Outreach

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Contents

1: Tables of Contents from October’s Respiratory journals

2: Latest relevant Systematic Reviews from the Cochrane Library.

3: NHS Behind the Headlines

4: Current Awareness database articles
Tables of Contents from Respiratory journals

The links below will take you to the full Tables of Contents.

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Thorax
October 2015, Volume 70, Issue 10

Chest
October 2015, Volume 148, Issue 4

European Respiratory Journal
October 2015, Volume 46, Issue 4

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The BIG 4 Bulletin
Latest relevant Systematic Reviews from the Cochrane Library

Beta2-agonists for acute cough or a clinical diagnosis of acute bronchitis

Macrolides for chronic asthma

NHS Behind the Headlines

Smoking linked to raised diabetes risk – including passive smoking

Friday Sep 18 2015

"Passive smoking raises risk of type 2 diabetes," The Guardian reports. A major new analysis of previous studies found a significant association between exposure to tobacco smoke – including secondhand smoke – and type 2 diabetes…

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October (12pm)
Thurs 8th Statistics
Fri 16th Literature Searching
Mon 19th Understanding articles
Tues 27th Statistics

November (1pm)
Wed 4th Literature Searching
Thurs 12th Understanding articles
Fri 20th Statistics
Mon 23rd Literature Searching
**Title:** Proteomic analysis of ofloxacin-mono resistant Mycobacterium tuberculosis isolates.  
**Citation:** Journal of proteomics, Sep 2015, vol. 127, p. 114-121 (September 8, 2015)  
**Author(s):** Lata, Manju, Sharma, Divakar, Deo, Nirmala, Tiwari, Pramod Kumar, Bisht, Deepa, Venkatesan, Krishnamurthy

**Abstract:** Drug resistance particularly, multi drug resistance tuberculosis (MDR-TB) has emerged as a major problem in the chemotherapy of tuberculosis. Ofloxacin (OFX) has been used as second-line drug against MDR-TB. The principal target of the OFX is DNA gyrase encoded by gyrA and gyrB genes. Many explanations have been proposed for drug resistance to OFX but still some mechanisms are unknown. As proteins manifest most of the biological processes, these are attractive targets for developing drugs and diagnostics/therapeutics. We examined the OFX resistant Mycobacterium tuberculosis isolates by proteomic approach (2DE-MALDI-TOF-MS) and bioinformatic tools under OFX induced conditions. Our study showed fourteen proteins (Rv0685, Rv0363c, Rv2744c, Rv3803c, Rv2534c, Rv2140c, Rv1475c, Rv0440, Rv2245, Rv1436, Rv3551, Rv0148, Rv2882c and Rv0733) with increased intensities in OFX resistant and OFX induced as compared to susceptible isolates. Bioinformatic analysis of hypothetical proteins (Rv2744c, Rv2140c, Rv3551 and Rv0148) revealed the presence of conserved motifs and domains. Molecular docking showed proper interaction of OFX with residues of conserved motifs. These proteins might be involved in the OFX modulation/neutralization and act as novel resistance mechanisms as well as potential for diagnostics and drug targets against OFX resistance. This article is part of a Special Issue entitled: Proteomics in India. Copyright © 2015 Elsevier B.V. All rights reserved.

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**Title:** Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis.  
**Citation:** Cold Spring Harbor perspectives in medicine, Sep 2015, vol. 5, no. 9 (September 2015)  
**Author(s):** Seung, Kwonjune J, Keshavjee, Salmaan, Rich, Michael L

**Abstract:** The continuing spread of drug-resistant tuberculosis (TB) is one of the most urgent and difficult challenges facing global TB control. Patients who are infected with strains resistant to isoniazid and rifampicin, called multidrug-resistant (MDR) TB, are practically incurable by standard first-line treatment. In 2012, there were approximately 450,000 new cases and 170,000 deaths because of MDR-TB. Extensively drug-resistant (XDR) TB refers to MDR-TB strains that are resistant to fluoroquinolones and second-line injectable drugs. The main causes of the spread of resistant TB are weak medical systems, amplification of resistance patterns through incorrect treatment, and transmission in communities and facilities. Although patients harboring MDR and XDR strains present a formidable challenge for treatment, cure is often possible with early identification of resistance and use of a properly designed regimen. Community-based programs can improve treatment outcomes by allowing patients to be treated in their homes and addressing socioeconomic barriers to adherence. Copyright © 2015 Cold Spring Harbor Laboratory Press; all rights reserved.

