A Systematic Review of The Barriers, Prescribing Trends And Adherence to Standard Treatment Guidelines for the Management of Pulmonary Tuberculosis.

[1]Madeeha Malik*, [2]Fouzia Houshiar Din, [3]Azhar Hussain
[1*]Director/Associate Professor, Hamdard University, Islamabad, Pakistan.
[2]M.Phil Scholar, Hamdard Institute Of Pharmaceutical Sciences, Hamdard University, Islamabad Pakistan.
[3]Dean/Professor, Hamdard University, Pakistan.
Director/Associate Professor, Hamdard University, Islamabad Pakistan

Abstract: Evidence suggests that practitioners in developing countries are not equipped with sufficient knowledge and training to carry out proper case management of TB. A good number of these practitioners do not adhere to the norms of standard treatment guidelines for treating tuberculosis in their daily practice and are not much familiar with DOTs program. The aim of this review paper is to summarize research findings regarding management of pulmonary tuberculosis in terms of barriers, prescribing trends and adherence to standard treatment guidelines in developed and developing countries as well as Pakistan. A total of 66 studies were reviewed out of which 53 were from developed and developing countries and thirteen from Pakistan. It was concluded that extensive research has been conducted in developed countries regarding availability, perceptions, acceptance and adherence of prescribers to internationally available standard treatment guidelines for management of tuberculosis and barriers to adherence which has led to improved control of tuberculosis in these countries. On the other hand, in developing countries including Pakistan limited data is available in this regard. Extensive research is required to explore role of DOTs program in control of TB, barriers in its effective implementation and healthcare system collaborative models to promote active case detection and appropriate treatment which can lead to improved patient compliance and control of tuberculosis.
Keywords: Adherence, Barriers, Prescribing trends, Perceptions, Pulmonary Tuberculosis, Pakistan and Standard Treatment guidelines.

I. Introduction

Tuberculosis (TB) remains a major public health problem globally for centuries. Pulmonary tuberculosis has been estimated to be accounted for one third of the world's total population [1]. The incidence of this infection is alarming mainly due to increase in the number of HIV patients, elderly population and the emergence of resistance to anti-tuberculosis drugs worldwide [2]. Misinterpretation of early symptoms and frequent use of antibiotics in the treatment of the disease always encounters risks of inappropriate prescribing practices resulting in drug resistance and increased healthcare costs. STGs are one of the tools to support effective clinical practice and promote rational use of drugs [3, 4]. Treatment guidelines are designed with the collective opinion of a wide group of recognized national experts and are used as a reference for appropriate treatment choices [5, 6]. To enable reliable, therapeutically effective and cost effective use of drugs rational prescribing in accordance with the standard treatment guidelines is required. This can influence positively on patient compliance and outcomes of therapy [7-9].

Evidence suggests that practitioners in developing countries are not equipped with sufficient knowledge and training to carry out proper case management of TB. A good number of these practitioners do not adhere to the norms of standard treatment guidelines for treating tuberculosis in their daily practice and are not much familiar with DOTs program [10-14]. A study conducted in Iran showed that although most of the prescribers were aware of the correct diagnostic criteria for TB but were not familiar and adhering with the standard treatment guidelines [15, 16]. Another study from South Africa, highlighted the need for adherence to STG's for improving prescribing practices resulting in better treatment outcomes [17, 18]. Lack of adherence of prescribers to existing recommendations for the overall management of pulmonary tuberculosis, is one of the major factor contributing towards the poor control of disease. Extensive research has been conducted in developed countries regarding availability, perceptions, acceptance and adherence of prescribers to available standard treatment guidelines for management of pulmonary tuberculosis and barriers to adherence have also been identified which has led to improved control of pulmonary tuberculosis in these countries. But in developing countries including Pakistan limited data is available in this regard. The aim of this review paper is to summarize research findings regarding management of pulmonary tuberculosis in terms of barriers,

prescribing trends and adherence to standard treatment guidelines in developed and developing countries as well as Pakistan.

