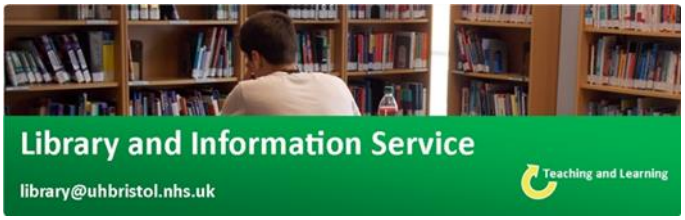
University Hospitals Bristol NHS
NHS Foundation Trust

TB Clinic

Evidence Update

August 2017 (Quarterly)

Respecting everyone
Embracing change
Recognising success
Working together
Our hospitals.



Training Calendar 2017

All sessions are one hour

August (12.00-13.00)

4th (Fri)	Critical Appraisal
9th (Wed)	Literature Searching
15th (Tues)	Interpreting Statistics
24th (Thurs)	Critical Appraisal

September (13.00-14.00)

Fri 1st	Literature Searching
Mon 4th	Critical Appraisal
Tue 12th	Interpreting Statistics
Wed 20th	Literature Searching
Thu 28th	Critical Appraisal

October (12.00-13.00)

Fri 6th	Interpreting Statistics
Mon 9th	Literature Searching
Tue 17th	Critical Appraisal
Wed 25th	Interpreting Statistics

Contents

Your Outreach Librarian: Jo Hooper

Whatever your information needs, the library is here to help. As your outreach librarian I offer **literature searching services** as well as training and guidance in **searching the evidence** and **critical appraisal** – just email me at library@uhbristol.nhs.uk

OUTREACH: Your Outreach Librarian can help facilitate evidence-based practise for all in the Orthopaedics team, as well as assisting with academic study and research. We can help with **literature searching, obtaining journal articles and books**, and setting up individual **current awareness alerts**. We also offer one-to-one or small group training in **literature searching, accessing electronic journals, and critical appraisal**. Get in touch: library@uhbristol.nhs.uk

LITERATURE SEARCHING: We provide a literature searching service for any library member. For those embarking on their own research it is advisable to book some time with one of the librarians for a one-to-one session where we can guide you through the process of creating a well-focused literature research and introduce you to the health databases access via NHS Evidence.

Updates

NICE National Institute for Health and Care Excellence

Tuberculosis | Treatment summary
Source: British National Formulary for Children - BNFc - 15 August 2017

Tuberculosis | Treatment summary
Source: British National Formulary - BNF - 15 August 2017

BEDAQUILINE | Drug
Source: British National Formulary - BNF - 15 August 2017

DELAMANID | Drug
Source: British National Formulary - BNF - 15 August 2017

MOXIFLOXACIN | Drug
Source: British National Formulary for Children - BNFc - 15 August 2017

MOXIFLOXACIN | Drug
Source: British National Formulary - BNF - 15 August 2017

Compounded Triamicinolone and Moxifloxacin Product for Intravitreal Injection by Guardian Pharmacy Services: Alert to Health Professionals - Serious Adverse Events Reported
Source: US Food and Drug Administration - FDA - 28 July 2017 Read Summary

Tuberculosis: Surrey and Sussex health needs assessment
Source: Public Health England - Source: GOV UK - 03 August 2017

Diagnostic accuracy of nucleic acid amplification tests (NAATs) in urine for genitourinary tuberculosis: a systematic review and meta-analysis
Source: PubMed - 05 June 2017 - Publisher: Bmc Infectious Diseases Read Summary

The strategic framework of tuberculosis control and prevention in the elderly: a scoping review towards End TB targets
Source: PubMed - 01 June 2017 - Publisher: Infectious Diseases Of Poverty Read Summary

Treatment of Latent Tuberculosis Infection: An Updated Network Meta-analysis
01 August 2017 - Publisher: Annals of Internal Medicine Read Summary

Tuberculosis (TB): regional and devolved administration reports
Source: Public Health England - Source: GOV UK - 16 June 2017
Annual regional reports for the recent epidemiology of TB.

Cochrane Library

No relevant up to date evidence

UpToDate®

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

Clinical manifestations and complications of pulmonary tuberculosis
- Primary tuberculosis
- Laboratory findings
- Summary
- TB chest radiograph 1 (Diagnostic Images)

Tuberculosis disease in children
- Treatment
- Clinical manifestations
- Summary and recommendations

Treatment of drug-susceptible pulmonary tuberculosis in HIV-uninfected adults
- Extrapulmonary TB
- Culture-negative TB
- Summary and recommendations

Tuberculosis transmission and control
- Surveillance
- Summary

Natural history, microbiology, and pathogenesis of tuberculosis
- Microbiology
- Pathogenesis
- Summary

Treatment of latent tuberculosis infection in HIV-uninfected adults
- Continuation of LTBI treatment after presumptive treatment for TB disease
- Summary and recommendations

Clinical manifestations, diagnosis, and treatment of miliary tuberculosis
- Molecular tests
- Laboratory findings
- Summary

Epidemiology of tuberculosis
- M. tuberculosis complex
- Summary

KnowledgeShare

What is KnowledgeShare?

Provides regular, targeted, personalised evidence updates to staff, based on their specific professional interests. Subject-specific bulletins can also be produced.

Targeted evidence updates

These are individualised, based on a staff member's interest in particular conditions or lifestyle factors, age groups, settings of care, interventions and management topics.

Collaboration and knowledge sharing

As more library and knowledge services join KnowledgeShare it becomes more powerful for sharing evidence and generating communities of practice.

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Journal Tables of Contents

Click on the hyperlinked journal title or image (+Ctrl) for the most recent tables of contents. If you would like any of these papers in full text then get in touch: library@uhbristol.nhs.uk

European Respiratory Journal

August 2017; volume 50, issue 2

Thorax

September 2017; Volume 72, issue 9

Recent Database Articles related to Tuberculosis Treatment

Below is a selection of articles related to orthopaedics recently added to the healthcare databases.

Drugs and Multidrug-resistance

Prevalence and Molecular Characterization of Second-Line Drugs Resistance among Multidrug-Resistant Mycobacterium tuberculosis Isolates in Southwest of China

Author(s): Hu Y.; Liu J.; Shen J.; Zhu D.M.; Feng X.; Xu L.; He Y.L.; Lu N.; Yang C.; Pang Y.; Wang Y.W.

Source: BioMed Research International; 2017; vol. 2017

Publication Type(s): Article

Available in full text at BioMed Research International - from EBSCOhost

Abstract: This study aimed to investigate the prevalence of multidrug-resistant tuberculosis (MDR-TB) isolates resistant to the second-line antituberculosis drugs (SLDs) and its association with resistant-related gene mutations in Mycobacterium tuberculosis (M.tb) isolates from Southwest of China. There were 81 isolates resistant to at least one of the SLDs among 156 MDR-TB isolates (81/156, 51.9%). The rates of general resistance to each of the drugs were as follows: OFX (66/156, 42.3%), KAN (26/156, 16.7%), CAP (13/156, 8.3%), PTO (11/156, 7.1%), PAS (22/156, 14.1%), and AMK (20/156, 12.8%). Therefore, the most predominant pattern was resistant to OFX compared with other SLDs (P

Knowledge, attitudes and practices about multidrug-resistant tuberculosis (MDR-TB) and preventive therapy among adult and adolescent household contacts of MDR-TB index cases

Author(s): Suryavanshi N.; Gupte N.; Mave V.; Murrill M.; Gupta A.; Hesseling A.; Garcia-Prats A.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract:RATIONALE: Household contacts (HHCs) of multidrug-resistant tuberculosis (MDR-TB) cases are at high risk of infection due to prolonged exposure in shared environments. The importance of preventing transmission is substantiated by poor treatment outcomes, toxic regimens and high social and economic costs of MDR-TB disease. Understanding knowledge, attitudes and practices (KAP) related to MDR-TB among this at-risk population is key to informing targeted interventions and clinical research. METHODS: Within a feasibility study for a multi-site MDR-TB preventive therapy trial, a cross-sectional KAP study of HHCs (>=13 years of age) of adult MDR-TB index cases was conducted at 16 sites in 8 countries: Botswana(1 site), Brazil(1), Haiti(1), India(2), Kenya(1),

Peru(2), South Africa(7) and Thailand(1). HHCs were interviewed using a structured instrument including questions on demographics, education and MDR-TB-related KAP. A composite indicator of MDR-TB knowledge was created, where knowledge was defined as identifying all of the following correctly: Cough >3 weeks is a TB symptom, TB transmission is airborne, MDR-TB is a curable disease, and cure is possible through directly observed therapy (DOT). Attitude and practice questions were analyzed separately. RESULTS: Complete KAP data was available for 741 (99.6%) of 744 consenting HHCs of 278 MDR-TB index cases. Median age of HHCs was 33 years (IQR: 22-49), and 62% were women. HHC education level was 12% with none, 31% primary, 46% secondary and 11% college or higher. Overall, MDR-TB knowledge was demonstrated by 67% of HHCs (Figure). Although 87% of HHCs reported that TB transmission is airborne, 49% also stated that transmission occurs through sharing utensils, 37% by sharing clothes/towels and 22% by touching items in public places. A majority of HHCs (64%) reported concern about being infected with MDR-TB by their diagnosed household member, 24% would be uncomfortable telling family/friends if they were diagnosed with MDR-TB, and 84% stated that someone can die from MDR-TB without proper treatment. If a new MDR-TB preventive therapy existed, HHC willingness to take this medication was high overall (79%) and was more likely with MDR-TB knowledge (90% vs. 56%) and concern about becoming infected (85% vs. 68%). CONCLUSION: This research among MDR-TB HHCs identified a high prevalence of concern about transmission as well as basic knowledge gaps and perceived stigma with the potential to negatively impact efforts to identify, treat and prevent MDR-TB. The high percentage of HHCs willing to consider MDR-TB preventive therapy demonstrates potential high uptake and utility when proven therapy is implemented.

