

SYSTEMATIC REVIEW

Assessing quality of life for multidrug-resistant and extensively drug-resistant tuberculosis patients

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Abstract

Objective: One can hypothesize that Mycobacterium genus originated more than 150 million years ago and has evolved to become one of the leading lethal infectious diseases. Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) patients are directly affected by the disease and other subjective issues, such as related diseases, medical costs and social issues, which all have negative impacts on patient quality of life (QOL). Our purpose is to define the status of health-related QOL for international MDR-TB and XDR-TB patients.

Methods: Systematic review is a good method for searching and selecting related researches and articles. As such, we have searched for and cited related articles on reputable databases, such as PubMed, Cochrane, and Google Scholar. A data overview was performed to draw conclusions and results on the QOL of MDR-TB and XDR-TB patients.

Results: A total of 18 articles were included, using instruments from the World Health Organization, Euroqol, Short Form, AQ and the Seattle Obstructive Lung Disease Questionnaire. The QOL of MDR-TB and XDR-TB patients was found to be compromised due to the strong resistance of Mycobacterium tuberculosis, economic pressure and community alienation.

Conclusions: A number of QOL and health-related QOL studies on MDR-TB and XDR-TB patients are limited, especially with XDR-TB patients. Significant numbers of MDR-TB and XDR-TB patients still have sequelae after completing treatment, reducing the health-related QOL among these patients.

Keywords: Extensively drug-resistant tuberculosis, Health-related quality of life, Multidrug-resistant tuberculosis, Quality of life. (JPMA 69: S-137 (Suppl. 2); 2019)

Introduction

Mycobacterium tuberculosis was discovered in monuments and fossil specimens from hundreds of millions of years ago. With strong adaptation throughout geological and climate change stages, as well as the migration of continents, Mycobacterium tuberculosis has spread and eventually become the most dangerous infectious disease in the world known as tuberculosis.^{1,2} Due to the mutability and adaptability of tuberculosis bacteria against antibiotics and environment, as well as patient non-compliance with medication regimens, anti-tuberculosis drug resistance has occurred.² While tuberculosis patients suffer from severe medical pressures, drug-resistance makes it significantly more difficult to manage and successfully treat multidrug-resistant tuberculosis (MDR-TB) and extensively drug-

resistant tuberculosis (XDR-TB) cases.³

Because of MDR-TB and XDR-TB, these patients must use second-line drugs, which are more expensive, cause more serious side effects and require longer treatment durations. These drugs also cause other health-related, economic and social patient burdens which affect the quality of life (QOL) of these patients.⁴

There has been some research on the health-related quality of life (HRQOL) of MDR-TB and XDR-TB patients which has shown such patients being significantly affected, but most of these studies were conducted in particular countries.⁵⁻⁸ Thus, our study shall evaluate QOL among international MDR-TB and XDR-TB cases to produce a positive solution to QOL improvement for MDR-TB and XDR-TB patients.

Methods

A systematic review was conducted from 30 January to 18 April 2019 using the following three databases: PubMed (www.ncbi.nlm.nih.gov/pubmed), Cochrane (www.cochranelibrary.com) and Google Scholar (www.scholar.google.com.vn). The found articles were sent to Endnote X9 for the creation of citation files. Using Endnote X9, we looked for duplicates and removed

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them.

The syntax we used in the PubMed and Cochrane databases was as follows: ("Health-related quality of life" or "HRQOL" or "HRQoL" or "HRQL" or "Quality of Life" or "QOL" or "QoL") and ("multidrug-resistant tuberculosis"[MeSH Terms] or "extensively drug-resistant tuberculosis"[MeSH Terms]). In the Google Scholar database, we used the

following search terms to match the scope of the other database searches: "health-related quality of life", "quality of life", "multidrug-resistant tuberculosis" and "extensively drug-resistant tuberculosis". The Google Scholar search combined the terms with matching words "and" and "or".

These found articles were subsequently screened by title, abstract and full-text to determine appropriate articles.

Table-1: Inclusion/exclusion criteria.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> - Studies related to quality of life and health-related quality of life of MDR-TB and XDR-TB patients. - Conducted internationally. - Written in English. 	<ul style="list-style-type: none"> - Studies were conducted on MDR-TB and XDR-TB patients worldwide, but did not evaluate patient quality of life or health-related quality of life. - Publications were published on non-English journals.

