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Impact of Pharmacist-Delivered Patient Education on Tuberculosis Drug Therapy Adherence

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A Systematic Review: The Impact of Pharmacist-Delivered Patient Education on Tuberculosis Drug Therapy Adherence

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Abstract

Treatment of tuberculosis poses unique clinical challenges that make successful completion of treatment traditionally low compared with other infectious diseases. Specifically, patient adherence to the long medication regimen is crucial for the success of treatment. Are pharmacists, the medications experts, being optimized with their clinical knowledge to assist in the management of tuberculosis treatment and does their impact provide a benefit to the patient? In order to determine the pharmacists impact on adherence to therapy for tuberculosis treatment, a systematic literature review utilizing OVID Medline was conducted. A search term criteria was formulated then used to generate literature pertaining to the clinical question. The initial search resulted in 21 hits, which were subsequently screened using the predetermined exclusion and inclusion criteria. Of the 21 initial results 17 were excluded from the review. The included studies demonstrated positive impact pharmacists had on the adherence and completion of prescribed tuberculosis medications. This trend presents an opportunity for pharmacists to provide clinical services that utilize their strength and ensure positive therapeutic outcomes for patients. Although the findings are encouraging, the included studies have drawbacks that while addressed, present the direction for future study.

1 Introduction

Tuberculosis (TB), an infectious disease that affects the lungs caused by the bacterium *Mycobacterium tuberculosis*, is a major global burden. According to the World Health Organization, in 2014, 9.6 million people worldwide fell ill with TB and 1.5 million people died from the disease (1). TB affects people worldwide, but over 95% of TB cases and deaths occur in developing countries. TBs disease progression profile and symptoms (cough, chest pain, weakness, weight loss, fever, and night sweats) greatly decrease ones quality of life and increase risk for mortality, morbidity, and leads to loss of productivity. Global leaders and professionals have identified TB as a priority by making it a health target within the Sustainable Development Goals (2).

Tuberculosis can be cured with the use of antimicrobial drugs and drug therapy adherence is vital to its success. The Infectious Disease Society of America recommends newly diagnosed patients with active tuberculosis infection not drug or multidrug resistant, the use of isoniazid, rifampin, pyrazinamide, and ethambutol for 8 weeks at a dosing regimen of 7 doses a week or 5 doses a week during the intensive phase of therapy (9). This is followed up in the continuation phase of therapy with isoniazid and rifampin at either the above stated dosing regimens for an additional 18 weeks (9). Patients that have drug resistant or multidrug resistant tuberculosis infections present with the additional challenge of treating the infection while not promoting additional resistance. Latent infections changes the duration of therapy but with both cases the duration of therapy is enormously longer compared to other antimicrobial treatment durations. Like with all antimicrobial therapy, adherence to the regimen is key in order to effectively treat the infection.

Pharmacists can play a pivotal role in promoting patient adherence to drug therapy, which leads to optimization of drug therapy goals and outcomes (3,4). As medication experts, pharmacists can utilize their clinical training to reduce drug interactions, optimize therapy for patients presenting resistant microbes, provide education on the importance of adherence to therapies, and make recommendations for therapy when necessary. In this systematic literature review, we determine how pharmacist-led patient education and monitoring affects patient adherence to tuberculosis drug therapy regimens.

2 Methods

2.1 Data Sources and Search Terms

We conducted a systematic literature review using OVID Medline that includes literature published on or after 2003 through 2016 to determine how pharmacist-led education affects patient adherence to tuberculosis drug therapy regimens.

The following combination of search terms were entered in OVID Medline:

- tuberculosis
- extensively drug-resistant tuberculosis
- latent tuberculosis
- mycobacterium tuberculosis
- multidrug-resistant tuberculosis
- Pharmacist
- pharmacist-led education
- pharmacist-led intervention
- Pharmacist-managed
- medication adherence
- patient compliance
- medication therapy management
- pharmaceutical services
- antimicrobial therapy

All search terms are MeSH terms except for pharmacist-led education, pharmacist-led intervention, and pharmacist-managed which are keyword search terms. Literature hits from the search will also be additionally filtered by inputting from 2003 to 2016 in the specific year range search option in OVID.

Randomized control trials, observational studies, and systematic literature reviews conducted in any care facility around the world were eligible to be included in this systematic review if they include pharmacist-led tuberculosis drug therapy education with outcomes measuring patient drug therapy adherence such as the median missed time if therapy, the rate of misses drug doses, and the therapeutic failure rate. The study or literature review mustve had pharmacists as part of the care team to be included in this review. We included studies with study subjects who have either active or latent tuberculosis infections. Studies and literature not published in the English language or published before 2003 were excluded from this review.