II.   Methodology

The electronic databases Pub Med, Google Scholar and Science direct were searched for articles published from 2000 to 2014. The search terms used were prescriber adherence, hypertension, and treatment guidelines. Full research papers and abstracts were searched and included in this review. A total of 66 studies were included in this review. Fifty three studies were from developed countries and developing countries whereas only thirteen studies were from Pakistan regarding adherence of prescribers to treatment guidelines for the management of hypertension (Table 1).

Table 1. Details of Country and Number of Included Papers

Regions	Number of Studies	Countries
Developed & Developing Countries	53	USA, Australia, UK, Japan, Germany, Belgium, Switzerland, Sweden, Canada, Denmark, Greece, Spain, Italy, South Korea, Finland, Ireland, Netherlands, Turkey, China, South Africa, Cyprus, Croatia, Ghana, Ethopia, Malaysia, India, Taiwan, Brazil, Iran, Saudi Arabia, Qatar, Austria, Eritrea, Jordan, Israel
Pakistan	13	
Total	**66**	

III.   Results and Discussion

Tuberculosis has remained a major concern for public health globally. In the year 2012, 8.6 million cases of active TB disease were reported among which 2.9 million case were reported to be females. The disease is found to be most prevalent in Asia and Africa (58% and 27% respectively) with India on the highest number with 2.0-2.4 million cases reported per year followed by China with 0.9-1 million cases per year. Both these countries account 38% of the total global burden of disease [2]. According to Global Tuberculosis Report 2015, 9.6 million new disease cases were reported in the year 2014 among which 65.4 million were males and 3.2 million cases were females. Mortality rate for the disease was high with about 1.5 million deaths reported due to tuberculosis [19].

Factors affecting Adherence to Standard Treatment of Tuberculosis Prescriber Perceptions Regarding Tuberculosis Management

Most of the prescribers were of the view that implementation of rational guidelines and designing an appropriate antibiotic policy for treating diseases like tuberculosis in all healthcare settings will improve tuberculosis management. Majority of the physician agreed that antibiotics are prescribed frequently and there is always an overuse with a risk of resistance and increasing costs, therefore rational drug prescribing is essential for minimizing the health care costs and for reducing the resistance as well as for decreasing the rate of poor adherence [20]. A survey on the perceptions of medical students shows that most of them are overestimating the current burden of resistant bacteria and they want further education on antibiotic prescribing. Misinterpretation of early symptoms led to delays in seeking health care and in non-adherence to the standard treatment guidelines resulting in resistance development and worsening of tuberculosis [15, 21, 22].

Lack of Knowledge of Prescribers Regarding Standard Treatment Guidelines

One of the main factors for irrational prescribing was lack of knowledge among the prescribers treating tuberculosis [13, 23]. A treatment regimen, drug dosage or treatment duration is considered to be inappropriate if it is not recommended by national guidelines or by the World Health Organization (WHO). Researchers have alarmed the policy makers with enormous challenge of facing drawbacks occurring in the result of low level of knowledge among medical professionals and students which are promoting wrong selection of treatment regimen, improper drug dosage or treatment duration [11, 24]. A study reported high proportion of prescribers who had correct knowledge about diagnostic criteria but inappropriate knowledge and practice of TB management [25]. A survey was conducted to analyze the knowledge of the private practitioners regarding tuberculosis control, diagnosis, treatment and monitoring reported that the practitioners were not well informed about the anti-tuberculosis treatment methodologies. A few available anti-tuberculosis drugs were being irrationally used which can lead to drug resistance. Beside this deficiencies in management and selection of treatment for tuberculosis were reported [3, 26]. Studies reported the need of regular medical education training programs to keep health professionals upgraded with the current status of diseases and its treatment [27, 28].

Unavailability of Standard Treatment Guidelines at Health Facilities

Standard treatment guidelines have been proved as an important tool, by world health organization, in the support of effective clinical practice as well as in the promotion of rational drug use [29]. In developing countries, irrational use of drugs has become a serious problem. One of the causes of irrational drug use is the absence and lack of implementation of standard treatment guidelines (STGs) for the most common diseases in these countries [30, 31]. This has resulted in following the practice of prescribing and dispensing of same drugs for different diseases, resulting in development of resistance of drugs and promoting non-uniform treatment [32]. Significant number of physicians did not adhere to the standard norms for prescribing anti-tuberculosis treatment specifically in developing countries which results in increasing the proportion of drug-resistant TB [33].

