Treatment of latent tb guidelines

The guidelines recommend three preferred and two alternative treatment regimens. The three preferred regimens chosen for efficacy, safety and high treatment completion rates are based on rhymcycin. This is three months of razoniazid plus rifapentin for adults and children over 2 years of age, regardless of HIV status; four months of daily rifampina; or three months of daily isoniazid plus rifampin. Rhymamicin-based regimens have a long list of drug interactions, including warfarin, oral contraceptives, azolam and HIV antiretroviral therapy. Alternative recommended schemes are six or nine months of daily isoniazid, with six months preferred for HIV-negative adults and children. These schemes are also recommended for individuals who are unable to adopt a rhyming-based regime because of drug intolerance or drug interaction. Sarah Coles, M.D., Phoenix, a member of the AAFP Public Health and Science Commission, told AAFP News that management reported shorter duration regimes had higher completion rates and less toxicity, with similar effectiveness to longer monotherapy regimens with isoniazid. Make sure to carefully check your patient's drug list to assess possible drug interactions before prescribing rhyamcin-based circuits, she added. Screening for the LTBI United States Preventive Care Task Force recommends LTBI screening in populations that are at increased risk, a recommendation supported by AAFP. These include patients born in countries with high rates of tuberculosis or former residents, as well as people who live or have lived in high-risk places, such as homeless shelters or correctional facilities, Coles said. The best way to catch these people is to be familiar with risk factors, identify risk factors during office visits and to screen these patients for either TB skin tests or interferon-gamma-release analyses like T-Spot or quantiferon-TB Gold, she said. Hidden TB is defined as an infection of M. tuberculosis in the absence of clinical diseases. Individuals with LTBI are imptomatic but have an immune response to M. tuberculosis antigens. Family doctors should remember that just because the patient is askiptomatic, this does not mean that their hidden infection will not pass on to active TB. To diagnose LTBI, active TB must be eliminated, Coles said. This will require a history and physical search for signs and symptoms of active tuberculosis, as well as chest X-rays, she said. If X-rays show lung penetration, lymphadenapathy, damage to the cavity or if the patient has symptoms consistent with active TB, sputum should be obtained for smear bacilli and culture. Symptoms of active tuberculosis include coughing, fever, haemoptism, night sweats and weight loss. Coles said she treated LTBI in her practice, and on cases identified by LTBI through screening and managed treatment. My last case was of a woman who immigrated from a county with a high prevalence of tuberculosis, she said. Due to numerous drug drug interactions, she was unable to get a rhyfacin-based regimen. She has completed a six-month isoniazid regimen and is very well-treated. Final thoughts Coles said the new guidelines sought to answer the question Which ltBI treatment regimens have the greatest efficacy and least toxicity? With regard to the limitations of the manual, she said hepatotoxicity was the only comparative indicator of toxicity assessment, and she noted that the guidelines did not recommend or evaluate evidence on who to test and treat or to manage side effects. In addition, Coles noted that periodic regimens are recommended to be administered with directly observed therapy that may increase the cost or create a barrier for patients who have difficulty getting an appointment. In addition, when choosing a regimen, she said, family doctors should take into account the cost, feasibility, comorbidities, drug interactions and patient preferences. Finally, Coles said that LTBI treatment is good within family medicine. Family doctors should screen high-risk individuals and then provide treatment as needed, she said. Patients feel safe and most supported in their primary care home, and we can help monitor adherence to treatment regimens, assess side effects and identify the right patients for treatment. Timothy R. Sterling, MD1; Jibril Njier, MPH2; Dominique Senner, MD3; David L. Cohn, MD4; Randall Reves, MD4; Amina Ahmed, MD5; Dick Menzies, MD6; C. Robert Horsburgh Jr., MD7; Charles M. Crane, MD8; Marcos Burgos, MD8.9; Philip Lobu, MD2; Carla A. Winston, PhD2; Robert Belknap, MD4.8 (View Author Affiliation) View offered a quote summary of the Comprehensive Guidelines for the Treatment of Hidden Tuberculosis Infection (LTBI) among individuals living in the United States was last