Latent Tuberculosis Therapy Outcomes in Dialysis Patients: A Retrospective Cohort

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Rationale & Objectives: Maintenance dialysis patients are at an increased risk for active tuberculosis (TB). In 2012, British Columbia, Canada, began systematically screening maintenance dialysis patients for latent TB infection (LTBI) and treating people with evidence of LTBI when appropriate. We examined LTBI treatment outcomes and compared treatment outcomes before and after rollout of the systematic screening program.

Study Design: Retrospective cohort study.

Setting & Participants: The study comprised 365 people in British Columbia, Canada, initiating at least 90 days of dialysis from January 1, 2001, to May 31, 2017, and starting LTBI therapy: 290 (79.5%) people in the recent cohort and 75 (20.5%) in the historical cohort. People starting LTBI therapy from January 1, 2012, onward were classified as the recent cohort, whereas people starting LTBI therapy before January 1, 2012, were classified as the historical cohort.

Exposure: Systematic LTBI screening and therapy.

Outcomes: Proportion of people who experience grade 3 to 5 adverse events (AEs) or any grade rash and end-of-treatment outcomes.

Analytical Approach: Outcomes were reported using descriptive statistics. 2-sample test of proportions using χ^2 distribution was used to test for statistical significance between the recent and historical cohorts.

Results: 298 (81.6%) people successfully completed LTBI therapy. The proportion of people experiencing a grade 3 to 4 AE or any grade rash was 21.1%. Most AEs were related to gastrointestinal events, general malaise, or pruritus that resulted in regimen changes. 2 (0.5%) people were hospitalized for AEs related to LTBI therapy. No significant difference was found between the recent and historical cohorts in all outcomes of interest. No grade 5 AEs (deaths) were attributed to LTBI therapy.

Limitations: Retrospective data and generalizability outside low-TB-burden settings.

Conclusions: Our findings suggest that a high proportion of people receiving maintenance dialysis can complete LTBI therapy. The rate of grade 3 to 4 AEs was high and associated with frequent medication changes during therapy. LTBI therapy in maintenance dialysis may be safe but requires close monitoring.

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Maintenance dialysis is associated with an increased risk for developing active tuberculosis (TB).[1,2] The risk for active TB in people receiving maintenance dialysis is estimated to be close to 10 times higher than in the general population.[1] This increased risk may be attributed to impaired cellular immunity associated with maintenance dialysis or with immunosuppressive therapy and is further compounded by comorbid conditions such as diabetes and HIV infection.[3,4] Additionally, people receiving maintenance dialysis may be at increased risk for TB exposure through increased health care interactions in the communal setting of dialysis units. In low-TB-incidence settings such as Canada, people born in high-TB-incidence regions are disproportionally represented in maintenance dialysis populations, increasing their background risk for exposure to infectious TB.[2,3,5,6]

World Health Organization (WHO) guidelines recommend latent TB infection (LTBI) screening and treatment in maintenance dialysis patients living in low-TB-incidence regions.[7] However, several potential barriers to LTBI therapy are encountered in this population, including the perception that maintenance dialysis patients are at increased risk for adverse events (AEs) from LTBI therapy. Increased risk for AEs during treatment may be due to numerous factors, including advanced age, frequent comorbid illness, and multiple potential drug-drug interactions.[8,9] Knowledge gaps remain in the literature regarding LTBI therapy outcomes among maintenance dialysis patients, as well as in studies that address AEs in this population.

In 2012, British Columbia, Canada, began rollout of a systematic TB screening program for all people initiating maintenance dialysis in the province. The rollout occurred over approximately 3 years, with full implementation of the TB screening program province-wide by late 2015. The screening program intervention includes a TB risk assessment questionnaire, interferon gamma release assay (IGRA), and chest x-ray before dialysis initiation.[10] Results from the screening are then interpreted by TB physicians, who provide recommendations for LTBI therapy. During the study period, isoniazid supplemented with pyridoxine (vitamin B_6) was most commonly recommended, while rifampin and rifabutin were used on a case-by-case basis, particularly given that rifamycin derivatives interact with multiple medications frequently prescribed to maintenance dialysis patients.[11] Before screening program

