# TB and Hepatitis C Virus

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**Askar Yedibayev**

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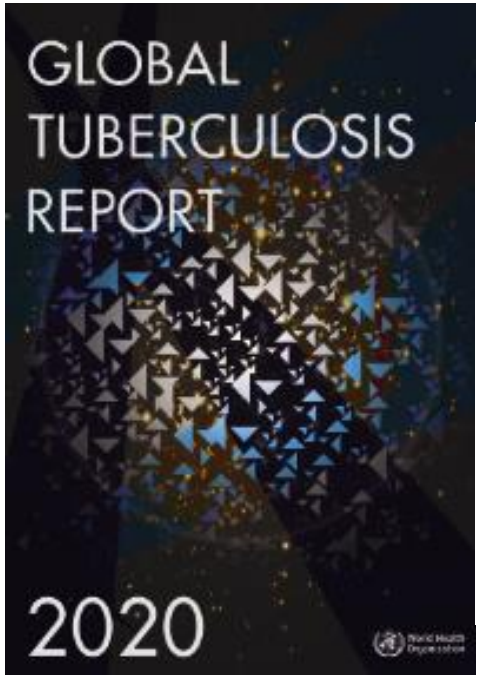
09 December 2020

# WHO European Region




- High burden in EECA countries, 7 countries account for more than 90% of the global MDR-TB burden: RUS, UKR, KAZ, BEL, KGZ, UZB, MDA (more than 1 000 recorded cases);
- More than 70% of the global XDR-TB burden
- MDR-TB treatment success rate – 59% (2017)
- XDR-TB treatment success rate – 39.1% (2018)

Global TB Report, 2020. World Health Organization.

# WHO Guidelines on Drug-Resistant Tuberculosis, June 2020

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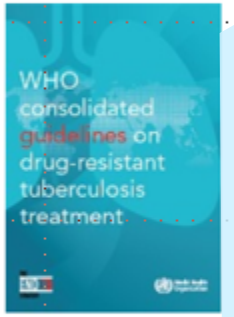
**WHO consolidated guidelines on drug-resistant tuberculosis treatment**

**Authors**:
WHO

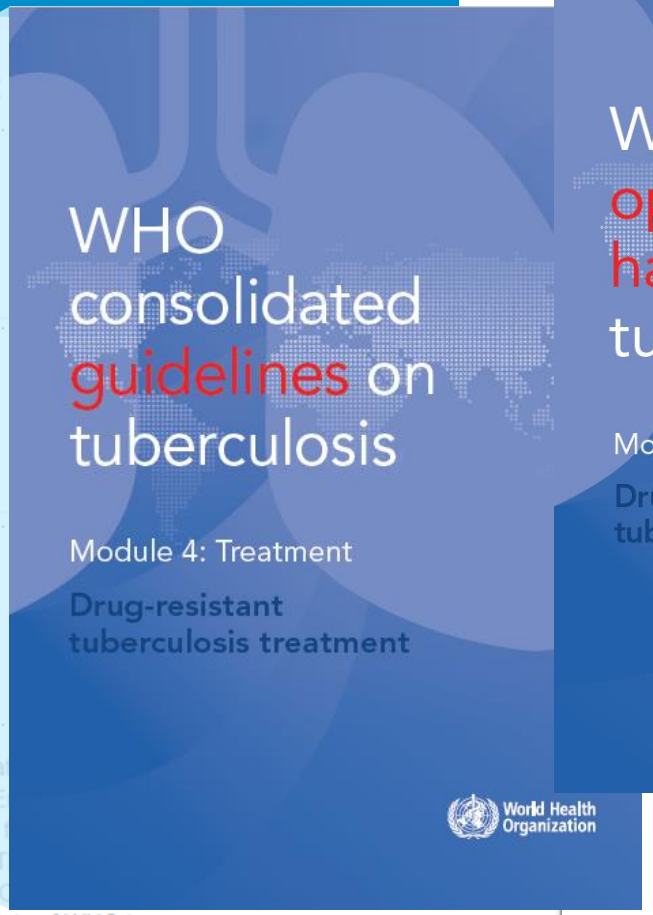


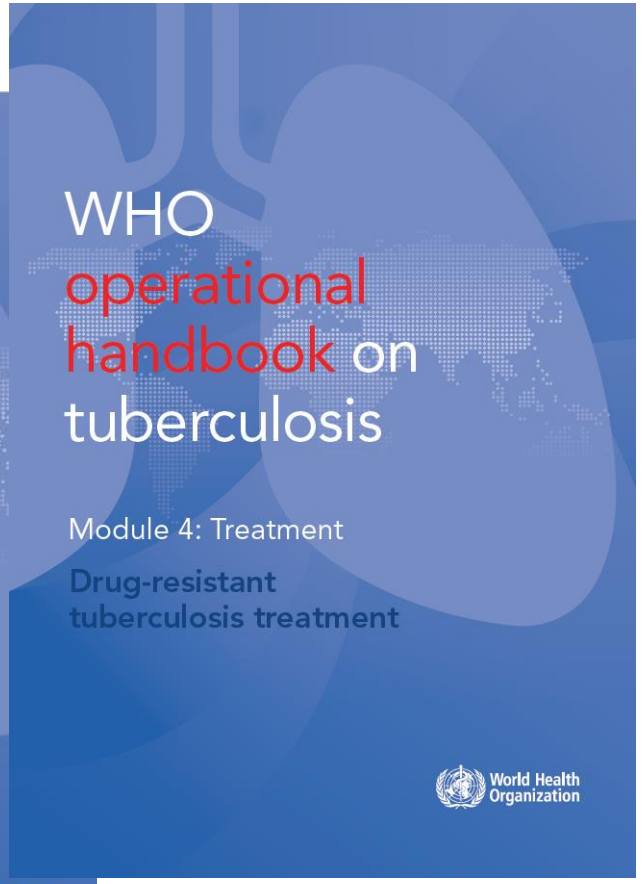

Publication details
Publication date: 2019
Languages: English
WHO reference number:
WHO/CDS/TB/2019.3