We would also like to mention an addendum to our search methods. We also systematically assessed the reference sections of screened articles to determine if any additional literature satisfied our criteria to be included in our review, which we may have missed upon our initial search, that may not have appeared as hits under our designated search terms.

2.2 Literature Screening

The sources included in this review were determined from appraising the hits obtained from the various search terms via databases as mentioned above. All three authors determined if each of the abstracts from the search hits satisfied our inclusion and exclusion criteria and what type of source (observational study, randomized control trial, etc.) each hit is. Should a discrepancy arise amongst the authors, a further discussion was held to determine the source of the discrepancy and to resolve the discrepancy. If a resolution could not be made, the source was set aside for reconsideration after completion of the screening process for the remaining sources.

If a literature source made it through the initial screen but does not contain the desired outcomes upon data abstraction that aim to answer our research question, we did not completely disregard the literature but set it aside to be considered in the review if warranted later on.

2.3 Strengths and Weaknesses of Databases

The usage of OVID Medline offers both strengths and weaknesses for identifying relevant primary literature sources. The underlying database is regulated by the reputable National Library of Medicine, and Ovid is a sensitive search engine which allows for narrowing the scope of a given search to provide high quality hits based on the search terms. OVID has MeSH (medical subject headings) terms which allows for specific, defined searches within a hierarchical system instead of relying solely on keyword searching. The sensitivity of OVID as a search engine also confers some inherent difficulty on the search process as minor wording adjustments to search terms significantly narrow or widen the scope of the resulting hits.

2.4 Data Abstraction

All three authors followed the data abstraction template, as shown below, and systematically abstracted and recorded data from each of the screened literature sources included in the review starting with the study population heading and moving down to the quality rating heading. The information abstracted includes: the study population, demographic characteristics, (total population size, age of study subjects, gender of study subjects, ethnicity of study subjects, and socioeconomic status of study subjects), the intervention (specific program or method of a pharmacist-led tuberculosis drug therapy education), the comparison (no medication counseling or a healthcare professional counseling that is not the pharmacist), the study design (randomized control trial, observation study, or literature review), the study setting (country and geographical area study was conducted and type of care setting pharmacist-led education was delivered), the outcomes as mentioned previously above (median missed time of therapy, rate of missed doses, and therapeutic failure rate), and the quality rating of each study which we will determine based on the 2011 CEBM level of evidence criteria. Upon completing the data abstraction phase, the three authors met to discuss and compare what was abstracted for each literature source. If there were disagreements, the authors referred back to the respective literature source to come to an agreement.

Literature sources that went through data abstraction but didnt support our research question, due to factors such as low external validity, werent completely disregarded. They were put into a separate category that could be included in the review if the clinical outcomes were deemed significant enough to outweigh extenuating factors such as low external validity.

Data Abstraction Table	
Study Population	• Total size • Adult or Pediatric
Intervention/Exposure	• Pharmacist-led drug therapy education
Comparison	• No pharmacist medication counseling • A healthcare professional providing counseling beside the pharmacist
Study Design	• Randomized Control Trial • Observational Study • Literature Review
Study Setting	• Country/geographical area of study • Care Setting – Clinic – Pharmacy – Inpatient or outpatient hospital
Outcome	• Median missed time of therapy • Rate of missed doses • Therapeutic failure rate • Other measurements of drug therapy adherence
Quality Rating	• Assign quality rating to each source based on the 2011 CEBM criteria to define levels of evidence