PLAIN-LANGUAGE SUMMARY

People receiving maintenance dialysis are at an increased risk for active tuberculosis (TB). However, preventative therapy for people receiving maintenance dialysis with latent TB infection (LTBI) is often not provided due to the perceived risks for adverse events (AEs) and potential drug-drug interactions in this population. To study the treatment outcomes and AEs associated with LTBI therapy in this population, we retrospectively analyzed and compared data for British Columbians receiving maintenance dialysis established on a course of LTBI therapy from 2001 to 2017. We found that despite experiencing AEs, a high proportion of maintenance dialysis patients were able to safely complete LTBI therapy.

implementation, there was no population-based systematic TB screening program for people receiving maintenance dialysis, and LTBI screening practices varied across the province. A more systematic and thus less selective approach to LTBI screening and treatment raised concern about the potential for increased risk for AEs in maintenance dialysis patients on LTBI therapy.

This study sought to examine outcomes of LTBI therapy among maintenance dialysis patients screened for LTBI as a part of the provincial program. Our objectives were to: (1) examine the proportion of maintenance dialysis patients with LTBI that completed LTBI therapy, (2) examine the proportion of people who experienced grade 3 to 5 AEs or any rash attributable to LTBI therapy, and (3) compare treatment outcomes between those who were offered LTBI therapy before implementation of the screening program with those who were offered LTBI therapy as a result of the screening program.

Methods

Data Sources and Study Population

We performed a retrospective cohort study to examine LTBI treatment outcomes in people receiving maintenance dialysis in British Columbia, Canada. This study was approved by the University of British Columbia Research Ethics Board (H14-01977). In British Columbia, care of maintenance dialysis patients undergoing LTBI screening is jointly operated through BC Renal, Provincial TB Services at the BC Centre for Disease Control (BCCDC), and the BCCDC Public Health Laboratories. BC Renal is a provincial government-funded network that spans all of British Columbia's health authorities and coordinates renal care for all people living with kidney disease. It also manages the Patient Records and Outcome Management Information System (PROMIS), a province-wide integrated registry and clinical information system that houses individual-level information on people with kidney disease in the province. The BCCDC is a provincial government-funded organization that provides centralized TB screening and treatment services in coordination with health care providers across British Columbia. It stores TB care information for individuals with LTBI or active TB through an electronic provincial TB registry. BCCDC Public Health Laboratories began funding for IGRA screening in select high-TB-risk groups in 2009, and in 2012 began funding for a program of systematic IGRA screening in people initiating maintenance dialysis.

To create our study cohort, we extracted data from PROMIS for all people initiating at least 90 days of dialysis between January 1, 2001, and May 31, 2017. Using unique provincial personal health number (PHN) identifiers, we linked this data to the BCCDC TB registry to identify all people starting LTBI therapy. We further categorized people into 2 groups: people initiating LTBI therapy from January 1, 2012, onward were categorized as the recent cohort, while people starting therapy from January 1, 2001, to December 31, 2011, were categorized as the historical cohort. These dates were chosen to reflect the systematic LTBI screening policy change in 2012. People without a PHN, people with more than 1 month of LTBI therapy before initiation of maintenance dialysis, and people with ongoing LTBI therapy at the time of review were excluded from our study.

Information for AEs and treatment outcomes were obtained through chart review of health care providers' notes and narratives within the electronic provincial TB registry by 2 independent reviewers (L.Y.C. and B.B.) from January 1 to 31, 2019. All extracted data were maintained in private access folders within secured network servers at the BCCDC. Individual-level informed consent for historical records was not required given ethics approval and anonymized data.

Treatment Outcomes

Successful treatment completion was defined as completing a 9-month daily dose regimen of isoniazid and vitamin B_6 (9H) within 12 months or a 4-month daily dose regimen of rifampin or rifabutin (4R) within 6 months.[12] In accordance with the Canadian TB Standards 7th edition, 9H is used in British Columbia instead of the 6-month isoniazid regimen recommended in WHO guidelines.[13] Incomplete treatment was categorized into 5 types: drug intolerance, death, lost to follow-up, nonadherence, and other. The category death was used for all-cause mortality and other was used when treatment was discontinued due to other mental or physical health circumstances unrelated to LTBI therapy at the time. People who required modified regimens to complete LTBI therapy were considered treatment incomplete due to drug intolerance if the regimen was not listed as an acceptable alternative LTBI regimen according to the Canadian TB Standards 7th edition.[13]