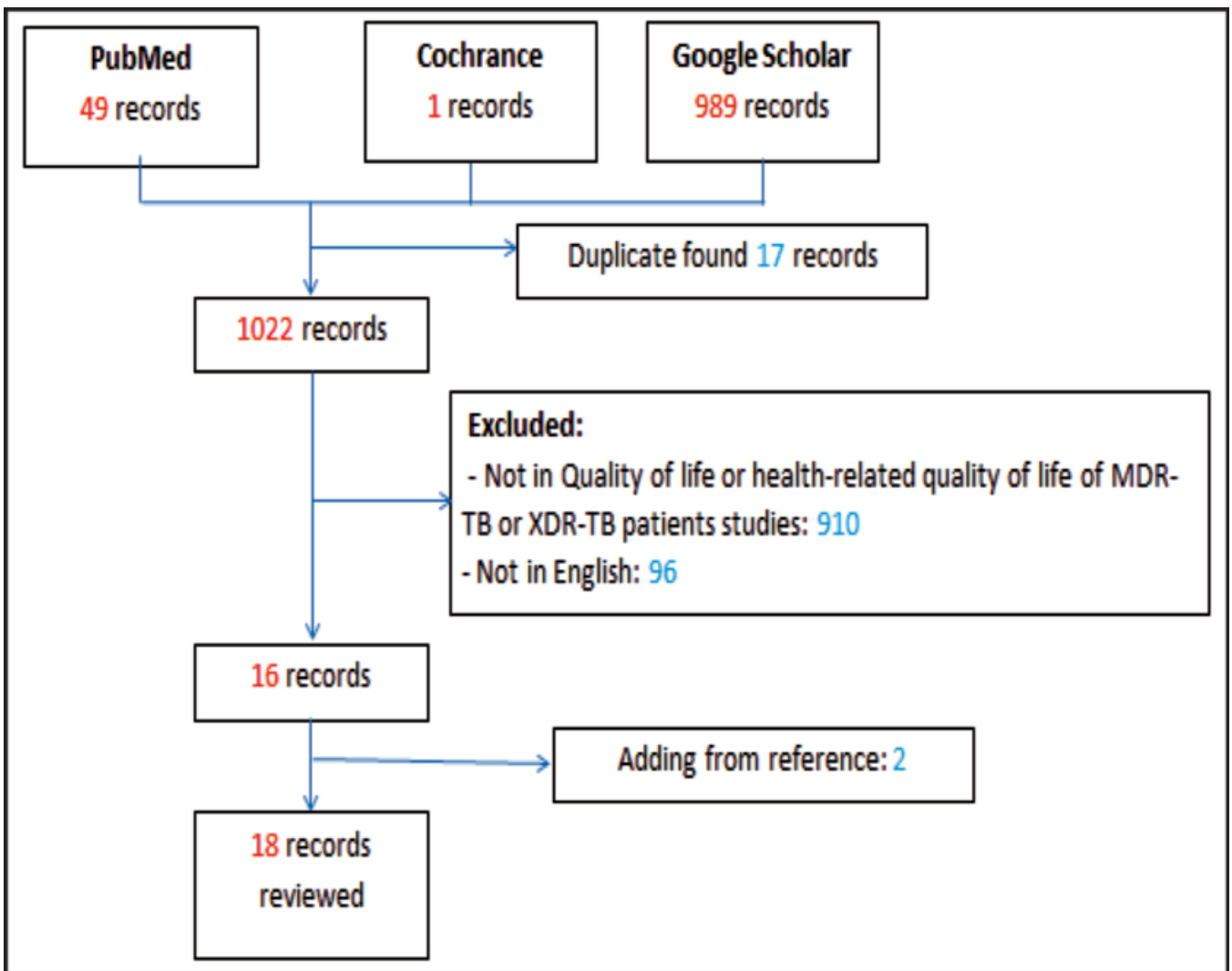


Figure-1: The selection process.

The criteria used for selection is shown in Table-1 and the process selected to identify which articles should be chosen for collecting indispensable information is shown in Figure-1.

