk compared with placebo after breast cancer surgery (6 trials, 1708 participants; RR 0.74, 95% CI 0.56 to 0.98; high-certainty evidence - assessed by overview authors). (3) Antibiotic prophylaxis probably reduce SSI risk in caesarean sections compared with no antibiotics (82 relevant trials, 14,407

participants; RR 0.40, 95% CI 0.35 to 0.46; moderate-certainty evidence; downgraded once for risk of bias - assessed by review authors). (4) Antibiotic prophylaxis probably reduces SSI risk for hernia repair compared with placebo or no treatment (17 trials, 7843 participants; RR 0.67, 95% CI 0.54 to 0.84; moderate-certainty evidence; downgraded once for risk of bias - assessed by overview authors); (5) There is currently no clear difference in the risk of SSI between iodine-impregnated adhesive drapes compared with no adhesive drapes (2 trials, 1113 participants; RR 1.03, 95% CI 0.66 to 1.60; moderate-certainty evidence; downgraded once for imprecision - assessed by review authors); (6) There is currently no clear difference in SSI risk between short-term compared with long-term duration antibiotics in colorectal surgery (7 trials; 1484 participants; RR 1.05 95% CI 0.78 to 1.40; moderate-certainty evidence; downgraded once for imprecision - assessed by overview authors). There was only one comparison showing negative effects associated with the intervention: adhesive drapes increase the risk of SSI compared with no drapes (5 trials; 3082 participants; RR 1.23, 95% CI 1.02 to 1.48; high-certainty evidence - rated by review authors).

**AUTHORS' CONCLUSION** This overview provides the most up-to-date evidence on use of intraoperative treatments for the prevention of SSIs from all currently published Cochrane Reviews. There is evidence that some interventions are useful in reducing SSI risk for people undergoing surgery, such as antibiotic prophylaxis for caesarean section and hernia repair, and also the timing of prophylactic intravenous antibiotics administered before caesarean incision. Also, there is evidence that adhesive drapes increase SSI risk. Evidence for the many other treatment choices is largely of low or very low certainty and no quality-of-life or cost-effectiveness data were reported. Future trials should elucidate the relative effects of some treatments. These studies should focus on increasing participant numbers, using robust methodology and being of sufficient duration to adequately assess SSI. Assessment of other outcomes such as mortality might also be investigated as part of non-experimental prospective follow-up of people with SSI of different severity, so the risk of death for different subgroups can be better understood.

**Database:** Medline

### **11. Quality improvement initiative: Preventative Surgical Site Infection Protocol in Vascular Surgery.**

**Author(s):** Parizh, David; Ascher, Enrico; Raza Rizvi, Syed Ali; Hingorani, Anil; Amaturro, Michael; Johnson, Eric

**Source:** Vascular; Feb 2018; vol. 26 (no. 1); p. 47-53

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28708024

**Abstract:** Objective A quality improvement initiative was employed to decrease single institution surgical site infection rate in open lower extremity revascularization procedures. **SUMMARY BACKGROUND DATA** In an attempt to lower patient morbidity, we developed and implemented the Preventative Surgical Site Infection Protocol in Vascular Surgery. Surgical site infections lead to prolonged hospital stays, adjunctive procedure, and additive costs. We employed targeted interventions to address the common risk factors that predispose patients to post-operative complications. **Methods** Retrospective review was performed between 2012 and 2016 for all surgical site infections after revascularization procedures of the lower extremity. A quality improvement protocol was initiated in January 2015. Primary outcome was the assessment of surgical site infection rate reduction in the pre-protocol vs. post-protocol era. Secondary outcomes evaluated patient demographics, closure method, perioperative antibiotic coverage, and management outcomes. **Results** Implementation of the protocol decreased the surgical site infection rate from 6.4% to 1.6% ( $p = 0.0137$ ). Patient demographics and comorbidities were assessed and failed to

demonstrate a statistically significant difference among the infection and no-infection groups. Wound closure with monocryl suture vs. staple proved to be associated with decreased surgical site infection rate ( $p < 0.005$ ). Conclusions Preventative measures, in the form of a standardized protocol, to decrease surgical site infections in the vascular surgery population are effective and necessary. Our data suggest that there may be benefit in the incorporation of MRSA and Gram-negative coverage as part of the Surgical Care Improvement Project perioperative guidelines.

**Database:** Medline

### **12. Temporal trends and epidemiology of Staphylococcus aureus surgical site infection in the Swiss surveillance network: a cohort study.**

**Author(s):** Abbas, M; Aghayev, E; Troillet, N; Eisenring, M-C; Kuster, S P; Widmer, A F; Harbarth, S; SwissNoso

**Source:** The Journal of hospital infection; Feb 2018; vol. 98 (no. 2); p. 118-126

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28988937

**Abstract:**BACKGROUND Staphylococcus aureus is the leading pathogen in surgical site infections (SSI). AIM To explore trends and risk factors associated with S. aureus SSI. METHODS Risk factors for monomicrobial S. aureus SSI were identified from the Swiss multi-centre SSI surveillance system using multi-variate logistic regression. Both in-hospital and postdischarge SSI were identified using standardized definitions. FINDINGS Over a six-year period, data were collected on 229,765 surgical patients, of whom 499 (0.22%) developed monomicrobial S. aureus SSI; 459 (92.0%) and 40 (8.0%) were due to methicillin-susceptible S. aureus (MSSA) and methicillin-resistant S. aureus (MRSA), respectively. There was a significant decrease in the rate of MSSA SSI ( $P = 0.007$ ), but not in the rate of MRSA SSI ( $P = 0.70$ ). Independent protective factors for S. aureus SSI were older age [ $\geq 75$  years vs  $< 50$  years: odds ratio (OR) 0.60, 95% confidence interval (CI) 0.44-0.83], laparoscopy/minimally invasive surgery (OR 0.68, 95% CI 0.50-0.92), non-clean surgery [OR 0.78 (per increase in wound contamination class), 95% CI 0.64-0.94] and correct timing of pre-operative antibiotic prophylaxis (OR 0.80, 95% CI 0.65-0.98). Independent risk factors were male sex (OR 1.38, 95% CI 1.14-1.66), higher American Society of Anesthesiologists' score (per one-point increment: OR 1.30, 95% CI 1.13-1.51), re-operation for non-infectious reasons (OR 4.59, 95% CI 3.59-5.87) and procedure type: cardiac surgery, laminectomy, and hip or knee arthroplasty had two-to nine-fold increased odds of S. aureus SSI compared with other procedures. CONCLUSIONS SSI due to S. aureus are decreasing and becoming rare events in Switzerland. High-risk procedures that may benefit from specific preventive measures were identified. Unfortunately, many of the independent risk factors are not easily modifiable.

**Database:** Medline

### **13. The Impact of a Reported Penicillin Allergy on Surgical Site Infection Risk.**

**Author(s):** Blumenthal, Kimberly G; Ryan, Erin E; Li, Yu; Lee, Hang; Kuhlen, James L; Shenoy, Erica S

**Source:** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Jan 2018; vol. 66 (no. 3); p. 329-336

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29361015

**Abstract:**Background A reported penicillin allergy may compromise receipt of recommended antibiotic prophylaxis intended to prevent surgical site infections (SSIs). Most patients with a reported penicillin allergy are not allergic. We determined the impact of a reported penicillin allergy on the development of SSIs. Methods In this retrospective cohort study of Massachusetts General Hospital hip arthroplasty, knee arthroplasty, hysterectomy, colon surgery, and coronary artery bypass grafting patients from 2010 to 2014, we compared patients with and without a reported penicillin allergy. The primary outcome was an SSI, as defined by the Centers for Disease Control and Prevention's National Healthcare Safety Network. The secondary outcome was perioperative antibiotic use. Results Of 8385 patients who underwent 9004 procedures, 922 (11%) reported a penicillin allergy, and 241 (2.7%) had an SSI. In multivariable logistic regression, patients reporting a penicillin allergy had increased odds (adjusted odds ratio, 1.51; 95% confidence interval, 1.02-2.22) of SSI. Penicillin allergy reporters were administered less cefazolin (12% vs 92%;  $P < .001$ ) and more clindamycin (49% vs 3%;  $P < .001$ ), vancomycin (35% vs 3%;  $P < .001$ ), and gentamicin (24% vs 3%;  $P < .001$ ) compared with those without a reported penicillin allergy. The increased SSI risk was entirely mediated by the patients' receipt of an alternative perioperative antibiotic; between 112 and 124 patients with reported penicillin allergy would need allergy evaluation to prevent 1 SSI. Conclusions Patients with a reported penicillin allergy had a 50% increased odds of SSI, attributable to the receipt of second-line perioperative antibiotics. Clarification of penicillin allergies as part of routine preoperative care may decrease SSI risk.