Grading of AEs

All patients underwent standard baseline testing, as well as monthly blood work and treatment monitoring throughout the course of LTBI therapy, according to provincial standards, with results entered into the Provincial TB registry.[12] All new or worsening adverse signs and/or symptoms reported by the patient and/or health care provider that developed during LTBI therapy were considered AEs unless clearly attributed to an alternative cause in clinical notes. During the chart review process, AEs were categorized into 8 types: hepatotoxicity, rash, presyncope, gastrointestinal events, general malaise, pruritus, peripheral neuropathy, or other. All AEs were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, with the exception of hepatotoxicity and gastrointestinal events that were graded according to the adapted American Thoracic Society and CTCAE guidelines.[14–16]

Because blood work is regularly entered into the TB registry, elevated liver enzyme levels are regularly compared with the patient's baseline levels, allowing for grading for hepatotoxicity according to the test parameters set by the adapted American Thoracic Society and CTCAE guidelines. When AEs experienced by the patient were not encompassed in the CTCAE terms, AEs were graded according to the CTCAE's general guidelines: "Grade 1 – mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated, Grade 2 – moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living, Grade 3 – severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living, Grade 4 – life-threatening consequences; urgent intervention indicated, Grade 5 – death related to AE."[14] AEs leading to hospitalization, discontinuation of LTBI therapy, or regimen change were classified as grade 3 at minimum. The latter indicated that an AE related to the medication was either intolerable to the individual or that the individual displayed signs or symptoms that led to the clinical decision of prescribing of an alternative regimen in the interest of the individual's general well-being. Hospitalizations for all other causes were not considered in our analysis.

Data Analysis

Demographic information, proportions of AEs, and treatment outcomes were reported using descriptive statistics. Statistical analysis was performed using the open source R statistical analysis software developed by the R Core Team version 3.4.1, for summary statistics using Base R. A 2-sample test of proportions using χ^2 distribution was used to test for statistical significance between recent and historical cohort outcomes and AEs and for potential AE-related differences between sexes at the $P < 0.05$ level.

Results

Participants and Population Characteristics

We identified 12,607 people with a PHN who initiated at least 90 days of dialysis between January 1, 2001, and May 31, 2017. Of those, 365 people initiated LTBI therapy no more than 1 month before dialysis and had a treatment outcome at the time of review. Overall, 290 (79.5%) maintenance dialysis patients were in the recent cohort, while 75 (20.5%) were in the historical cohort (Fig 1). Baseline characteristics of our study population at the time of LTBI therapy initiation are shown in Table 1. Median age at the start of LTBI therapy was 65 (interquartile range, 56-72) years, and there was a male preponderance in the study population (65.2%; n = 238). People born outside of Canada comprised 73.4% (n = 268) of the study population. Most LTBI screening in the historical cohort was performed using tuberculin skin tests (50.7%; n = 38), whereas most LTBI screening in the recent cohort was performed using IGRA (79.7%; n = 231). Most people starting LTBI therapy were initially prescribed 9H (91.2%; n = 333). With the exception of 2014 and 2017, increases in LTBI therapy uptake were observed each year after 2009 (Fig 2).

Adverse Events

Grade 3 to 4 AEs or any grade rash developed in 21.1% (n = 77) of the study population, with no occurrences of grade 5 AEs (ie, death; Table 2). Proportions of grade 3 to 4 AEs or any grade rash among the study population, stratified by AE type, are shown in Figure 3. Analyses for the recent and historical cohorts are provided in Fig S1A and B. The most common grade 3 to 4 AEs were gastrointestinal events. The most common intervention was a regimen change among those who experienced grade 3 to 4 AEs or any grade rash. No differences were found in subanalyses comparing the recent and historical cohorts in all categories listed in Table 2 and in comparing these outcomes between male and female patients in the recent cohort (Table S1).