Downloads
– English
– Annex 3–9

**Overview**

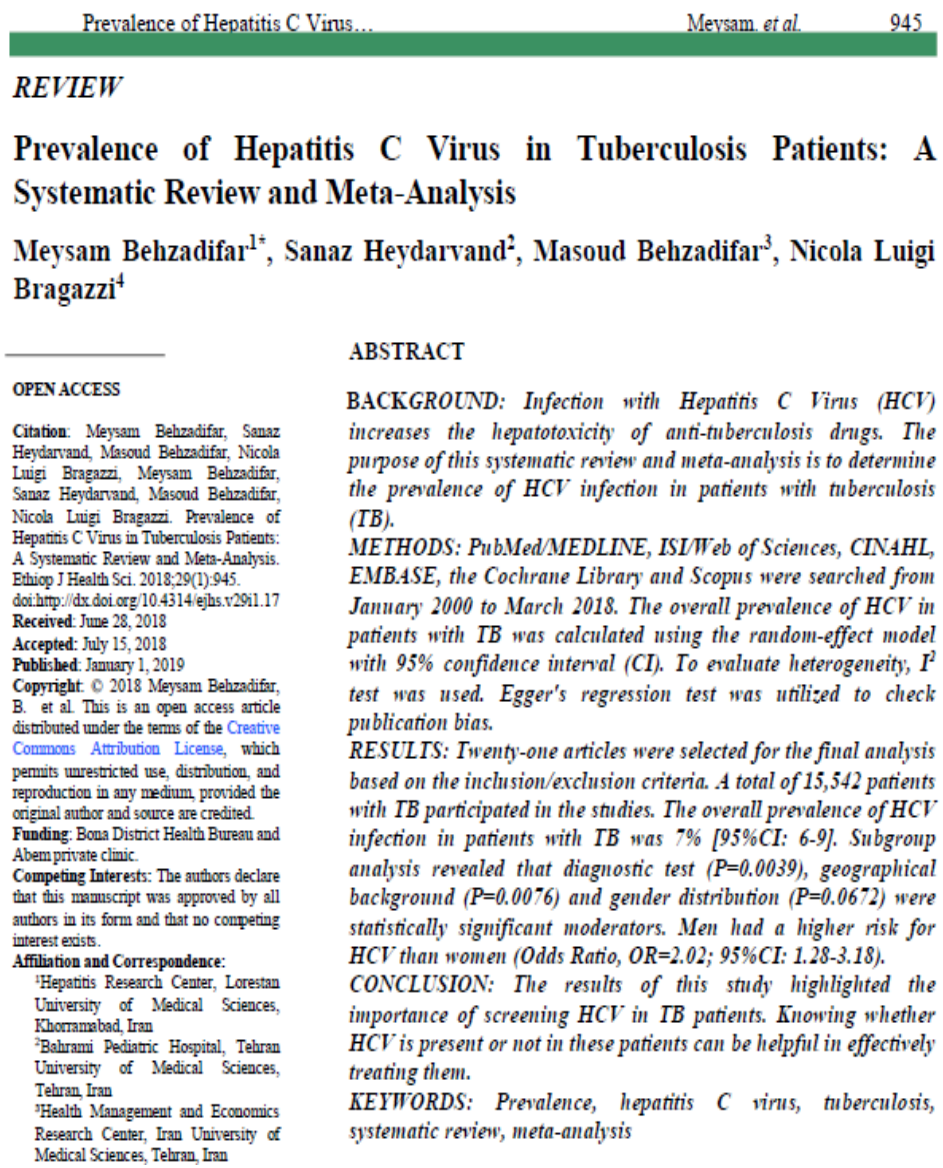
Tuberculosis (TB) strains with drug resistance (DR-TB) are more difficult to trea
susceptible ones, and threaten global progress towards the targets set by the E
Strategy of the World Health Organization (WHO). There is thus a critical need f
based policy recommendations on the treatment and care of patients with DR-T
the most recent and comprehensive evidence available. In this regard, the WH
consolidated guidelines on drug-resistant tuberculosis treatment fulfil the mandate of WHO to
inform health professionals in Member States on how to improve treatment and care for



# Grouping of Drugs for Longer MDR-TB Treatment Regimens

| Group | Drug | Abbreviation |
|---|---|---|
| **Group A**<br>Priority drugs | Levofloxacin (Lfx) OR Moxifloxacin (Mfx)<br>Bedaquiline<br>Linezolid | Lfx / Mfx<br>Bdq<br>Lzd |
| **Group B**<br>Added to priority drugs | Clofazimine<br>Cycloserine | Cfz<br>Cs |
| **Group C**<br>Agents are added when a regimen can not be composed of Group A and B drugs | Ethambutol<br>Delamanid<br>Pyrazinamide<br>Imipenem-cilastatin OR Meropenem<br>Amikacin (OR Streptomycin)<br>Ethionamide OR Prothionamide<br>*p*-aminosalicilic acid | E<br>Dlm<br>Z<br>Imi-cln / Mpn<br>Am (S)<br>Eto / Pto<br>PAS |





*REVIEW*

**Prevalence of Hepatitis C Virus in Tuberculosis Patients: A Systematic Review and Meta-Analysis**

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OPEN ACCESS

**Citation**: Meysam Behzadifar, Sanaz Heydarvand, Masoud Behzadifar, Nicola Luigi Bragazzi, Meysam Behzadifar, Sanaz Heydarvand, Masoud Behzadifar, Nicola Luigi Bragazzi. Prevalence of Hepatitis C Virus in Tuberculosis Patients: A Systematic Review and Meta-Analysis. Ethiop J Health Sci. 2018;29(1):945. doi:http://dx.doi.org/10.4314/ejhs.v29i1.17
**Received**: June 28, 2018
**Accepted**: July 15, 2018
**Published**: January 1, 2019

**Funding**: Bona District Health Bureau and Abem private clinic.
**Competing Interests**: The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.
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ABSTRACT