**Database:** Medline

#### **14. Impact of choice of skin preparation solution in cardiac surgery on rate of surgical site infection: a propensity score matched analysis.**

**Author(s):** Raja, Shahzad G; Rochon, Melissa; Mullins, Clair; Morais, Carlos; Kourliouros, Antonios; Wishart, Ellie; De Souza, Anthony; Bhudia, Sunil

**Source:** Journal of infection prevention; Jan 2018; vol. 19 (no. 1); p. 16-21

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29317910

**Abstract:**Background Antiseptic skin preparations containing chlorhexidine gluconate and povidone iodine are routinely used to reduce the risk of surgical site infection (SSI). This study assesses the efficacy of two alcohol-based solutions, 2% chlorhexidine-alcohol and 10% povidone iodine-alcohol, on the incidence of cardiac SSI. Methods A total of 738 consecutive patients undergoing cardiac surgery had skin preparation with 2% chlorhexidine gluconate in 70% isopropanol (ChlorPrep, BD Ltd, UK) were propensity matched to 738 patients with skin prepared with 10% povidone-iodine in 30% industrial methylated spirit (Videne Alcoholic Tincture, Ecolab Ltd, UK). Continuous, prospective SSI surveillance data were collected for all these patients. A retrospective analysis of prospectively collected perioperative data was performed. Results The overall rate of SSI was similar in the chlorhexidine-alcohol and povidone-iodine-alcohol groups (3.3% versus 3.8%;  $P = 0.14$ ; relative risk [RR] = 0.98; 95% confidence interval [CI] = 0.52-1.78). Superficial (1.2% versus 1.8%;  $P = 0.18$ ; RR = 0.97; 95% CI = 0.48-1.80) and deep incisional (1.2% versus 1.6%;  $P = 0.24$ ) SSI rates were also similar with 10% povidone-iodine-alcohol being marginally more effective against organ-space infections (0.8% versus 0.4%;  $P = 0.05$ ; RR = 0.38; 95% CI = 0.20-1.01). Conclusion Our analysis confirms that alcohol-based skin preparation in cardiac surgery with povidone-iodine reduces the incidence of organ-space infections with no significant superiority in preventing incisional SSI compared with chlorhexidine-alcohol.

**Database:** Medline

### 15. Impact of a surgical site infection bundle on surgical site infection rates in cesarean deliveries

**Author(s):** Davidson C.; Enns J.; Dempster C.; Eppes C.

**Source:** American Journal of Obstetrics and Gynecology; Jan 2018; vol. 218 (no. 1)

**Publication Date:** Jan 2018

**Publication Type(s):** Conference Abstract

**Abstract:**OBJECTIVE: To investigate cesarean delivery (CD) surgical site infection (SSI) rates before and after implementation of an SSI care bundle. STUDY DESIGN: In April 2014, our hospital, a public tertiary care academic center, introduced an SSI bundle for CD to reduce the SSI rate. The bundle, adopted from the colorectal surgery literature, included the following: 1) pre-and post-operative instructions regarding antiseptic skin cleansing, wound care, and glycemic control in diabetics; 2) intraoperative use of antiseptic skin and vaginal preparations, double-gloving, and changing of gloves and instrument tray for fascial closure; and 3) follow up nurse phone calls after discharge. Following bundle implementation, we performed a retrospective case/cohort review of maternal records from an aggregate database for demographic characteristics and used hospital reported SSI rates from infection prevention services. Cases were women who underwent CD post-SSI bundle implementation and controls were those who underwent CD pre-SSI bundle. Women were included if they had a gestational age of at least 23 0/7 weeks and delivered a liveborn neonate(s) between January 1, 2012 and December 31, 2015. Primary outcome was SSI rate. Secondary outcomes included patient demographics and co-morbidities. Students t test was used for continuous outcomes and chi squared for categorical. RESULTS: During the study time period, 4014 total CD were performed (2147 pre-bundle, 1867 post-bundle). Demographics of women undergoing CD were similar before and after the infection prevention bundle (Table 1), with the exception of body mass index, gestational diabetes, substance abuse, smoking, history of venous thromboembolism, and number of women with prior CD. The mean SSI rate significantly decreased after the bundle (2.44 to 1.10,  $p = 0.013$ ). Figure 1 illustrates the quarterly SSI rate, with the arrow representing the implementation of the SSI bundle. CONCLUSION: Implementation of an infection prevention bundle led to a significantly decreased SSI rate in our population. While differences in SSI related demographics of the populations before and after the bundle may have contributed, in general, these risk factors were higher in the post-bundle population and therefore are unlikely to have confounded the impact of the infection prevention bundle.

**Database:** EMBASE

### 16. Prophylactic retention suture for surgical site infection: a retrospective cohort study

**Author(s):** Ito E.; Yoshida M.; Suzuki N.; Imakita T.; Tsutsui N.; Ohdaira H.; Kitajima M.; Suzuki Y.

**Source:** Journal of Surgical Research; Jan 2018; vol. 221 ; p. 58-63

**Publication Date:** Jan 2018

**Publication Type(s):** Article

**PubMedID:** 29229153

**Abstract:**Background Surgical site infection (SSI) is a common complication of gastrointestinal surgery. Because retention suture is known to prevent abdominal wound dehiscence, it is only considered indicated in high-risk patients. At present, there are no clear indications for retention suture. The purpose of this study was to analyze the effect of prophylactic retention suture and to determine what situations indicate prophylactic retention suture against SSI. Material and methods Between January 2014 and January 2016, 135 patients who underwent midline laparotomy in our hospital were analyzed. Inclusion criteria for this study were patients with American Society Anesthesiologists' physical status classification system (ASA-PS score)  $\geq 3$  or emergent surgery. Results Of the 135 patients, 30 (22.2%) received prophylactic retention suture. Diabetes mellitus,

surgical wound classification, large incision, and retention suture were associated with SSI in multivariate analysis. In subgroup analysis, SSI risk factors were analyzed in each surgical wound classification. Only in surgical wound classification class II and III did retention suture significantly reduce the risk of SSI (odds ratio = 0.100 [0.012-0.837], P = 0.034). In class IV, however, half the patients developed SSI, regardless of retention suture. Table 3 summarizes the results of the subgroup analysis. Conclusions The present data suggest that prophylactic retention suture reduces SSI for surgical wound classification class II or III. For class IV operations, however, other methods to prevent SSI are necessary.

**Database:** EMBASE

## Influenza

### 1. The influence of prebiotic or probiotic supplementation on antibody titers after influenza vaccination: a systematic review and meta-analysis of randomized controlled trials.