Irrational Prescribing Practices for TB Management

Studies have reported lack of knowledge regarding national treatment guidelines which promotes irrational practice of treating tuberculosis resulting in resistance development and non-adherence to the standards [1]. A serious deficiency exists in adoption of clinical practice guidelines in practice among the prescribers or health care givers. A noteworthy number of physicians mostly do not adhere to the norms of standard treatment guidelines for treating tuberculosis and have less knowledge about DOT program and this is the major reason in promoting irrational practice and prescribing patterns for tuberculosis treatment amongst doctors [34-36]. Prescribers working in public sectors, private sector and family physicians have less knowledge about TB and hence follow wrong practice. Therefore, there is need of arranging more educational programs for specialists treating tuberculosis as great diversity was seen between daily practice of doctors and national guidelines [2]. Effective and fruitful research might support in finding gaps in knowledge and prescribing among caregivers of tuberculosis. Implementation of different interventions and then their systematic reviews of may support in making important and strategic decisions in both public-private sectors of care providers [8, 37, 38].

Prescribers Adherence to Standard Treatment Guidelines

Guidelines are designed by converting research and expert opinion into recommendations for everyday practice, but health care providers are often slow to incorporate these guidelines into their daily practices [39, 40]. Unfortunately, in clinical practices, guidelines are not routinely followed and the overall compliance with recommendations is low [40-43].The reason for suboptimal adherence to published guidelines may be lack of awareness, particularly primary care providers who might be less aware of these guidelines [44]. Poor adherence to anti-tuberculosis treatment is the most important hurdle to tuberculosis control. In the negligence and absence of standard policies and public health interventions, most of the patients defaulted treatment which leads to further worsening the current status of tuberculosis [45].

Patient Related Issues

As the rates of TB have increased during the past 10 years throughout the world, it has been noticed that along with the prescribers, patients are also major factor who play an important role in non-adherence to the treatment guidelines [46]. Lack of a comprehensive understanding about barriers to treatment adherence is currently a major hinder to find effective solutions [47]. Poor adherence to anti-tuberculosis treatment is the most important hurdle to tuberculosis control. In the negligence and absence of standard policies and public health interventions, most of the patients defaulted treatment which leads to further worsening the current status of tuberculosis [48]. It has also been observed that tuberculosis among migrant pulmonary tuberculosis patients is getting more worst due to non adherence to standard treatment guidelines. No doubt, adherence to continuous course of TB treatment is a complex procedure with a wide range of factors impacting on treatment-taking behavior. There is need of evolution of structural barriers for prescribers as well as patients regarding treatment adherence [49].

Public-Private Mix Project

Significant conflict were found in perceptions of prescribers working in public sector vs. private sector on general facts, attitudes, and social implications of programs which results in caginess, conflicts and unwillingness to co-operate with each other [50]. Many studies have revealed that although prescribers of both public and private sectors initially get agree for the showing compliance to each other, only for the benefits of patients but at the end many reasons exist in their respective sectors that they failed to comply with the commitment [35, 51]. In most of the countries, DOTS implementation is limited specifically to public sector under the tuberculosis program, however, in reality many patients do seek care from healthcare providers outside the network of the tuberculosis program and these providers, mostly do not coordinate with the national program or apply to DOTS. In order to control this weakness globally, the World Health Organization gave concept of Public-Private Mix (PPM) initiative. Important goal of developing PPM is to promote access to

quality TB care worldwide which will reduce chances of worsening of tuberculosis and will also control arising rate of new cases with tuberculosis [50]. Public-private mix project is new innovation to solve problem of conflicts among prescribers of both sectors. Training, supervision, standard guidelines, efficient information system and financial incentives are kept in mind in this project. Presence of subsidization of drug costs and powers of regulatory affairs can result in producing best outcomes [52, 53]. Effective rates of case detection and good percentage of treatment success can be achieved by collaborative efforts between private health care providers and the government [54].