Bedaquiline and linezolid for the operational treatment of multidrug-resistant and extensively drug-resistant tuberculosis in a high burden HIV setting (blix study)

Author(s): Bionghi N.; Padayatchi N.; Naidoo K.; Master I.; O'Donnell M.R.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Rationale: Global rates of multi drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) continue to increase despite intensive focus by national tuberculosis (TB) treatment programs. Bedaquiline, a novel diarylquinoline, and Linezolid, a repurposed oxazolidinone, have shown promise in treatment regimens for MDR- and XDR-TB. However, there are critical knowledge gaps for outcomes outside of clinical trials and in specific populations, such as HIV-co-infected patients. Methods: Retrospective cohort study of adult patients with microbiologically confirmed drug-resistant TB admitted to a TB referral hospital in KwaZulu-Natal, South Africa initiated on treatment including Bedaquiline and/or Linezolid between January and September 2015 and followed for at least 6 months. Results: Complete data for 153/183 consecutive eligible TB patients newly initiated on Bedaquiline-containing regimens was available with partial data on the remainder. The majority had XDR-TB (42%) or pre-XDR-TB (42%) with 11% MDR-TB and 5% Rifampicin monoresistant. 77% were HIV co-infected, 99% on antiretroviral therapy at baseline. 24 patients were initiated on Bedaquiline and 129 on Bedaquiline and Linezolid containing regimens. Rationale for initiation on these regimens included XDR or pre-XDR TB diagnosis (N=126), ototoxicity (N=49) due to aminoglycoside antibiotics, previous treatment failure (N=21) or renal impairment (N=8). Median number of drugs in regimen was 8 (IQR 7-8). During treatment, 22% of patients were lost to retention in care, with 52% (N=17) occurring during Bedaquiline treatment. 90% of patients with culture data converted their sputum TB culture to negative. Median time to culture conversion was 65 days (IQR 40-91). Among patients who were TB culture negative at Bedaquiline initiation, 98% remained culture negative. Six month outcomes for 180 patients were death (4%; N=7),

treatment failure (5%; N=9), loss to retention in care (23%; N=41), and culture negative on treatment at 6 months (68%; N=123). Loss to retention in care on Bedaquiline (OR 0.03, CI 0.002-0.281, p=0.002) was associated with failure to culture convert. Conclusions: Among patients with drug-resistant TB in this high HIV burden setting, initiation of treatment with Bedaquiline and Linezolid was associated with high rates of TB culture conversion and maintenance of culture conversion. Loss to retention in care even in our short follow-up period was unacceptably high and associated with failure to convert TB culture to negative, raising concern for amplification of drug resistance on treatment. Important further areas of investigation include strengthening adherence support, monitoring for emergence of drug-resistance to Bedaquiline and Linezolid, and identifying optimal drug regimens and patient selection.

Case Report: Culture Conversion In Bedaquiline Contain Regiment Of Pre-Xdr And Xdr Tb Treatment In Persahabatan Hospital In Indonesia

Author(s): Isbaniah F.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Introduction Extensively drug Resistant-Tuberculosis (XDR-TB) is TB caused by strains of M. Tuberculosis that resistant to isoniazid, rifampicin, at least one injectable second-line anti-TB drugs and any of the fluoroquinolone. Extensively drug resistant had been reported by 105 countries by 2015. An estimated 9.7% of people of MDR-TB have XDR-TB. Indonesia is the one of high MDR-TB country with 1.9% estimated of new TB cases with MDR-TB. Persahabatan hospital as the national referral of respiratory disease and the first center for TB resistant program in Indonesia including emerging and re-emerging diseases such as MDR and XDR TB. Until now there are 1.582 MDR-TB patients being treated and 175 patients are pre-XDR and XDR TB. National TB program have 2 kind of regimens for pre XDR and XDR TB cases. First is Kanamycin-Levofloxacin-Ethionamid-Cicloserin-Pirazinamid-Ethambutol and second is bedaquiline containing regimen. The bedaquiline contain regimen is the new program and piloting only in 4 hospitals in Indonesia. From 175 patients, 13 patients being treated with Bedaquiline containing regimen. Other patients being treating with conventional regimen. A single dose of Bedaquiline 400 mg per day in the first two weeks followed by 200 mg three times a week at 22 the next week. Method We report 14 pre-XDR and XDR patients with Bedaquilline containg regimen It is 11 males and 3 females. Range of age is 22-50 years old. Two patient converted in first month, Two patients in second month, one patient in third month, one patient in fourth month, two patients in fifth month. Eight (61.5%) patients had culture conversion below sixth month. Three patients (23%) not converted until yet. One patient died and one patient drop out due social problem. Chest pain and increased heart beat with QTc prolongation reported in two patients. Increased lipase enzyme reported in two patients. Other symptom such as nausea is common reported in Bedaquiline contain regimen or conventional regimen. One patient died due to respiratory failure. Conclusion There need more time and analysis in Bedaquiline containing program for pre-XDR and XDR patients in Persahabatan hospital.

Multi-drug resistant TB treatment regimen, including bedaquiline and linezolid, failed to reduce transmission over 14 days

Author(s): Stoltz A.C.; Keulder S.; De Kock E.J.; Nathavitharana R.R.; Lederer P.; Kruger J.A.; Jensen P.; Nardell E.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Abstract:BACKGROUND Retrospective observations at the South African Airborne Infection Research (AIR) Facility, indicate that patients with multidrug-resistant tuberculosis (MDR-TB), like drug susceptible TB, become rapidly non-infectious soon (less than 72 hours) after starting effective anti-TB therapy. We sought to evaluate the impact of the current South African standard regimen for MDR/XDR-TB, containing bedaquiline and linezolid, using our established human to guinea pig transmission model. These data are essential for determining the duration of quarantine required. METHODS We selectively admitted 5 M. tuberculosis smear positive patients, potentially bedaquiline suitable, to the AIR facility and measured baseline infectivity for an average of 8 days, by exhausting ward air to one of two guinea pig exposure chambers (Control), each containing 90 Hartley guinea pigs. Once bedaquiline suitability was confirmed, and pre-treatment clinical evaluation completed, patients were initiated on standard South African treatment, including bedaquiline and linezolid, amongst others. . During the initial 72 hours of treatment, no ward air was exhausted to either animal room. After 72 hours, ward air was exhausted to the second guinea pig exposure chamber (Intervention) for an average of 8 days. Infectiousness during exposure before and after starting MDR/XDR treatment in the same patients, was compared by Guinea Pig tuberculin skin test (TST, 100 TU) induration, 6 weeks following the end of exposure. Note that one patient was withdrawn early, during the baseline infectivity period. RESULTS Pre-treatment, MDR/XDR TB patients infected 24 of 90 guinea pigs (Control), whereas post-treatment initiation over 3 to 14 days, the same patients (minus the patient who was withdrawn), infected 25 of 90 guinea pigs (Intervention), clearly demonstrating no difference. Results of bedaquiline pharmacokinetics are pending. CONCLUSIONS The current South African MDR/XDR TB regimen, including bedaquiline and linezolid over 3 to 14 days, failed to inhibit transmission. Although our PK data are pending, we hypothesize that the absence of impact of these regimens on MDR/XDR-TB transmission may be due to a delayed bactericidal activity. Follow up study is planned to test the effect of a longer duration of therapy or additional drugs (Delamamid, PA-824) on MDR/XDR-TB transmission.

Factors associated with mortality among patients with multidrug-resistant tuberculosis-United States, 1993-2013

Author(s): Salinas J.L.; Armstrong L.R.; Cegielski J.P.; Haddad M.B.; Silk B.J.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Abstract: Background: Multidrug-resistant tuberculosis (MDR TB) is diagnosed when the patient's Mycobacterium tuberculosis isolate is resistant to at least isoniazid and rifampin. Completing treatment reduces mortality and prevents TB recurrence and transmission to others. Although directly observed therapy (DOT) is standard care for ensuring treatment completion, some patients' therapy is self-administered. In a large cohort of U.S. MDR TB patients, we examined patient and clinical characteristics and treatment administration mode in association with mortality over time. Methods: We analyzed surveillance data for MDR TB patients treated in the United States during

1993-2013. We used Cox proportional hazards models to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) for the association of treatment administration mode (DOT versus self-administered therapy) with all-cause mortality during TB treatment, accounting for age (per 5-year increments), sex, race/ethnicity, HIV infection, previous TB disease, site of disease (i.e., pulmonary versus extrapulmonary), and additional drug resistance (i.e., resistance to at least one fluoroquinolone or a second-line injectable drug). Stratified models were also fit for origin (U.S.-born or foreign-born) and period of treatment (1993-2002 or 2003-2013). Results: Among 3,434 MDR TB patients, 709 (21%) died during TB treatment. Most patients were foreign-born of Asian (50%) or Hispanic (33%) race/ethnicity. Among those with available data, 710 (34%) had HIV infection reported, 606 (18%) had previous TB disease, and 577 (17%) had additional drug resistance. DOT increased from 74% during 1993-2002 to 95% during 2002-2013; all-cause mortality decreased from 31% to 11% during these periods. Older age (aHR: 1.15; 95% CI: 1.11-1.20) and reported HIV infection (aHR: 7.11; 95% CI: 5.46-9.24) were risk factors for all-cause mortality irrespective of patient's origin or period of treatment. Receiving DOT (aHR: 0.23; 95% CI: 0.19-0.28) was protective in all stratified models. Conclusions: In the United States, all-cause mortality during treatment has declined among patients with MDR TB. DOT coverage has increased and remained protective over time against all-cause mortality, after adjusting for demographic and clinical characteristics known to be associated with mortality. A continued emphasis on maximizing DOT coverage can help reduce all-cause mortality.