published in 2000 (American Thoracic Society). The CDC targeted TB testing and treatment of a latent tuberculosis infection. Am J Respir Crit Care Med 2000;161:S221-47). Since then, several new schemes have been carried out in clinical trials. To update previous guidelines, the National Association of TB Controllers (NTCA) and the CDC convened a committee to conduct a systematic review of literature and make new recommendations on the most effective and least toxic treatment regimens for LTBI among individuals living in the United States. A systematic review of the literature included clinical trials of LTBI treatment regimens. evidence (high, moderate, low or very low) in clinical trials was evaluated using recommendation, development and evaluation criteria (GRADE). In addition, meta-analysis evaluated patterns that were not directly compared in clinical trials. The result of efficiency was tuberculosis disease; the result of toxicity was hepatotoxicity. Strong GRADE recommendations required at least moderate evidence of efficacy and that the desired effects outweighed the undesirable effects in most patients. GRADE conditional recommendations were aligned in cases where the definition of desirable effects outweighed the undesirable effects, was uncertain (e.g. through substandard evidence). These updated 2020 LTBI treatment guidelines include NTCA- and CDC-recommended treatment regimens that include three preferred rhyming-based regimens and two alternative monotherapy regimens with daily isoniazid. All recommended treatment regimens are intended for individuals infected with mycobacterium tuberculosis, which is supposed to be susceptible to isoniazid or rifampin. These updated guidelines do not apply where there is evidence that the M. tuberculosis infecting strain is resistant to both isoniazid and

rifampine; Recommendations for the treatment of contacts exposed to multidrug-resistant tuberculosis were published in 2019 (Nahid P, Mase SR Migliori GB, etc. Treatment of Drug-Resistant Tuberculosis. Am J Respir Crit Care Med 2019;200:e93-e142). Three rhymamicin-based preferred regimes 3 months once a week isoniazid plus rifapentine, 4 months daily rifamping, or 3 months of daily isoniazid plus rifampin. The appointment of suppliers or pharmacists who are unfamiliar with rifamping and rifapentin can confuse the two drugs. They are not interchangeable and caution should be exercised to ensure that patients receive the correct medication for the intended regimen. Preference for these reef-based regimens was based on efficacy, safety and high treatment completion rates. Two alternative treatments daily for 6 or 9 months; monotherapy isoniazid is effective, but has a higher risk of toxicity and lower completion rates than shorter rhymes. Thus, short courses (3 to 4 months) of rhymamicin-based treatment regimens are preferable to a longer course (6-9 months) of isoniazid monotherapy to treat LTBI. These updated guidelines can be used by physicians, public health officials, policy makers, health organizations, and other state stakeholders and local stakeholders who may need to adapt them in appropriate clinical settings. By one quarter of the world's population (approximately 2 billion people) is infected with mycobacterium tuberculosis (1), including approximately 13 million people in the United States (2). Most infected people are askiptoma and are classified as having a latent tb infection (LTBI). If left untreated, about 5%-10% 5%-10% LTBI progress to tuberculosis (TB) disease during its lifetime (3-5). Progression from untreated LTBI accounts for about 80% of TB cases in the U.S. (6). LTBI treatment is effective in preventing progression to tuberculosis disease (7). The most recent comprehensive guidelines for LTBI treatment in the United States were published in 2000 (8). In 2003, the CDC and the American Thoracic Society recommended not to use a 2-month regimen of rifampina plus pirazinamide due to the risk of severe hepatotoxicity (9). Since then, several new schemes have been carried out in clinical trials. To update the treatment guidelines of 2000 and 2003, the National Association of Tb Controllers (NTCA) and the CDC convened a committee to conduct a systematic literary review of clinical trials for LTBI treatment. Evaluation, development and evaluation criteria (GRADE) were applied to evidence of effectiveness, networked meta-analysis of selected evidence was carried out, and evidence was used to support the 2020 LTBI treatment guidelines. These updated LTBI 2020 treatment guidelines apply to individuals with LTBI who live in the United States. In addition, these guidelines apply to persons infected with M. tuberculosis, who are believed to be susceptible to isoniazid or