Overview of Management of Tuberculosis in Developed & Developing Countries

WHO's recently announced Global Plan to Stop TB highlights the need to expand DOTS through standardized treatment, under proper case management conditions, including directly observed treatment to reduce the risk of acquiring drug resistance, and support of patients to increase adherence to treatment and chance of cure [3]. Clinical practice guidelines for pulmonary tuberculosis have been developed from many years, but its quality is not reaching to an acceptable standard. A study was conducted to identify and assess the quality of tuberculosis guidelines which proved that methodological quality of tuberculosis guidelines was disappointingly low [2]. A study was conducted in New Jersey to evaluate physician prescribing practices for initial therapy of tuberculosis as per recommendations of the Centers for Disease Control and Prevention (CDC) and American Thoracic Society (ATS). It was found that a substantial proportion of physicians were not treating their tuberculosis patients initially according to the standard recommendations. Drug resistance was increasing day by day as tuberculosis patients were receiving inappropriate initial therapy [55]. In a study conducted on physician's knowledge and practice regarding treatment of the patients who were positive victims of human immune virus and could also suffer from tuberculosis reported that most of the physicians were not aware of the standards of care for preventing tuberculosis among HIV-infected patients, even in a geographic area with a high prevalence of mycobacterium tuberculosis and HIV [56]. It was also observed that treating tuberculosis according to the standard treatment guidelines for the specific time period proposed by the national tuberculosis program is reducing the risk of resistance development in the patients and before choosing regimen for the patients having multi drug resistance, there was need of confirmatory formal trials to have efficient results [57]. Inappropriate anti-tuberculosis (TB) treatment, particularly at the beginning of the disease, is a major cause of drug resistance. Many of the contributing factors were found to be the basic reasons of development of resistance.

These factors include wrong perceptions of the physicians, lack of knowledge and irrational prescribing practice. A study reported the standard retreatment regimen was adequate to determine acquired drug resistance among failure or relapse cases after treatment of new smear-positive tuberculosis. The study concluded that relapse of cases of tuberculosis was found to be the reason for development of primary drug resistance. As 80% of failure cases had multi drug resistance, therefore it was proved that standard re-treatment regimen was inadequate for failure or relapse cases and there was need of renewal of the strategies regarding treatment guidelines and management of tuberculosis [14]. In a study conducted in South Africa, regarding patient and health worker perspectives on adherence to tuberculosis preventive therapy (TBPT) among human immunodeficiency virus (HIV) infected patients in resource-poor areas concluded that need of interventions to improve accessibility and quality of the care delivery system to promote adherence to tuberculosis preventive therapy and other antiretroviral therapy [58]. A study conducted in Iraq concluded that good percentage of health care workers had good knowledge, but had negative attitudes and practices towards tuberculosis and towards adherence to standard treatment guidelines. The national tuberculosis program in Iraq had a good impact on knowledge of tuberculosis health care workers [15].

A great diversity was seen in a survey performed in Tanzania, between daily practice of doctors and national guidelines about tuberculosis as well as among the private doctors [59]. Similarly another study reported that the first step practice physicians had insufficient knowledge and need sporadically more education and practice to enhance the knowledge, attitude and behaviour related to the tuberculosis treatment and management [60]. A survey conducted to analyze the knowledge of the private practitioners regarding tuberculosis control, diagnosis, treatment and monitoring reported that the practitioners were not well informed about the anti-tuberculosis treatment methodologies [11].

A prospective cohort study conducted to determine reasons for adherence to tuberculosis standard treatment therapy among human immune virus infected patients concluded that although an isoniazid preventive therapy program for human immune virus infected patients was shown to be feasible, still there were further adjustments required to increase the adherence as resistance and spread of tuberculosis was found controlled in Thailand [61]. Significant number of physicians did not adhered to the standard norms for prescribing anti-tuberculosis treatment specifically in developing countries which resulted in increasing the proportion of drug-resistant TB. Therefore effective training programs are required to improve knowledge of prescribers [33, 62].