*BACKGROUND: Infection with Hepatitis C Virus (HCV) increases the hepatotoxicity of anti-tuberculosis drugs. The purpose of this systematic review and meta-analysis is to determine the prevalence of HCV infection in patients with tuberculosis (TB).*
*METHODS: PubMed/MEDLINE, ISI/Web of Sciences, CINAHL, EMBASE, the Cochrane Library and Scopus were searched from January 2000 to March 2018. The overall prevalence of HCV in patients with TB was calculated using the random-effect model with 95% confidence interval (CI). To evaluate heterogeneity, $I^2$ test was used. Egger's regression test was utilized to check publication bias.*
*RESULTS: Twenty-one articles were selected for the final analysis based on the inclusion/exclusion criteria. A total of 15,542 patients with TB participated in the studies. The overall prevalence of HCV infection in patients with TB was 7% [95%CI: 6-9]. Subgroup analysis revealed that diagnostic test (P=0.0039), geographical background (P=0.0076) and gender distribution (P=0.0672) were statistically significant moderators. Men had a higher risk for HCV than women (Odds Ratio, OR=2.02; 95%CI: 1.28-3.18).*
*CONCLUSION: The results of this study highlighted the importance of screening HCV in TB patients. Knowing whether HCV is present or not in these patients can be helpful in effectively treating them.*
*KEYWORDS: Prevalence, hepatitis C virus, tuberculosis, systematic review, meta-analysis*

*Ethiop J Health Sci. 2019 Jan: 29(1) 945-956

# HCV Prevalence in TB Patients*

- A total of 15,542 TB patients were included in the review of 21 studies in 4 WHO geographical regions: EURO, SEARO, AMRO and AFRO.
- The prevalence of HCV ranged from 2 to 27%, with a cumulative prevalence of 7% [95%CI: 6-9].
- HCV screening among TB patients is very important. Information about HCV infection can contribute to effective treatment outcome.
- Urgent measures are needed to improve the knowledge and roll out screening of people at risk for HCV and TB.

# HCV Prevalence in TB Patients

| First author | Year | Country | Age (Mean±SD) | Test | Prevalence | No. of participants |
|---|---|---|---|---|---|---|
| Richards | 2006 | Georgia | 35 | ELISA | 22% | 272 |
| Kuniholm | 2008 | Georgia | NA | ELISA | 12.00% | 300 |
| Pando | 2008 | Argentina | 34.8±14.1 | ELISA | 11.80% | 187 |
| Khalili | 2009 | Iran | 43.21±18.27 | ELISA | 27.45% | 102 |
| Khan | 2010 | UK | NA | ELISA | 2.00% | 245 |
| Chien | 2010 | Taiwan | NA | ELISA | 10% | 295 |
| Wang | 2011 | Taiwan | NA | PCR | 6.70% | 360 |
| Reis | 2011 | Brazil | NA | ELISA | 7.50% | 402 |
| Badawy | 2011 | Egypt | NA | ELISA | 6.40% | 135 |
| Lomtadze | 2013 | Georgia | 21-92 | ELISA | 21% | 326 |
| Akhtar | 2013 | Pakistan | 42±18.2 | ELISA | 9.10% | 110 |
| Beasley | 2013 | UK | NA | ELISA | NA | 192 |
| Zhang | 2013 | China | NA | ELISA | 3.80% | 2296 |
| Potter | 2014 | UK | 37.7±15.3 | ELISA | 2.00% | 302 |
| Campo | 2014 | USA | NA | ELISA | 3.60% | 1421 |
| Agha | 2015 | Egypt | NA | PCR | 17.02% | 94 |
| Ahmadi Nooredinvand | 2015 | UK | NA | ELISA | 1.60% | 429 |
| Abdallah | 2015 | Sudan | 36.03± 13.3 | ELISA | 1% | 98 |
| Bushnell | 201+5 | USA | NA | ELISA | 4.20% | 7624 |
| Merza | 2016 | Iraq | 40.34±20.29 | ELISA | 0.90% | 214 |
| Costi | 2017 | Brazil | 38.0± 12.9 | PCR | 20% | 138 |

THE AMERICAN JOURNAL OF GASTROENTEROLOGY

Published by Elsevier Science Inc.

Vol. 98, No. 1, 2003
ISSN 0002-9270/03/$30.00
PII S0002-9270(02)05844-6

World Health Organization
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# Association Between Hepatitis C Infection and Other Infectious Diseases: A Case for Targeted Screening?

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## Hepatitis C Virus Infection Is Associated With an Increased Risk of Active Tuberculosis Disease

*A Nationwide Population-Based Study*

*Ping-Hsun Wu, MD, Yi-Ting Lin, MD, Kun-Pin Hsieh, PhD, Hung-Yi Chuang, PhD, and Chau-Chyun Sheu, MD*

**Abstract:** Tuberculosis (TB) and hepatitis C virus (HCV) infection contribute to major disease mortality and morbidity worldwide. However, the causal link between HCV infection and TB risk remains unclear. We conducted a population-based cohort study to elucidate the association between HCV infection and TB disease by analyzing Taiwan National Health Insurance Database. We enrolled 5454 persons with HCV infection and 54,274 age- and sex-matched non-HCV-infected persons between January 1998 and December 2007. Time-dependent Cox proportional hazards regression analysis was used to measure the association between HCV infection and active TB disease. Incidence rate of active TB disease was higher among HCV infection than in control (134.1 vs 89.1 per 100,000 person-years; incidence rate ratio 1.51; $P = 0.014$). HCV infection was significantly associated with active TB disease in multivariate Cox regression (adjusted hazard ratio [HR] 3.20; 95% confidence interval [CI], 1.85–5.53; $P < 0.001$) and competing death risk event analysis (adjusted HR 2.11; 95% CI, 1.39–3.20; $P < 0.001$). Multivariate stratified analysis further revealed that HCV infection was a risk of active TB disease in most strata. This nationwide cohort study suggests that HCV infection is associated with a higher risk of developing active TB disease.