Results

Among the databases, 1039 articles were found with 49, 1 and 989 originating from Pubmed, Cochrane and Google Scholar, respectively. After the selection process, 17 duplicates, 96 non-English and 910 unrelated articles were removed. The resulting 16 articles were chosen for review and two additional references were selected to make up the 18 articles included for systematic review.

As we summarized these publications, we divided them into three categories: year of publication, the number of study participants and target samples (Table-2).

According to publication years, one study was published in 2004, 2014 and 2019. The other years ranged from two to five articles with the most prolific being 2016 and 2018. The number of participants ranged from under 100 (6 articles), to between 100 and 200 (5 articles) and over 200 (4 articles), with the rest having unlimited participants. There were 11, 1 and 6 publications targeting MDR-TB patients, XDR-TB patients and MDR-TB patients with other subjects, respectively. Furthermore, we also summarized the study designs of these reviewed articles (Table-3), obtaining data showing cross-sectional design accounted for more than 10 studies (around 55.56%) while other types of study design represented less than 20%.

Among these articles, many HRQOL and QOL instruments were used to evaluate the lives of MDR-TB and XDR-TB patients (Table-4). The most commonly used instrument was the World Health Organization quality of life (WHOQOL) (used by 5 articles) and the second most common was the SF (using in 3 articles).

Most of the 18 reviewed articles researched adult aged subjects (>18 years) and evaluated their lives in four domains: physical, psychological, social and environmental. Instances of depression, anxiety and lack

Table-3: Summary of study designs used by reviewed articles.

Study designs	Number of publications
Follow-up	1
Case-control	1
Cross-sectional	11
Meta-analysis and systematic review	3

Table-4: Summary of QOL and HRQOL instruments used by reviewed articles.

Instruments	Number of publications	Specific questionnaires
EQ-5D	2	EQ-5D, EQ-VAS
WHOQOL	5	WHOQOL-BREF
SF	3	1 SF-8 2 SF-36v2
Others	8	1 AQ-20 1 SOLDQ 5 N/A 1 SSRS

Table-5: Summary of research locations selected by reviewed articles.

Places	Number of publications
India	5
Africa	4
China	1
Thailand	1
Brazil	1

of social support were noted during treatments, which reduced the QOL of MDR-TB patients in all domains.^{6,9,10} Moreover, these reductions were dependent on the age and gender of the MDR-TB patients. For instance, the elderly may have a lower HRQOL than those aged 18-30 years. Females were found more likely to experience poor HRQOL than males.¹¹ In countries such as India and China, the well-being of living or social support of MDR-TB patients were seen to be comparatively low.^{8,12} Therefore, encouragement is a vital factor to enhance the lives of

Table-2: Summary of publications.

Year of publication	2004	2012	2014	2015	2016	2018	2019
Number of publications	1	2	2	3	4	5	1
Study participants	Under 100		100 - 200		Over 200		Not available
Number of publications	6		5		4		3
Target samples	MDR-TB patients		XDR-TB patients		MDR-TB patients + others		
Number of publications	11		1		6		

Table-6: Summary of reviewed articles.