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**Title:** Limited sampling strategies for therapeutic drug monitoring of amikacin and kanamycin in patients with multidrug-resistant tuberculosis.
Amikacin and kanamycin are considered important and effective drugs in the treatment of multidrug-resistant tuberculosis (MDR-TB). Unfortunately, the incidence of toxicity is high and is related to elevated drug exposure. In order to achieve a balance between efficacy and toxicity, a population pharmacokinetic (PPK) model may help to optimize drug exposure. Patients with MDR-TB who had received amikacin or kanamycin as part of their treatment and who had routinely received therapeutic drug monitoring were evaluated. A PPK model was developed and subsequently validated. Using this model, a limited sampling model was developed. Eleven patients receiving amikacin and nine patients receiving kanamycin were included in this study. The median observed 24-h area under the concentration-time curve (AUC0\textsubscript{24h}) was 77.2mg/L (IQR 64.7-96.2mg/L) for amikacin and 64.1mg/L (IQR 55.6-92.1mg/L) for kanamycin. The PPK model was developed and validated using n-1 cross-validation. A robust population model was developed that is suitable for predicting the AUC0\textsubscript{24h} of amikacin and kanamycin. This model, in combination with the limited sampling strategy developed, can be used in daily routine to guide dosing but also to assess AUC0\textsubscript{24h} in phase 3 studies. Copyright © 2015 Elsevier B.V. and the International Society of Chemotherapy. All rights reserved.

Tuberculosis (TB) is an infectious bacterial disease that has historically created a high global health burden. Unfortunately, the emergence of drug-resistant TB (DR-TB), which includes multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), has greatly affected the treatment of TB. Anti-TB chemotherapy drugs are classified into five groups to facilitate application of effective guidelines for the treatment regimen. However, chemotherapy has a limited ability to treat DR-TB, and therefore a novel alternative treatment for DR-TB is required. In this review, we focused on photodynamic therapy (PDT) as potential treatment for DR-TB. PDT is a widely used cancer treatment that combines photosensitizers and harmless laser light to produce reactive oxygen species that selectively damage the target cells. Initially, PDT was originally developed to target pathogenic microorganisms but fell into disuse because of adverse reactions. Recently, photodynamic antimicrobial chemotherapy is attracting attention again as an alternative treatment for bacterial infections. In our previous study, we suggested that PDT could be a novel option to treat MDR- and XDR-TB in vitro. Despite the limited previous studies regarding PDT in TB models, fast-developing bronchoscopic technologies and clinician experience will soon facilitate the clinical application of safe and minimally invasive PDT for TB. Copyright © 2015 Elsevier B.V. All rights reserved.

Costs to Health Services and the Patient of Treating Tuberculosis: A Systematic Literature Review.