rifampine; they are not used when there is evidence that the M. tb infecting strain is resistant to both isoniazids and rifampine. Local and government TB programs in the United States answer questions about the diagnosis and treatment of individuals with LTBI in their jurisdictions (badge). Members of the LTBI treatment committee, who are the authors of this report, have been appointed based on their experience in LTBI treatment. The Committee has expertise in epidemiology, domestic and international TB control, clinical trials and LTBI treatment in adults and children. Methodology, experience in the GRADE approach, has worked as a consultant on the guidelines committee. The Evidence Search Committee has determined that the following clinical issue should be addressed in the updated guidelines: Which treatment regimens for latent tuberculosis infection have the greatest efficacy and least toxicity? The question was written in the format of population, intervention, comparator, results (PICO), and then the results were assessed as critical, important or not important. Comparison of the toxicity of the regime was limited by hepatotoxicity because it was the only toxicity that could be consistent compared to studies. In December 2017, a systematic literary check was launched. Electronic databases including MEDLINE, Embase, CINAHL, ClinicalTrials.gov, Cochrane Central Register (CENTRAL) and grey grey studies have been conducted assessing the effectiveness of LTBI treatment regimens. Search terms included hidden tuberculosis, hidden TB, LTBI, mikobacteria tuberculosis, tuberculosis infection and isoniazid, rifampin, rifapentin or pirazinamide. Articles were included if the design of the study was a randomized controlled trial and the results included the prevention of tuberculosis and drug-related hepatotoxicity. Studies that included persons with suspected or confirmed TB were excluded from the review. The initial search revealed a high-quality systematic review and meta-analysis published in August 2017 that examined the effectiveness of LTBI treatment regimens (10). The authors of the study were contacted and asked to access the extracted data. Study characteristics, participants' types, interventions, measured results and results were extracted from each study. If the data is prepared for the merger, the effects are evaluated by meta-analysis. A random effects model was used for meta-analysis, unless otherwise stated, and effect estimates were reported as coefficients. All statistical analyses were conducted using a packet of metaphors in R, versions 3.4.3 (11). The Cochrane Bias Risk Tool was used to assess bias (12). The analyses conducted in 2018 included combined research data from the previous review and articles from an updated study survey published in June 2017-August 2018 (Figure) (13.14). All treatment regimens were analyzed using Bayesian Network Meta-Analysis (NMA), which allowed indirect comparisons of treatment regimens in the presence of direct comparisons. However, the preferred method was direct, paired meta-analysis; network analysis is presented in this report only if no direct comparisons have been made. A full description of the network analysis method (10.15) was previously published. The NMA allows indirect comparisons of treatment regimens through the withdrawal of evidence from the network. For this analysis, WinBUGS Software (Version 1.4; Department of Biostatistics of the Medical Research Council of the University of Cambridge) was used to create a Bayesian network with a rear distribution based on 20,000 samples after a period of burning 10,000 iterations (15). Convergence was assessed by checking the parameters of the chains and diagnosing Helman-Rubin (16). Brief statistics and 95% of reliable intervals were derived from rear distributions. The network inconsistency that can occur if indirect comparisons contradict direct pair estimates was assessed compared to standard meta-analysis and an omnibus consistency test (17). Total evidence quality using the GRADE approach, and GRADEpro software was used to develop evidence it summarizes the quality of the evidence for each result (high, moderate, low or very low) and the quality of the evidence estimate (18). Comparison of regimes assessed in clinical trials was assessed in accordance with the study population: adults, children, HIV-positive and HIV-negative. There are references to all studies included in the analysis (Additional tables; . The Committee discussed the evidence in face-to-face meetings and teleconferences. The GRADE data tables were prioritized in line with research schemes, comparisons, and populations that were found to be most clinically relevant to the United States. If discrepancies were