**Author(s):** Yeh, Tzu-Lin; Shih, Pei-Ching; Liu, Shu-Jung; Lin, Chao-Hsu; Liu, Jui-Ming; Lei, Wei-Te; Lin, Chien-Yu

**Source:** Drug design, development and therapy; 2018; vol. 12 ; p. 217-230

**Publication Date:** 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29416317

Available at [Drug Design, Development and Therapy](#) - from Europe PubMed Central - Open Access

Available at [Drug Design, Development and Therapy](#) - from EBSCO (MEDLINE Complete)

Available at [Drug Design, Development and Therapy](#) - from PubMed Central

**Abstract:**Background Influenza infection is a common disease with a huge disease burden. Influenza vaccination has been widely used, but concerns regarding vaccine efficacy exist, especially in the elderly. Probiotics are live microorganisms with immunomodulatory effects and may enhance the immune responses to influenza vaccination. Methods We conducted a systematic review and meta-analysis to determine the influence of prebiotics/probiotics/synbiotics supplementation on vaccine responses to influenza vaccination. Studies were systematically identified from electronic databases up to July 2017. Information regarding study population, influenza vaccination, components of supplements, and immune responses were extracted and analyzed. Twelve studies, investigating a total of 688 participants, were included in this review. Results Patients with prebiotics/probiotics supplements were found to have higher influenza hemagglutination inhibition antibody titers after vaccination (for A/H1N1, 42.89 vs 35.76, mean difference =7.14, 95% CI =2.73, 11.55, P=0.002; for A/H3N2, 105.4 vs 88.25, mean difference =17.19, 95% CI =3.39, 30.99, P=0.01; for B strain, 34.87 vs 30.73, mean difference =4.17, 95% CI =0.37, 7.96, P=0.03). Conclusion Supplementation with prebiotics or probiotics may enhance the influenza hemagglutination inhibition antibody titers in all A/H1N1, A/H3N2, and B strains (20%, 19.5%, and 13.6% increases, respectively). Concomitant prebiotics or probiotics supplementation with influenza vaccination may hold great promise for improving vaccine efficacy. However, high heterogeneity was observed and further studies are warranted.

**Database:** Medline

## 2. Randomized controlled trial on promoting influenza vaccination in general practice waiting rooms.

**Author(s):** Berkhout, Christophe; Willefert-Bouche, Amy; Chazard, Emmanuel; Zgorska-Maynard-Moussa, Suzanna; Favre, Jonathan; Peremans, Lieve; Ficheur, Grégoire; Van Royen, Paul

**Source:** PloS one; 2018; vol. 13 (no. 2); p. e0192155

**Publication Date:** 2018

**Publication Type(s):** Randomized Controlled Trial Journal Article

**PubMedID:** 29425226

Available at [PLoS ONE](#) - from Public Library of Science (PLoS)

Available at [PLoS ONE](#) - from Europe PubMed Central - Open Access

Available at [PLoS ONE](#) - from EBSCO (MEDLINE Complete)

Available at [PLoS ONE](#) - from Europe PubMed Central

**Abstract:**BACKGROUND Most of general practitioners (GPs) use advertising in their waiting rooms for patient's education purposes. Patients vaccinated against seasonal influenza have been gradually lessening. The objective of this trial was to assess the effect of an advertising campaign for influenza vaccination using posters and pamphlets in GPs' waiting rooms. METHODS AND FINDINGS Registry based 2/1 cluster randomized controlled trial, a cluster gathering the enlisted patients of 75 GPs aged over 16 years. The trial, run during the 2014-2015 influenza vaccination campaign, compared patient's awareness from being in 50 GPs' standard waiting rooms (control group) versus that of waiting in 25 rooms from GPs who had received and exposed pamphlets and one poster on influenza vaccine (intervention group), in addition to standard mandatory information. The main outcome was the number of vaccination units delivered in pharmacies. Data were extracted from the SIAM-ERASME claim database of the Health Insurance Fund of Lille-Douai (France). The association between the intervention (yes/no) and the main outcome was assessed through a generalized estimating equation. Seventy-five GPs enrolled 10,597 patients over 65 years or suffering from long lasting diseases (intervention/control as of 3781/6816 patients) from October 15, 2014 to February 28, 2015. No difference was found regarding the number of influenza vaccination units delivered (Relative Risk (RR) = 1.01; 95% Confidence interval: 0.97 to 1.05; p = 0.561). CONCLUSION Effects of the monothematic campaign promoting vaccination against influenza using a poster and pamphlets exposed in GPs' waiting rooms could not be demonstrated.

**Database:** Medline

## 3. Effect of probiotics and prebiotics on immune response to influenza vaccination in adults: A systematic review and meta-analysis of randomized controlled trials

**Author(s):** Lei W.T.

**Source:** Journal of Allergy and Clinical Immunology; 2018; vol. 141 (no. 2)

**Publication Date:** 2018

**Publication Type(s):** Conference Abstract

Available at [Journal of Allergy and Clinical Immunology](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**RATIONALE: To summarize the evidence from RCTs to investigate the effect of probiotics / prebiotics on the immune response of adult accept influenza vaccination. METHODS: Databases were searched from inception to July 2017. We used Cochrane Review risk-of-bias assessment tools of RCT for quality assessment. Our objective is seroprotection and seroconversion rate of the influenza vaccination influenced by probiotics / prebiotics. RESULTS: A total of 20 RCTs comprising

1,979 adults were included in our systematic review. Nine RCTs including 623 participants were pooled through a meta-analysis. Participants who take probiotics / prebiotics showed a significant improvement in H1N1 seroprotection rate (OR 5.83, 95% CI 1.19 - 2.82,  $p=0.006$ , I<sup>2</sup>50%), in H3N2 seroprotection rate (OR 2.85, 95% CI 1.59 - 5.10,  $p<0.001$ , I<sup>2</sup>50%) and in B strain seroconversion rate (OR 2.11, 95% CI 1.38 - 3.21,  $p<0.001$ , I<sup>2</sup>50%). In subgroup analysis according to intervention type, participants using probiotics had a significant better seroconversion rate in H3N2 (OR 5.52, 95% CI 1.45 - 8.53,  $p=0.005$ , I<sup>2</sup>63%). Meta-regression disclosed the effect of probiotics / prebiotics was significantly positive correlated with the duration of supplement on seroconversion rate for influenza B strain and seroconversion rate for influenza H1N1 strain. Subgroup analysis also showed that health elders supplemented with probiotics / prebiotics exhibited significant better response to all of the influenza strains than health adults and unhealthy elders. **CONCLUSIONS:** This meta-analysis suggests that probiotics / prebiotics is effective to elevate the immunogenicity of seroconversion and seroprotection rate for adults inoculated with influenza vaccine, especially the health elders and longer treatment duration.

**Database:** EMBASE

#### **4. Incidence of narcolepsy after H1N1 influenza and vaccinations: Systematic review and meta-analysis.**

**Author(s):** Sarkanen, Tomi O; Alakuijala, Anniina P E; Dauvilliers, Yves A; Partinen, Markku M

**Source:** Sleep medicine reviews; Apr 2018; vol. 38 ; p. 177-186

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 28847694

**Abstract:** An increased incidence of narcolepsy was seen in many countries after the pandemic H1N1 influenza vaccination campaign in 2009-2010. The H1N1 vaccine - narcolepsy connection is based on observational studies that are prone to various biases, e.g., confounding by H1N1 infection, and ascertainment, recall and selection biases. A direct pathogenic link has, however, remained elusive. We conducted a systematic review and meta-analysis to analyze the magnitude of H1N1 vaccination related risk and to examine if there was any association with H1N1 infection itself. We searched all articles from PubMed, Web of Science and Scopus, and other relevant sources reporting the incidence and risk of post-vaccine narcolepsy. In our paper, we show that the risk appears to be limited to only one vaccine (Pandemrix®). During the first year after vaccination, the relative risk of narcolepsy was increased 5 to 14-fold in children and adolescents and 2 to 7-fold in adults. The vaccine attributable risk in children and adolescents was around 1 per 18,400 vaccine doses. Studies from Finland and Sweden also appear to demonstrate an extended risk of narcolepsy into the second year following vaccination, but such conclusions should be interpreted with a word of caution due to possible biases. Benefits of immunization outweigh the risk of vaccination-associated narcolepsy, which remains a rare disease.