Multidrug-resistant tuberculosis in The United States, 1993-2014: Trends and characteristics

Author(s): Chen M.P.; Miramontes R.; Hill A.N.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract:INTRODUCTION: The World Health Organization estimated 480,000 multidrug-resistant tuberculosis (MDR TB) incident cases and 190,000 deaths globally in 2014. In the United States (US), MDR TB cases have declined since national MDR TB data became available in 1993. What changes have occurred in the US MDR TB case counts, HIV co-infection, cases in previously treated persons, and MDR TB proportions in foreign-born persons? METHODS: We obtained 1993-2014 TB data from CDC's Online Tuberculosis Information System, used Join-point regression to estimate annual-percentage-changes (APCs) for MDR TB cases, analyzed proportions of HIV co-infection and patients with previous TB, and calculated the rate-ratio of foreign-born/US-born with previous TB. RESULTS: There were 91 reported MDR TB cases in 2014, a decrease from 484 in 1993. Associated APCs (%) were -20.7 (95% confidence interval (CI): -24.8,-16.2; 1993-1998) and -3.3 (-4.2,-1.4; 1998-2014). APCs were -28.7 (-33.9,-23.1; 1993-1999) and -10.0 (-11.7,-8.3; 1999-2014) for US-born and -2.2% (-2.9,-1.4; 1993-2014) for foreign-born. The proportion of known MDR TB/HIV co-infection declined from 49% to 15% among US-born and from 8% to 5% among foreign-born cases (1993-1999 to 2007-2014). For individuals with previous TB, the proportion decreased from 12% to 10% in US-born and from 25% to 19% in foreign-born cases (1993-1999 to 2007-2014, Figure). The rate-ratio of foreign-born/US-born with previous TB cases during 1993-2014 was 1.9 (95%CI: 1.6-2.2). CONCLUSIONS: Ongoing TB control efforts have been associated with markedly reduced MDR TB, especially MDR TB/HIV co-infection among US-born cases. The low proportions of MDR TB patients with previous TB may indicate that most MDR TB cases did not acquire resistance as a result of previous TB treatment, especially for the US-born. The low number of US-born cases could indicate successful control of recent MDR TB infections. (Figure Presnted).

The diaspora of multidrug-resistant tuberculosis: Whole-genome analysis of globally migrant MDR clades

Author(s): Cohen K.A.; Manson A.; Desjardins C.; Birren B.; Earl A.M.; Abeel T.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Abstract: Background: International spread of drug-resistant M. tuberculosis strains is a threat to tuberculosis control efforts everywhere. While the global dissemination of Beijing strains has been previously studied, less is known about international movement of non-Beijing strains. A whole-genome analysis to characterize the international migration of multidrug-resistant (MDR) tuberculosis has not yet been performed to date. Methods: From a global dataset of 5,310 M. tuberculosis whole genome sequences isolated from five continents, we performed a phylogenetic analysis and used parsimony to assign known drug resistance mutation evolutions to nodes on the phylogeny. For each high confidence node at which genotypic MDR evolved, we examined the geographic origins of descendent strains and determined the number of SNPs that separated the two most closely related isolates that derived from different countries. Results: We identified a total of 213 high confidence phylogenetic clades of genotypic MDR that contained two or more descendent strains. Of these 213 clades, we identified 32 (15%) migrant clades that contained descendent strains isolated in two or more countries, including 22 clades with members in two or more UN geographic regions. Notable MDR dissemination included strain migration between Europe and Africa, as well as Asia and Europe. With respect to genetic background, in addition to 20 Beijing MDR migrant clades, there were also 12 non-Beijing migrant clades identified. Migrant MDR clade members differed by as few as four SNPs, indicating relatively recent last common ancestry. Conclusion: Whole-genome analysis revealed extensive global spread of MDR tuberculosis clades. Relatively recent strain movement between Europe, Asia and Africa was observed from both Beijing and non-Beijing genetic backgrounds. Infection control efforts will be necessary to reverse this worrisome trend and stem the global tide of MDR migration.

High incidence of fluoroquinolone resistance and effect of efflux pump inhibitors on moxifloxacin resistance among Mycobacterium tuberculosis isolates causing urinary tract infection in Taiwan

Author(s): Chien J.-Y.; Yu C.-J.; Hsueh P.-R.

Source: International Journal of Antimicrobial Agents; 2017

Publication Type(s): Article In Press

Abstract: This study explored the prevalence of urinary tract tuberculosis (UTB) and whether efflux pump activation accounts for resistance to moxifloxacin in Taiwan. Of 3034 patients with culture-confirmed TB from 2005-2012, 47 patients (1.5%) with UTB were included in this study. Minimum inhibitory concentrations (MICs) of moxifloxacin were determined in the presence and absence of efflux pump inhibitors (EPIs), including verapamil, reserpine and carbonyl cyanide 3-chlorophenylhydrazone (CCCP). EPI responders were defined as isolates with at least a four-fold reduction in MICs in the presence of EPIs. Among the 47 isolates, 24 (51.1%) were resistant to ofloxacin and 22 (46.8%) were resistant to moxifloxacin by the agar proportion method. Among the 22 moxifloxacin-resistant isolates, 19 (86.4%) had low-level resistance (MIC = 1.0-2.0 mg/L). Patients with prior exposure to fluoroquinolones were more likely than non-exposed patients to have moxifloxacin-resistant isolates [14/22 (63.6%) vs. 8/25 (32.0%); P = 0.030]. All 3 isolates with high-level moxifloxacin resistance (MIC >= 4.0 mg/L) had mutations in the gyrA or gyrB genes; however, among the 19 isolates with low-level resistance, only 1 (5.3%) had a mutation in the gyrA gene. Among the 19 isolates with low-level moxifloxacin resistance, 16 isolates (84.2%) were EPIs

responders, but none of the high-level resistant isolates were EPIs responders. Approximately one-half (46.8%) of the isolates from patients with UTB were resistant to moxifloxacin, and activation of efflux pumps accounted for most low-level moxifloxacin-resistant isolates.

Social support a key factor for adherence to multidrug-resistant tuberculosis treatment

Author(s): Deshmukh R.D.; Sreenivas A.N.; Parmar M.; Dhande D.J.; Sachdeva K.S.; Kumar A.M.V.

Source: Indian Journal of Tuberculosis; 2017

Publication Type(s): Article In Press

Abstract: Background: Multidrug-resistant tuberculosis (MDR-TB) is emerging as a major public health problem globally. Treatment success rates in MDR-TB across the globe are not encouraging as completing MDR-TB treatment successfully is challenging due to high proportion of lost to follow up. Methods: Using qualitative methods and grounded theory approach, in-depth interviews were conducted with MDR-TB patients and treatment providers. The social cognitive framework was explored as a way to guide understanding of the factors affecting treatment adherence among MDR-TB patients. Results: Multiple factors influenced patient's decision to adhere to MDR-TB treatment. Self-motivation, awareness about disease and treatment, counselling support, family support, nutritional support and social support were important drivers for successful treatment. Providers related that motivational counselling, nutritional support, family support and social support encouraged treatment adherence. Conclusion: To improve MDR-TB treatment adherence, a patient-centric approach should be considered at the programmatic level. There is a need to formulate strategy that includes motivational counselling, nutritional supplementation and social support mobilisation for treatment adherence. Participants suggested a Patient Support Group led treatment care model for better adherence and treatment success rates in MDR-TB treatment.

Genetic diversity of multidrug-resistant Mycobacterium tuberculosis strains isolated from tuberculosis patients in Iran using MIRU-VNTR technique

Author(s): Khosravi A.D.; Dezfuli S.K.; Hashemzadeh M.; Goodarzi H.; Shahraki A.H.; Mohajeri P.

Source: Kaohsiung Journal of Medical Sciences; 2017

Publication Type(s): Article In Press

Abstract: Tuberculosis (TB) is considered as one of the most important infectious diseases in the world, and recent rise and spread of multidrug-resistant (MDR) Mycobacterium tuberculosis (MTB) strains, have made the matter worsened. Due to the importance of TB prevalence in Iran, this study was designed to investigate the genetic diversity among MDR strains of MTB by MIRU-VNTR typing scheme. A total of 88 drug resistant M. tuberculosis isolates belong to pulmonary TB cases were collected from several TB reference centers of Iran. Drug susceptibility testing for Isoniazid and Rifampin was performed using the agar proportion method and MDR isolates were underwent genotyping by using 12-locus- based MIRU-VNTR typing. On performing proportion method, 22 isolates were identified as MDR. By typing of MDR isolates using 12-loci MIRU-VNTR technique, high diversity were demonstrated in MDR strains and these were classified into 20 distinct MIRU-VNTR genotypes. MIRU loci 10 and 26 were the most discriminatory loci with 8 and 7 alleles respectively; while MIRU loci 2, 20, 24 and 39 were found to be the least discriminatory with 1-2 alleles each. We noticed a mixed infection in isolate 53, as this isolate comprised simultaneous two alleles in MIRU loci 40, 10, 16 and 39. In conclusion, this result represents MIRU-VNTR typing as a useful tool for studying genetic diversity of MDR-MTB in regional settings, and will help the health sectors to construct a preventive program for MDR-TB. Additionally, it can detect mixed infection which can facilitate management of treatment.

Population implications of the use of bedaquiline in people with extensively drug-resistant tuberculosis: Are fears of resistance justified?

Author(s): Kunkel A.; Cohen T.; Furin J.

Source: The Lancet Infectious Diseases; 2017

Publication Type(s): Article In Press

Available in full text at Lancet Infectious Diseases, The - from ProQuest

Abstract: Global rollout of the new antituberculosis drug bedaquiline has been slow, in part reflecting concerns about spread of bedaquiline resistance. Acquired resistance to bedaquiline is especially likely in patients with extensively drug-resistant (XDR) tuberculosis. However, the very high mortality rates of patients with XDR not receiving bedaquiline, and promising cohort study results, suggest these patients also have greatest need for the drug. In this Personal View, we argue that resistance concerns should not forestall use of bedaquiline in patients with XDR tuberculosis. Our position in favour of increased access to bedaquiline for these patients is based on three arguments. First, the use of drug combinations that include bedaquiline might prevent spread of XDR disease to others in the community. Second, until new combination regimens of novel drugs for XDR tuberculosis become available, patients with XDR disease and their infected contacts will face equivalent outcomes if bedaquiline is either not provided because of policy, or not effective because of resistance. Finally, because resistance to bedaquiline and other antituberculosis drugs is caused by mutations within a single bacterial chromosome, use of bedaquiline in patients with XDR tuberculosis will not substantially increase the risk of bedaquiline resistance in patients with drug-susceptible or multidrug-resistant (non-XDR) tuberculosis strains.