found between GRADE head-to-head comparisons and network meta-analysis results, the committee prioritized GRADE comparison. The recommendations were based on the following considerations: the balance of the desirable effects of intervention (benefits) and adverse effects (complexity of the regime, adverse effects and cost), the quality of the evidence, the values and preferences of patients and feasibility (19). The desirable and undesirable consequences considered by the Committee include both the effects on individuals and on general public health. A strong GRADE recommendation for the regimen was made if the team concluded that the desired effects of the intervention outweighed the undesirable effects, most well-informed patients would choose the regimen, and the evidence was of at least moderate quality (18.19). A conditional review of the GRAD for the regime was made when there was uncertainty as to whether the undesirable effects outweighed the undesirable effects (e.g., the poor quality of evidence for a critical outcome so that additional evidence could alter the key findings, hence the recommendation) (18.19). The conditional recommendation indicates that well-informed patients may choose differently whether to choose a regimen (18.19). The group also prioritized recommended regimes as preferred or alternative. Preferred regimens have been identified as having excellent tolerability and effectiveness, shorter duration of treatment and higher completion rates. Alternative regimens have been identified as having excellent efficacy, but longer treatment durations and lower completion rates. The rationale for regime priorities was that the completion rates were higher for shorter regimens (20); if the modes have similar efficacy and security, the shorter mode is more effective because the completion rates are higher. Draft recommendations were publicly presented at the meeting U.S. Tuberculosis Elimination Council december 11, 2018 and at the NTCA meeting on April 23, 2019. The recommendations were well received on the and there have been no significant changes to the recommendation since then. Presented are THE GRADE evidence tables (table 1) (Additional tables; . Additional tables contain all links; Selected links are included in this report. A total of 55 clinical trials rated efficacy (7,13,14,21-74), and 31 trials assessed toxicity (13,14,27,35-3 8.43-46,49,51-53,55,61-66,68,71,72,75-82). Presented the results of the updated network meta-analysis for 2018 (table 2); 63 studies of 16 schemes (7,13,14,21-82) were evaluated. A summary of the evidence and recommendations of the recommended treatment regimens include three preferred and two alternative treatment regimens (tables 3 and 4). Rhophamicin-based schemes, including 3 months once a week isoniazid plus rifapentine, 4 months of daily rifampin, and 3 months of daily isoniazid plus rifampin are preferred recommended regimens because of their effectiveness, safety and high treatment completion rates. Six or nine months of daily isoniazid regimes are alternative recommended modes; although they are effective, they have a higher risk of toxicity and lower completion rates that reduce effectiveness. Based on the most recent comprehensive GUIDELINES for LTBI treatment in the United States, which were published in 2000 (8), 9 months of daily isoniazid was considered a standard comparator regimen to evaluate shorter course regimes. Data on the efficacy and toxicity of 9 months of daily isoniazid are provided, as well as data on other recommended modes. The reef-based regimen refers to a treatment that includes either rifampin or rifapentine. The preferred three month weekly Isoniazid Plus Rifapentine regime of 3 months once a week isoniazid plus rifapentin is the preferred regimen, which is highly recommended for adults and children aged 2 years, including HIV-positive individuals (as drug interactions allow). This regimen, administered through directly observed therapy, had an equivalent efficacy and was no more toxic than the standard 9 month daily isoniazid regimen in adults and children aged 2 years (53.68.83). The completion rates were higher with a 3-month regimen. In HIV-negative individuals in the study noninferiority, 3 months of isoniazid and rifapentine was equivalent and was associated with less hepatoxyity than 9 months of isoniazid, despite a greater cessation due to side effects (68). There was no significant difference in the comparison of isoniazid plus rifapentin in all outcomes with 6 or 9 months of isoniazid (22.53). In a study of noninferiority 3 months of weekly isoniazid plus rifapentin, the rate of completion of self-therapy was speed with direct observation, but noninferior in the foreseeable foreseeable