Title: Costs to Health Services and the Patient of Treating Tuberculosis: A Systematic Literature Review.
Citation: PharmacoEconomics, Sep 2015, vol. 33, no. 9, p. 939-955 (September 2015)
Author(s): Laurence, Yoko V, Griffiths, Ulla K, Vassall, Anna
Abstract: Novel tuberculosis (TB) drugs and the need to treat drug-resistant tuberculosis (DR-TB) are likely to bring about substantial transformations in TB treatment in coming years. An evidence base for cost and cost-effectiveness analyses of these developments is needed. Our objective was to perform a review of papers assessing provider-incurred as well as patient-incurred costs of treating both drug-susceptible (DS) and multidrug-resistant (MDR)-TB. Five databases (EMBASE, Medline, the National Health Service Economic Evaluation Database, the Cost-Effectiveness Analysis Registry, and Latin American and Caribbean Health Services Literature) were searched for cost and economic evaluation full-text papers containing primary DS-TB and MDR-TB treatment cost data published in peer-reviewed journals between January 1990 and February 2015. No language restrictions were set. The search terms were a combination of 'tuberculosis', 'multidrug-resistant tuberculosis', 'cost', and 'treatment'. In the selected papers, study methods and characterisitics, quality indicators and costs were extracted into summary tables according to pre-defined criteria. Results were analysed according to country income groups and for provider costs, patient costs and productivity losses. All values were converted to $US, year 2014 values, so that studies could be compared. We selected 71 treatment cost papers on DS-TB only, ten papers on MDR-TB only and nine papers that included both DS-TB and MDR-TB. These papers provided evidence on the costs of treating DS-TB and MDR-TB in 50 and 16 countries, respectively. In 31 % of the papers, only provider costs were included; 26 % included only patient-incurred costs, and the remaining 43 % estimated costs incurred by both. From the provider perspective, mean DS-TB treatment costs per patient were US$14,659 in high-income countries (HICs), US$840 in upper middle-income countries (UMICs), US$273 in lower middle-income (LMICs), and US$258 in low-income countries (LICs), showing a strong positive correlation. The respective costs for treating MDR-TB were US$83,365, US$5284, US$6313 and US$1218. Costs incurred by patients when seeking treatment for DS-TB accounted for an additional 3 % of the provider costs in HICs. A greater burden was seen in the other income groups, increasing the costs of DS-TB treatment by 72 % in UMICs, 60 % in LICs and 31 % in LMICs. When provider costs, patient costs and productivity losses were combined, productivity losses accounted for 16 % in HICs, 29 % in UMICs, 40 % in LMICs and 38 % in LICs. Cost data for MDR-TB treatment are limited, and the variation in delivery mechanisms, as well as the rapidly evolving diagnosis and treatment regimens, means that it is essential to increase the number of studies assessing the cost from both provider and patient perspectives. There is substantial evidence available on the costs of DS-TB treatment from all regions of the world. The patient-incurred costs illustrate that the financial burden of illness is relatively greater for patients in poorer countries without universal healthcare coverage.

Title: ABCs of asthma inhaler and device training
Citation: International Forum of Allergy and Rhinology, September 2015, vol./is. 5/(S71-S75), 2042-6976;2042-6984 (01 Sep 2015)
Author(s): Boise E., Rotella M.

Abstract: Background: The impact of poor adherence and medication administration is well documented, as are the difficulties with asthma inhaler and device usage. However, difficulties with these devices and inhalers continue to present significant challenges to many healthcare providers and patients. Methods: A systematic review of the published, peer-reviewed international literature was performed to identify likely teaching needs as well as available and recommended resources to address same. Results: Asthma inhaler and device use and educational needs vary as widely as do the types and severity of usage errors committed. Multiple interventions have been studied and found to be effective at improving both patient technique and overall asthma outcomes. Conclusion: Providers must ensure that patient teaching is performed by suitably prepared staff members. Education should be device-specific, patient-centered, and repeated at frequent intervals. Providers must frequently reassess patient understanding and ability with regard to asthma inhalers and devices in order to maximize therapeutic outcomes.
Title: Systematic review of mutations in pyrazinamidase associated with pyrazinamide resistance in mycobacterium tuberculosis clinical isolates

Citation: Antimicrobial Agents and Chemotherapy, September 2015, vol./is. 59/9(5267-5277), 0066-4804;1098-6596 (01 Sep 2015)

Author(s): Ramirez-Busby S.M., Valafar F.

Abstract: Pyrazinamide (PZA) is an important first-line drug in the treatment of tuberculosis (TB) and of significant interest to the HIV-infected community due to the prevalence of TB-HIV co-infection in some regions of the world. The mechanism of resistance to PZA is unlike that of any other anti-TB drug. The gene pncA, encoding pyrazinamidase (PZase), is associated with resistance to PZA. However, because single mutations in PZase have a low prevalence, the individual sensitivities are low. Hundreds of distinct mutations in the enzyme have been associated with resistance, while some only appear in susceptible isolates. This makes interpretation of molecular testing difficult and often leads to the simplification that any PZase mutation causes resistance. This systematic review reports a comprehensive global list of mutations observed in PZase and its promoter region in clinical strains, their phenotypic association, their global frequencies and diversity, the method of phenotypic determination, their MIC values when given, and the method of MIC determination and assesses the strength of the association between mutations and phenotypic resistance to PZA. In this systematic review, we report global statistics for 641 mutations in 171 (of 187) codons from 2,760 resistant strains and 96 mutations from 3,329 susceptible strains reported in 61 studies. For diagnostics, individual mutations (or any subset) were not sufficiently sensitive. Assuming similar error profiles of the 5 phenotyping platforms included in this study, the entire enzyme and its promoter provide a combined estimated sensitivity of 83%. This review highlights the need for identification of an alternative mechanism(s) of resistance, at least for the unexplained 17% of cases.