Phenotypic and Genotypic Analysis of Multidrug-Resistant Mycobacterium tuberculosis Isolates from Sudanese Patients.

Author(s): Sabeel, Solima M A; Salih, Mohamed Ahmed; Ali, Manasik; El-Zaki, Salah-Eldin;

Source: Tuberculosis research and treatment; 2017; vol. 2017 ; p. 8340746

Publication Date: 2017

Publication Type(s): Journal Article

PubMedID: 28197340

Abstract: Background. Currently, mutations in rpoB, KatG, and rrs genes and inhA promoter were considered to be involved in conferring resistance to rifampicin, isoniazid, and streptomycin in Mycobacterium tuberculosis (MTB). Objective. The aims of this study were to detect the prevalence of first-line tuberculosis (TB) drug resistance among a group of previously treated and newly detected TB patients, to determine the association between prevalence of multidrug resistance (MDR) and demographic information (age and sex), to explain genes correlated with MDR Mycobacterium tuberculosis, and to characterize MTB via 16S ribosomal RNA (16S rRNA) analysis. Methods. A hundred MTB isolates from Sudanese pulmonary TB patients were included in the study. The proportional method of drug susceptibility test was carried out on Löwenstein-Jensen media. Multiplex PCR of rpoB and KatG genes and inhA promoter was conducted; then rrs genes were amplified by conventional PCR and were sequenced. The sequences of the PCR product were compared with known rrs gene sequences in the GenBank database by multiple sequence alignment tools. Result. The prevalence of MDR was 14.7% among old cases and 5.3% among newly diagnosed cases. Conclusion. Mutations in rrs could be considered as a diagnostic marker.

Evaluation of a nurse practitioner-physician task-sharing model for multidrug-resistant tuberculosis in South Africa.

Author(s): Farley, Jason E; Ndjeka, Norbert; Kelly, Ana M; Whitehouse, Erin; Lachman, Simmi;

Source: PloS one; 2017; vol. 12 (no. 8); p. e0182780

Publication Type(s): Journal Article

Available in full text at PLoS One - from ProQuest

Abstract:BACKGROUNDTreatment success rates for multidrug-resistant tuberculosis (MDR-TB) in South Africa remain close to 50%. Lack of access to timely, decentralized care is a contributing factor. We evaluated MDR-TB treatment outcomes from a clinical cohort with task-sharing between a clinical nurse practitioner (CNP) and a medical officer (MO).METHODSWe completed a retrospective evaluation of outcomes from a prospective, programmatically-based MDR-TB cohort who were enrolled and received care between 2012 and 2015 at a peri-urban hospital in KwaZulu-Natal, South Africa. Treatment was provided by either by a CNP or MO.FINDINGSThe cohort included 197 participants with a median age of 33 years, 51% female, and 74% co-infected with HIV. The CNP initiated 123 participants on treatment. Overall MDR-TB treatment success rate in this cohort was 57.9%, significantly higher than the South African national average of 45% in 2012 (p<0·0001) and similar to the provincal average of 60% (p = NS). There were no significant differences by provider type: treatment success was 61% for patients initiated by the CNP and 52.7% for those initiated by the MO.INTERPRETATIONClinics that adopted a task sharing approach for MDR-TB demonstrated greater treatment success rates than the national average. Task-sharing between the CNP and MO did not adversely impact treatment outcome with similar success rates noted. Task-sharing is a feasible option for South Africa to support decentralization without compromising patient outcomes. Models that allow sharing of responsibility for MDR-TB may optimize the use of human resources and improve access to care.

Correction: Prevalence and extent of heteroresistance by next generation sequencing of multidrug-resistant tuberculosis.

Author(s): Operario, Darwin J; Koeppel, Alexander F; Turner, Stephen D; Bao, Yongde;

Source: PloS one; 2017; vol. 12 (no. 7); p. e0181284

Publication Type(s): Published Erratum

Available in full text at PLoS One - from ProQuest

Abstract:[This corrects the article DOI: 10.1371/journal.pone.0176522.].

Off-Label Use of Bedaquiline in Children and Adolescents with Multidrug-Resistant Tuberculosis.

Author(s): Achar, Jay; Hewison, Cathy; Cavalheiro, Ana P; Skrahina, Alena; Cajazeiro, Junia;

Source: Emerging infectious diseases; Oct 2017; vol. 23 (no. 10)

Publication Type(s): Journal Article

Available in full text at Emerging infectious diseases [Emerg Infect Dis] NLMUID: 9508155 - from EBSCOhost

Abstract: We describe 27 children and adolescents <18 years of age who received bedaquiline during treatment for multidrug-resistant tuberculosis. We report good treatment responses and no cessation attributable to adverse effects. Bedaquiline could be considered for use with this age group for multidrug-resistant tuberculosis when treatment options are limited.

Bedaquiline and Delamanid Combination Treatment of 5 Patients with Pulmonary Extensively Drug-Resistant Tuberculosis.

Author(s): Maryandyshev, Andrey; Pontali, Emanuele; Tiberi, Simon; Akkerman, Onno;

Source: Emerging infectious diseases; Oct 2017; vol. 23 (no. 10)

Publication Type(s): Journal Article

Available in full text at Emerging infectious diseases [Emerg Infect Dis] NLMUID: 9508155 - from EBSCOhost

Abstract: We report the experiences of 5 patients taking bedaquiline with delamanid in combination: 1 patient was cured; 3 culture converted, with 2 continuing and 1 changing therapy; and 1 died from respiratory insufficiency. For 2 patients, QT-interval prolongation but no arrhythmias occurred. Use of this therapy is justified for patients with limited options.

Six-Month Response to Delamanid Treatment in MDR TB Patients.

Author(s): Hewison, Cathy; Ferlazzo, Gabriella; Avaliani, Zaza; Hayrapetyan, Armen;

Source: Emerging infectious diseases; Oct 2017; vol. 23 (no. 10)

Publication Type(s): Journal Article

Available in full text at Emerging infectious diseases [Emerg Infect Dis] NLMUID: 9508155 - from EBSCOhost

Abstract: Delamanid, recently available for the treatment of multidrug-resistant tuberculosis (MDR TB), has had limited use outside clinical trials. We present the early treatment results for 53 patients from 7 countries who received a delamanid-containing treatment for MDR TB. Results show good tolerability and treatment response at 6 months.

Bedaquiline and Linezolid for Extensively Drug-Resistant Tuberculosis in Pregnant Woman.

Author(s): Jaspard, Marie; Elefant-Amoura, Elisabeth; Melonio, Isabelle; De Montgolfier, Inés

Source: Emerging infectious diseases; Oct 2017; vol. 23 (no. 10)

Publication Type(s): Journal Article

Available in full text at Emerging infectious diseases [Emerg Infect Dis] NLMUID: 9508155 - from EBSCOhost

Abstract:A woman with extremely drug-resistant tuberculosis treated with a drug regimen including linezolid and bedaquiline during her last 3 weeks of pregnancy gave birth to a child without abnormalities. No fetal toxicities were noted by 2 years after delivery. This drug combination might be safe during the late third trimester of pregnancy.

Molecular detection of Isoniazid, Rifampin and Ethambutol resistance to M. tuberculosis and M. bovis in multidrug resistant tuberculosis (MDR-TB) patients in Pakistan

Author(s): Munir S.; Mahmood N.; Shahid S.; Khan M.I.

Source: Microbial Pathogenesis; Sep 2017; vol. 110 ; p. 262-274

Publication Type(s): Article

Abstract: The various aspects of MDR-TB, type of pathogen, different drug sensitive methods and mutation (s) in specific genes were determined. The histone-like protein (hupB) gene of M. tuberculosis was targeted by using primer sets: N & S and M & S (produced 645 bp & 318 bp fragment respectively). The most significant risk factors were the poverty and male gender of ages 11-25 years. All samples were detected as M. tuberculosis. By Drug Proportion method, the highest

percentage (37%) was found resistant to only Rifampin. By MGIT method, the highest percentage (82.2%) was found resistant with the triple combination (Rifampin-RIF + Isoniazid-INH + Ethambutol-EMB) of the drugs. The highest mutations (76.92%) were found in gene rpoB (codon 531) in MDR TB patients. By, MAS-PCR, the highest percentage (34%) were found resistant to combination (INH + RIF) of the drugs. Minimum samples were resistant to RIF and RIF + INH drugs by MGIT, while proportionate results were observed from MAS-PCR and DP. Moreover, by MAS-PCR mutation in gene embB (306) caused EMB resistance (51.64%). We found that M. tuberculosis was the main cause of MDR-TB. Our findings may further be used for an early diagnosis of multi-drug resistant tuberculosis.

Real-time PCR followed by high-resolution melting curve analysis: A rapid and pragmatic approach for screening of multidrug-resistant extrapulmonary tuberculosis.