3 Results

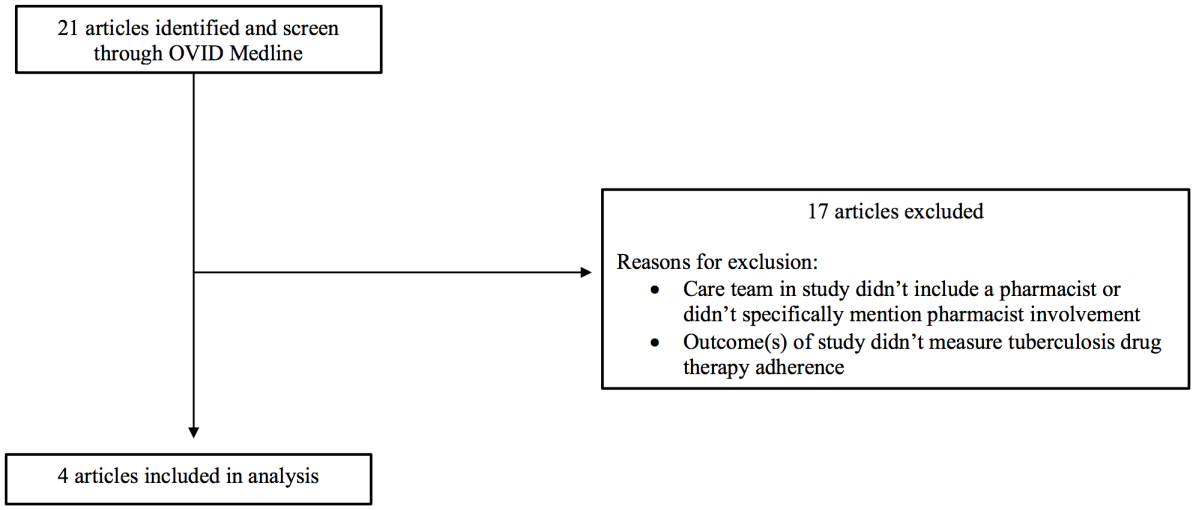

Figure 1: Study section flow diagram

Table 2. Summary of studies evaluating impact of pharmacist-led TB therapy education

Study	Population	Design	Setting	Specific intervention(s) by pharmacist(s)	Results	Quality of Evidence
Hess, Goad, Wu, Johnson, 2009	348 university college students diagnosed with latent TB infection	Retrospective observational study	Pharmacist-managed community clinic/pharmacy at university	• Pharmacists provided comprehensive therapy management, counseling, and support to help encourage students to finish their therapies	9-month isoniazid completion rate of 59% and 6-month completion rate of 67%	Level 4
Clark, Karagoz, Apikoglu-Rabus, Izzettin, 2007	114 first time TB infected patients from Istanbul, Turkey	Prospective randomized case-control study: pharmacist-delivered TB therapy education or education delivered by other medical professionals (medical doctors, nurses)	Inpatient and outpatient pharmacy	• Patients randomized into pharmacist-delivered TB therapy education group were provided with oral and written patient education by pharmacists in the inpatient and outpatient setting	Patient attendance at scheduled visits and urine analysis for presence of isoniazid had better results in pharmacist-delivered education group ($P<0.05$)	Level 2
Last and Kozakiewicz, 2009	80 adult and pediatric latent TB patients in Haven, CT	Prospective observational study	Clinic at Hospital of Saint Raphael in New Haven, CT	• Pharmacist called patient to schedule appointment (length of appointment was about 45 minutes) upon referral by physician • Pharmacist were responsible for reconciling all pertinent patient information (medical, social, family histories) during appointment • Pharmacist educated patient on pathology of	Rate of treatment completion among patients receiving entire 9 months of therapy in pharmacist-managed clinic was 74% compared to 26% from 2004 before pharmacist-managed clinic was opened	Level 4

				latent TB infections and how it's treated • Pharmacist assessed for patient adherence to medication therapy, changes in lab values, provided recommendations for therapy course, and determined next follow up appointment • Pharmacist followed up with patients for about 20 minutes monthly in clinic and called patients to reschedule follow up appointment if patient didn't show		
Tavitian, Spalek, Bailey, 2003	131 adult health care workers with latent TB infection	Retrospective observational study	Clinic at Cedars-Sinai Hospital in Los Angeles, CA	• Initial patient assessment and education on medication regimens conducted by pharmacist • Monthly follow-up visits with pharmacist for first 3 months of therapy where pharmacist evaluated treatment adherence and assessed for adverse effects • Pharmacist conducted monthly telephone interviews with patient after first 3 months of treatment until therapy was completed	93% of enrolled patients completed the prescribed LTBI treatment regimen	Level 4

4 Discussion

In this systematic literature review, our goal is to determine the impact of pharmacist-led patient education and monitoring affects patient adherence to tuberculosis drug therapy regimens. Four articles were included in the final analysis, and these studies offer varying strength and weakness profiles with respect to study design and external validity. These publications unanimously demonstrated improved medication adherence and/or treatment completion rates in patients receiving pharmacist-delivered medication education and ongoing monitoring.

Hess et al. (5) conducted a retrospective observational study which looked at medication records of university college students in Southern California with latent TB infections receiving care from the universitys pharmacist managed community pharmacy to determine their 9-month and 6-month isoniazid completion rate. The 9-month isoniazid completion rate of 59% and 6-month completion rate of 67%. The large population of foreign-born patients at the pharmacy could have impacted study results as language and culture may be barriers hindering communication. The possibility of medication count inaccuracy may also pose as a weakness of this study as patients mayve discard tablets or misrepresented number of tablets taken to finish TB treatment.