Title: The Salford Lung Study protocol: A pragmatic, randomised phase III real-world effectiveness trial in chronic obstructive pulmonary disease

Citation: Respiratory Research, September 2015, vol./is. 16/1, 1465-9921;1465-993X (September 04, 2015)


Abstract: Background: New treatments need to be evaluated in real-world clinical practice to account for co-morbidities, adherence and polypharmacy. Methods: Patients with chronic obstructive pulmonary disease (COPD), >40 years old, with exacerbation in the previous 3 years are randomised 1:1 to once-daily fluticasone furoate 100μg/vilanterol 25μg in a novel dry-powder inhaler versus continuing their existing therapy. The primary endpoint is the mean annual rate of COPD exacerbations; an electronic medical record allows real-time collection and monitoring of endpoint and safety data. Conclusions: The Salford Lung Study is the world’s first pragmatic randomised controlled trial of a pre-licensed medication in COPD. Trial registration: Clinicaltrials.gov identifier NCT01551758.

Full Text:
Available from ProQuest in Respiratory Research
Available from BioMed Central in Respiratory Research
Available from National Library of Medicine in Respiratory Research

Title: Tiotropium for the treatment of adolescents with moderate to severe symptomatic asthma: A systematic review with meta-analysis
Citation: Annals of Allergy, Asthma and Immunology, September 2015, vol./is. 115/3(211-216), 1081-1206;1534-4436 (01 Sep 2015)

Author(s): Rodrigo G.J., Castro-Rodriguez J.A.

Abstract: Background: The role of tiotropium for the treatment of adolescents with asthma has not yet been clearly defined. Objective: To assess the efficacy and safety of inhaled tiotropium in adolescents with moderate to severe symptomatic asthma. Methods: Randomized, placebo-controlled trials were included in this systematic review. Primary outcomes were peak and trough forced expiratory volume in 1 second (FEV$_1$). Results: Three studies (approximately 1,000 patients) were included. Tiotropium was associated with significant improvements in FEV$_1$ peak (mean change from baseline) by 120 mL (P < .001) and trough by 100 mL (P < .001) compared with placebo. Tiotropium significantly reduced the percentage of patients who experienced an Asthma Control Questionnaire 7 worsening episode defined as a change from trial baseline of 0.5 points or more compared with placebo (2.1% vs 4.8%, number needed to treat = 38) and also was associated with a significantly decreased in the number of patients with at least one exacerbation compared with placebo (17.6 vs 23.8%, number needed to treat = 16). Finally, no significant differences were found in rescue medication use, withdrawals, withdrawals due to adverse events (AEs), AEs (27.3% vs 27.1%), and serious AEs (6.5% vs 7.1%). Tiotropium in doses of 2.5 mug once daily or 5.0 mug once daily resulted in equivalent effects. Conclusions: Tiotropium was well tolerated and efficacious as an addition to maintenance treatment with an inhaled corticosteroid or an inhaled corticosteroid plus a long-acting beta-agonist in adolescents with moderate to severe asthma. Available data do not suggest an advantage of the 5-mug once-daily dose (used in adults) compared with the 2.5-mug once-daily dose of tiotropium.

Title: The outcome of acute respiratory distress syndrome in relation to body mass index and diabetes mellitus

Citation: Heart and Lung: Journal of Acute and Critical Care, September 2015, vol./is. 44/5(441-447), 0147-9563;1527-3288 (01 Sep 2015)

Author(s): Soubani A.O., Chen W., Jang H.

Abstract: Objective: To determine the 28 day mortality of patients with ARDS in relation to body mass index (BMI) and presence diabetes mellitus (DM). Design: Retrospective cohort study of patients enrolled in the ARDS Network randomized controlled trials. Results: 2914 patients were enrolled in these trials. 112 patients were underweight (BMI < 18.5), 948 patients were normal range (18.5 < BMI < 25.0), 801 patients were overweight (25.0 < BMI < 30.0), 687 patients were obese (30.0 < BMI < 40.0), and 175 patients were severely obese (BMI > 40.0). 469 patients had DM. There was no significant difference in the 28 day mortality in relation to BMI or presence of DM (underweight adjusted OR, 1.217; 95% CI, 0.749-1.979; overweight adjusted OR, 0.887; 95% CI, 0.696-1.131; obese adjusted OR, 0.812; 95% CI, 0.624-1.056; severely obese adjusted OR, 1.102; 95% CI, 0.716-1.695; and DM adjusted OR, 0.938; 95% CI, 0.728-1.208). Conclusions: The short term mortality in patients with ARDS is not affected by BMI or the presence of DM.