The proportion of people who permanently discontinued LTBI therapy due to drug intolerance was 6.3% (n = 23). Two (0.5%) people were hospitalized due to LTBI therapy; both individuals belonged to the recent cohort and were hospitalized for symptomatic hepatotoxicity while receiving isoniazid, which improved on treatment discontinuation. Two (0.7%) people in the recent cohort and 2 (2.7%) people in the historical cohort visited the emergency department due to AEs attributable to LTBI therapy; both people in the historical cohort reported nausea or vomiting, while in the recent cohort, 1 person experienced general malaise and the other person reported presyncope.

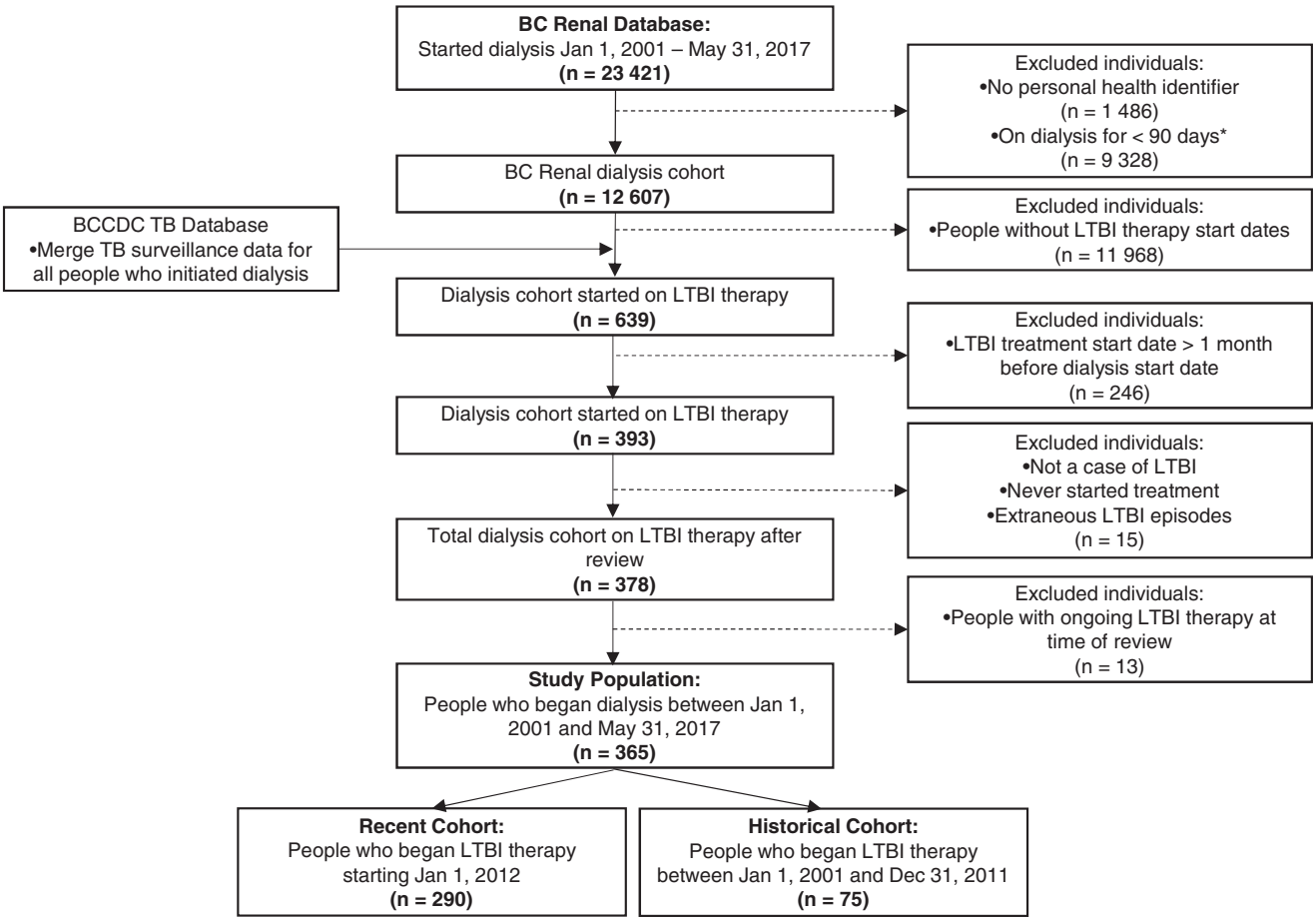

Figure 1. Latent tuberculosis (TB) infection (LTBI) therapy cascade of care among maintenance dialysis patients. *BC Renal database includes people with acute kidney injury, which contribute to the high proportion of patients receiving dialysis for less than 90 days. Abbreviations: BCCDC, BC Centre for Disease Control.