Overview of Management of Tuberculosis in Pakistan

It is universally accepted that a partially treated TB patient is worse than an untreated one as the chronic cases are the ones who excrete multi drug resistant organisms and increase the community burden of TB. Pakistan is ranked fifth amongst the twenty two countries designated as highly burdened by TB in the Eastern Mediterranean Region [63]. It also accounts to have the fourth highest prevalence of multidrug-resistant TB (MDR-TB) worldwide [19]. X-ray examination, clinical lab tests and blood tests are usually used for TB detection and diagnosis instead of sputum examination in Pakistan. Tuberculin is rarely available but still few practitioners rely on Mantoux results [64]. Active case detection suffers from a chronic lack of resumes especially that of widely available trained laboratory technicians and X-ray facilities. Treatment of cases is often inadequate and inappropriate owing to lack of training of health care workers, scarcity of medicines in health care facilities, absence of control on drug sales and hence over the counter sales and self medication by patients and widespread lack of patient compliance with therapy in Pakistan [27].

Another most important factor for rapid rise in multi-drug resistant (MDR) TB in Pakistan is inadequate treatment with inappropriate regimens with respect to dosage and duration. In 1993, WHO declared TB as a global emergency and the DOTS strategy was endorsed by Government of Pakistan in the country [65]. In 1994, the Ministry of Health in collaboration with WHO revised the TB control policy and national guidelines were drafted. Pakistan was declared 1 of the 16 countries without an appropriate NTP in 1998. Since then, although a steady progress has been made in TB case detection and treatment success rate but Pakistan is still far away from meeting the targets related to Millennium Development Goal (MDG) by 2015 [19]. Studies conducted in Pakistan have reported poor knowledge of prescribers regarding national standard treatment guidelines as one of the main reasons for this slow progress. Most of the prescribers in Pakistan diagnose and treat tuberculosis by their own choices rather complying with standard treatment guidelines [63, 66].

IV.   Conclusion

This review paper concluded that although available guidelines for management of pulmonary tuberculosis aim at seeking the desired therapeutic goals but still adherence to these guidelines by prescribers is inadequate especially in developing counties. This highlights the need of refreshing or updating the knowledge of the physicians regarding these guidelines and ensuring the availability and implementation of the DOT strategy within the hospitals as compulsory unit for control of tuberculosis. Moreover, extensive research is required to explore role of DOTs program in control of TB, barriers in its effective implementation and healthcare system collaborative models to promote active case detection and appropriate treatment which can lead to improved patient compliance and control of tuberculosis in developing countries including Pakistan.