(*Medicine* 94(33):e1328)

**Abbreviations**: CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, HBV = hepatitis B virus, HCV = hepatitis C virus, HIV = human immunodeficiency virus, ICD-9 = International Classification of Diseases, 9th Revision, IRR = incidence rate ratio, LHID = Longitudinal Health Insurance Database, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, TB = tuberculosis.

### INTRODUCTION

Tuberculosis (TB), an infectious disease caused by *Mycobacterium tuberculosis*, is the most prevalent infectious disease and the major leading cause of death worldwide, especially in developing countries. According to the Global Tuberculosis Report by World Health Organization, there were an estimated 8.6 million incident cases of TB and approximately 1.3 million people died of TB in 2012.[1] It is endemic in southeastern Asia, as well as Taiwan. An epidemiological study declared the incidence of active TB disease in Taiwan was 74 per 100,000 person-years.[2]

TB is considered as an immunodeficiency-related infection. Our recent work demonstrated that liver cirrhosis was associated with increased risk of active TB disease.[3] Liver cirrhosis, and subsequent complications of both hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are major health problems in Taiwan.[4] However, a comprehensive evaluation from HCV patients without cirrhosis remains unavailable. HCV infection is one of the contributing factors for developing TB infection is our hypothesis. Previous observation study showed that HCV infection and TB share the same high risks population, especially in homeless people,[5] prisoners,[6] and human immunodeficiency virus (HIV) patients.[7] Furthermore, one case-control study using the US Veterans data demonstrated that HCV infection is associated with TB disease.[8] However, results from this hospital-based, case-control study cannot be extended to the general population. In order to fill this knowledge gap, this nationwide cohort study analyzed healthcare data to clarify the association between HCV and active TB disease using large-scale data from the Taiwan National Health Insurance (NHI).

**Table 1.** Comparison Between HCV-Infected Patients (Cases) and Controls Without HCV Among Hospitalized Veterans (1992–1999)

| | Cases (n = 34,204) | Controls (n = 136,816) | Unadjusted Odds Ratio (95% CI) | *p* |
|---|---|---|---|---|
| Demographic features | | | | |
| Age (mean ± SD) | 48.4 ± 9.3 | 59.8 ±13.4 | | <0.0001 |
| Ethnicity (Caucasian) | 21,039 (61.5) | 100,526 (73.5) | 0.6 (0.5–0.6) | <0.0001 |
| Gender (men) | 33,576 (98.2) | 132,713 (97.0) | 1.7 (1.5–1.8) | <0.0001 |
| Period of service (Vietnam) | 23,294 (68.1) | 45,210 (33.0) | 4.3 (4.2–4.4) | <0.0001 |
| Blood-borne viral infections | | | | |
| Human immunodeficiency virus | 4,832 (14.1) | 4,090 (3.0) | 5.3 (5.1–5.6) | <0.0001 |
| Hepatitits B | 7,665 (22.4) | 985 (0.7) | 39.8 (37.22–42.62) | <0.0001 |
| Hepatitits D | 570 (1.7) | 45 (0.03) | 51.5 (38.0–69.8) | <0.0001 |
| Infections related to immunodeficiency | | | | |
| Toxoplasmosis | 88 (0.3) | 79 (0.06) | 4.5 (3.3–6.1) | <0.0001 |
| Cytomegalovirus | 194 (0.6) | 213 (0.2) | 3.7 (3.0–4.5) | <0.0001 |
| Cryptococcosis | 121 (0.4) | 119 (0.1) | 4.1 (3.2–5.3) | <0.0001 |
| Pneumocystosis | 513 (1.5) | 530 (0.4) | 3.9 (3.5–4.4) | <0.0001 |
| Kaposi sarcoma | 93 (0.3) | 150 (0.1) | 2.5 (1.9–3.2) | <0.0001 |
| Candida | 1,382 (4.0) | 2,407 (1.8) | 2.4 (2.2–2.5) | <0.0001 |
| Herpes simplex (excluding genital) | 449 (1.3) | 862 (0.6) | 2.1 (1.9–2.4) | <0.0001 |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| Tuberculosis | 1,124 (3.3) | 1,717 (1.3) | 2.7 (2.5–2.9) | <0.0001 |
| [illegible] | | | | |
| Peritonitis | 1,325 (3.9) | 1,067 (0.8) | 5.13 (4.7–5.6) | <0.0001 |
| Sepsis | 2,289 (6.7) | 6,575 (4.8) | 1.42 (1.4–1.5) | <0.0001 |
| Endocarditis | 811 (2.4) | 2,052 (1.5) | 1.60 (1.5–1.7) | <0.0001 |
| Cellulitis | 5,966 (17.44) | 16,394 (12.0) | 1.55 (1.5–1.6) | <0.0001 |
| Carbuncles | 1,172 (3.43) | 3,301 (2.4) | 1.44 (1.3–1.5) | <0.0001 |
| Sexually transmitted diseases | | | | |
| Gonococcus | 155 (0.5) | 179 (0.1) | 3.47 (2.8–4.3) | <0.0001 |
| Viral warts | 1,259 (3.7) | 3,037 (2.2) | 1.68 (1.6–1.8) | <0.0001 |
| Chlamydia | 544 (1.6) | 1,011 (0.7) | 2.17 (2.0–2.4) | <0.0001 |
| Syphilis | 687 (2.0) | 755 (0.6) | 3.69 (3.3–4.1) | <0.0001 |
| Gential herpes | 354 (1.0) | 408 (0.3) | 3.50 (3.0–4.0) | <0.0001 |
| Trichomoniasis | 106 (0.3) | 211 (0.2) | 2.01 (1.6–2.5) | <0.0001 |
| Molluscum | 45 (0.1) | 82 (0.1) | 2.20 (1.5–3.2) | <0.0001 |

Values are n (%) unless otherwise noted.

World Health Organization Europe

# Hepatitis C virus infection increases hepatitis risk during anti-tuberculosis treatment

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SUMMARY

OBJECTIVE: To study the impact of hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infection on clinically significant transaminase elevation during short-course anti-tuberculosis treatment.