**Database:** Medline

#### **5. Impact of ageing and a synbiotic on the immune response to seasonal influenza vaccination; a randomised controlled trial.**

**Author(s):** Enani, Sumia; Przemaska-Kosicka, Agnieszka; Childs, Caroline E; Maidens, Catherine; Dong, Honglin; Conterno, Lorenza; Tuohy, Kieran; Todd, Susan; Gosney, Margot; Yaqoob, Parveen

**Source:** Clinical nutrition (Edinburgh, Scotland); Apr 2018; vol. 37 (no. 2); p. 443-451

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28215759

Available at [Clinical Nutrition](#) - from PubMed Central

**Abstract:**BACKGROUND & AIMS Ageing increases risk of respiratory infections and impairs the response to influenza vaccination. Pre- and pro-biotics offer an opportunity to modulate anti-viral defenses and the response to vaccination via alteration of the gut microbiota. This study investigated the effect of a novel probiotic, *Bifidobacterium longum* bv. *infantis* CCUG 52486, combined with a prebiotic, gluco-oligosaccharide, on the B and T cell response to seasonal influenza vaccination in young and older subjects. METHODS In a double-blind, randomized controlled trial, 58 young (18-35 y) and 54 older (60-85 y) subjects were supplemented with the synbiotic for 8 weeks. At 4 weeks they were administered with a seasonal influenza vaccine. B and T cell phenotype and responsiveness to in vitro re-stimulation with the vaccine were assessed at baseline, 4, 6 and 8 weeks. RESULTS B and T cell profiles differed markedly between young and older subjects. Vaccination increased numbers of memory, IgA+ memory, IgG+ memory and total IgG+ B cells in young subjects, but failed to do so in older subjects and did not significantly alter T cell subsets. Seroconversion to the H1N1 subunit in the older subjects was associated with higher post-vaccination numbers of plasma B cells, but seroconversion was less consistently associated with T cell phenotype. B and T cell subsets from both young and older subjects demonstrated a strong antigen-specific recall challenge, and although not influenced by age, responsiveness to the recall challenge was associated with seroconversion. In older subjects, CMV seropositivity was associated with a significantly lower recall response to the vaccine, but the synbiotic did not affect the responsiveness of B or T cells to re-stimulation with influenza vaccine. CONCLUSIONS Antigen-specific B and T cell activation following an in vitro recall challenge with the influenza vaccine was influenced by CMV seropositivity, but not by a synbiotic. Registered under ClinicalTrials.gov Identifier no. NCT01066377.

**Database:** Medline

## **6. Influenza vaccination during pregnancy for prevention of influenza confirmed illness in the infants: A systematic review and meta-analysis.**

**Author(s):** Nunes, Marta C; Madhi, Shabir A

**Source:** Human vaccines & immunotherapeutics; Mar 2018; vol. 14 (no. 3); p. 758-766

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28708952

**Abstract:** Infants younger than 6 months of age are at particular risk for serious illness from influenza infection. Currently available influenza vaccines are, however, not licensed for use in infants <6 months old. Influenza vaccination during pregnancy elicits robust antibody responses in the women that will protect the infants against influenza infection during the first few months of life. We aimed to determine the impact of influenza vaccination during pregnancy to prevent laboratory-confirmed influenza infection and influenza-associated hospitalisations in infants <6 months old. An electronic search identified all studies assessing the proposed outcomes in infants after administration of influenza vaccine during pregnancy. Two meta-analyses were performed accordingly to studies restricting the evaluation to influenza-associated hospitalisations or not. Four randomized control trials and 3 observational studies reported on the prevention of laboratory-confirmed influenza infection in infants <6 months old. Maternal influenza vaccination was associated with a 48% [95% confidence interval (CI): 33 to 59] reduced risk of infants having laboratory-confirmed influenza infection. Four observational studies reported on the prevention of

hospitalizations associated with laboratory-confirmed influenza infection and the pool estimate was 72% (95%CI: 39% to 87%). Receipt of influenza vaccine during pregnancy was associated with decreased risk of laboratory-confirmed influenza infection in the infants.

**Database:** Medline

### **7. Does Vitamin D Deficiency Affect the Immunogenic Responses to Influenza Vaccination? A Systematic Review and Meta-Analysis.**

**Author(s):** Lee, Ming-Dar; Lin, Chao-Hsu; Lei, Wei-Te; Chang, Hung-Yang; Lee, Hung-Chang; Yeung, Chun-Yan; Chiu, Nan-Chang; Chi, Hsin; Liu, Jui-Ming; Hsu, Ren-Jun; Cheng, Yu-Jyun; Yeh, Tzu-Lin; Lin, Chien-Yu

**Source:** Nutrients; Mar 2018; vol. 10 (no. 4)

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29587438

Available at [Nutrients](#) - from Europe PubMed Central - Open Access

Available at [Nutrients](#) - from mdpi.com

**Abstract:**Influenza virus infection is a major global public health problem, and the efficacy of influenza vaccination is not satisfactory. Vitamin D is involved in many immune-mediated inflammatory processes. The impact of vitamin D levels on the immunogenic response to influenza vaccination is not clear. We performed a comprehensive literature search and systematic review of studies that investigated vitamin D and influenza vaccination. Data pertaining to study population, vaccine components, vitamin D levels, and immunogenic response were analyzed. Nine studies, with a combined study population of 2367 patients, were included in the systematic review. Four studies were included in the meta-analysis to investigate the influence of vitamin D deficiency (VDD) on the seroprotection (SP) rates and seroconversion (SC) rates following influenza vaccination. We found no significant association between vitamin D level and the immunogenic response to influenza vaccination. However, strain-specific differences may exist. We observed lower SP rates of influenza A virus subtype H3N2 (A/H3N2) and B strain in VDD patients than patients with normal vitamin D levels (A/H3N2: 71.8% vs. 80.1%, odds ratio (OR): 0.63, 95% confidence interval (CI): 0.43-0.91,  $p = 0.01$ ; B strain: 69.6% vs. 76.4%, OR: 0.68, 95% CI: 0.5-0.93,  $p = 0.01$ ). However, the SP rates of A/H1N1 and SC rates of all three strains were not significantly different in VDD and control groups. In conclusion, no association was observed between VDD and immunogenic response to influenza vaccination.

**Database:** Medline

### **8. Influenza vaccine effectiveness among high-risk groups: A systematic literature review and meta-analysis of case-control and cohort studies.**

**Author(s):** Restivo, Vincenzo; Costantino, Claudio; Bono, Stefania; Maniglia, Marialuisa; Marchese, Valentina; Ventura, Gianmarco; Casuccio, Alessandra; Tramuto, Fabio; Vitale, Francesco

**Source:** Human vaccines & immunotherapeutics; Mar 2018; vol. 14 (no. 3); p. 724-735

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28481673

**Abstract:** Vaccination represents the most effective intervention to prevent infection, hospitalization and mortality due to influenza. This meta-analysis quantifies data reporting influenza vaccine effectiveness (VE) on influenza visits and hospitalizations of case-control and cohort studies among high-risk groups. A systematic literature review including original articles published between 2007 and 2016, using a protocol registered on Prospero with No. 42017054854, and a meta-analysis were conducted. For 3 high-risk groups (subjects with underlying health conditions, pregnant women and health care workers) only a qualitative evaluation was performed. The VE quantitative analysis demonstrated a clear significant overall effect of 39% (95%CI: 32-46%) for visits and 57% (95%CI: 30-74%) for hospitalization among children. Considering the elderly influenza VE had a clear effect of 25% (95%CI: 6-40%) for visits and 14% (95%CI: 7-21%;  $p < 0.001$ ) for hospitalization. This study showed the high VE of influenza vaccination among high-risk groups, representing a tool for public health decision-makers to develop evidence-based preventive interventions to avoid influenza outcomes.