Title: Risk factors for asthma: Is prevention possible?

Citation: The Lancet, September 2015, vol./is. 386/9998(1075-1085), 0140-6736;1474-547X (12 Sep 2015)

Author(s): Beasley R., Semprini A., Mitchell E.A.

Abstract: Asthma is one of the most common diseases in the world, resulting in a substantial burden of disease. Although rates of deaths due to asthma worldwide have reduced greatly over the past 25
years, no available therapeutic regimens can cure asthma, and the burden of asthma will continue to be driven by increasing prevalence. The reasons for the increase in asthma prevalence have not been defined, which limits the opportunities to develop targeted primary prevention measures. Although associations are reported between a wide range of risk factors and childhood asthma, substantiation of causality is inherently difficult from observational studies, and few risk factors have been assessed in primary prevention studies. Furthermore, none of the primary prevention intervention strategies that have undergone scrutiny in randomised controlled trials has provided sufficient evidence to lead to widespread implementation in clinical practice. A better understanding of the factors that cause asthma is urgently needed, and this knowledge could be used to develop public health and pharmacological primary prevention measures that are effective in reducing the prevalence of asthma worldwide. To achieve this it will be necessary to think outside the box, not only in terms of risk factors for the causation of asthma, but also the types of novel primary prevention strategies that are developed, and the research methods used to provide the evidence base for their implementation. In the interim, public health efforts should remain focused on measures with the potential to improve lung and general health, such as: reducing tobacco smoking and environmental tobacco smoke exposure; reducing indoor and outdoor air pollution and occupational exposures; reducing childhood obesity and encouraging a diet high in vegetables and fruit; improving feto-maternal health; encouraging breastfeeding; promoting childhood vaccinations; and reducing social inequalities.

Full Text:
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Title: Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with chronic respiratory conditions
Citation: General Hospital Psychiatry, September 2015, vol./is. 37/5(399-407), 0163-8343;1873-7714 (01 Sep 2015)
Author(s): Ho S.Y., Alnashri N., Rohde D., Murphy P., Doyle F.

Abstract: Objective: To systematically review the impact of depression on subsequent smoking cessation in prospective studies of chronic respiratory patients. Method: A systematic search of electronic databases (MEDLINE, PsycINFO, CINAHL) was conducted to identify prospective studies of chronic respiratory patients that measured depression at baseline and smoking status at follow-up, dating from 1st January 1990 to 21st February 2014. The standardized mean difference (SMD) and 95% confidence interval (CI) for the association between baseline depressive symptoms and subsequent smoking cessation was estimated from available data using random effects meta-analysis. Results: A total of 1314 citations were retrieved and 197 articles were further evaluated by two reviewers. Seven articles provided sufficient data to estimate the association between depressive symptoms and subsequent smoking cessation. Those with elevated depressive symptoms were significantly less likely to quit smoking at follow-up than those not reporting elevated depressive symptoms (SMD=-.31, 95% CI -.43 to -.19; I<sup>2</sup>=0%, P =506). Conclusions: The association between depression and subsequent smoking was poorly reported or omitted in most studies. However, the available evidence suggests that depression decreases the likelihood that patients with chronic respiratory conditions will quit smoking. Future research is needed to determine how best to manage depression and smoking cessation in this population.