References

[1].   Lienhardt, C. and J.A. Ogden, Tuberculosis control in resource-poor countries: have we reached the limits of the universal paradigm? Tropical Medicine & International Health, 2004. **9**(7): p. 833-841.
[2].   Langendam, M.W., et al., Prevalence of inappropriate tuberculosis treatment regimens: a systematic review. European Respiratory Journal, 2012. **39**(4): p. 1012-1020.
[3].   Nnoaham, K., et al., Perceptions and experiences of tuberculosis among African patients attending a tuberculosis clinic in London. The International Journal of Tuberculosis and Lung Disease, 2006. **10**(9): p. 1013-1017.
[4].   Grimshaw, J.M. and I.T. Russell, Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. The Lancet, 1993. **342**(8883): p. 1317-1322.
[5].   Nahid, P., M. Pai, and P.C. Hopewell, Advances in the diagnosis and treatment of tuberculosis. Proceedings of the American Thoracic Society, 2006. **3**(1): p. 103-110.
[6].   Garner, P., et al., Promoting adherence to tuberculosis treatment. Bulletin of the World Health Organization, 2007. **85**(5): p. 404-406.
[7].   Shah, S., et al., Do private doctors follow national guidelines for managing pulmonary tuberculosis in Pakistan? 2003.
[8].   Gallardo, C., et al., Quality of tuberculosis guidelines: urgent need for improvement. The International Journal of Tuberculosis and Lung Disease, 2010. **14**(8): p. 1045-1051.
[9].   Grol, R. and J. Grimshaw, From best evidence to best practice: effective implementation of change in patients' care. The Lancet, 2003. **362**(9391): p. 1225-1230.
[10].   Shehzadi, R., et al., Knowledge regarding management of tuberculosis among general practitioners in northern areas of Pakistan. JOURNAL-PAKISTAN MEDICAL ASSOCIATION, 2005. **55**(4): p. 174.
[11].   Nojoomi, M., L. Mokhberal-Safa, and A. Jamali, Study of Knowledge and Attitude of Private General Physicians of Karaj City Regarding National TB Programs–2002. Tanaffos, 2003. **2**(6): p. 67-73.
[12].   Balamurugan, S.S. and S.R. Swaminathan, The Awareness about Tuberculosis and DOTS among the Aspiring Doctors in a Tertiary Medical College Hospital, Salem, Tamil Nadu. National Journal of Research in Community Medicine, 2013. **2**: p. 133-9.
[13].   Mala, G., et al., Why tuberculosis service providers do not follow treatment guideline in Ethiopia: a qualitative study. Journal of evaluation in clinical practice, 2014. **20**(1): p. 88-93.
[14].   Irani, A.D., et al., Lack of optimum practice among health care workers regarding tuberculosis in Iran: A knowledge, attitude, and practice study. American Journal of Infection Control, 2015.
[15].   Hashim, D., W. Al Kubaisy, and A. Al Dulayme, Knowledge, attitudes and practices survey among health care workers and tuberculosis patients in Iraq. 2003.
[16].   Dato, M.I. and M.S. Imaz, Tuberculosis control and the private sector in a low incidence setting in Argentina. Revista de Salud Pública, 2009. **11**(3): p. 370-382.