DESIGN: Retrospective observation study.

RESULTS: During standard anti-tuberculosis treatment of 295 patients with active pulmonary tuberculosis (TB) and normal baseline liver biochemical tests, 25 (8.5%) developed hepatitis and had a significantly higher mortality rate (32% vs. 7%, OR 6.22, 95%CI 2.0–17.6, $P = 0.001$). Multivariate analysis showed that HCV co-infected individuals were more likely to develop transaminase elevations (OR 3.43, 95%CI 1.14–10.35, $P = 0.03$) than

40.4 vs. 13.5 ± 8.6 days, $P = 0.01$). Co-infection with HBV was not associated with a higher rate of hepatitis but was associated with later onset (102 ± 68.7 vs. 37.0 ± 31.9 days, $P = 0.01$), higher peak alanine aminotransferase level and slower recovery (55.5 ± 62.9 vs. 15.4 ± 10.8 days, $P = 0.01$).

CONCLUSION: Even with normal baseline liver bio-

**Conclusion: Even with normal baseline liver biochemical tests, HCV co-infection is associated with a higher incidence and longer exacerbation of drug-induced hepatitis during anti-TB therapy. We suggest that screening for HCV infection before starting anti-TB treatment is helpful in planning the frequency of treatment monitoring.**

# Risk of Drug-Induced Hepatitis in Patients with HCV during TB Treatment

**Table 2: Factors associated with the development of drug-induced hepatitis during TB treatment**

| Characteristic | No hepatitis ($n$ = 270) $n$ (%) or mean ± SD | Hepatitis ($n$ = 25) $n$ (%) or mean ± SD | $P$ value |
|---|---|---|---|
| Age, years | 64 ± 20 | 68 ± 17 | 0.35 |
| Male | 175 (65) | 17 (68) | 0.83 |
| Baseline AST, IU/l | 21.8 ± 6.6 | 22.4 ± 6.2 | 0.67 |
| Baseline ALT, IU/l | 15.8 ± 8.1 | 14.0 ± 7.5 | 0.30 |
| Baseline bilirubin, mg/dl | 0.55 ± 0.30 | 0.45 ± 0.21 | 0.12 |
| HBV (+) | 22 (8) | 3 (12) | 0.46 |
| HCV (+) | 18 (7) | 7 (28) | 0.006 |
| INH+EMB+RMP+PZA | 260 (96) | 24 (96) | 1.00 |
| INH+EMB+RMP | 10 (4) | 1 (4) | 1.00 |
| Mortality | 19 (7) | 8 (32) | 0.001 |

SD = standard deviation; AST = aspartate aminotransferase; ALT = alanine aminotransferase; IU = international unit; HBV(+) = hepatitis B virus co-infection; HCV(+) = hepatitis C virus co-infection; INH = isoniazid; EMB = ethambutol; RMP = rifampicin; PZA = pyrazinamide.

INT J TUBERC LUNG DIS 22(7):766–772

http://dx.doi.org/10.5588/ijtld.17.0840

World Health Organization
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# Is 6 months of bedaquiline enough? Results from the compassionate use of bedaquiline in Armenia and Georgia

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SUMMARY

BACKGROUND AND SETTING: Bedaquiline (BDQ) was initially only available through compassionate use programmes.

OBJECTIVE: To assess the effectiveness and safety of multidrug-resistant tuberculosis (MDR-TB) treatment containing BDQ.

METHOD: Retrospective analysis of data from patients receiving BDQ through compassionate use in Armenia and Georgia from April 2013 to April 2015. Logistic regression was used to assess the risk factors associated with unsuccessful treatment outcomes.

RESULTS: Of 82 patients included, 84.2% (69/82) had fluoroquinolone-resistant MDR-TB and 43.4% (23/53) were seropositive for the hepatitis C virus (HCV). The culture conversion rate was 84.4% (54/64), and 18.5% (10/54) reverted back to positive. In total, 79.3% (65/82) of the patients reported at least one adverse event. Serious adverse events were reported in 14 patients, with 10/14 patients experiencing fatal outcomes—6/10 related to advanced TB and 2/10 assessed as possibly related to BDQ. Treatment outcomes were as follows: 58.5% treatment success, 12.2% deaths, 7.3% failures and 21.9% lost to follow-up. HCV coinfection was associated with unsuccessful outcomes (adjusted OR 4.45, 95%CI 1.23–16.13).

CONCLUSION: BDQ through compassionate use showed relatively good success rates and safety profiles in a cohort with difficult-to-treat MDR-TB. High rates of reversion may indicate that >24 weeks of BDQ is necessary in some cases. HCV coinfection should be diagnosed and treatment considered in MDR-TB patients.

KEY WORDS: MDR-TB; treatment; new anti-tuberculosis drugs; duration; hepatitis C

# Table 2: Risk Factors for Unfavorable Treatment Outcomes Among Patients Receiving Bedaquiline at Treatment Start (n = 82)

**Table 2** Risk factors for unfavourable treatment outcomes among patients receiving BDQ at treatment start ($n = 82$)

| Characteristics | OR (95%CI) | *P* value | aOR (95%CI) | *P* value |
|---|---|---|---|---|
| Male sex | 1.34 (0.40–4.42) | 0.632 | | |
| Age ⩾ 35 years | 2.16 (0.83–5.60) | 0.113 | | |
| Former prison inmate | 2.73 (0.97–7.68) | 0.057 | | |
| Contact of an MDR-TB case | 1.12 (0.37–3.38) | 0.836 | | |
| BMI < 18.5 kg/m$^2$ | 2.13 (0.84–5.56) | 0.112 | | |
| Cavities on CXR | 8.68 (1.05–71.48) | 0.044 | | |
| Bilateral disease on CXR | 3.26 (1.19–8.93) | 0.021 | | |
| HIV-positive | 1.37 (0.18–10.28) | 0.756 | | |
| Hepatitis C antibody-positive | 4.27 (1.31–19.92) | 0.016 | 4.45 (1.23–16.13) | 0.023 |
| Smear positive at treatment start | 3.53 (1.33–9.36) | 0.011 | 2.59 (0.88–7.57) | 0.083 |
| XDR-TB strain at treatment start | 0.89 (0.37–2.14) | 0.793 | | |
| Previous use of CFZ | 0.95 (0.38–2.33) | 0.902 | | |
| CFZ at BDQ initiation | 1.34 (0.41–4.42) | 0.632 | | |
| Imipenem at BDQ initiation | 1.43 (0.50–4.08) | 0.501 | | |