Title: Vitamin D deficiency is associated with the severity of COPD: A systematic review and meta-analysis
Abstract: Purpose: To explore the association between host serum 25-hydroxyvitamin D (25(OH)D) and the susceptibility and severity of COPD. Methods: Previous studies on the association between host 25(OH)D and the susceptibility and severity of COPD were collected on the basis of a systematic literature search of PubMed and Web of Science up to June 2015. Continuous variable data were presented as standard mean difference (SMD) or weighted mean difference with 95% confidence interval (CI). The dichotomous variable data were analyzed as relative ratio (RR) or odds ratio with 95% CI for cohort and case-control studies. A systematic review was conducted to understand the curative and side effects of vitamin D intake. Results: A total of 18 studies including eight cohort, five case-control, and five randomized studies met the inclusion criteria. The serum level of 25(OH)D in COPD patients was comparable with controls with a pooled SMD of 0.191 (95% CI: -0.126 to 0.508, P=0.237) based on pooled analyses of cohort studies. However, the serum level of 25(OH)D in COPD patients was lower with a pooled SMD of 0.961 (95% CI: 0.476-1.446, P<0.001) compared with controls based on pooled analyses of case-control studies. The deficiency rates of 25(OH)D were comparable between controls and COPD patients with a pooled RR of 0.955 (95% CI: 0.754-1.211, P=0.705) based on analyses of cohort studies, and the same results were observed based on pooled analyses of case-control studies. Interestingly, the deficiency rate of 25(OH)D was significantly lower in moderate or severe COPD patients with a pooled RR of 0.723 (95% CI: 0.632-0.828, P<0.001) compared with that in mild COPD patients. The four randomized studies showed that vitamin D intake provided benefit for COPD patients. Conclusion: Low serum levels of 25(OH)D were not associated with COPD susceptibility, but the high deficiency rate of 25(OH)D was associated with COPD severity. Vitamin D supplementation may prevent COPD exacerbation.

Full Text: Available from National Library of Medicine in International Journal of Chronic Obstructive Pulmonary Disease
based doublets as first-line chemotherapy may be related to higher incidence of acute exacerbation-ILD in first line chemotherapy (AE, 8.47%; 95% CrI, 5.04-12.6). The data selection bias and small patient number make the metaanalysis of treatment response and conclusions generated from these data inaccurate. The present meta-analysis suggests that chemotherapy might be an effective therapy for patients with NSCLC-ILD, but it might be associated with higher incidence of acute exacerbation.

Title: Cochrane commentary: Probiotics for prevention of acute upper respiratory infection
Citation: Explore: The Journal of Science and Healing, September 2015, vol./is. 11/5(418-420), 1550-8307;1878-7541 (01 Sep 2015)
Authors: Quick M.

Abstract: Background Probiotics may improve a person's health by regulating their immune function. Some trials have shown that probiotic strains can prevent respiratory infections. Even though the previous version of our review showed benefits of probiotics for acute upper respiratory tract infections (URTIs), several new studies have been published. Objectives To assess the effectiveness and safety of probiotics (any specified strain or dose), compared with placebo, in the prevention of acute URTIs in people of all ages, who are at risk of acute URTIs. Search Methods We searched CENTRAL (2014, Issue 6), MEDLINE (1950 to July week 3, 2014), EMBASE (1974 to July 2014), Web of Science (1900 to July 2014), the Chinese Biomedical Literature Database, which includes the China Biological Medicine Database (from 1978 to July 2014), the Chinese Medicine Popular Science Literature Database (from 2000 to July 2014) and the Masters Degree Dissertation of Beijing Union Medical College Database (from 1981 to July 2014). We also searched the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov for completed and ongoing trials on 31 July 2014. Selection Criteria Randomised controlled trials (RCTs) comparing probiotics with placebo to prevent acute URTIs. Data Collection and Analysis Two review authors independently assessed the eligibility and quality of trials, and extracted data using the standard methodological procedures expected by The Cochrane Collaboration. Main Results We included 13 RCTs, although we could only extract data to meta-analyze 12 trials, which involved 3720 participants including children, adults (aged around 40 years) and older people. We found that probiotics were better than placebo when measuring the number of participants experiencing episodes of acute URTI [at least one episode: odds ratio (OR): 0.53; 95% CI = 0.37-0.76, P <.001, low quality evidence; at least three episodes: OR: 0.53; 95% CI = 0.36-0.80, P =.002, low quality evidence]; the mean duration of an episode of acute URTI [mean difference (MD): -1.89; 95% CI = -2.03 to -1.75, P <.001, low quality evidence]; reduced antibiotic prescription rates for acute URTIs (OR: 0.65; 95% CI = 0.45-0.94, moderate quality evidence) and cold-related school absence (OR: 0.10; 95% CI = 0.02-0.47, very low quality evidence). Side effects of probiotics were minor and gastrointestinal symptoms were the most common. We found that some subgroups had a high level of heterogeneity when we conducted pooled analyses and the evidence level was low or very low quality. Authors' Conclusions Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTI, the mean duration of an episode of acute URTI, antibiotic use and cold-related school absence. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs. However, the quality of the evidence was low or very low.