No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
1	Effects of Multidrug Resistant Tuberculosis Treatment on Patients' Health Related Quality of Life: Results from a Follow Up Study ⁹	Ahmad, N., Javaid, A., Syed Sulaiman, S. A., Basit, A., Afridi, A. K., Jaber, A. A., Khan, A. H.	2016	2012	SF-36v2	Follow up	N/A	68	>18	A total of 68 MDR-TB patients completed SF-36v2 questionnaire at the three time points. Patients' mean PCS scores at the three time points were 38.2±4.7, 38.6±4.4 and 42.2±5.2, respectively, and the mean MCS were 33.7±7.0, 35.5±6.9 and 40.0±6.9, respectively. Length of sickness prior to the diagnosis of MDR-TB was predictive of a difference in PCS scores, while patients' gender and length of sickness prior to diagnosis were predictive of a difference in MCS scores.	Despite the positive impact of MDR-TB treatment on patients' HRQOL, the scores on component summary measures suggested compromised physical and mental health even at the end of treatment. A large multicentre study is recommended to confirm the present findings.
2	Health-related quality of life of tuberculosis Patients in Bagdad and Socio-demographic Factors Associated with Multiple Drug Resistant Tuberculosis (MDR TB) ⁵	Ahmed Abed Marzook	2016	2015	WHOQOL-BREF	Cross-sectional study	Baghdad/ Iraq	100	43.46 ± 14.8 (MDR-TB) and 37 ± 16.16 (non-DR-TB)	. Males constituted a majority in both participant groups (64% in DR-TB and 59% in non-DR-TB). Smoking was higher in DR-TB than non-DR-TB (57% and 38%, respectively). Significant differences were found between DR-TB and non-DR-TB in global QOL, health, physical, psychological, social and environmental domains (P=0.004, 0.014, 0.001, 0.0019, 0.001 and 0.001, respectively).	Patients with MDR-TB had lower mean scores than non-DR-TB for overall HRQOL domains. There was an association found between getting MDR-TB and being older, having a lower educational level, smoking and being unemployed.
3	Tuberculosis patients are physically challenged and socially isolated: A mixed methods case-control study of Health Related Quality of Life in Eastern Ethiopia ¹⁷	Akili Abrham Robal, Tamirat Tesfaye Dasa, Fitsum Weldegebreal, Abyot Asfaw, Habtamu Mitiku, Zelalem Teklemariam, Mahantash Naganuri, Bahubali Jinnappa Geddugold1, Frehiwot Mesfin1, Hilina Befikadu2, Eden Tesfaye3	2018	2017	SF-36v2	Case-control	Eastern Ethiopia	400	27.4±10.5	HRQOL between cases and controls had no statistically significant differences in mean scores (57.61±16.42 and 59.13±22.10, respectively) as well as no significant differences in physical functioning, and no role disruption due to physical problems, vitality, social functioning, emotional distress or overall mental health. With significantly poorer HRQOL (p<0.05), MDR-TB patients were more likely to be single, a current student, have lower education and have more than 5 people in family than individuals with drug sensitive tuberculosis. The scale scores had good internal consistency, with a Cronbach's alpha value of 0.73.	Individuals with MDR-TB reported statistically worse general health but less bodily pain than individuals with drug sensitive tuberculosis. To regain lost role function, we recommend that health facilities, media and all other stakeholders educate the community, households and students about pulmonary tuberculosis, its treatment, prevention methods and therapeutic approaches towards tuberculosis patients, specifically MDR-TB.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
4	Mental health disorders, social stressors, and health-related quality of life in patients with multidrug-resistant Tuberculosis: A systematic review and meta-analysis ¹⁰	Alene, K. A.; Clements, A. C. A.; McBryde, E. S.; Jaramillo, E.; Lonroth, K.; Shaweno, D.; Gulliver, A.; Viney, K.	2018	N/A	N/A	Retrospective cohort, prospective cohort, cross-sectional and intervention studies	African Region, American Region, Southeast Region, European Region, Eastern Mediterranean Region, Western Pacific Region	40 articles	N/A	We included a total of 40 studies conducted in 20 countries. Depression, anxiety and psychosis were the most common mental health disorders reported in the studies. The overall prevalence of depression, anxiety and psychosis were 25%, 24% and 10%, respectively. There was considerable heterogeneity in the estimates. Stratification analysis showed that the incidence of psychosis was 4% before and 9% after starting MDR-TB treatment. The most common social stressors reported were stigma, discrimination, isolation and lack of social support. HRQOL was significantly lower in patients with MDR-TB when compared to drug-susceptible tuberculosis patients ($Q = 9.88$, $p = 0.01$, $I^2 = 80\%$).	Mental health and social functioning of MDR-TB patients are significantly compromised due to this review, which is confirmed by the poor HRQOL reported. Therefore, it is important to integrate mental health services, social protection and social support into the clinical and programming management of MDR-TB.