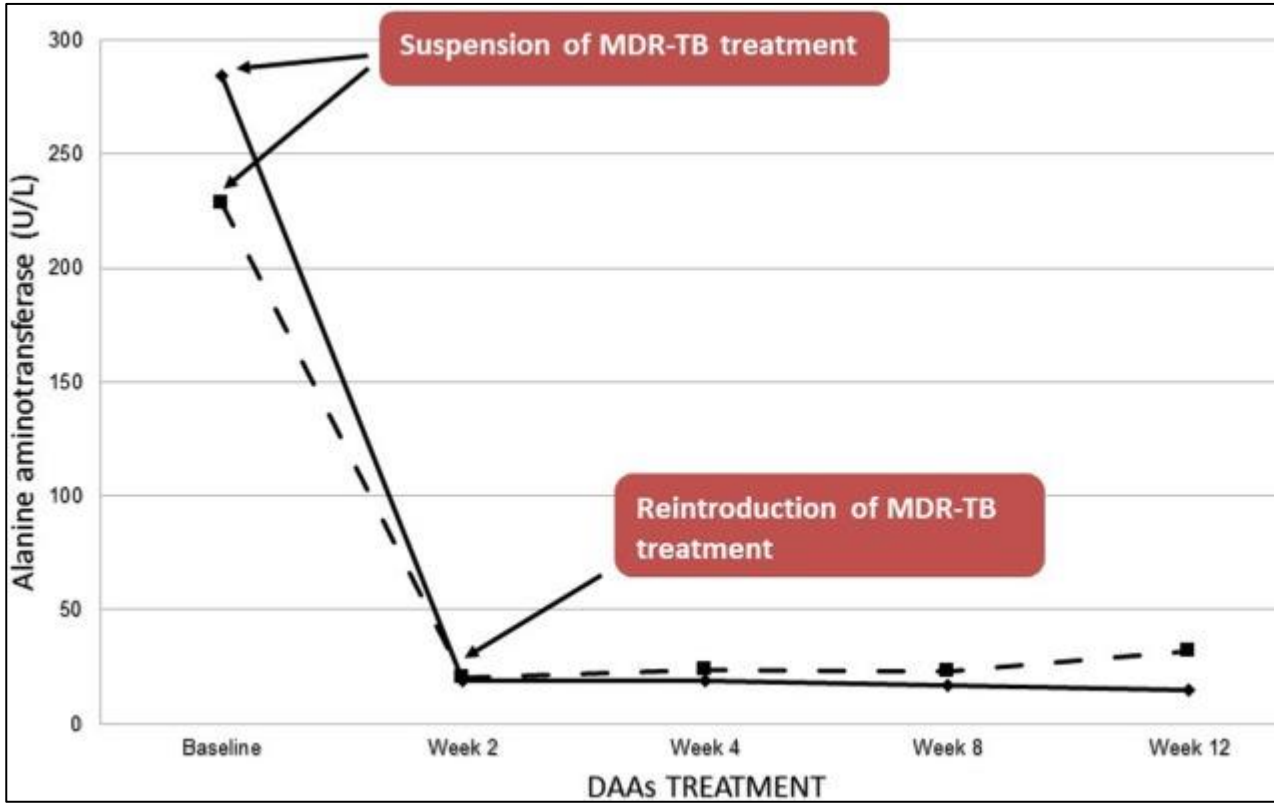
BDQ = bedaquiline; OR = odds ratio; CI = confidence interval; aOR = adjusted OR; MDR-TB = multidrug-resistant tuberculosis; BMI = body mass index; HIV = human immunodeficiency virus; CXR = chest X-ray; XDR-TB = extensively drug-resistant TB; CFZ = clofazimine.

# Drug-Induced Hepatitis can Occur During TB Treatment

*Serious Adverse Events (SAE in patients on longer MDR-TB treatment regimens)*

| Drug | Absolute Risk of AE | |
|---|---|---|
| | ***Median %*** | ***95% Bayesian CI*** |
| **Bedaquiline** | 2,4 | [0.7, 7.6] |
| **Moxifloxacin** | 2,9 | [1.4, 5.6] |
| **Amoxicillin clavulanic acid** | 3,0 | [1,5, 5,8] |
| **Clofazimine** | 3,6 | [1,3, 8,6] |
| **Ethambutol** | 4,0 | [2,4, 6,8] |
| **Levofloxacin** | 4,1 | [1,9, 8,8] |
| **Streptomycin** | 4,5 | [2,3, 8,8] |
| **Cycloserine /terizidone** | 7,8 | [5,8, 10,9] |
| **Capreomycin** | 8,4 | [5,7, 12,2] |
| **Pyrazinamide** | 8,8 | [5,6, 13,2] |
| **Ethionamide / protionamide** | 9,5 | [6,5, 14,5] |
| **Amikacin** | 10,3 | [6,6, 17,0] |
| **Kanamycin** | 10,8 | [7,2, 16,1] |
| ***p-aminio salicylic acid*** | 14,3 | [10,1, 20,7] |
| **Thioacetazone** | 14,6 | [4,9, 37,6] |
| **Linezolid** | 17,2 | [10,1, 27,0] |

# Drug-Induced Liver Toxicity (DILI)




Musso *et al. BMC Infectious Diseases* (2019) 19:882
https://doi.org/10.1186/s12879-019-4494-1

BMC Infectious Diseases

CASE REPORT Open Access

## Hepatitis C virus infection: a challenge in the complex management of two cases of multidrug-resistant tuberculosis

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**Abstract**

**Background:** Multidrug-resistant tuberculosis (MDR-TB) requires lengthy use of second-line drugs, burdened by many side effects. Hepatitis C virus (HCV) chronic infection increases risk of drug-induced liver injury (DILI) in these patients. Data on MDR-TB patients with concurrent HCV chronic infection treated at the same time with second-line antitubercular drugs and new direct-acting antivirals (DAAs) are lacking. We evaluate if treating at the same time HCV infection and pulmonary MDR-TB is feasible and effective.