United States (84). Potential drawbacks of this regimen include the cost of drugs which is greater than most alternatives, the potential additional costs if provided directly observed therapy (with the completion of treatment is the highest with directly observed therapy, although self therapy is an approved option) (85), the need to take numerous pills simultaneously (10 tablets once a week compared to two or three tablets per day for other regimens for most adults), and a link with a systemic drug reaction or flu-like syndrome, which can include syncopation and hypotoni. Severe events requiring hospitalization occurred in 0.1% of people (68.86). The systemic reaction of the drug is self-sufficient and usually mild; There were no reports of casualties. Potential drug interactions and acquired drug resistance are also important considerations for all treatment regimens if tb disease is not properly ruled out. The four month daily Rifampin regimen of 4 months daily is the preferred treatment, which is highly recommended for HIV-negative adults and children of all ages. (There is no evidence of efficacy in HIV-infected people.) The effectiveness of this regimen was clinically equivalent and less toxic than the standard 9 month daily isoniazid regimen in adults and children (13,14,78,79). Four months of daily rifampina had a non-inferior effectiveness in preventing tuberculosis disease compared to 9 months of daily isoniazid, as well as lower discontinuation due to side effects, lower hepatotoxicity and higher completion rate (13.14). Potential drawbacks of rhofamicin-based regimens are numerous drug interactions, including warfarin, oral contraceptives, azol antifungal drugs and HIV antiretroviral therapy (87). Rifabutin has less or less pronounced medicinal interactions and can be used instead of rifampin when rifampin is contraindicated due to medicinal interactions and isoniazid cannot be used (87). The medicinal interactions with weekly rifapentine are less than with rifampin, and appear to be less than with rifabutin; therefore, weekly isoniazid and rifapentin can be considered when rifampin is not suitable, although clinical data are limited (88). Drug interactions between rhyamycin and antiretroviral therapy are regularly updated by the U.S. Department of Health and Human Services (badge). HIV-positive people with low lymphocytes CD4 risk of developing a amptomy or tuberculosis disease is on the rise, which may contribute to rifampin resistance if tuberculosis is inadvertently treated with rifampine monotherapy (89). Three months daily Isoniazid Plus Rifammpin regimen 3 months daily isoniazid plus rifampin is the preferred treatment which recommended for adults and children of all ages and for HIV-positive people as it allows medicinal interactions. HIV-negative adults and children with a positive tuberculin skin test (TST) who received 3 months of daily isoniazid plus rifampin appear to have a similar risk of tuberculosis, hepatotoxicity, and side effects requiring discontinuation of therapy as those who received ≥6 months of isoniazid (23.35,44,51,90). Among children aged 15 years, in particular, the 3-month course of daily isoniazid plus rifampin was as effective as a 6-month or longer course of isoniazid, because direct comparisons found no difference in tuberculosis diseases and no differences in side effects requiring discontinuation of therapy or hepatotoxicity (67). THERE was no difference in TB incidence among those who received 3 months of daily isoniazid plus rifampin compared to those who received isoniazid monotherapy in ≥6 months, regardless of whether they were positive, TST negative or anergic (34,46,63,72). Hepatotoxicity was less common among those receiving a shorter course of therapy, although discontinuation of therapy due to side effects was more frequent (63). Potential drug interactions with rifampin and acquired drug resistance are also important considerations if TB disease is not properly ruled out (see the previous section on 4 months of daily rifamping). In addition, the risk of hepatotoxicity may be greater with the two drugs given together than with any drug given alone (91). Alternative schemes: Six or nine months of daily isoniazid Regimens 6 or 9 months of daily isoniazid are alternative recommended modes; 6 months a day is highly recommended for HIV-negative adults and children of all ages and conditionally for HIV-positive adults and children of all ages and 9 months daily is conditionally recommended for adults and children of all ages, both HIV-negative and HIV-positive. Isoniazid reduces the risk of developing TB in people with TST-positive, including HIV-negative adults and children (7,23,28,43,47,73), HIV-positive adults (27,38,42,46,60,72), and