Title: Association of vitamin D-binding protein variants with chronic obstructive pulmonary disease: A meta-analysis
Abstract: Gene polymorphism of vitamin D-binding protein (VDBP) correlates with chronic obstructive pulmonary disease (COPD), but the results remain inconclusive. We aimed to explore the association between VDBP gene polymorphism and COPD. We searched MEDLINE, Embase, Web of Science, and China National Knowledge Infrastructure for publications addressing the association between VDBP gene polymorphism and COPD. After qualitative evaluation, randomized controlled trials were pooled using either a fixed- or a random-effect model depending upon the degree of heterogeneity. Eleven studies with 3144 subjects were included. The genotype group-specific component (GC)*1F-1F was significantly associated with COPD in Asians [odds ratio (OR) = 1.73, 95% confidence interval (CI) = 1.07-2.81, P = 0.03], but not in Caucasians (OR = 1.44, 95%CI = 0.57-3.66, P = 0.45). A protective effect of GC*1F-1S was observed in Asians (OR = 0.70, 95%CI = 0.55-0.89, P = 0.03) but not in Caucasians (OR = 0.93, 95%CI = 0.69-1.24, P = 0.61). There was no association of GC*1S-1S, GC*2-1S and GC*1F-2 with COPD. As for alleles, GC*1F was a risk factor, whereas GC*1S was protective against COPD in Asians; GC*2 was not protective. The genotype GC*1F-1F or allele GC*1F was associated with increased susceptibility to COPD in Asians. No protective effect of genotype GC*2-2 against COPD was found. The protective effects of GC*1F-1S and GC*1S were observed in Asians but not in Caucasians. The VDBP gene polymorphism could be a potential marker for screening of COPD.

Title: Safety and efficacy of diaphragm pacing in patients with respiratory insufficiency due to amyotrophic lateral sclerosis (DiPALS): A multicentre, open-label, randomised controlled trial

Abstract: Background: Non-invasive ventilation is part of the standard of care for treatment of respiratory failure in patients with amyotrophic lateral sclerosis (ALS). The NeuRx RA/4 Diaphragm Pacing System has received Humanitarian Device Exemption approval from the US Food and Drug Administration for treatment of respiratory failure in patients with ALS. We aimed to establish the safety and efficacy of diaphragm pacing with this system in patients with respiratory muscle weakness due to ALS. Methods: We undertook a multicentre, open-label, randomised controlled trial at seven specialist ALS and respiratory centres in the UK. Eligible participants were aged 18 years or older with laboratory supported probable, clinically probable, or clinically definite ALS; stable riluzole treatment for at least 30 days; and respiratory insufficiency. We randomly assigned participants (1:1), via a centralised web-based randomisation system with minimisation that balanced patients for age, sex, forced vital capacity, and bulbar function, to receive either non-invasive ventilation plus pacing with the NeuRx RA/4 Diaphragm Pacing System or non-invasive ventilation alone. Patients, carers, and outcome assessors were not masked to treatment allocation. The primary outcome was overall survival, defined as the time from randomisation to death from any cause. Analysis was by intention to treat. This trial is registered, ISRCTN number 53817913. Findings: Between Dec 5, 2011, and Dec 18, 2013, we randomly assigned 74 participants to receive either non-invasive ventilation alone (n=37) or non-invasive ventilation plus diaphragm pacing (n=37). On Dec 18, 2013, the Data Monitoring and Ethics Committee (DMEC) recommended
suspension of recruitment on the basis of overall survival figures. Randomly assigned participants continued as per the study protocol until June 23, 2014, when the DMEC advised discontinuation of pacing in all patients. Follow-up assessments continued until the planned end of the study in December, 2014. Survival was shorter in the non-invasive ventilation plus pacing group than in the non-invasive ventilation alone group (median 110 months [95% CI 83-136] vs 225 months [136-not reached]; adjusted hazard ratio 2.27, 95% CI 1.22-4.25; p=0.009). 28 (76%) patients died in the pacing group and 19 (51%) patients died in the non-invasive ventilation alone group. We recorded 162 adverse events (59 events per person-year) in the pacing group, of which 46 events were serious, compared with 81 events (25 events per person-year) in the non-invasive ventilation alone group, of which 31 events were serious. Interpretation: Addition of diaphragm pacing to standard care with non-invasive ventilation was associated with decreased survival in patients with ALS. Our results suggest that diaphragmatic pacing should not be used as a routine treatment for patients with ALS in respiratory failure. Funding: The National Institute for Health Research Health Technology Assessment Programme; the Motor Neurone Disease Association of England, Wales, and Northern Ireland.