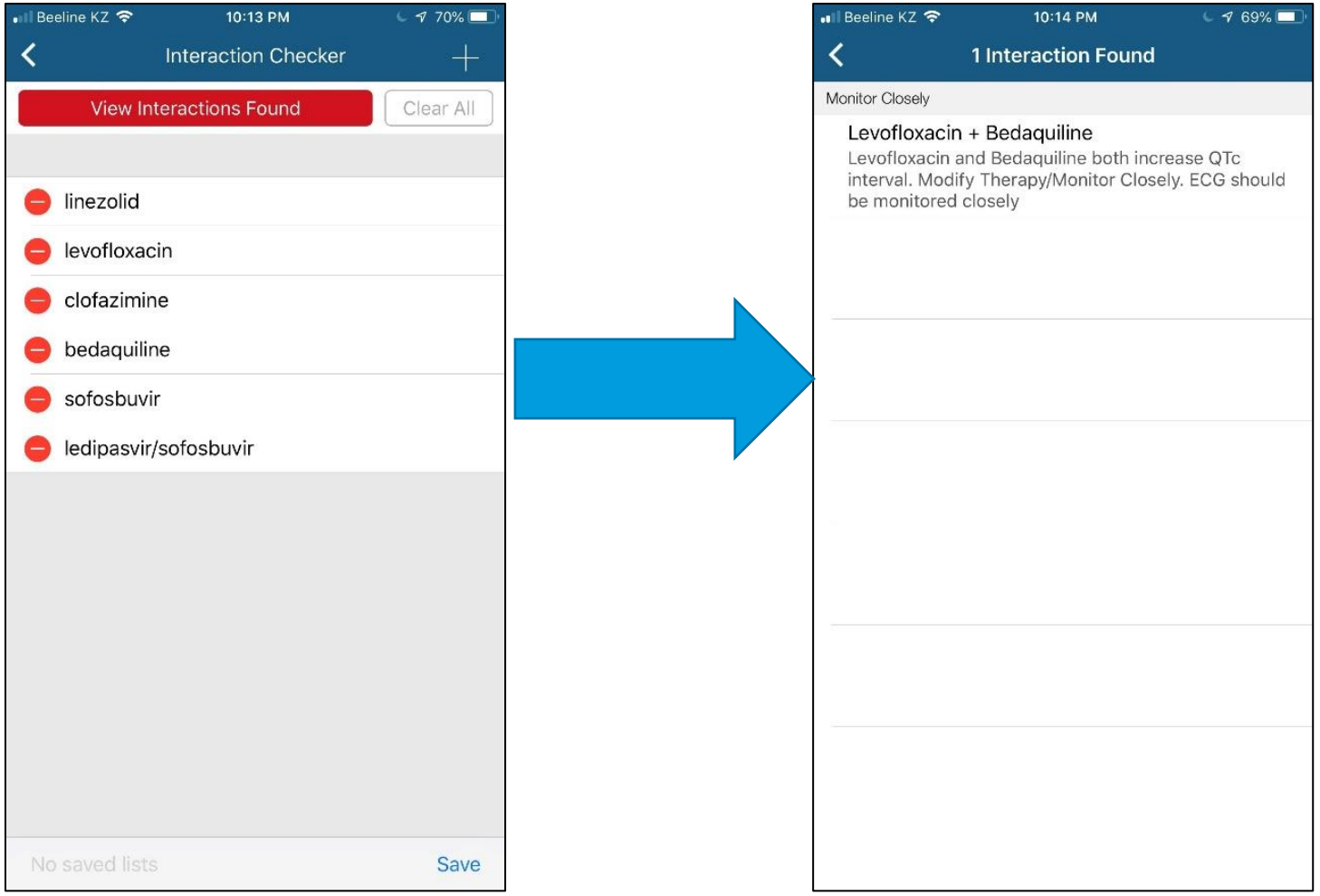
**Cases presentation:** In this study, we described two cases of patients with pulmonary MDR-TB and concurrent HCV chronic infection cured with DAAs at a Tertiary Infectious Diseases Hospital in Italy. During antitubercular treatment, both patients experienced a DILI before treating HCV infection.
After DAAs liver enzymes normalized and HCV RNA was undetectable. Then antitubercular regimen was started according to the institutional protocol, drawn up following WHO MDR-TB guidelines. It was completed without further liver side effects and patients were declared cured from both HCV infection and MDR-TB.

**Conclusions:** We suggest to consider treatment of chronic hepatitis C with DAAs as a useful intervention for reintroduction of second-line antitubercular agents in those patients who developed DILI, reducing the risk of treatment interruption when re-exposed to these drugs.