Clark et al. (6) conducted a prospective, randomized case-control study among first time TB-infected patients in Turkey to determine the impact of pharmacist-delivered TB therapy education on management on success of patients to attend scheduled follow up visits and adherence to drug therapy. First time infected patients admitted to the hospital were either randomized to receive pharmacist-delivered TB education or no routine care by medical doctors and nurses but not pharmacists. Patient attendance at scheduled follow up clinic visits and urine analysis for presence of isoniazid had better results among the pharmacist-delivered education group. A strength of this study is patients were randomized to receive pharmacist-delivered education or not and besides evaluating adherence qualitatively, patients agreed to urine analyses which measures adherence quantitatively and provides further evidence for or against the impact of pharmacist-delivered education. Because this study was conducted in Turkey, a weakness may be the difference between care practices in Turkey to those in the United States. However, the results are still applicable to TB care in general.

Last and Kozakiewicz (7) conducted a prospective observational study at the Hospital of Saint Raphael in New Haven, CT. The study followed 80 adult and pediatric patients through Tuberculosis treatment for either latent or active infections in a pharmacist led clinic within the hospital. The diagnosis is made by primary care physician or a specialist in infectious disease or pulmonary medicine. After the diagnosis the patient is referred to the TB clinic which places in them in the care of the pharmacist. The initial appointment between the patient and pharmacist lasts approximately 45 minutes with subsequent visits lasting 15 to 20 minutes and occur on a monthly basis. All pediatric patients were started on isoniazid dosed at 10mg/kg while adult patients were started on isoniazid 300 mg and pyridoxine 50 mg combination therapy for 9 months. The primary outcome looked at patient completion of therapy percentage before pharmacist led intervention to current model. Before pharmacist led intervention, the 9 month completion percentage was 26%. When pharmacist led the treatment intervention the 9 month completion percentage rose to 74%. Only 2 patients of those in the study reported any type of adverse drug reaction. The cost of the medications was eliminated and made free to patients in the study to help minimize confounding variable which may influence the completion of therapy. Areas of the study that needed improvement which are addressed are improving methods of documentation of missed appointments as well as patient follow up appointments. The other was widening the recruitment of patients in order to increase the sample size.

Tavitian et al. (8) evaluated treatment completion rates of healthcare workers with latent TB infection treated at a Cedars-Sinai clinic who received pharmacist-led medication and disease-state education upon treatment initiation as well as ongoing follow-up by a pharmacist assessing for adverse effects of therapy and providing adherence reminders. Over a four year period, 122/131 (93%) of the patients enrolled in this treatment protocol completed the prescribed medication course. The external validity of this study may be impaired by the possibility that the patient population, consisting entirely of healthcare workers, had an increased basal level of health literacy, and the exact contribution of pharmacist involvement in the care process is difficult to assess as this was not a controlled study design.

Overall, the studies analyzed demonstrate the trend of pharmacists having positive impact on adherence as well as completion to therapy regimen. The studies included have a moderate quality of evidence and despite their shortcomings demonstrate the positive impact pharmacists have on therapy outcomes. The body of literature for this topic appears to lack high quality randomized control trials which evaluate the impact pharmacist led, managed, delivered interventions have on therapy outcomes for patients with TB. Speculation as to why there is a lack of these types of studies include that adherence can be a measure difficult to analyze as it is more qualitative in nature and laborious through lots of follow up and monitoring.

There is a lack of studies based in the United States, where TB is not endemic or afflicting a high enough percentage of the population to generate the same volume of studies in therapy outcomes compared to a cardiovascular disease. Finally, many of the studies that showed positive impact pharmacists played came from areas of the world where the disease is more endemic to the population, many of these areas are developing countries. This also makes the study population vast, and highly variable in nature. Both factors may influence the body of literature available. Replication of these studies in the United States that look at patient populations who either emigrated from endemic areas with TB or those who contract it in the United States through exposure will help solidify the potential pharmacists have in the management of TB therapy to ensure successful completion of therapy by the patient.

5 Conclusion

Our analysis of the literature indicates that pharmacist-led patient education and therapy monitoring increase adherence to prescribed treatment regimens and treatment completion rates. These results suggest that health systems and clinics have an opportunity to expand the role of pharmacists in the care of patients with TB infection. Further research in the form of large, randomized, controlled trials is needed in order to demonstrate outcome-based value of pharmacist-led patient education and monitoring in terms of disease-specific goals of therapy.

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