Author(s): Sharma, Kusum; Sharma, Megha; Singh, Shreya; Modi, Manish; Sharma, Aman

Source: Tuberculosis (Edinburgh, Scotland); Sep 2017; vol. 106 ; p. 56-61

Publication Type(s): Journal Article

Abstract:INTRODUCTIONMultidrug resistance (MDR) in extrapulmonary tuberculosis (EPTB) is a diagnostic challenge in an endemic country like India. Timely detection of MDR-TB can contribute to a better patient outcome.OBJECTIVETo perform real-time PCR (qPCR) using rpoB, mpb64 and IS6110 gene on a variety of EPTB samples and to compare the performance of different gene targets. All qPCR positive samples were subjected to high resolution melt-curve analysis (HRM analysis) for rpoB and katG gene to evaluate its potential for MDR screening among different sample types.METHODSReal-time PCR using rpoB, mpb64 and IS6110 genes was carried out on 200 cases of study group and 100 cases of non-TB control group. The study group consisted of 100 culture-confirmed and 100 clinically suspected cases of EPTB. Phenotypic drug susceptibility testing (DST) for culture isolates was performed by the 1% indirect agar proportion method. DNA extracted from all qPCR positive samples was subjected to rpoB and katG HRM analysis for screening of MDR. Sequencing was used to confirm the results of HRM analysis and the results were also compared with phenotypic DST in all culture positive cases.RESULTSThe sensitivity of qPCR using rpoB, mpb64 and IS6110 was 86.5%, 86.5% and 76.5%, respectively. All isolates from the control group were negative by all the three targets, giving a specificity of 100%. HRM analysis detected MDR in 22/200 (11%) isolates. 3/200 (1.5%) had mono-rifampicin resistance while 8/200 (4%) had mono-isoniazid resistance. HRM analysis identified an additional 4 MDR cases directly from the samples which were negative by culture. On sequencing, mutations were observed at codon 531 (60%); 533 (16%); 516 (12%) and 526 (12%) of the rpoB gene and at codon 315 (100%) of the katG gene. There was 100% concordance in the results of phenotypic DST, HRM analysis and sequencing.CONCLUSIONThe HRM analysis can play a promising role in the reliable and rapid screening of EPTB samples for detection of MDR.

Are moxifloxacin and levofloxacin equally effective to treat XDR tuberculosis?

Author(s): Maitre T.; Chauffour A.; Bernard C.; Jarlier V.; Reibel F.; Aubry A.; Veziris N.; Petitjean G.; El Helali N.; Chavanet P.

Source: Journal of Antimicrobial Chemotherapy; Aug 2017; vol. 72 (no. 8); p. 2326-2333

Publication Type(s): Article

Abstract: Background: Moxifloxacin retains partial activity against some fluoroquinolone-resistant mutants of Mycobacterium tuberculosis. Levofloxacin is presumed to be as active as moxifloxacin against drug-susceptible tuberculosis and to have a better safety profile. Objectives: To compare the in vivo activity of levofloxacin and moxifloxacin against M. tuberculosis strains with various levels of fluoroquinolone resistance. Methods: BALB/c mice were intravenously infected with 106 M.

tuberculosis H37Rv and three isogenic mutants: GyrA A90V, GyrB E540A and GyrB A543V. Treatment with 50 or 100 mg/kg levofloxacin and 60 or 66 mg/kg moxifloxacin was given orally every 6 h, for 4 weeks. Results: Levofloxacin 50 and 100 mg/kg q6h and moxifloxacin 60 and 66 mg/kg q6h generated AUCs in mice equivalent to those of levofloxacin 750 and 1000mg/day and moxifloxacin 400 and 800 mg/day, respectively, in humans. Moxifloxacin 60 and 66 mg/kg q6h had bactericidal activity against strain H37Rv (MIC>=0.25 mg/L) and mutants GyrB E540A and GyrB A543V (MIC=0.5 mg/L). Against mutant GyrA A90V (MIC=2 mg/L), moxifloxacin 60 mg/kg q6h did not prevent bacillary growth, whereas 66 mg/kg q6h had bacteriostatic activity. Levofloxacin 50 mg/kg q6h had bactericidal activity against H37Rv (MIC>=0.25 mg/L) but not against the mutant strains. Levofloxacin 100 mg/kg q6h had bactericidal activity against H37Rv and mutants GyrB E540A (MIC"0.5 mg/L) and GyrB A543V (MIC=1 mg/L) but not against mutant GyrA A90V (MIC=4 mg/L). Conclusions: All mutations reduced fluoroquinolone activity, even those classified as susceptible according to phenotypic tests. High-dose levofloxacin is less effective than high-dose moxifloxacin against both fluoroquinolone-resistant and -susceptible M. tuberculosis strains in mice.

Outcomes of multidrug-resistant tuberculosis in Zambia: a cohort analysis

Author(s): Kapata N.; Chanda-Kapata P.; Ngosa W.; Mwaba P.; Grobusch M.P.; Chongwe G.; Tembo M.; Musonda S.; Katemangwe P.; Bates M.; Zumla A.; Cobelens F.

Source: Infection; Aug 2017 ; p. 1-9

Publication Type(s): Article In Press

Abstract: Purpose: The purpose of this study was to establish a baseline for measuring the impact of the programmatic management of drug-resistant TB program by following up on outcomes of all patients diagnosed with multidrug-resistant tuberculosis in Zambia between 2012 and 2014. Methods: A cohort study of all the MDR-TB patients diagnosed at the national TB reference laboratory from across Zambia. MDR-TB was diagnosed by culture and DST, whereas outcome data were collected in 2015 by patient record checks and home visits. Results: The total number of patients diagnosed was 258. Of those, 110 (42.6%) patients were traceable for this study. There were 67 survivor participants (60.9%); 43 (39.1%) were deceased. Out of the 110 patients who were traced, only 71 (64.5%) were started on second-line treatment. Twenty-nine (40.8%) patients were declared cured and 16.9% were still on treatment; 8.4% had failed treatment. The survival rate was 20.2 per 100 person-years of follow-up. Taking ARVs was associated with a decreased risk of dying (hazard ratio 0.12, p = 0.002). Sex, age, marital status and treatment category were not important predictors of survival in MDR-TB patients. Conclusions: More than half of the patients diagnosed with MDR-TB were lost to follow-up before second-line treatment was initiated.

Modeling the impact of bedaquiline treatment strategies on the multidrug-resistant tuberculosis burden in India

Author(s): Mehra M.; Kambili C.; Rhines A.; Thomas A.; Potluri R.; Singh V.

Source: International Journal of Tuberculosis and Lung Disease; Aug 2017; vol. 21 (no. 8); p. 902-909

Publication Date: Aug 2017

Publication Type(s): Article

Abstract:E T T ING: Bedaquiline (BDQ) has been approved in India for the treatment of multidrug-resistant tuberculosis (MDR-TB), but is currently recommended for MDR-TB patients who have failed initial treatment with standard regimens. While some have argued that such deferred BDQ use allows a second line of defense with a potent drug, this strategy may not be optimal. OBJECTIVE : To

compare several distinct scenarios of BDQ access and use, and their potential impact on the MDR-TB disease burden and the associated net economic benefit in India. METHOD: We used a state-Transition model to carry out this evaluation. The scenarios differed in the timing and breadth of BDQ access. RESULT S : The simulations showed that a strategy reliant on reserving the use of BDQ for those who have failed other MDR-TB regimens is likely to result in worse treatment outcomes for patients and in inferior public health outcomes for communities, leading to reduced net monetary benefit. CONCLUS ION: Our study suggests that deferring patient access to new drugs such as BDQ until front-line regimens have failed, in order to 'save' these drugs for later use, could be detrimental to patients and to public health, and could reduce the economic benefit of treating MDR-TB.

The novel gene mtb192 is a candidate marker for the detection of multidrug-resistant Mycobacterium tuberculosis strains.

Author(s): Chen, Junhua; Jiang, Li; Su, Wei; Zheng, Gaihuan; Hongmei, Xu

Source: Gene; Aug 2017; vol. 626 ; p. 264-268

Publication Type(s): Journal Article

Abstract:BACKGROUNDMulti-drug resistant tuberculosis (TB) is one of the most main threats to the global TB control work at present. And it's very difficult to detect. From a screen of differentially expressed genes in multidrug-resistant tuberculosis (MDR-TB) strains, we identified a new gene, mtb192. In the present study, we verified the association of mtb192 with TB drug resistance by detecting its expression in clinical isolates from paediatric TB patients.MATERIALS AND METHODSThe homology of mtb192 was analysed by gene blasting in GenBank. The drug resistance of clinical TB isolates was tested, and mtb192 gene expression was compared using reverse transcription polymerase chain reaction (RT-PCR) and quantitative PCR.RESULTSGene homology suggested that mtb192 is a new gene sequence. Among the 120 clinical isolates, 14 were positive for mtb192, including 12 in the MDR group, 2 in the single drug-resistant group, 1 in the poly-resistant group, and 1 in the sensitive group. The mtb192 positive expression rate was significantly higher in the MDR group than all other groups, and the mtb192 mRNA expression level was significantly higher in the MDR group than in the non-MDR group.CONCLUSIONSThe new gene mtb192 showed significantly higher expression in MDR-TB strains and could be related to the development of MDR in Mycobacterium tuberculosis, highlighting it as a new genetic marker in the detection of MDR-TB.

Isothermal Point Mutation Detection: Toward a First-Pass Screening Strategy for Multidrug-Resistant Tuberculosis.

Author(s): Ng, Benjamin Y C; Wee, Eugene J H; Woods, Kyra; Anderson, Will; Antaw, Fiach; Tsang, Hennes Z H; West, Nicholas P; Trau, Matt

Source: Analytical chemistry; Aug 2017

Publication Type(s): Journal Article

Abstract: Point mutations in DNA are useful biomarkers that can provide critical classification of disease for accurate diagnosis and to inform clinical decisions. Conventional approaches to detect point mutations are usually based on technologies such as real-time polymerase chain reaction (PCR) or DNA sequencing, which are typically slow and require expensive lab-based equipment. While rapid isothermal strategies such as recombinase polymerase amplification (RPA) have been proposed, they tend to suffer from poor specificity in discriminating point mutations. Herein, we describe a novel strategy that enabled exquisite point mutation discrimination with isothermal DNA amplification, using mismatched primers in conjunction with a two-round enrichment process. As a proof of concept, the method was applied to the rapid and specific identification of drug-resistant Mycobacterium tuberculosis using RPA under specific conditions. The assay requires just picogram levels of genomic DNA input, is sensitive and specific enough to detect 10% point mutation loading,

and can discriminate between closely related mutant variants within 30 min. The assay was subsequently adapted onto a low-cost 3D-printed isothermal device with real-time analysis capabilities to demonstrate a potential point-of-care application. Finally, the generic applicability of the strategy was shown by detecting three other clinically important cancer-associated point mutations. We believe that our assay shows potential in a broad range of healthcare screening processes for detecting and categorizing disease phenotypes at the point of care, thus reducing unnecessary therapy and cost in these contexts.