Title: Rationale and design of a comparative effectiveness trial of home- and clinic-based self-management support coaching for older adults with asthma
Citation: Contemporary Clinical Trials, September 2015, vol./is. 44/(103-111), 1551-7144;1559-2030 (September 01, 2015)

Abstract: Older adults with asthma face numerous barriers to effective self-management and asthma control, and experience worse outcomes than younger asthmatics. Yet, there have been no controlled trials of interventions specifically designed to improve their care and outcomes. Through a multi-stakeholder collaboration (patients, academia, community-based organizations, a state department of health, and an advocacy organization) we developed a multi-component asthma self-management support intervention to address the myriad psychosocial, functional, health status, and cognitive barriers to effective asthma self-management in adults ages 60 and older. We are recruiting 425 New Yorkers in Manhattan and the Bronx for a pragmatic randomized controlled trial with 3 arms: the intervention delivered in primary care settings or in their home, or usual care. In the intervention, care coaches use a novel screening tool to identify the specific barriers to asthma control and self-management they experience. Once identified, the coach and patient choose from a menu of actions to address it. The intervention emphasizes efficiency, flexibility, shared decision making and goal setting, communication strategies appropriate for individuals with limited cognition and literacy skills, and ongoing reinforcement and support. Additionally, we introduced asthma-specific enhancements to the electronic health records of all participating clinical practices, including an asthma severity assessment, clinical decision support, and a patient-tailored asthma action plan. Patients will be followed for 12 months and interviewed at baseline, 3, 6, and 12 months and data on emergency department visits and hospitalizations will be obtained through the New York State Statewide Planning and Research Cooperative System.

Title: Smoking cessation interventions for adults aged 50 or older: A systematic review and meta-analysis
Citation: Drug and Alcohol Dependence, September 2015, vol./is. 154/(14-24), 0376-8716;1879-0046 (01 Sep 2015)
Author(s): Chen D., Wu L.-T.

Abstract: Background: The older population size has increased substantially, and a considerable proportion of older adults are cigarette smokers. Quitting smoking is associated with reduced health risk. This review is among the first to quantitatively assess the relative efficacy of types of cessation interventions for smokers aged >50 years. Methods: We conducted searches of the Cochrane Library, Embase, MEDLINE, and PsycINFO to identify smoking cessation studies on adults aged >50 years. Twenty-nine randomized clinical trials met the inclusion criteria. Three main types of interventions were identified. We analyzed relative cessation rates or Risk Ratios (RRs) between the type of intervention groups and the control group by fixed- and random-effects meta-analyses at the study level. We conducted a weighted least squares meta-regression of cessation rates on trial and sample characteristics to determine sources of outcome heterogeneity. Results: Fixed-effects analysis showed significant treatment effects for pharmacological (RR. = 3.18, 95% CI: 1.89-5.36), non-pharmacological (RR. = 1.80, 95% CI: 1.67-1.94), and multimodal interventions (RR. = 1.61, 95% CI: 1.41-1.84) compared with control group. Estimations based on meta-regression suggested that pharmacological intervention (mean point prevalence abstinence rate (PPA). = 26.10%, CI: 15.20-37.00) resembled non-pharmacological (27.97%, CI: 24.00-31.94), and multimodal interventions (36.64%, CI: 31.66-41.62); and non-pharmacological and multimodal interventions had higher PPAs than the control group (18.80%, CI: 14.48-23.12), after adjusting for a number of trial and sample characteristics. Conclusions: A small number of smoking cessation studies examined smokers aged >50 years. Additional research is recommended to determine smoking cessation efficacy for diverse older population groups (e.g., ethnic minorities).
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