presumably also HIV-positive children. The drug can cause hepatotoxicity and be associated with discontinuation due to side effects, although these effects are more common in adults than children (23.43). In HIV-positive people with negative TST, anergia or unknown TST, the benefits of isoniazid are uncertain in conditions of low tb incidence (38). For these HIV-infected people, there is potential to reduce the incidence of tuberculosis and increase the side effects of isoniadide therapy; However, the likelihood of these remains uncertain due to wide confidence intervals resulting from too few events. The synthesis of evidence included several durations of isoniazid therapy in individuals with TST (3, 6 and 12 months in HIV-negative people and 6 months in HIV-infected people) (7.72). Among HIV-negative people with inactive tuberculosis (defined as the presence of tuberculosis, stable pulmonary lesions and negative sputum cultures in individuals who had not previously been treated), 6 and 12 months of therapy were more effective than 3 months of therapy, demonstrating the benefit of LTBI treatment isoniazid in this subset of high-risk LTBI (7) patients. Studies of other schemes have individuals with LTBI and fibrous lesions, but in much smaller amounts (14.68). A systematic review of 6 months of therapy among HIV-positive people was highly effective (72), and the effect of other durations was unknown. In addition, an analysis was considered that included different, smaller trials than included in this report and found that 9 months of daily isoniazid therapy may be more effective than 6 months and similar to 12 months (25.92-94). However, there was no clinical trial data available directly comparing 9 months of isoniazide with placebo, 6 months of isoniazid, or 12 months of isoniazid. Among HIV-positive people living in areas with high TB incidence, isoniazid complements antiretroviral therapy in the prevention of tuberculosis. Two randomized controlled trials have shown that isoniazid plus antiretroviral therapy reduced the incidence of tuberculosis more than isoniazid alone or antiretroviral therapy (27.61). Potential deficiencies in the regimen include its long duration, hepatoxyity and low completion rates (primarily due to the first two factors). A systematic review of clinical trial data on the efficacy and toxicity of LTBI treatment was carried out, including studies published after the 2018 World Health Organization's LTBI guidelines (95). The quality of the evidence was evaluated using the GRADE approach, and a networked meta-analysis was conducted, updated to include data from studies published after the previous meta-analysis of the network (10), to compare circuits not evaluated head-to-head in clinical trials. The recommendations were based on a balance of the desirable and undesirable effects of intervention, the quality of evidence, the values and preferences of patients, and feasibility. These factors also reported priority rank schemes as preferred or alternative, with a preference for shorter circuits, given their similar effectiveness compared to 6-9 months of isoniazid, but favourable tolerance and higher completion rates. This combination of characteristics should lead to greater effectiveness of shorter circuits in clinical settings. More LTBI treatment will facilitate the elimination of tuberculosis (96). The appointment of suppliers or pharmacists who are unfamiliar with rifampin and rifippentine can confuse Drugs. They are not interchangeable and caution should be exercised to ensure that patients receive the correct medication for the intended regimen. Although 9 months of isoniazid was the preferred regimen in the guidelines published in 2000, both 6 and 9 months of isoniazid were recommended at that time (8). In these current guidelines, the application of THE criteria has led to strong recommendations within 6 months of isoniazid as an alternative for those individuals who cannot adopt a shorter preferred regimen (e.g. due to intolerance to drugs or interactions with drugs), especially in HIV-negative individuals. Two months of rifampina plus pirazinamide are not recommended for LTBI treatment due to the risk of hepatotoxicity. However, in persons empirically treated for tuberculosis with isoniazid, rifampina and pirazinamide within 2 months, this regime will effectively treat LTBI in persons who have subsequently been identified as patients with LTBI, not tuberculosis. Here are a number of considerations for the use of these guidelines. First, the Committee does not include cost-effectiveness in the evaluation of evidence; recommendations were based on an assessment of the effectiveness and toxicity of the regimes. Secondly, the committee did not