GenoType MTBDRplus assay for screening and characterization of isoniazid and rifampicin resistance-associated mutations in multidrug-resistant Mycobacterium tuberculosis from India.

Author(s): Sethi, Sunil; Yadav, Rakesh; Singh, Shreya; Khaneja, Rajiv; Aggarwal, Ashutosh; Agarwal, Priyanka; Behera, Digambar

Source: Letters in applied microbiology; Aug 2017

Publication Type(s): Journal Article

Abstract: Multidrug resistant tuberculosis (MDR-TB) is rising and World health organization has recommended the line probe assay (LPA) for screening. In this study we assess LPA at a tertiary care center from North India in 1758 samples from suspected MDR-TB cases. All smear positive and/or M.tuberculosis culture confirmed cases (n=1170) were subjected to GenoType-MTBDR assay. Amongst these the majority were retreatment cases, smear positive at diagnosis (n=637). MDR prevalence of 7.8% was observed with the highest cases reported amongst MDR contacts (33.3%). Most common rifampicin resistance encoding mutation seen overall and in individual patient groups was H531L (53.3%). Higher prevalence of H526D mutation was observed in retreatment cases, smear positive at 4th month of ATT vs. other patient groups (p=0.052). The most common mutation encoding isoniazid resistance was S315T1 in katG (79.9%) and C-15T in inhA gene (91.1%).Thirty rifampicin and 9 isoniazid resistant isolates had Wild type gene deletion but no detectable mutation by LPA. Although LPA is practical and rapid screening method for most mutations expected to result in MDR-TB, we observed is that it only detects the known major mutations in specific genes. Such studies can provide the knowledge required to formulate customized strips based on prevalent mutations in our region and in specific patient groups. This article is protected by copyright. All rights reserved.

The Effect of Genetic Variation in UGT1A and ABCB1 on Moxifloxacin Pharmacokinetics in South African Patients with Tuberculosis.

Author(s): Naidoo, A.; Ramsuran, V.; Chirehwa, M.; Denti, P.; McIlleron, H.; Naidoo, K.; Yende-Zuma, N.; Singh, R.; Ngapu, S.; Pepper, M.; Chaudhry, M.; Padayatchi, N.

Source: Clinical Therapeutics; Aug 2017; vol. 39

Publication Type(s): Academic Journal

Treatment Outcomes and Cohort Studies

Changes in Host Immune-Endocrine Relationships during Tuberculosis Treatment in Patients with Cured and Failed Treatment Outcomes.

Author(s): Kleynhans, Léanie; Ruzive, Sheena; Ehlers, Lizaan; Thiart, Lani; Chegou, Novel N;

Source: Frontiers in immunology; 2017; vol. 8 ; p. 690

Publication Type(s): Journal Article

Abstract:A bidirectional communication between the immune and endocrine systems exists and facilitates optimum responses in the host during infections. This is in part achieved through changes in secretion patterns of hypothalamic hormones induced by inflammatory cytokines. The aim of this study was to elucidate the immune-endocrine alterations during tuberculosis (TB) treatment in patients with cured and failed TB treatment outcomes. **[ABSTRACT EDITED]**

Childhood tuberculosis: management and treatment outcomes among children in Northwest Ethiopia: a cross-sectional study.

Author(s): Kebede, Zemene Tigabu; Taye, Belaynew Wasie; Matebe, Yohannes Hailu

Source: The Pan African medical journal; 2017; vol. 27 ; p. 25

Publication Type(s): Journal Article

Available in full text at Pan African Medical Journal, The - from National Library of Medicine

Abstract:INTRODUCTIONChildhood tuberculosis (TB) treatment is becoming a major challenge in the TB control efforts of the Ethiopian health system. This study assessed childhood tuberculosis management, and treatment outcomes among children who completed anti-TB treatment in Northwest Ethiopia. **[ABSTRACT EDITED]**

Mycobacterium tuberculosis Induction of Heme Oxygenase-1 Expression Is Dependent on Oxidative Stress and Reflects Treatment Outcomes.

Author(s): Rockwood, Neesha; Costa, Diego L; Amaral, Eduardo P; Du Bruyn, Elsa; Kubler, Andre;

Source: Frontiers in immunology; 2017; vol. 8 ; p. 542

Publication Type(s): Journal Article

Abstract: The antioxidant enzyme heme oxygenase-1 (HO-1) is implicated in the pathogenesis of tuberculosis (TB) and has been proposed as a biomarker of active disease. Nevertheless, the mechanisms by which Mycobacterium tuberculosis (Mtb) induces HO-1 as well as how its expression is affected by HIV-1 coinfection and successful antitubercular therapy (ATT) are poorly understood. **[ABSTRACT EDITED]**

Delay in initiation of treatment after diagnosis of pulmonary tuberculosis in primary health care setting: eight year cohort analysis from district Faridabad, Haryana, North India.

Author(s): Kant, Shashi; Singh, Arvind K; Parmeshwaran, Giridara G; Haldar, Partha;

Source: Rural and remote health; 2017; vol. 17 (no. 3); p. 4158

Publication Type(s): Journal Article

Abstract:INTRODUCTIONDelay in initiation of tuberculosis (TB) treatment may have a tremendous impact on disease transmission, development of drug resistance, poor outcome and overall survival of TB patients. The delay can occur at various levels. Delay in initiation of treatment after diagnosis is

mostly due to health system failure and has immense programmatic implications. It has not been studied extensively in the Indian setting. **[ABSTRACT EDITED]**

Predicting tuberculosis risk in the foreign-born population of British Columbia, Canada: Retrospective population-based cohort study

Author(s): Ronald L.; Balshaw R.; Roth D.; Romanowski K.; Cook V.; Johnston J.; Campbell J.; Marra F.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract:RATIONALE: Improved understanding of risk factors for developing active tuberculosis (TB) will better inform decisions about diagnostic testing and treatment for latent TB infection (LTBI) in migrant populations. Our objective was to examine TB risk factors among the foreign-born population in British Columbia (BC), Canada and to develop a clinically relevant predictive model for the risk of active TB. **[ABSTRACT EDITED]**

Tuberculin skin test conversion in infants from Cape Town, South Africa: A longitudinal birth cohort study

Author(s): Martinez L.; Le Roux D.; Barnett W.; Stadler A.; Zar H.J.; Nicol M.P.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Transmission of Mycobacterium tuberculosis is driving the current global tuberculosis epidemic, especially in areas with a high burden of HIV, such as South Africa. Few studies have investigated prenatal and early life risk factors for the development of tuberculosis infection and most knowledge comes from case reports before 1950. We report the prevalence of TB infection in the Drakenstein Child Health study, a birth cohort in South Africa, a country with the highest tuberculosis incidence globally. **[ABSTRACT EDITED]**

The effect of diabetes and comorbidities on tuberculosis treatment outcomes

Author(s): Degner N.R.; Golub J.E.; Wang J.-Y.; Karakousis P.C.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Rationale: The global diabetes mellitus (DM) epidemic threatens progress made in reducing tuberculosis (TB)-related morbidity and mortality worldwide. Previous clinical studies have not fully evaluated or controlled for potential confounding variables in addressing the impact of DM on TB treatment outcomes. Objectives: We assessed the effect of DM and poor glycemic control on mortality during TB treatment and 2-month TB sputum culture conversion, controlling for confounding variables. We also evaluated the effect of metformin use on these endpoints. **[ABSTRACT EDITED]**

Are there factors that predict intensive care unit admission in patients with active mycobacterium tuberculosis infection: A retrospective, cohort study

Author(s): Patel S.; Shah N.M.; Malhotra N.M.; Hussain N.; Myall K.; Milburn H.; Breen R.A.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Introduction There is a paucity of data on patients in the UK with active Mycobacterium tuberculosis (MTB) that require intensive care unit admission. We sought to characterise this cohort and identify risk factors for intensive care admission and compare them to those requiring standard inpatient care. **[ABSTRACT EDITED]**

Characterization of a 2013-2016 cohort of patients with multi-drug resistant tuberculosis (MDR-TB) with major surgical management in fundacion valle del lili, a reference hospital in latin america

Author(s): Fernandez L.; Monroy K.; Velasquez M.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Introduction MDR-TB prevents global control of TB and is a serious public health issue. WHO estimates that in 2014 there were 480.000 new MDR-TB cases in the world, defined as resistance to Rifampin and Isoniazid; 8.7% of the cases were extensively drug-resistant tuberculosis (XDR-TB). This includes resistance to a fluoroquinolone and at least one of three injectable second-line drugs. Currently lung resection is accepted as a complementary and alternative intervention in the management of MDR-TB that presents with destruction of lung parenchyma with cavitated lesions, bronchiectasis and persistence of positive sputum smears. Surgery tries to reduce the inoculum and areas of poor drug penetration, the risks are similar to those of surgery for lung cancer. We present the experience in 38 patients with MDR-TB managed with major surgery in a reference hospital in Latin America. **[ABSTRACT EDITED]**

Outcomes, infectiousness and transmission dynamics of patients with extensively drug resistant tuberculosis and home-discharged patients with programmatically incurable TB: A prospective cohort study