**Database:** Medline

### **9. Factors influencing seasonal influenza vaccination behaviour among elderly people: a systematic review.**

**Author(s):** Kan, T; Zhang, J

**Source:** Public health; Mar 2018; vol. 156 ; p. 67-78

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 29408191

**Abstract:** OBJECTIVE To explore the behaviour-related factors influencing influenza vaccination among elderly people using a framework derived from the Health Belief Model (HBM) and the Theory of Reasoned Action (TRA). STUDY DESIGN Systematic review. METHODS Five databases were searched using predetermined strategies in March 2016, and 1927 citations were identified. Articles were selected according to inclusion and exclusion criteria. Key information was extracted from selected studies using a predesigned sheet. Both authors assessed study quality using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) or Critical Appraisal Skills Programme (CASP) checklist. RESULTS Thirty-six articles were selected. A new framework was proposed that contributes to shared understanding of factors influencing health behaviour. Possible determinants of influenza vaccination among elderly people were knowledge, health promotion factors, all constructs of the HBM, and some concepts of the TRA. Key factors were threat perception, behavioural beliefs, subjective norms, recommendations, past behaviour and perceived barriers. CONCLUSION This is the first systematic review to analyse the factors influencing influenza vaccination behaviour of elderly people using a framework integrating the HBM and the TRA. The framework identified key factors of influenza vaccination and presented the inter-relation of behaviour-related variables. However, further well-designed studies are required to explore the inter-relationships accurately and comprehensively.

**Database:** Medline

### **10. Immunogenicity, safety, and effectiveness of seasonal influenza vaccination in patients with diabetes mellitus: A systematic review.**

**Author(s):** Dos Santos, Gael; Tahrat, Halima; Bekkat-Berkani, Rafik

**Source:** Human vaccines & immunotherapeutics; Mar 2018 ; p. 1-30

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29517396

**Abstract:**Influenza is associated with an increased risk of complications, especially in diabetic mellitus patients who are more susceptible to influenza infection. Despite recommendations of the WHO and public health authorities, vaccination uptake in this population remains suboptimal. This systematic review identified 15 studies published between January 2000-March 2017 in PubMed, Embase and Cochrane Library, which provided data on immunogenicity, safety, effectiveness, and/or cost-effectiveness of seasonal influenza vaccination in diabetic patients. Immunogenicity of seasonal influenza vaccination in diabetic patients was generally comparable to that of healthy participants. One month after vaccination of diabetic patients, seroconversion rates and seroprotection ranged from 24.0-58.0% and 29.0-99.0%, respectively. Seasonal influenza vaccination reduced the risk of hospitalization and mortality in diabetic patients, particularly those aged  $\geq 65$  years. These review results demonstrate and reinforce the need and value of annual influenza vaccination in diabetic patients, particularly in alleviating severe complications such as hospitalization or death.

**Database:** Medline

**11. A Randomized, Double-Blind, Active-Controlled Clinical Trial of a Cell Culture-Derived Inactivated Trivalent Influenza Vaccine (NBP607) in Healthy Children 6 Months Through 18 Years of Age.**

**Author(s):** Oh, Chi Eun; Choi, Ui-Yoon; Eun, Byung Wook; Lee, Taek Jin; Kim, Ki Hwan; Kim, Dong Ho; Kim, Nam Hee; Jo, Dae Sun; Shin, Sun Hee; Kim, Kyung-Ho; Kim, Hun; Kim, Yun-Kyung

**Source:** The Pediatric infectious disease journal; Mar 2018

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29528914

**Abstract:**BACKGROUNDAlthough a number of cell culture-derived influenza vaccines have been approved for use in adults, there have been few clinical trials of cell culture-derived seasonal influenza vaccines for young children.METHODSWe conducted a randomized, double-blind phase III clinical trial to evaluate the safety and immunogenicity of a cell culture-derived subunit trivalent inactivated influenza vaccine (NBP607, SK Chemicals Co., Ltd., Seongnam, Korea) in healthy children aged 6 months through 18 years. Subjects were randomized to receive either a study vaccine or an egg-based control vaccine. Antibody levels were measured by the hemagglutination inhibition assay, using cell-derived antigens. Solicited adverse events were assessed for seven days after each injection. Serious adverse events were collected for 6 months after vaccination.RESULTSA total of 374 participants completed the study. No deaths, vaccine-related serious adverse events, or withdrawals due to adverse events were reported. Rates of solicited and unsolicited adverse events were similar in two groups. Overall, NBP607 met the immunogenicity criteria of the Committee for Proprietary Medicinal Products for the three influenza strains. Between the NBP607 group and the control group, immunogenicity endpoints were comparable. Participants younger than three years of age had lower immunologic responses against the influenza B virus in both the NBP607 group and the control group.CONCLUSIONThe immunogenicity and safety were comparable between the NBP607 group and the control group. NBP607 is well-tolerated and immunogenic in children aged 6 months through 18 years.

**Database:** Medline

### **12. Safety, immunogenicity, and lot-to-lot consistency of a split-virion quadrivalent influenza vaccine in younger and older adults: A phase III randomized, double-blind clinical trial.**

**Author(s):** Sesay, Sanie; Brzostek, Jerzy; Meyer, Ingo; Donazzolo, Yves; Leroux-Roels, Geert; Rouzier, Régine; Astruc, Béatrice; Szymanski, Henryk; Toursarkissian, Nicole; Vandermeulen, Corinne; Kowalska, Edyta; Van Damme, Pierre; Salamand, Camille; Pepin, Stephanie

**Source:** Human vaccines & immunotherapeutics; Mar 2018; vol. 14 (no. 3); p. 596-608

**Publication Date:** Mar 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28968138

Available at [Human Vaccines & Immunotherapeutics](#) - from PubMed Central

**Abstract:** Here, we report a randomized multicenter phase III trial assessing the lot-to-lot consistency of the 2014-2015 Northern Hemisphere quadrivalent split-virion inactivated influenza vaccine (IIV4; Sanofi Pasteur) and comparing its immunogenicity and safety with that of trivalent inactivated influenza vaccine (IIV3) in younger and older adults (EudraCT no. 2014-000785-21). Younger (18-60 y, n = 1114) and older (>60 y, n = 1111) adults were randomized 2:2:2:1:1 to receive a single dose of one of three lots of IIV4, the licensed IIV3 containing the B Yamagata lineage strain, or an investigational IIV3 containing the B Victoria lineage strain. Post-vaccination (day 21) hemagglutination inhibition antibody titers were equivalent for the three IIV4 lots. For the pooled IIV4s vs. IIV3, hemagglutination inhibition antibody titers were also non-inferior for the A strains, non-inferior for the B strain when present in the comparator IIV3, and superior for the B strain lineage when absent from the comparator IIV3. For all vaccine strains, seroprotection rates were  $\geq 98\%$  in younger adults and  $\geq 90\%$  in older adults. IIV4 also increased seroneutralizing antibody titers against all three vaccine strains of influenza. All vaccines were well tolerated, with no safety concerns identified. Solicited injection-site reactions were similar for IIV4 and IIV3 and mostly grade 1 and transient. This study showed that in younger and older adults, IIV4 had a similar safety profile as the licensed IIV3 and that including a second B strain lineage in IIV4 provided superior immunogenicity for the added B strain without affecting the immunogenicity of the three IIV3 strains.