evaluate the evidence on how to implement these schemes in a programmatic way (e.g., who to test and treat and treat side effects). Thirdly, the guidelines focus on treatment regimens for people with LTBI living in countries with low TB incidence. These guidelines do not apply to other strategies for preventing empirical tuberculosis (e.g., 1 month of isoniazid plus rifapentine among HIV-positive people living in high TB incidence, regardless of TST results or interferon-gamma emission analysis(97). Finally, shorter regimens should not be used for patients who have non-drugs, including those taking drugs with significant drug interactions with rhyamycin. For patients without drug tolerability or drug-drug interactions, short-term (3-4 months) rhyming-based treatment regimens are preferable for a longer course (6-9 months) of isoniazid monotherapy to treat LTBI. These guidelines can be used by physicians, public health officials, policy makers, health organizations, and other stakeholders in the states and locals who may need to adapt these guidelines to individual clinical conditions. Local government TB programs in the United States answer questions about the diagnosis and treatment of individuals with LTBI in their jurisdictions (badge). 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One month of rifapentine plus plus HIV-related tuberculosis prevention. N Engl J Med 2019;380:1001-11. CrossRefexternal icon PubMedexternal icon Abbreviation: LTBI - Hidden Tuberculosis Infection. Existing systematic review search: The results of the 2017 analysis were published, citing all the initial studies included in the analysis (Senner D, Beer N, Harris RJ, Lipman MC, Stagg HR, van der Werf MJ. Treatment of latent tuberculosis infection: updated network meta-analysis. Ann Intern Honey 2017;167:248-5). Updated search: The analyses included combined data from studies included in the previous review and articles identified in an updated study search published in June 2017-August 2018. Population Test Number Experimental Mode Comparison Mode Efficiency Toxicity 3 mos isoniazid plus rifapentin given once a week 9 mos isoniazid HIV-positive adults 1 1 3 mos iszid plus rifapentin given once a week 9 mos isoniazid HIV-negative adults and children 1 1 3 moszioniad plus rifapentin, given once a week 9 mos isoniazid HIV-negative children 1 1 3 mos isoniazid plus rifapentin given once a week 6 mos isoniazid HIV-positive adults 1 1 3 mos isoniazid plus rifampin, Given daily 9 mos isonia zid HIV-negative adults 1 1 1 3 mos isoniazid plus rifampin is given daily 6 mos isoniazid HIV negative adults and children 3 2 3 mos isoniazid plus rifampin is given daily 6 mos isoniazid HIV-positive adults 4 4 3 mos iszionia d plus rifampin , given the daily placebo or without treatment of HIV-positive adults 2 1 3 mos isoniazid plus rifampin, given daily Placebo or without treatment of HIV-negative adults and children 2 0 4 mos rifampin, given daily 9 mos isoniazid HIV-negative adults 1 2 4 mos rifampin is given

daily 9 mos isoniazid HIV-negative children 1 1 4 mos rifampin is given daily 6 mos isoniazid HIV-negative children 1 0 6 mos isoniazid given daily Placebo HIV-negative adults and children 4 x 2 6 isonia is Daily Placebo or No Treatment of HIV-Positive Adults 5 3 9 mos isoniazid daily No treatment for HIV-negative adults and children 2 0 12 mos isoniazid given daily No treatment for HIV-positive adults 2 0 12 mos isoniazid given daily Placebo HIV-positive Adults and children 5 3 12 mos isoniazid given daily Placebo HIV-positive children 3 1 12 mos isoniazid given daily placebo or without treatment HIV-negative adults and children 15 15 5 3 mos isoniazid reef pluspentin given once a week Continuous Isoniazid (up to 6 years) HIV-positive adults 1 1 1 2 mos rifampin and pirazinamide, given daily or twice a week 6 mos isoniazid , 12 mos isoniazid HIV-positive adults and children 4 2 Abbreviation: GRADE - Assessment of recommendations, development and evaluation. Detailed information is available and information on the quality of evidence (Additional tables; . Risk and Treatment Ratio 2017 (unpublished) Coefficient Ratio (95% Reliable Interval) Odds (95% (95% interval) Tuberculosis risk compared with no treatment No treatment 1 (ref) 1 (ref) 3 mos isoniazid plus rifapentine given once weekly 0.36 (0.18–0.73) 0.36 (0.18–0.72) 3–4 mos rifampin given daily 0.25 (0.11–0.57) 0.25 (0.12–0.50) 3 mos isoniazid plus rifampin given daily 0.33 (0.20–0.54) 0.33 (0.20–0.53) 6 mos isoniazid given daily 0.40 (0.26–0.60) 0.40 (0.26–0.59) 9 mos isoniazid given daily 0.46 (0.22–0.95) 0.47 (0.24–0.90) Hepatotoxicity risk compared with no treatment No treatment 1 (ref) 1 (ref) 3 mos isoniazid plus rifapentine given once weekly 