End-of-Treatment Outcomes

In total, 81.6% of people achieved treatment completion, with similar proportions in the recent and historical cohorts (80.7% and 85.3%, respectively; $P = 0.5$; Table 2). During the course of treatment, 6.3% (n = 23) of the study population died (Fig 4). No deaths were attributed to LTBI therapy; however, cause of death was unknown for 2 (0.7%) people in the recent cohort and 1 (1.3%) person in the historical cohort. One person belonging to the recent cohort developed active TB after a course of LTBI therapy consisting of 1 month of 4R and 6 months of 9H. This person had a positive IGRA result 3 years after initiating dialysis and developed fully susceptible active TB lymphadenitis within 2 years of discontinuing LTBI therapy and 1 year after kidney transplantation. End-of-treatment outcomes stratified by recent and historical cohorts are provided in Fig S2.

Discussion

To our knowledge, this is the largest study investigating LTBI treatment outcomes in maintenance dialysis patients under programmatic conditions. Despite the advanced age, frequent comorbid conditions, and potential drug-drug interactions common in this population, LTBI treatment was successfully initiated and completion remained high, comparable to provincial and national performance indicators.[13,17]

In the United States and Canada, LTBI treatment completion rates have differed widely, and interventions to improve adherence have shown inconsistent effectiveness across studies.[18] However, for this cohort, the high proportion of treatment completion despite AEs is likely attributed to the close monitoring and active management of LTBI therapy in this group by both renal and TB health care providers through a patient-centered approach. Although monthly visits are part of routine care at the BCCDC for people on LTBI therapy, patients are seen more frequently if needed. During follow-up visits, clinicians and program staff ask patients to self-report on their treatment progress through a series of questions and cross-checking with the number of medications dispensed and the number of remaining medications. If clinicians suspect poor adherence, they attempt to identify and address patients' unique barriers to adherence, including recommendations for managing AEs, assessing and mitigating

Table 1. Population Characteristics

	Study Population (N = 365)	Recent Cohort (n = 290)	Historical Cohort (n = 75)
Male sex	238 (65.2%)	180 (62.1%)	58 (77%)
Age, y	65 [56-72]	65 [57-72]	62 [51-72]
Place of birth			
Foreign-born	268 (73.4%)	221 (76.2%)	47 (63%)
Canadian-born	53 (14.5%)	39 (13.4%)	14 (19%)
Unknown	44 (12.1%)	30 (10.3%)	14 (19%)
Dialysis modality			
Hemodialysis	263 (72.1%)	208 (71.7%)	55 (73%)
Peritoneal	102 (27.9%)	82 (28.3%)	20 (27%)
LTBI screening result			
IGRA positive	252 (69.0%)	231 (79.7%)	21 (28%)
TST positive	51 (14.0%)	13 (4.5%)	38 (51%)
Clinical evaluation only[a]	62 (17.0%)	46 (15.9%)	16 (21%)
Drug initiation type			
Isoniazid	333 (91.2%)	264 (91.0%)	69 (92%)
Rifampin or rifabutin	32 (8.8%)	26 (9.0%)	6 (8%)
Comorbid conditions			
Diabetes	175 (47.9%)	145 (50.0%)	30 (40%)
Current smoker	27 (7.4%)	19 (6.6%)	8 (11%)
Immune suppression[b]	3 (0.8%)	2 (0.7%)	1 (1%)
Alcohol use disorder	16 (4.4%)	13 (4.5%)	3 (4%)

Values for categorical variables given as count (percentage); for continuous variables, as median [interquartile range].
Abbreviations: IGRA, interferon gamma release assay; LTBI, latent tuberculosis infection; TST, tuberculin skin test.
[a]Represents people recommended LTBI therapy despite negative immune testing. For example, LTBI therapy may be offered if IGRA is negative with a chest x-ray suggesting prior tuberculosis infection.
[b]Defined as transplantation before dialysis or any other connective tissue disease as defined by BC Renal database.