**Keywords:** Multidrug-resistant tuberculosis, Chronic hepatitis C, Treatment, Drug-induced liver injury

*Hepatitis C virus infection: a challenge in the complex management of two cases of multidrug-resistant tuberculosis.* Musso et al. BMC Infectious Diseases (2019) 12:882

# Medscape: drug interaction monitoring



# University of Liverpool Hep Drug Interaction Checker

https://www.hep-druginteractions.org/checker#

Do Not Coadminister | Potential Interaction | Potential Weak Interaction | No Interaction Expected

Results Key

| | DCV | LED/SOF | SOF/VEL | SOF/VEL/VOX |
|---|---|---|---|---|
| Bedaquiline | ◆ | ■ | ◆ | ◆ |
| Clofazimine | ◆ | ◆ | ◆ | ◆ |
| Delamanid | ◆ | ◆ | ◆ | ◆ |
| Levofloxacin | ◆ | ◆ | ◆ | ◆ |
| Linezolid | ◆ | ◆ | ◆ | ◆ |

**Concomitant use has not been studied. Bedaquiline is metabolized by CYP3A4 and its concentration may increase due to moderate CYP3A4 inhibition by Ledipasvir. It should be prescribed with caution due to the narrow therapeutic index of Bedaquiline and the risk of SAE. If concomitant use is necessary, than more frequent ECG and transaminases monitoring is recommended.**

# Opportunities: Operational Research and Programmatic Components


# Conclusion

Hepatotoxicity occurs during treatment of TB and drug-resistant tuberculosis

HCV is associated with increased hepatotoxicity

Lack of clear recommendations on treatment of HCV in patients with DR-TB

In many sites where DAAs are available for HCV treatment, they are not available for DR-TB patients

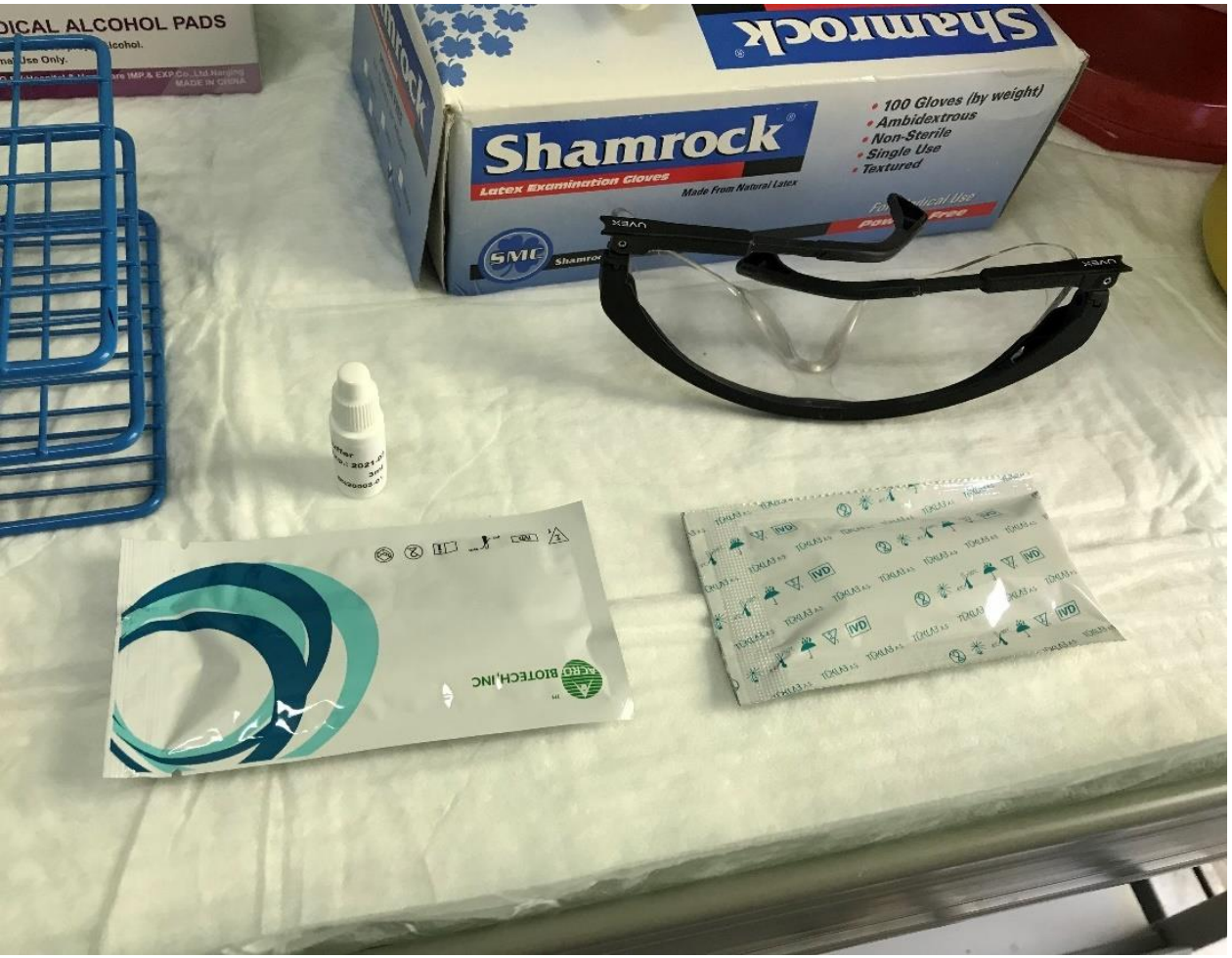
Most DR-TB patients in EECA have history of TB treatment

Risk factors for HCV are very common in patients with DR-TB (history of incarceration, IDU, long-term contact with the health system, and high prevalence of HCV in the region)

# Conclusion

- Screening for active HCV should be performed systematically at the beginning of treatment in all TB patients, especially in those with DR-TB in regions with high HCV prevalence.
- HCV treatment may be considered in patients with DR-TB who are unable to receive treatment due to hepatotoxicity and a high risk of liver cirrhosis.
- Current treatment of HCV with DAA agents is compatible with the DR-TB treatment, and there is no drug interaction with the majority of drugs for the treatment of DR-TB.
- Dual therapy for DR-TB and HCV is possible with close monitoring and direct observation at the PHC level.
- Active drug safety monitoring during TB treatment and the use of patient-centered models of care that are used in TB control programs can ensure proper treatment of patients with comorbidities and increase treatment success rate.
- Operational research in the field of DR-TB, in particular in the WHO European Region, is an opportunity to improve treatment outcomes, improve patients' quality of life, strengthen integration with the infection disease services and inform the development of new recommendations by the World Health Organization.

# HIV, HCV and TB Screening




# Thank you!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