[17]. Rowe, K., et al., Adherence to TB preventive therapy for HIV-positive patients in rural South Africa: implications for antiretroviral delivery in resource-poor settings? The International Journal of Tuberculosis and Lung Disease, 2005. **9**(3): p. 263-269.
[18]. Croft, R. and R. Croft, Knowledge, attitude and practice regarding leprosy and tuberculosis in Bangladesh. Leprosy review, 1999. **70**(1): p. 34-42.
[19]. WHO., Global Tuberculosis Report 2014. 2014: World Health Organization.
[20]. van der Werf, M.J., et al., Knowledge of tuberculosis-treatment prescription of health workers: a systematic review. European Respiratory Journal, 2012. **39**(5): p. 1248-1255.
[21]. Deveci, S., et al., [The knowledge, attitude and behavior related to the tuberculosis and approaches of tuberculosis therapy by the physicians providing first step service]. Tuberkuloz ve toraks, 2002. **51**(1): p. 40-47.
[22]. Cramm, J.M., et al., TB treatment initiation and adherence in a South African community influenced more by perceptions than by knowledge of tuberculosis. BMC public health, 2010. **10**(1): p. 72.
[23]. Chaudhry, R., M. Saeed Zaheer, and N.H. Sheikh, Awareness of dots regarding management of pulmonary tuberculosis among resident doctors and final year medical students in tertiary level health care facility. Biomedical, 2012. **28**(1): p. 82-87.
[24]. Dasgupta, A. and A. Chattopadhyay, A study on the perception of general practitioners of a locality in Kolkata regarding RNTCP and DOTS. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine, 2010. **35**(2): p. 344.
[25]. Arif, K., et al., Physician compliance with national tuberculosis treatment guidelines: a university hospital study. The International Journal of Tuberculosis and Lung Disease, 1998. **2**(3): p. 225-230.
[26]. Barker, R.D., Clinical tuberculosis. Medicine, 2008. **36**(6): p. 300-305.
[27]. Rizvi, N. and M. Hussain, Survey of knowledge about tuberculosis amongst family physicians. JOURNAL-PAKISTAN MEDICAL ASSOCIATION, 2001. **51**(9): p. 333-336.
[28]. Amin, A., et al., Review of prescriber approach towards rational drug practice in hospitalised patients. J Ayub Med Coll Abbottabad, 2011. **23**(1).
[29]. Raviglione, M.C. and M.W. Uplekar, WHO's new Stop TB Strategy. The Lancet, 2006. **367**(9514): p. 952-955.
[30]. Wells, W., et al., Implications of the current tuberculosis treatment landscape for future regimen change. The International Journal of Tuberculosis and Lung Disease, 2011. **15**(6): p. 746-753.
[31]. Moran-Mendoza, O., et al., Risk factors for developing tuberculosis: a 12-year follow-up of contacts of tuberculosis cases. The International Journal of Tuberculosis and Lung Disease, 2010. **14**(9): p. 1112-1119.
[32]. Vallejo, J.G., L.T. Ong, and J.R. Starke, Clinical features, diagnosis, and treatment of tuberculosis in infants. Pediatrics, 1994. **94**(1): p. 1-7.
[33]. Zazueta-Beltran, J., et al., Increasing drug resistance of Mycobacterium tuberculosis in Sinaloa, Mexico, 1997–2005. International Journal of Infectious Diseases, 2011. **15**(4): p. e272-e276.
[34]. Frieden, T.R. and J.A. Sbarbaro, Promoting adherence to treatment for tuberculosis: the importance of direct observation. Bulletin of the World Health Organization, 2007. **85**(5): p. 407-409.
[35]. Vyas, R., P. Small, and K. DeRiemer, The private-public divide: impact of conflicting perceptions between the private and public health care sectors in India. The International Journal of Tuberculosis and Lung Disease, 2003. **7**(6): p. 543-549.
[36]. Shamaei, M., et al., First-line anti-tuberculosis drug resistance patterns and trends at the national TB referral center in Iran—eight years of surveillance. International Journal of Infectious Diseases, 2009. **13**(5): p. e236-e240.
[37]. Quy, H., et al., Treatment results among tuberculosis patients treated by private lung specialists involved in a public-private mix project in Vietnam. The International Journal of Tuberculosis and Lung Disease, 2003. **7**(12): p. 1139-1146.
[38]. Ormerod, L. and C. Bentley, The management of pulmonary tuberculosis notified in England and Wales in 1993. Journal of the Royal College of Physicians of London, 1996. **31**(6): p. 662-665.
[39]. Ayaya, S., et al., Knowledge, attitudes and practices of private medical practitioners on tuberculosis among HIV/AIDS patients in Eldoret, Kenya. East African medical journal, 2003. **80**(2): p. 83-90.
[40]. Remesh, A., et al., The Knowledge, Attitude and the Perception of Prescribers on the Rational Use of Antibiotics and the Need for an Antibiotic Policy–A Cross Sectional Survey in a Tertiary Care Hospital. Journal of clinical and diagnostic research: JCDR, 2013. **7**(4): p. 675.
[41]. Kiefer, E.M., et al., Knowledge and attitudes of tuberculosis management in San Juan de Lurigancho district of Lima, Peru. The Journal of Infection in Developing Countries, 2009. **3**(10): p. 783-788.
[42]. Prasad, R., et al., Treatment of new pulmonary tuberculosis patients: what do allopathic doctors do in India? The International Journal of Tuberculosis and Lung Disease, 2002. **6**(10): p. 895-902.
[43]. Szakacs, T.A., et al., Adherence with isoniazid for prevention of tuberculosis among HIV-infected adults in South Africa. BMC infectious diseases, 2006. **6**(1): p. 97.
[44]. Xu, W., et al., Adherence to anti-tuberculosis treatment among pulmonary tuberculosis patients: a qualitative and quantitative study. BMC Health Services Research, 2009. **9**(1): p. 169.
[45]. Dyar, O.J., et al., European medical students: a first multicentre study of knowledge, attitudes and perceptions of antibiotic prescribing and antibiotic resistance. Journal of Antimicrobial Chemotherapy, 2013: p. dkt440.
[46]. Kutare, A., M. Rosario, and N. Goudb, A study on knowledge of tuberculosis, DOTS and MDR-TB among interns of medical colleges in Bangalore. International Journal of Health Sciences & Research, 2012. **2**(3): p. 33-39.
[47]. Olle-Goig, J., J. Cullity, and R. Vargas, A survey of prescribing patterns for tuberculosis treatment amongst doctors in a Bolivian city. The International Journal of Tuberculosis and Lung Disease, 1999. **3**(1): p. 74-78.
[48]. Davis, D.A. and A. Taylor-Vaisey, Translating guidelines into practice: a systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. Canadian Medical Association Journal, 1997. **157**(4): p. 408-416.
[49]. Cabana, M.D., et al., Why don't physicians follow clinical practice guidelines?: A framework for improvement. Jama, 1999. **282**(15): p. 1458-1465.
[50]. Murthy, K., et al., Public-private partnership in tuberculosis control: experience in Hyderabad, India. The International Journal of Tuberculosis and Lung Disease, 2001. **5**(4): p. 354-359.
[51]. Husain, M.O., et al., The relationship between anxiety, depression and illness perception in tberculosis patients in Pakistan. Clinical Practice and Epidemiology in Mental Health, 2008. **4**(1): p. 4.
[52]. Uplekar, M., et al., Tuberculosis management in private practice and its implications. Indian Journal of Tuberculosis, 1996. **43**: p. 19-22.
[53]. Lönnroth, K., et al., Private tuberculosis care provision associated with poor treatment outcome: comparative study of a semi-private lung clinic and the NTP in two urban districts in Ho Chi Minh City, Vietnam. The International Journal of Tuberculosis and Lung Disease, 2003. **7**(2): p. 165-171.