financial barriers to treatment, and arranging transportation for clinic visits. Evidence suggests that LTBI therapy adherence is affected by patients' AE concerns, financial barriers, and transportation barriers.[19] Additionally, because maintenance dialysis patients regularly access renal services, renal health care providers likely contributed to treatment monitoring, such as providing blood work and TB appointment reminders or notifying TB services of patients' health concerns and issues with treatment adherence.

The increased uptake of LTBI therapy starting in 2010 coincided with the start of IGRA funding for select dialysis units, followed by a further increase in LTBI therapy uptake after 2012, coinciding with the introduction of the systematic provincial IGRA-based TB screening program in people starting maintenance dialysis. In our study population, there was no significant difference when comparing proportions of people with grade 3 to 4 AEs or any grade rash in the historical versus the recent cohort, suggesting that the earlier approach of selective screening and LTBI treatment in the maintenance dialysis population did not lead to reduced individual risk for significant AEs. In addition, although nearly a quarter of the study population experienced grade 3 to 4 AEs or rashes attributed to LTBI therapy, the proportion that required permanent treatment discontinuation due to AEs was only 6.3%, similar to historical local data.[20] This suggests that the high frequency of grade 3 to 4 AEs may be explained by the nature of AE reporting and limitations of retrospective study data rather than serious or life-threatening AEs. It is important to note that grade 3 AEs include any TB regimen change and/or discontinuation.

It appears that in our study population, physicians were prompt to adjust medications in an effort to minimize the risk for serious AEs and improve chances for treatment completion. However, AEs associated with LTBI therapy often coincided with symptoms associated with dialysis treatment, and despite reporting only new AEs and preexisting symptoms that intensified during the course of treatment, misattribution of AEs to LTBI therapy may have occurred in some circumstances. This reflects the complex nature of AE detection and management for LTBI therapy among the maintenance dialysis cohort and underlines the importance of close follow-up and a patient-centered approach to achieving adequate LTBI treatment outcomes.

Existing research on LTBI therapy outcomes among people receiving maintenance dialysis has focused on the relative risks for TB in comparison to nontreated individuals, with biomarkers for hepatotoxicity often used in isolation to detect AEs.[21–23] Although analyzing the risks for hepatotoxicity and protective effects of LTBI therapy are important, literature on other potential AEs associated with treatment in maintenance dialysis patients is lacking. The current study findings have broadened the evidence base by documenting that the most common AE among these cohorts was not hepatotoxicity, but gastrointestinal events, general malaise, and pruritus. Despite our study population's older median age, hospitalization related to LTBI therapy remained comparable to that of an administrative data study reporting a crude hospital admission rate of 1.3 per 100 individuals for hepatic, allergic, gastrointestinal, hematologic, or poisoning events among a Canadian provincial population undergoing LTBI therapy.[24] Again, we believe this can be related to the close monitoring and patient-centered approach, which allows clinicians to intervene earlier when a patient experiences AEs, preventing the escalation to serious AEs and hospital admissions. However, the ability for clinicians to closely monitor patients is likely facilitated by British Columbia's existing centralized TB treatment infrastructure and systems. In this province, all LTBI therapy is managed by a health care team dedicated to TB screening and treatment, with particular experience in treating people with advanced age and multiple comorbid conditions. This experience and infrastructure likely improved treatment