**Database:** Medline

### **13. Age-related changes in the natural killer cell response to seasonal influenza vaccination are not influenced by a synbiotic: A randomised controlled trial**

**Author(s):** Przemaska-Kosicka A.; Childs C.E.; Maidens C.; Dong H.; Yaqoob P.; Todd S.; Gosney M.A.; Tuohy K.M.

**Source:** Frontiers in Immunology; Mar 2018; vol. 8

**Publication Date:** Mar 2018

**Publication Type(s):** Article

Available at [Frontiers in Immunology](#) - from Europe PubMed Central - Open Access

Available at [Frontiers in Immunology](#) - from frontiersin.org

**Abstract:** Natural killer (NK) cells are an important component of the immune response to influenza infection, but are subject to alteration during aging, which may play a role in impaired response to infection and vaccination in older people. Enhancement of NK cell activity could, therefore, present a means to improve the immune response to vaccination in older subjects, and pre- and probiotics offer an opportunity to modulate antiviral defenses via alteration of the gut microbiota. This study investigated the effect of a novel probiotic, *Bifidobacterium longum* bv. *infantis* CCUG 52486, combined with a prebiotic, gluco-oligosaccharide (B. longum + GI-OS), on the NK cell response to

seasonal influenza vaccination in young and older subjects in a double-blind, randomized controlled trial. There were significant effects of aging on NK cell phenotype, the most notable of which were an increase in CD56dim cells, mainly reflected in the CD16+ subset, a decrease in CD56bright cells, mainly reflected in the CD16- subset, and greater expression of the immunosenescence marker, CD57, on NK cell subsets. However, these changes only partially translated to differences in NK cell activity, observed as trends toward reduced NK cell activity in older subjects when analyzed on a per cell basis. Influenza vaccination increased the proportion of CD56bright cells and decreased the proportion of CD56dim cells, in young, but not older subjects. Although NK cell activity in response to vaccination was not significantly different between the young and older subjects, low post-vaccination NK cell activity was associated with poor seroconversion in only the older subjects. There was no influence of the synbiotic on NK cell phenotype or activity, either before or after influenza vaccination. In conclusion, aging is associated with marked alteration of the phenotype of the NK cell population and there was evidence of an impaired NK cell response to influenza vaccination in older subjects. The effects of aging on NK cell phenotype and activity could not be offset by B. longum + GI-OS.

**Database:** EMBASE

#### **14. Duration of Influenza Vaccine Effectiveness: A Systematic Review, Meta-analysis, and Meta-regression of Test-Negative Design Case-Control Studies.**

**Author(s):** Young, Barnaby; Sadarangani, Sapna; Jiang, Lili; Wilder-Smith, Annelies; Chen, Mark I-Cheng

**Source:** The Journal of infectious diseases; Feb 2018; vol. 217 (no. 5); p. 731-741

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29220496

**Abstract:**BackgroundWhether influenza vaccination offers protection for the duration of an influenza season was called into question recently after analysis of data from test-negative design (TND) case-control studies.MethodThe published literature was systematically reviewed to identify TND studies that estimated the change in vaccine effectiveness (VE) with respect to time since vaccination.ResultsFourteen studies were identified through the literature search as meeting eligibility criteria. Meta-analyses were performed to compare VE 15-90 days after vaccination to VE 91-180 days after vaccination. A significant decline in VE was observed for influenza virus subtype A/H3 (change in VE, -33; 95% confidence interval [CI], -57 to -12) and type B (change in VE, -19; 95% CI, -33 to -6). VE declined for influenza virus subtype A/H1, but this difference was not statistically significant (change in VE -8; 95% CI, -27 to 21). A multivariable mixed-effects meta-regression model indicated that the change VE was associated with the proportion of study participants who were cases and the proportion who were vaccinated controls ( $P < .05$ ). This could reflect biological effects such as (1) mismatch between the vaccine received and the circulating strains (among cases), (2) herd immunity (among controls), or (3) the reduced power of individual TND studies in the later parts of an influenza outbreak.ConclusionsExploration of new influenza vaccination strategies must be a priority for influenza control, particularly in tropical countries with year-round influenza virus activity.

**Database:** Medline

**15. Change in the efficacy of influenza vaccination after repeated inoculation under antigenic mismatch: A systematic review and meta-analysis.**

**Author(s):** Morimoto, Nobuhisa; Takeishi, Kenta

**Source:** Vaccine; Feb 2018; vol. 36 (no. 7); p. 949-957

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article Review

**PubMedID:** 29373191

Available at [Vaccine](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:**OBJECTIVE To examine the effects of repeated influenza vaccination on medically-attended influenza (MAI) and acute respiratory illness (ARI) risk according to the antigenic matching between vaccine and circulating virus strains. METHODS We performed a systematic review and meta-analysis of randomized studies that compared the risk of MAI and ARI between subjects who had been vaccinated for two consecutive seasons (multiple vaccine group) and those who had been vaccinated in the current season and not in the previous season (single vaccine group). RESULTS Of 1467 articles identified, eight studies covering ten seasons were included in meta-analyses. Six studies assessed efficacy against MAI in children, yielding the risk ratios (RR) of 2.04 (95% CI 1.29-3.22) when circulating strains mismatched vaccine strains, and 0.64 (0.33-1.22) when circulating strains matched vaccine strains. When stratified by vaccine types, the reduced efficacy was significant for live-attenuated influenza vaccine only. Three studies investigated efficacy against ARI in children, with the RR of 0.96 (0.81-1.15). The results on adults and the elderly were scarce. CONCLUSIONS Influenza vaccine efficacy against mismatch strains was lower in repeatedly vaccinated children as compared with those vaccinated for the current season only. The scarcity of available studies may call for further randomized controlled trials on repeated influenza vaccination.

**Database:** Medline

**16. Estimating Influenza Vaccine Effectiveness With the Test-Negative Design Using Alternative Control Groups: A Systematic Review and Meta-Analysis.**

**Author(s):** Feng, Shuo; Cowling, Benjamin J; Kelly, Heath; Sullivan, Sheena G

**Source:** American journal of epidemiology; Feb 2018; vol. 187 (no. 2); p. 389-397

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28641373

**Abstract:**One important assumption in case-control studies is that control selection should be independent of exposure. Nevertheless, it has been hypothesized that virus interference might lead to a correlation between receipt of influenza vaccination and increased risk of infection with other respiratory viruses. We investigated whether such a phenomenon might affect a study design commonly used to estimate influenza vaccine effectiveness (VE). We searched publications in MEDLINE, PubMed, and Web of Science. We identified 12 studies using the test-negative design (2011-2017) that reported VE estimates separately derived by 3 alternative control groups: 1) all patients testing negative for influenza (FLU), VEFLU-; 2) patients who tested positive for other/another respiratory virus (ORV), VEORV+; and 3) patients who tested negative for all viruses in the panel (PAN), VEPAN-. These included VE estimates from 7 countries for all age groups from 2003/2004 to 2013/2014. We observed no difference in vaccination coverage between the ORV-positive and PAN-negative control groups. A total of 63 VEFLU- estimates, 62 VEORV+ estimates, and 33 VEPAN- estimates were extracted. Pooled estimates of the difference in VE ( $\Delta$ VE) were very similar between groups. In meta-regression, no association was found between the selection of

control group and VE estimates. In conclusion, we did not find any differences in VE estimates based on the choice of control group.

**Database:** Medline

**17. Immunogenicity and safety of the first indigenously developed Indian tetravalent influenza vaccine (split virion) in healthy adults  $\geq$  18 years of age: A randomized, multicenter, phase II / III clinical trial.**

**Author(s):** Sharma, Shrikant; Singh, Veer Bahadur; Kumar, Sanjay; Prajapati, Vipul; Patel, Jitendra; Vukkala, Rajesh; Jangid, Sanjay Kumar; Sanmukhani, Jayesh; Gupta, Gaurav; Patel, Pradip; Mittal, Ravindra; Glueck, Reinhard

**Source:** Human vaccines & immunotherapeutics; Feb 2018 ; p. 1-8

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29461913

**Abstract:** This phase II / III clinical trial was conducted to evaluate the immunogenicity and safety of the Tetravalent Influenza vaccine (Split virion) I.P. (TetIV) developed indigenously in the country for the first time by M/s Cadila Healthcare Limited, India containing two influenza A and two influenza B strains, one of each, Yamagata (B/Phuket) and Victoria (B/Brisbane) lineage and also compare it to that of an licensed seasonal Trivalent Influenza vaccine (TriIV) of Sanofi Pasteur India Private Limited, containing the two influenza A and only the Yamagata lineage (B/Phuket) strain. Three hundred and fifty subjects of either sex, aged more than 18 years of age, were randomized in a 1:1 ratio to receive either the TetIV or TriIV. Immunogenicity assessments (antibody against A/H1N1, A/H3N2, B/Phuket and B/Brisbane) were done by Haemagglutination Inhibition assay at baseline and 21 d after vaccination. Solicited (local and systemic) and unsolicited adverse events were recorded for up to 42 d following vaccination. The TetIV was found to fulfill the criteria set by the European and the US regulatory authorities and WHO guidance on the requirements of clinical data for licensure of seasonal inactivated influenza vaccines. The seroconversion rates with TetIV were 93.5% for A/H1N1, 90.0% for A/H3N2, 70.0% for B/Phuket and 82.9% for B/Brisbane strain. There was no significant difference in the seroconversion and seroprotection rates at day 21 for A/H1N1, A/H3N2 and B/Phuket in the two groups while the TetIV was superior to the TrivIV for the seroconversion and the seroprotection rate for the B/Brisbane strain (Victoria lineage). Both the vaccines were well tolerated by all the study participants; addition of the fourth strain in the TetIV did not compromise the safety as compared to TriIV. The most common systemic adverse event reported in both the groups was headache followed by fever.