Author(s): Limberis J.D.; Pietersen E.; Esmail A.; Lesosky M.; Smith L.; McNerney R.; Dheda K.U.J.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Background: The emergence of programmatically incurable tuberculosis (TB) threatens to destabilize control efforts. Prospective patient-orientated data are urgently needed to inform treatment and containment strategies. **[ABSTRACT EDITED]**

High efflux pump activity and gene expression at baseline linked to poor tuberculosis treatment outcomes

Author(s): Mazando S.; Zimudzi C.; Zimba M.; Sande S.; Gundidza M.; Mazorodze J.H.; Seepe P.M.M.;

Source: Journal of Medical and Biomedical Sciences; 2017; vol. 6 (no. 1); p. 8-17

Publication Type(s): Article

Abstract: Phenotypic TB drug resistance, also known as drug tolerance, has been previously attributed to slowed bacterial growth in vivo. The increased activity and expression of efflux systems can lower the intracellular concentration of many antibiotics thus reducing their efficacy. We hypothesized that efflux pump activation and expression could be a risk factor for TB drug tolerance in patients initiated on treatment. **[ABSTRACT EDITED]**

Obstructive pulmonary disease in patients with previous tuberculosis: Pathophysiology of a community-based cohort

Author(s): Allwood B.W.; Gillespie R.; Bateman M.; Olckers H.; Calligaro G.L.; Van Zyl-Smit R.;

Source: South African Medical Journal; 2017; vol. 107 (no. 5); p. 440-445

Publication Type(s): Article

Available in full text at South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde [S Afr Med J] NLMUID: 0404520 - from EBSCOhost

Abstract: Background. An association between chronic airflow limitation (CAL) and a history of pulmonary tuberculosis (PTB) has been confirmed in epidemiological studies, but the mechanisms responsible for this association are unclear. It is debated whether CAL in this context should be viewed as chronic obstructive pulmonary disease (COPD) or a separate phenotype. Objective. To compare lung physiology and high-resolution computed tomography (HRCT) findings in subjects with CAL and evidence of previous (healed) PTB with those in subjects with smoking-related COPD without evidence of previous PTB. **[ABSTRACT EDITED]**

Treatment outcomes of rifampin-sparing treatment in patients with pulmonary tuberculosis with rifampin-mono-resistance or rifampin adverse events: A retrospective cohort analysis

Author(s): Park S.; Jo K.-W.; Lee S.D.; Kim W.S.; Shim T.S.

Source: Respiratory Medicine; Oct 2017; vol. 131 ; p. 43-48

Publication Type(s): Article

Abstract: Background Rifampin (RIF) mono-resistant tuberculosis (RMR-TB) is a rare disease. Current guidelines recommend that RMR-TB be treated as multidrug-resistant TB (MDR-TB) but the evidence is scarce. **[ABSTRACT EDITED]**

The association between tuberculosis and the development of insulin resistance in adults with pulmonary tuberculosis in the Western sub-district of the Cape Metropole region, South Africa: a combined cross-sectional, cohort study.

Author(s): Philips, Lauren; Visser, Janicke; Nel, Daan; Blaauw, Renée

Source: BMC infectious diseases; Aug 2017; vol. 17 (no. 1); p. 570

Publication Type(s): Journal Article

Available in full text at BMC Infectious Diseases - from BioMed Central

Abstract:BACKGROUNDThe existence of a bi-directional relationship between tuberculosis (TB) and insulin resistance (IR)/diabetes has been alluded to in literature. Although diabetes has been linked

to increased tuberculosis risk, the relationship between tuberculosis as a causative factor for IR remains unclear. The study aimed to determine if an association existed between tuberculosis and IR development in adults with newly diagnosed pulmonary tuberculosis at baseline. It was additionally aimed to document changes in IR status during TB follow-up periods. **[ABSTRACT EDITED]**

Increased Risk of Tuberculosis in Patients With Rheumatologic Diseases Managed With Anti-Tnf-A Agents: A Nationwide Retrospective Pharmacoepidemiological Cohort Study in Turkey.

Author(s): Akici, A.; Aydin, V.; Kadi, E.; Isli, F.; Gursoz, H.

Source: Clinical Therapeutics; Aug 2017; vol. 39

Publication Type(s): Academic Journal

Social capital and adverse treatment outcomes of tuberculosis: a case-control study.

Author(s): Deshmukh, P R; Mundra, A; Dawale, A

Source: The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease; Aug 2017; vol. 21 (no. 8); p. 941-946

Publication Type(s): Journal Article

Abstract:SETTINGS'Social capital' refers to social norms, relationships, networks and values that affect the functioning and development of society. Social capital influences health positively, but its role in the treatment outcomes of tuberculosis (TB) is not known.OBJECTIVESTo study the role of social capital in determining adverse TB treatment outcomes. **[ABSTRACT EDITED]**

The neglected burden of tuberculosis disease among health workers: a decade-long cohort study in South Africa.

Author(s): O'Hara, Lyndsay M; Yassi, Annalee; Zungu, Muzimkhulu; Malotle, Molebogeng;

Source: BMC infectious diseases; Aug 2017; vol. 17 (no. 1); p. 547

Publication Type(s): Journal Article

PubMedID: 28784107

Available in full text at BMC Infectious Diseases - from BioMed Central

Abstract:BACKGROUNDHealth workers (HWs) in resource-limited settings are at high-risk of exposure to tuberculosis (TB) at work. The aim of this study was to estimate the rate of TB disease among HWs in the Free State Province of South Africa between 2002 and 2012 and to compare demographic and clinical characteristics between HWs and the general population with TB. This study also explores the effect of occupational variables on risk of TB among HWs. **[ABSTRACT EDITED]**

Prospective cohort study of the feasibility and yield of household child tuberculosis contact screening in Uganda.

Author(s): Bonnet, M; Kyakwera, C; Kyomugasho, N; Atwine, D; Mugabe, F

Source: The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease; Aug 2017; vol. 21 (no. 8); p. 862-868

Publication Type(s): Journal Article

Abstract:SETTINGScreening and isoniazid preventive therapy (IPT) of child contacts of tuberculosis (TB) patients is poorly implemented in resource-limited countries, in part due to difficulties in TB

diagnosis in children.OBJECTIVETo assess the feasibility and yield of hospital-based screening and IPT in Uganda, and to evaluate the utility of symptom-based screening. **[ABSTRACT EDITED]**

Prevalence of pyrazinamide resistance and Wayne assay performance analysis in a tuberculosis cohort in Lima, Peru.

Author(s): Calderón, R I; Velásquez, G E; Becerra, M C; Zhang, Z; Contreras, C C; Yataco, R M;

Source: The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease; Aug 2017; vol. 21 (no. 8); p. 894-901

Publication Type(s): Journal Article

Abstract:BACKGROUNDMultidrug-resistant tuberculosis (MDR-TB) regimens often contain pyrazinamide (PZA) even if susceptibility to the drug has not been confirmed. This gap is due to the limited availability and reliability of PZA susceptibility testing.OBJECTIVESTo estimate the prevalence of PZA resistance using the Wayne assay among TB patients in Lima, Peru, to describe characteristics associated with PZA resistance and to compare the performance of Wayne with that of BACTEC™ MGIT™ 960. **[ABSTRACT EDITED]**

Controlled Trials and Systematic Reviews

Prise en charge decentralisee de la tuberculose multiresistante: Revue systematique et meta-analyseAtencion descentralizada para la tuberculosis multirresistente: Una revision sistematica y un metaanalisis

Decentralized care for multidrug-resistant tuberculosis: A systematic review and meta-analysis

Author(s): Ho J.; Byrne A.L.; Linh N.N.; Jaramillo E.; Fox G.J.

Source: Bulletin of the World Health Organization; 2017; vol. 95 (no. 8); p. 584-593

Publication Type(s): Review

Available in full text at Bulletin of the World Health Organization [Bull World Health Organ] NLMUID: 7507052 - from EBSCOhost

Abstract: Objective To assess the effectiveness of decentralized treatment and care for patients with multidrug-resistant (MDR) tuberculosis, in comparison with centralized approaches. **[ABSTRACT EDITED]**

Cbnaat (xpert MTB/RIF) for rapid detection of childhood tuberculosis and rifampicin resistance: A systematic review and meta-analysis

Author(s): Singh M.; Jaiswal N.; Thumburu K.K.; Chauhan A.; Agarwal A.; Pant P.; Dhatwalia S.K.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Back ground Childhood Tuberculosis and drug resistance is difficult to diagnose due to paucibacilliary condition and atypical radiological findings. The available systematic reviews focus on the diagnostic accuracy of CBNAAT for adult tuberculosis. Present systematic review focuses on diagnostic accuracy of CBNAAT for detection of Mycobacterium tuberculosis and drug resistance in all forms of childhood Tuberculosis. **[ABSTRACT EDITED]**

Sputum quality and bacteriological positivity comparison between intervention of individually-guided active cycle breathing technique (ACBT) and video-guided ACBT in tuberculosis case detection: A randomized controlled trial

Author(s): Desianti G.; Burhan E.; Ratnawati A.

Source: American Journal of Respiratory and Critical Care Medicine; 2017; vol. 195

Publication Type(s): Conference Abstract

Available in full text at American journal of respiratory and critical care medicine [Am J Respir Crit Care Med] NLMUID: 9421642 - from EBSCOhost

Abstract: Background: Tuberculosis case finding plays an important role in decreasing complication and mortality rate. Sputum is an integral part for bacteriological diagnosis of pulmonary tuberculosis so it should be represent lower respiratory tract secretion. It could be described by good sputum quality so it will have a higher positivity rate in bacteriological result. Nowdays, it still felt quite hard for getting good sputum specimen for diagnostic procedure so it is needed a new method for increasing sputum expectoration, such as active cycle breathing technique (ACBT) method. So the primary aim of this research is to evaluate the effectivity of ACBT (2 type ACBT methods) in sputum result of pulmonary TB patient, both regarding sputum quality and also bacteriological sputum positivity level. **[ABSTRACT EDITED]**

Research on tuberculosis in tribal areas in India: A systematic review

Author(s): Rao V.G.; Bhat J.; Yadav R.; Sharma R.; Muniyandi M.