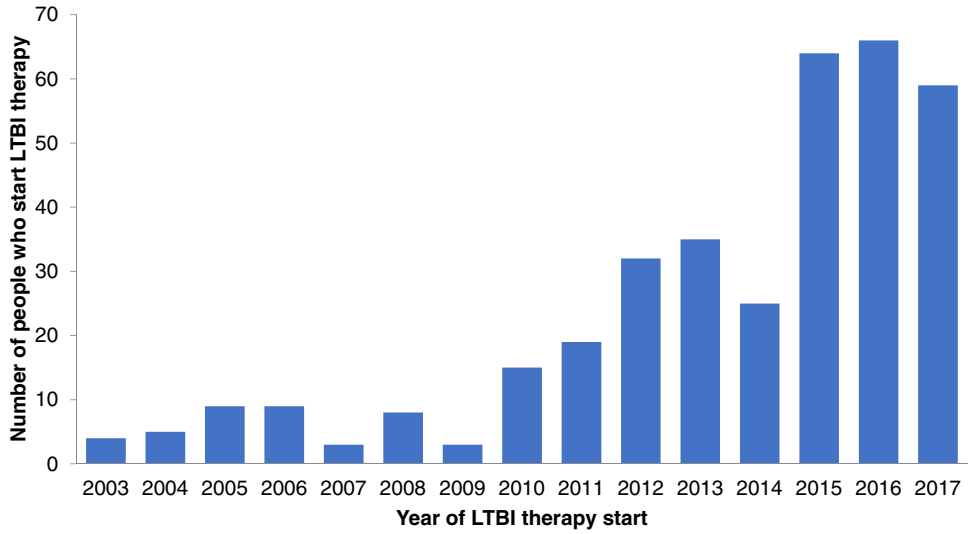

Figure 2. Latent tuberculosis infection (LTBI) therapy uptake over the years for people starting maintenance dialysis. Data in 2018 were excluded because patients who started LTBI therapy in 2018 were not fully captured given the methodological constraints of data extraction based on start of dialysis, ending on May 31, 2017.

completion and facilitated early identification of AEs with LTBI therapy, which may be less feasible in other settings without this existing system in place.

Although our cohort did not include individuals on the 12-week intermittent isoniazid and rifapentine (3HP) regimen because rifapentine was not routinely available during the study period, a recent study investigated outcomes of 3HP for 26 people receiving hemodialysis. Despite the small sample size and regimen difference, similar rates of mild AEs were reported, with low rates of guideline-defined hepatotoxicity and serious AEs.[25] However, that study reported a much lower completion rate of 65.4%.[25] This difference may be explained by health care provider approaches to AEs in this cohort. The current study confirmed that if AEs occurred during LTBI therapy, regimen changes using well-studied and safe drugs such as isoniazid, rifampin, or rifabutin were required to improve chances for successful treatment completion.

This study has several limitations, primarily related to the retrospective nature of the reported data. Treatment data reported by all nurses, physicians, and other potential specialized health care personnel were nonstandardized. Due to programmatic conditions, most reported AEs did not involve extensive confirmatory testing, with the exception of hepatotoxicity. Therefore, over- or underreporting of AEs may have occurred. Additionally, assessing AEs for causality and understanding the patient-level decisions behind LTBI regimen changes versus treatment continuation were often unfeasible. The number of physician office visits related to AEs could not be accurately estimated due to the routine nature of follow-up visits at TB services. Because hospital records were unavailable for analysis, hospitalizations were based on records within the TB registry, which limited the ability to understand the low numbers of hospitalizations attributed to LTBI therapy in this study. Potential underreporting by patients who

Table 2. Primary Outcomes

	Study Population (N = 365)	Recent Cohort (n = 290)	Historical Cohort (n = 75)	Percent Difference (95% CI)	*P*[a]
Grade 3-4 AEs or any grade rash[b]	77 (21.1%)	64 (22.1%)	13 (17.3%)	4.7% (−5.9%, 15.4%)	0.5
AE requiring treatment discontinuation	23 (6.3%)	18 (6.2%)	5 (6.7%)	−0.5% (−7.2%, 6.3%)	0.9[c]
AE requiring regimen change	51 (14.0%)	43 (14.8%)	8 (10.7%)	4.2% (−4.8%, 13.1%)	0.5
Grade 3-4 hepatotoxic event	16 (4.4%)	14 (4.8%)	2 (2.7%)	2.2% (−3.1%, 7.4%)	0.6[c]
Hospitalization related to LTBI therapy	2 (0.5%)	2 (0.7%)	0 (0%)	0.7% (−1.0%, 2.3%)	0.9[c]
Treatment completed	298 (81.6%)	234 (80.7%)	64 (85.3%)	−4.6% (−14.7%, 5.4%)	0.5

Abbreviations: AE, adverse event; LTBI, latent tuberculosis infection.
[a]*P* value based on the 2-sample test of proportions using $\chi 2$ distribution.
[b]An individual can be classified under more than 1 category among grade 3 to 4 AEs or any grade rash; therefore, frequencies between categories are not mutually exclusive.
[c]*P* value should be interpreted with caution due to small cell size.