**Database:** Medline

**18. Safety and immunogenicity of the novel seasonal preservative- and adjuvant-free influenza vaccine: Blind, randomized, and placebo-controlled trial.**

**Author(s):** Sarsenbayeva, Gulbanu; Volgin, Yevgeniy; Kassenov, Markhabat; Issagulov, Timur; Bogdanov, Nikolay; Sansyzbay, Abylay; Abitay, Ruslan; Nurpeisova, Ainur; Sagymbay, Altynay; Koshemetov, Zhumagali; Stukova, Marina; Buzitskaya, Zhanna; Kulmagambetov, Ilyas; Karabayeva, Dinara; Davlyatshin, Timur; Khairullin, Berik

**Source:** Journal of medical virology; Jan 2018; vol. 90 (no. 1); p. 41-49

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 28842994

**Abstract:**The producers of influenza vaccines are not capable today to meet the global demand for an influenza vaccine in case of pandemic, so the World Health Organization recommends to develop the own influenza vaccine production in each country. A domestic preservative- and adjuvant-free trivalent split vaccine against seasonal influenza was developed at the Research Institute for Biological Safety Problems. The paper presents the results of assessing safety and immunogenicity of the influenza split vaccine after single immunization of healthy volunteers aged 18-50 years in the course of Phase I Clinical Trials. This study was randomized, blind, and placebo-controlled. The volunteers were intramuscularly vaccinated with a dose of split vaccine or placebo. The study has shown that all local and systemic reactions had low degree of manifestation and short-term character, so there was no need in medication. Serious side effects were not observed. On day 21 post vaccination the portion of vaccinated persons with fourfold seroconversions to influenza A/H1N1pdm09 virus was 100.0%, to influenza A/H3N2 virus-95.5%, to influenza B virus-81.8%, and in placebo group this index was 0%. Seroprotection rates against influenza A/H1N1pdm09, A/H3N2 and B viruses were 95.5, 86.3, and 72.7%, respectively. Geometric mean titers (GMT) of antibodies by day 21 post vaccination reached 175.7 for influenza A/H1N1pdm09 virus, 64.2 for influenza A/H3N2 virus, and 37.6 for influenza B virus; in placebo group GMT growth was not observed. So, the seasonal influenza split vaccine is well tolerated and fits all immunogenicity criteria for human influenza vaccines.

**Database:** Medline

### **19. Preventive Effects of Vitamin D on Seasonal Influenza A in Infants: A Multicenter, Randomized, Open, Controlled Clinical Trial.**

**Author(s):** Zhou, Jian; Du, Juan; Huang, Leting; Wang, Youcheng; Shi, Yimei; Lin, Hailong

**Source:** The Pediatric infectious disease journal; Jan 2018

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29315160

**Abstract:**OBJECTIVE This study aimed to evaluate the clinical efficacy and safety of vitamin D for preventing influenza A in 400 infants in a multicenter, randomized, open, controlled clinical trial. METHOD The infants were randomized into low-dose and high-dose vitamin D groups, and serum calcium, inorganic phosphorus and 25-hydroxyvitamin D levels were detected thrice in 4 months. Infants infected with influenza A were monitored for symptoms including fever, cough, and wheezing. Pathogen levels and safety of vitamin D treatment were also evaluated. RESULTS Of 121 cases in total, 78 and 43 cases of influenza A infection occurred in the low-dose and high-dose vitamin D groups, respectively. There was a significant difference between the groups ( $\chi = 14.6324$ ,  $P = 0.0001$ ). Among the cases of influenza infection, the median durations for fever, cough, and wheezing were shorter in the high-dose vitamin D group than in the low-dose vitamin D group. The viral loads showed a downward trend in both groups, and were significantly different between the groups at the second and third detections. Additionally, the incidences of adverse events and severe adverse events were very low and not significantly different between the two groups. CONCLUSION High-dose vitamin D (1200 IU) is suitable for the prevention of seasonal influenza as evidenced by rapid relief from symptoms, rapid decrease in viral loads, and disease recovery. In addition, high-dose vitamin D is probably safe for infants. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

**Database:** Medline

**20. The risk of lower respiratory tract infection following influenza virus infection: A systematic and narrative review.**

**Author(s):** Malosh, Ryan E; Martin, Emily T; Ortiz, Justin R; Monto, Arnold S

**Source:** Vaccine; Jan 2018; vol. 36 (no. 1); p. 141-147

**Publication Date:** Jan 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29157959

Available at [Vaccine](#) - from ProQuest (Hospital Premium Collection) - NHS Version

Available at [Vaccine](#) - from PubMed Central

**Abstract:**BACKGROUND Lower respiratory tract infections (LRTI) are a major cause of morbidity and mortality worldwide, particularly in young children and older adults. Influenza is known to cause severe disease but the risk of developing LRTI following influenza virus infection in various populations has not been systematically reviewed. Such data are important for estimating the impact specific influenza vaccine programs would have on LRTI outcomes in a community. We sought to review the published literature to determine the risk of developing LRTI following an influenza virus infection in individuals of any age. METHODS AND FINDINGS We conducted a systematic review to identify prospective studies that estimated the incidence of LRTI following laboratory-confirmed influenza virus infection. We searched PubMed, Medline, and Embase databases for relevant literature. We supplemented this search with a narrative review of influenza and LRTI. The systematic review identified two prospective studies that both followed children less than 5 years. We also identified one additional pediatric study from our narrative review meeting the study inclusion criteria. Finally, we summarized recent case-control studies on the etiology of pneumonia in both adults and children. CONCLUSIONS There is a dearth of prospective studies evaluating the risk of developing LRTI following influenza virus infection. Determining the burden of severe LRTI that is attributable to influenza is necessary to estimate the benefits of influenza vaccine on this important public health outcome. Vaccine probe studies are an efficient way to evaluate these questions and should be encouraged going forward.

**Database:** Medline

**21. Risk factors for serious outcomes associated with influenza illness in high- versus low- and middle-income countries: Systematic literature review and meta-analysis**

**Author(s):** Coleman B.L.; Fadel S.A.; Fitzpatrick T.; Thomas S.-M.

**Source:** Influenza and other Respiratory Viruses; Jan 2018; vol. 12 (no. 1); p. 22-29

**Publication Date:** Jan 2018

**Publication Type(s):** Article

Available at [Influenza and Other Respiratory Viruses](#) - from Wiley Online Library Free Content - NHS

Available at [Influenza and Other Respiratory Viruses](#) - from Europe PubMed Central - Open Access

Available at [Influenza and Other Respiratory Viruses](#) - from EBSCO (MEDLINE Complete)

Available at [Influenza and Other Respiratory Viruses](#) - from PubMed Central

**Abstract:**Aim: To determine factors associated with a serious outcome (hospital admission or severe outcome: critical care or death) and associated with illness caused by laboratory-confirmed influenza, with a specific interest in low- and middle-income countries (LMIC). Method: Databases

were searched on 11 March 2016 for reports of influenza and factors associated with mortality or morbidity in humans, with no language restrictions. Pooled risks were estimated using random-effects models. Results: Despite the heterogeneity of results across studies, known risk factors for serious disease were associated with both hospital admission and severe outcomes (critical care and/or death). In LMIC, but not in high income countries (HIC), pregnant women, people with HIV/AIDS and children < 5 years old (compared with older children) were at increased risk of a severe outcome. Also, although all patients with neurological conditions were at higher risk of severe outcomes than those without, children were at higher risk than adults and children who lived in a LMIC were at significantly higher risk than those living in HIC. Adults were more likely than children to suffer a severe outcome if they had diabetes or a hematologic condition, were obese or had liver disease. Asthma is a risk factor for hospital admission but not for severe outcomes. Conclusion: Known risk factors for serious disease remain important predictors of hospital admission and severe outcomes with few differences between HIC and LMIC countries. These differences likely reflect differences in health-seeking behaviours and health services, but high heterogeneity between studies limits conclusions about the effect size.