0.52 (0.13–2.15) 0.53 (0.13–2.13) 3–4 mos rifampin given daily 0.14 (0.02–0.81) 0.13 (<0.02–0.72) 3 mos isoniazid plus rifampin given daily 0.72 (0.21–2.37) 0.73 (0.22–2.38) 6 mos isoniazid given daily 1.10 (0.40–3.17) 1.11 (0.41–3.15) 9 mos isoniazid given daily 1.70 (0.35–8.05) 1.77 (0.35–8.32) Abbreviation The results of the 2017 analysis were published, citing all the initial studies included in the analysis (Senner D, Beer N, Harris RJ, Lipman MC, Stagg HR, van der Werf. Treatment of latent tuberculosis infection: updated network meta-analysis. Ann Intern Med 2017;167:248-55.); The 2018 update includes data subsequently published (Diallo T, Adjobimey M, Ruslami R, etc. Safety and side effects of rifampin compared to isoniazid in children. N Engl J Med 2018;379:454-63; Menzies D, Adjobimey M, Ruslumi R, et al. Four months of rifampin or nine months of isoniazid in late-tb adults. N Engl J Med 2018;379:440-53). Priority Rank Recommendations (strong or conditional) Evidence (high, moderate, low, or very low) Preferred 3 mos isoniazid plus rifapentin, given once a week Strong Moderate Preferred 4 mos rifampin, given the daily Strong Moderate (HIV negative)† Preferred 3 mos isoniazid plus rifampin, given the daily Conditional Very Low (HIV-negative) Conditional Low (HIV-positive) Alternative 6 mos isoniazid given the daily strong (HIV-negative) Conditional Moderate (HIV-positive) Alternative 9 mos iszioniad Shorter duration of treatment, higher completion rates than longer regimens and therefore higher efficacy; Alternative: excellent efficacy, but concerns about longer-term treatment, Lower completion rates, and therefore lower efficacy.† No evidence recorded in HIV-positive individuals. Dose duration of the drug and age group Frequency Of General doses of Isoniazid and rifapentin† 3 mos Adults and children ≥12 years Once a week 12 Isoniazid: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum rifapentin: kg, 300 mg 14.1-25.0 kg, 450 mg 25.1-32.0 kg, 600 mg 32.1-49.9 kg, 750 mg ≥50.0 kg, 900 mg maximum Children aged 2-11 yrsoniazizzid: 25 mg/kg; 900 mg maximum rifupentin†: see above Rifammpina 4 mos Adults: 10 mg/kg Daily 120 Children: 15-20 mg/kg Maximum dose: 600 mg Isoniazid and rifampin 3 mos Adults Daily 90 Isoniazid: 5 mg/kg; 300 mg maximum Rifammpin: 10 mg/kg; 600 mg maximum Children's isoniazid: 10-20 mg/kg††; 300 mg maximum Rifamminga: 15-20 mg/kg; 600 mg maximum Isoniazid 6 m Adults: 5 mg/kg Daily 180 Children: 10-20 mg/kg†† Maximum dose: 300 mg Adults:15 mg/kg Twice a week 52 Children: 20-40 mg/kg†† Maximum dose: 900 mg 9 mg Adults: 5 mg/kg Daily 270 Children: 10-20 mg/kg†† dose: 300 mg Adults: 15 mg/kg Twice a week 76 Children: 20-40 mg/kg†† Maximum dose: 900 mg and isoniazid as 100 mg and 300-mg tablets.† Rifapentin formulated as 150-mg voldal pill packs that should be formulated before use. a health care worker watches medication. Rifampin (rifampicin) is formulated as a 150-mg and 300 mg capsule. The American Academy of Pediatrics recognizes that some experts use rifampin at 20-30 mg/kg for daily prescribing for infants and toddlers (Source: American Academy of Pediatrics. Red Book: 2018 Report by the Committee on Infectious Diseases. 31st o. Itasca, IL: American Academy of Pediatrics; 2018:829-53.†† the American Academy of Pediatrics recommends a dose of isoniazid 10-15 mg/kg for daily regimen and 20-30 mg/kg for a two-week regimen. Recommended quote for this article: Sterling TR, Njie G, zenner D, et al. Guidelines for the Treatment of Hidden Tuberculosis Infection: Recommendations from the National Association of Tuberculosis Controllers and the CDC, 2020. MMWR Recomm Rep 2020;69 (No. RR-1):1-11. DOI: icon. THE MMWR Morbidity and Mortality Report is a hallmark of the U.S. Department of Health and Human Services. The use of trade names and commercial sources only for identification does not imply approval from the U.S. Department of Health and Human Services. Links to non-CDC sites on the Internet are provided as a service to MMWR readers and do not or imply approval of these organizations or their programs by the CDC or the U.S. Department of Health and Human Services. The CDC is not responsible for the content of the pages found on these sites. The URLs listed in MMWR were up-to-date as of the publication date. All HTML versions of MMWR articles are generated from the final evidence through an automated process. conversion can cause character or format translation errors in html. Users refer to the electronic version of the PDF (and/or the original paper copy of MMWR to print official versions of official text, numbers and tables. Issues or messages about formatting errors should be addressed mmwrq@cdc.gov. mmwrq@cdc.gov. cdc guidelines for treatment of latent tb