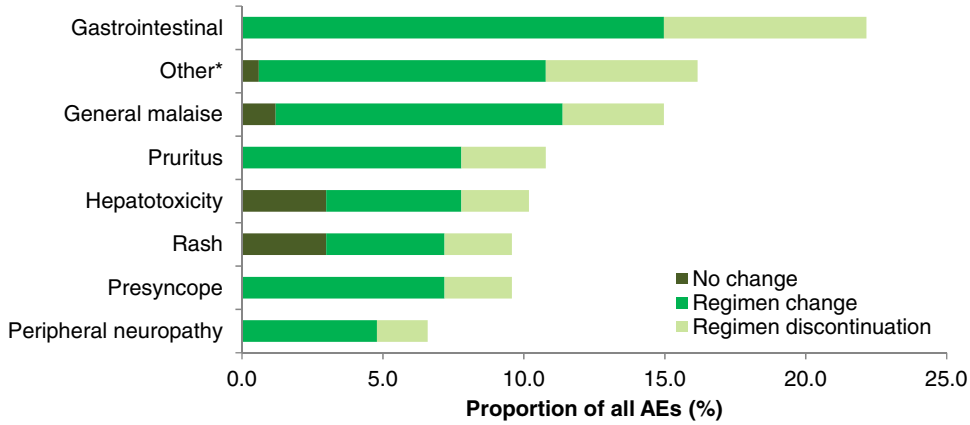

Figure 3. Proportion of grade 3 to 4 adverse events (AEs) or any grade rash among the study population. *All other reported side effects not commonly associated with latent tuberculosis infection therapy. Proportion based on all counts of grade 3 to 4 AEs (ie, an individual can experience more than 1 AE and experience the same AE more than once).

may have received care outside of TB services may have caused additional bias. Finally, these findings may only be generalizable to countries with similarly low TB burden because resource availability can greatly affect the ability for health professionals to provide ample follow-up care or to make the systematic changes required for centralized TB care.

Our results indicate that LTBI therapy in the maintenance dialysis population may be safe if combined with close follow-up and monitoring by experienced clinicians as part of a patient-centered approach to TB care. Further studies are required to assess the optimal approach to TB prevention and treatment in the maintenance dialysis population given their complex set of comorbid conditions and medication interactions.

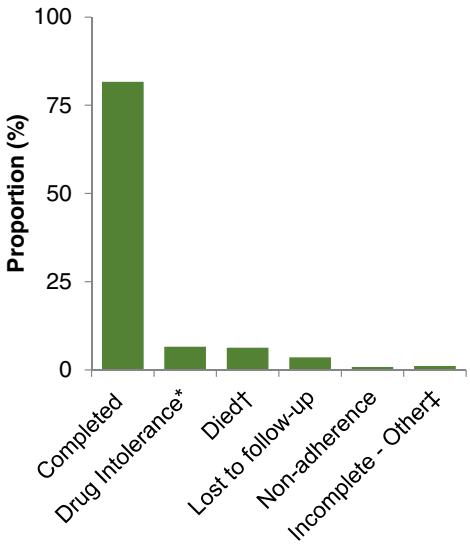

Figure 4. Treatment outcomes of patients who started latent tuberculosis infection (LTBI) therapy in the study population. *Includes patients who completed LTBI therapy on an alternative regimen of uncertain efficacy. †LTBI therapy was not noted as the underlying cause of death. Cause of death was unknown for 1 person in the recent cohort and 2 people in the historical cohort. ‡Stopped LTBI therapy due to other unrelated health concerns.

Supplementary Material

Supplementary File (PDF)

Figure S1: Proportion of grade 3 to 4 AEs or any grade rash among the recent and historical cohorts.

Figure S2: Treatment outcomes of patients who started LTBI therapy in the recent and historical cohorts.

Table S1: Primary outcomes among the recent cohort, by sex.

Article Information

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