[54]. Uplekar, M., et al., Tuberculosis patients and practitioners in private clinics in India. The International Journal of Tuberculosis and Lung Disease, 1998. **2**(4): p. 324-329.
[55]. Pablos-Méndez, A., et al., Nonadherence in tuberculosis treatment: predictors and consequences in New York City. The American journal of medicine, 1997. **102**(2): p. 164-170.
[56]. Ngamvithayapong, J., et al., Adherence to tuberculosis preventive therapy among HIV-infected persons in Chiang Rai, Thailand. Aids, 1997. **11**(1): p. 107-112.
[57]. Zhou, C., et al., Adherence to tuberculosis treatment among migrant pulmonary tuberculosis patients in Shandong, China: a quantitative survey study. PloS one, 2012. **7**(12): p. e52334.
[58]. Edginton, M., C. Sekatane, and S. Goldstein, PatientsÕ beliefs: do they affect tuberculosis control? A study in a rural district of South Africa. The International Journal of Tuberculosis and Lung Disease, 2002. **6**(12): p. 1075-1082.
[59]. Haasnoot, P.J., et al., Knowledge, attitudes, and practice of Tuberculosis among Maasai in Simanjiro District, Tanzania. The American journal of tropical medicine and hygiene, 2010. **83**(4): p. 902-905.
[60]. Dagli, C.E., et al., A multicentre study of doctors' approaches to the diagnosis and treatment of tuberculosis in Turkey. The Journal of Infection in Developing Countries, 2009. **3**(05): p. 357-364.
[61]. Hong, Y., et al., Survey of knowledge, attitudes and practices for tuberculosis among general practitioners. Tubercle and lung disease, 1995. **76**(5): p. 431-435.
[62]. Yimer, S.A., C. Holm-Hansen, and G. Bjune, Assessment of knowledge and practice of private practitioners regarding tuberculosis control in Ethiopia. The Journal of Infection in Developing Countries, 2011. **6**(01): p. 13-19.
[63]. Naseer, M., et al., How well can physicians manage Tuberculosis? A Public-Private sector comparison from Karachi, Pakistan. BMC Health Services Research, 2013. **13**(1): p. 439.
[64]. Khan, A., Z. Badini, and J. Parkash, Prescribing Practices of Consultants at Karachi, Pakistan. 2006.
[65]. Shiffman, J., T. Beer, and Y. Wu, The emergence of global disease control priorities. Health Policy and Planning, 2002. **17**(3): p. 225-234.
[66]. Mushtaq, M., et al., Knowledge, attitudes and practices regarding tuberculosis in two districts of Punjab, Pakistan. The International Journal of Tuberculosis and Lung Disease, 2010. **14**(3): p. 303-310.