**Database:** EMBASE

## Norovirus

### 1. Risk factors for hospital norovirus outbreaks: impact of vomiting, genotype, and multi-occupancy rooms

**Author(s):** Fraenkel C.J.; Johansson P.J.H.; Inghammar M.; Soderlund-Strand A.; Bottiger B.

**Source:** Journal of Hospital Infection; Apr 2018; vol. 98 (no. 4); p. 398-403

**Publication Date:** Apr 2018

**Publication Type(s):** Article

**Abstract:**Background: Norovirus is frequently introduced to the hospital and is a frequent cause of hospital outbreaks. Recognition of the factors that facilitate or impede norovirus transmission is an important step to effectively prevent hospital outbreaks. Aim: To investigate risk factors for norovirus outbreaks in hospital settings. Methods: Clinical data, ward setting, and norovirus genotype were collected from all 65 norovirus-positive index cases in outbreaks and all 186 sporadic norovirus cases at 192 wards in southern Sweden during 2010-2012 in a nested case-control study. Uni- and multivariate statistical analyses were conducted. Findings: Outbreak was independently associated with the number of patients sharing a room with the norovirus case (odds ratio (OR): 1.9 per additional patient in the room;  $P < 0.01$ ), vomiting (OR: 2.6;  $P = 0.04$ ), age >80 years (OR: 3.2;  $P < 0.01$ ), comorbidity (OR: 2.3;  $P = 0.05$ ), and onset of symptoms after admission to the ward (OR: 3.5;  $P < 0.01$ ) in the multivariate analysis. Infection with genotype GII.4 was found to be strongly associated with outbreak in the univariate analysis (OR: 5.7;  $P < 0.01$ ). Moreover, associations between GII.4 and vomiting (OR: 2.5;  $P = 0.01$ ) and old age (OR: 4.3;  $P < 0.01$ ) were found. Conclusion: This is the first study to investigate clinical, ward and genotype risk factors for norovirus hospital outbreaks. Recognition of these factors may help direct and prioritize infection control actions based on the outbreak risk. The results also suggest that the outbreak association with GII.4 partly may be explained by an enhanced ability to induce vomiting. Copyright © 2018 The Healthcare Infection Society

**Database:** EMBASE

## 2. Norovirus Illnesses in Children and Adolescents

**Author(s):** Shah M.P.; Hall A.J.

**Source:** Infectious Disease Clinics of North America; Mar 2018; vol. 32 (no. 1); p. 65-74

**Publication Date:** Mar 2018

**Publication Type(s):** Review

**Abstract:** Norovirus is a leading cause of childhood vomiting and diarrhea in the United States and globally. Although most illnesses caused by norovirus are self-resolving, severe outcomes may occur from dehydration, including hospitalization and death. A vast majority of deaths from norovirus occur in developing countries. Immunocompromised children are at risk for more severe outcomes. Treatment of norovirus illness is focused on early correction of dehydration and maintenance of fluid status and nutrition. Hand hygiene, exclusion of ill individuals, and environmental cleaning are important for norovirus outbreak prevention and control, and vaccines to prevent norovirus illness are currently under development.

**Database:** EMBASE

## 3. Estimating the Hospital Burden of Norovirus-Associated Gastroenteritis in England and its Opportunity Costs for Non-Admitted Patients.

**Author(s):** Sandmann, Frank G; Shallcross, Laura; Adams, Natalie; Allen, David J; Coen, Pietro G; Jeanes, Annette; Kozlakidis, Zisis; Larkin, Lesley; Wurie, Fatima; Robotham, Julie V; Jit, Mark; Deeny, Sarah R

**Source:** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Feb 2018

**Publication Date:** Feb 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29529135

**Abstract:** Background Norovirus places a substantial burden on healthcare systems, arising from infected patients, disease outbreaks, beds kept unoccupied for infection control, and staff absences due to infection. In settings with high rates of bed occupancy, opportunity costs arise from patients who cannot be admitted due to beds being unavailable. With several treatments and vaccines against norovirus in development, quantifying the expected economic burden is timely. Methods The number of inpatients with norovirus-associated gastroenteritis in England were modelled using infectious and non-infectious gastrointestinal Hospital Episode Statistics codes and laboratory reports of gastrointestinal pathogens collected at Public Health England. The excess length of stay from norovirus was estimated with a multi-state model and local outbreak data. Unoccupied bed-days and staff absences were estimated from national outbreak surveillance. The burden was valued conventionally using accounting expenditures and wages, which we contrasted to the opportunity costs from forgone patients using a novel methodology. Results Between July 2013 and June 2016, 17.7% (95%-confidence interval: 15.6%–21.6%) of primary and 23.8% (20.6%–29.9%) of secondary gastrointestinal diagnoses were norovirus-attributable. Annually, the estimated median 290,000 (interquartile range: 282,000–297,000) occupied and unoccupied bed-days used for norovirus displaced 57,800 patients. Conventional costs for the National Health Service reached £107.6 million; the economic burden approximated to £297.7 million and a loss of 6,300 quality-adjusted life years annually. Conclusions In England, norovirus is now the second-largest contributor of the gastrointestinal hospital burden. With the projected impact being greater than previously estimated, improved capture of relevant opportunity costs seems imperative for diseases like norovirus.

**Database:** Medline

#### 4. The unwelcome houseguest: Secondary household transmission of norovirus

**Author(s):** Marsh Z.A.; Grytdal S.P.; Leshem E.; Gastanaduy P.A.; Rha B.; Lopman B.A.; Hall A.J.; Beggs J.C.; Nyaku M.

**Source:** Epidemiology and Infection; Jan 2018; vol. 146 (no. 2); p. 159-167

**Publication Date:** Jan 2018

**Publication Type(s):** Article

Available at [Epidemiology and Infection](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:** Norovirus is the leading cause of acute gastroenteritis in the USA. Although secondary household transmission of norovirus is frequently reported in outbreaks, little is known about specific risk factors for susceptibility and infectiousness in the household. Three norovirus outbreaks were investigated and data were collected on individuals exposed in the primary outbreak setting and their household members. Potential individual- and household-level risk factors for susceptibility and infectiousness were assessed using univariate and multivariate generalised linear mixed models. In the univariate models, the secondary attack rate (SAR) was significantly higher when living in a household with two or more primary cases (incidence rate ratio (IRR) = 2.1; 95% confidence interval (CI) 1.37-3.29), more than one primary case with vomiting (IRR = 1.9; CI 1.11-3.37), and at least one primary case with diarrhoea (IRR = 3.0; CI 1.46-6.01). After controlling for other risk factors in the multivariate models, the SAR was significantly higher among those living in a household with two or more primary cases (adjusted IRR = 2.0; CI 1.17-3.47) and at least one primary case with diarrhoea (adjusted IRR = 2.8; CI 1.35-5.93). These findings underscore the importance of maintaining proper hygiene and isolating ill household members to prevent norovirus transmission in the household.

**Database:** EMBASE

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