Source: Indian Journal of Tuberculosis; 2017

Publication Type(s): Article In Press

Abstract: Background: Tuberculosis (TB) remains a major public health problem in resource-poor countries including India. Scientific knowledge is used to guide policy and practice. There is however, a limited, systematically collected data required for guiding the scale-up of interventions particularly amongst vulnerable populations including tribal groups in the country. In view of this, a systematic review of the TB research studies carried out in tribal areas of different parts of the country was undertaken. Objective: To undertake a systematic review of the TB research studies carried out in tribal areas of India between 1996 and 2016. **[ABSTRACT EDITED]**

Prevalence of and risk factors for multidrug-resistant tuberculosis in Iran and its neighboring countries: Systematic review and meta-analysis

Author(s): Jimma W.; Abdurahman A.A.; Ghazisaeedi M.; Shahmoradi L.; Kalhori S.R.N.; Safdari R.

Source: Revista da Sociedade Brasileira de Medicina Tropical; 2017; vol. 50 (no. 3); p. 287-295

Publication Type(s): Review

Available in full text at Revista da Sociedade Brasileira de Medicina Tropical - from ProQuest

Abstract: Tuberculosis, in partiular drug-resistant tuberculosis, is of global concern due to the high mortality and morbidity associated with it annually. The aim of this study was to determine the prevalence of and the risk factors for multidrug-resistant tuberculosis in Iran and its neighboring countries.

Systematic review on the proteomic profile of Mycobacterium tuberculosis exposed to drugs

Author(s): Campanerut-Sa P.A.Z.; Ghiraldi-Lopes L.D.; Meneguello J.E.; Teixeira J.J.V.; Scodro R.B.d.L.

Source: Proteomics - Clinical Applications; 2017

Publication Type(s): Article In Press

Abstract: The authors present an overview about proteomics studies in Mycobacterium tuberculosis exposed to some anti-tuberculosis drugs and new candidates, using two-dimensional gel electrophoresis and mass spectrometry. To date, that the authors have knowledge, this is the first studies that was performed specifically in M. tuberculosis using systematic review on electronic literature conducted in three databases using the following search terms: tuberculosis OR mycobacterium tuberculosis, proteome OR proteomics, and mass spectrometry electrospray ionization OR matrix-assisted laser desorption ionization OR two-dimensional gel electrophoresis. By electronic search, 622 abstracts of the original articles published from November 2003 to March 2016 were selected. After the selection, four articles fulfill proposed criteria and were included in this study. The studies reported changes in the protein profile of M. tuberculosis after exposure to isoniazid, ethambutol, streptomycin, ofloxacin, moxifloxacin and two new drugs candidates, SQ109 and ATB107. In conclusion, the proteins changes were related to the synthesis of mycolic acids, cellular metabolism pathways, bacterial stress and starvation.

Comparison of sputum collection methods for tuberculosis diagnosis: A systematic review and pairwise and network meta-analysis

Author(s): Datta S.; Evans C.A.; Shah L.; Gilman R.H.

Source: The Lancet Global Health; 2017

Publication Type(s): Article In Press

Abstract: Background: The performance of laboratory tests to diagnose pulmonary tuberculosis is dependent on the quality of the sputum sample tested. The relative merits of sputum collection methods to improve tuberculosis diagnosis are poorly characterised. We therefore aimed to investigate the effects of sputum collection methods on tuberculosis diagnosis. **[ABSTRACT EDITED]**

Effect of intermittency on treatment outcomes in pulmonary tuberculosis: An updated systematic review and metaanalysis

Author(s): Johnston J.C.; Campbell J.R.; Menzies D.

Source: Clinical Infectious Diseases; 2017; vol. 64 (no. 9); p. 1211-1220

Publication Type(s): Article

Abstract: Background. Intermittent regimens offer operational advantages in tuberculosis treatment, but their efficacy has been questioned. We updated a systematic review and metaanalysis to examine the efficacy of different intermittent dosing schedules in firstline pulmonary tuberculosis therapy. **[ABSTRACT EDITED]**

Risk of active tuberculosis in patients with cancer: A systematic review and metaanalysis

Author(s): Cheng M.P.; Yansouni C.P.; Chakra C.N.A.; Cnossen S.; Shrier I.; Greenaway C.; Menzies D.

Source: Clinical Infectious Diseases; 2017; vol. 64 (no. 5); p. 635-644

Publication Type(s): Review

Abstract: Background. Cancer is a known risk factor for developing active tuberculosis. We determined the incidence and relative risk of active tuberculosis in cancer patients compared to the general population. **[ABSTRACT EDITED]**

Systematic review and meta-analysis of the nitrate reductase assay for drug susceptibility testing of Mycobacterium tuberculosis and the detection limits in liquid medium

Author(s): Kwak M.; Lee W.-K.; Lim Y.J.; Lee S.H.; Ryoo S.

Source: Journal of Microbiological Methods; Oct 2017; vol. 141 ; p. 1-9

Publication Type(s): Article

Abstract: Recently, the need for rapid, reliable, and low-cost drug susceptibility testing (DST) methods has increased due to the emergence of multidrug-resistant Mycobacterium tuberculosis. Colorimetric methods of DST provide results more quickly than standard culture methods and are inexpensive than molecular methods. Thus, colorimetric methods, such as the nitrate reductase assay (NRA), are being recommended. **[ABSTRACT EDITED]**

Yield of community-based tuberculosis targeted testing and treatment in foreign-born populations in the United States: A systematic review

Author(s): Malekinejad M.; Parriott A.; Viitanen A.P.; Horvath H.; Kahn J.G.; Marks S.M.

Source: PLoS ONE; Aug 2017; vol. 12 (no. 8)

Publication Type(s): Article

Available in full text at PLoS One - from ProQuest

Abstract: Objective: To synthesize outputs and outcomes of community-based tuberculosis targeted testing and treatment (TTT) programs in foreign-born populations (FBP) in the United States (US). **[ABSTRACT EDITED]**

Child contact management in high tuberculosis burden countries: A mixed-methods systematic review

Author(s): Szkwarko D.; Hirsch-Moverman Y.; Du Plessis L.; Du Preez K.; Carr C.; Mandalakas A.M.

Source: PLoS ONE; Aug 2017; vol. 12 (no. 8)

Publication Type(s): Article

Available in full text at PLoS One - from ProQuest

Abstract: Tuberculosis (TB) remains a leading cause of morbidity and mortality worldwide. Considering the World Health Organization recommendation to implement child contact management (CCM) for TB, we conducted a mixed-methods systematic review to summarize CCM implementation, challenges, predictors, and recommendations. **[ABSTRACT EDITED]**

A systematic review of national policies for the management of persons exposed to tuberculosis

Author(s): Rodriguez C.A.; Sasse S.; Azzawi S.; Becerra M.C.; Yuen C.M.; Yuengling K.A.

Source: International Journal of Tuberculosis and Lung Disease; Aug 2017; vol. 21 (no. 8); p. 935-940

Publication Type(s): Review

Abstract:OBJECTIVE : To describe mandates and policy gaps in tuberculosis (TB) contact investigation and management. **[ABSTRACT EDITED]**

Exercise: Relative Risk

The relative risk is the ratio of probability of an event (a specified outcome) occurring in one group (i.e. those exposed to a particular intervention) compared to those in another group (i.e. those not exposed – a control group).

The relative risk can be interpreted using the following chart. First, you must determine whether the event (the outcome measure) is adverse or beneficial.

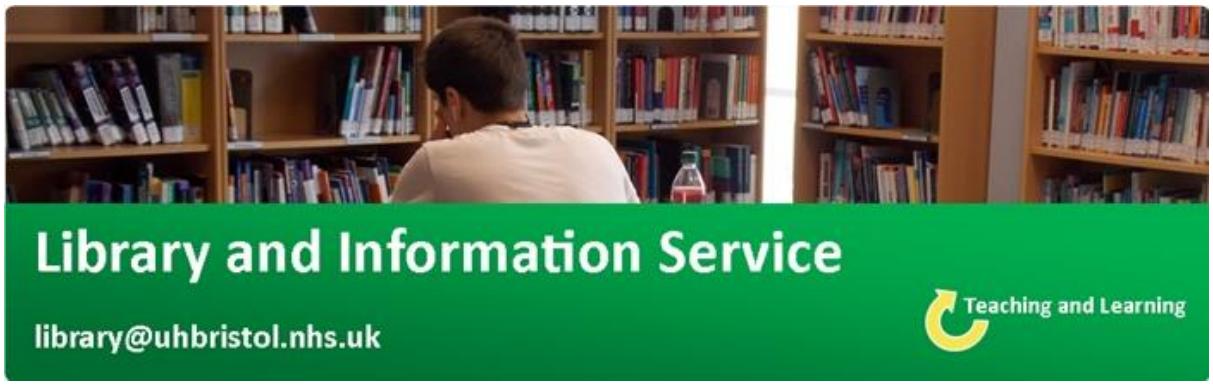
Relative Risk	Adverse outcome (e.g. death)	Beneficial outcome (e.g. recovery of limb function)
<1	Intervention better than control	Intervention worse than control
1	Intervention no better or worse than control	Intervention no better or worse than control
>1	Intervention worse than control	Intervention better than control

Have a go at interpreting the relative risks for these three studies using the chart above. Is the intervention better or worse than the control?

	Intervention	Population	Outcome measure (think: adverse or beneficial?)	Relative Risk
Study 1	Drug X	Adults at risk of a heart attack	Heart attack	1.2
Study 2	Therapy programme Y	Smokers	Smoking cessation	0.8
Study 3	Probiotic Z	Children on antibiotics	Diarrhoea	0.3

*Find out more about relative risk in one of our **Statistics** training sessions.*
For more details, email library@uhbristol.nhs.uk.

Answers: Study 1: worse; Study 2: worse; Study 3: better



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