5	Sequelae of multidrug-resistant tuberculosis: protocol for a systematic review and meta-analysis ¹⁰	Alene, K. A.; Clements, A. C. A.; McBryde, E. S.; Jaramillo, E.; Lonroth, K.; Shaweno, D.; Viney, K.	2018	2017	N/A	Retrospective cohort, prospective cohort, cross-sectional and intervention studies	N/A	N/A	N/A	Studies reporting on clinical, psychological, social and economic sequelae, as well as HRQOL in persons with MDR-TB treatment or illness.	This will provide pooled estimates of MDR-TB sequelae, which will identify the main risk factors for MDR-TB sequelae and provide empirical evidence necessary for clinicians, health professionals, researchers and decision-makers to better understand the risk factors, policy implications, future research needs and programming priorities for the treatment, care and follow-up of persons with MDR-TB.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
6	Adverse drug reactions and resultant health-related quality of life during multidrug-resistant tuberculosis treatment in South Africa ¹⁴	Ana Maria Kelly	2015	N/A	EQ-5D	Cross-sectional	KwaZulu-Natal, South Africa	121	≥18	Aim 1: Most of participants were co-infected with HIV (75%), female (51%), and did not have enough to eat on a daily basis. Aim 2: In the multivariable analysis, an increase in total ADRs was related to gender (female) and elevated liver enzymes when starting MDR-TB treatment. HIV status had no significant impact on ADRs. Aim 3: An increase in total ADRs was significantly related to a decrease in HRQOL.	This study helps complete the knowledge about ADR effects from MDR-TB treatment on HRQOL. For clinicians, this finding strengthens the requirement to improve detection, documentation and ADR management. Further research is needed to identify the effectiveness of ADR management techniques on improving HRQOL results for patients during treatment.
7	Quality of life among patients on MDR-TB treatment in a district tuberculosis centre of a metropolitan city ⁶	Apoorva E. Patel, K. Lalitha, Dinesh Rajaram, K. Radhika, N. S. Murthy	2018	2014	WHOQOL-BREF	Cross-sectional	Karnataka	159	22-50	The average age among MDR-TB cases, non-MDR-TB and TB-cured subjects were 35, 37 and 30.5 years old, respectively. The number of females in the 52 MDR-TB cases was 26 (50%), compared to 14 (26.4%) among the non-MDR-TB cases and 26 (48.1%) among the TB-cured subjects ($p = 0.0024$). The scores of physical and environmental domains in MDR-TB cases were significantly lower than non-MDR-TB cases ($p = 0.01$ and $p = 0.001$, respectively). Meanwhile, MDR-TB cases also had significantly lower physical and psychological scores compared to TB-cured subjects ($p < 0.001$ and $p < 0.001$, respectively).	Tuberculosis has negative effects on the QOL of patients which are made worse in MDR-TB cases. Thus, early diagnosis and prompt treatment will alleviate the severity of the disease while improving patient QOL after treatment.
8	Social support received by multidrug-resistant tuberculosis patients and related factors: a cross-sectional study in Zhejiang Province, People's Republic of China ¹²	Bin Chen, Yin Peng, Lin Zhou, Chengliang Chai, Hui-Chi Yeh, Songhua Chen, Fei Wang, Mingwu Zhang, Tieniu He, Xiaomeng Wang	2016	2014	SSRS	Cross-sectional	Zhejiang, China	212	20-59	The average social support score for MDR-TB patients was 32.56 ± 7.86 . Participants who were single, widowed or divorced, who were retired, had fewer family members and had lower family income were found to have lower social support scores. Participants unwilling to disclose their disease tended to have less social support ($31.59, 34.23, P = 0.010$). Participants who perceived great help from health care workers reported higher social support rating scale scores than those who perceived no help ($35.36, 29.89, P = 0.014$).	MDR-TB patients in the Zhejiang province were shown to have a low level of social support. Patients who were not married, had smaller families, and lower family income received less social support, suggesting that family harmony could be an important source of social support. Patient self-isolation may contribute to a decrease in support received from surroundings. Health care organizations need to offer more social support to MDR-TB patients.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
9	Beyond 'cure' and 'treatment success': quality of life of patients with multidrug-resistant tuberculosis ¹³	C. Laxmeshwar, A. G. Stewart, A. Dalal, A. M. V. Kumar, S. Kalaiselvi, M. Das, N. Gawde, S. S. Thi, P. Isaakidis	2019	2016	WHOQoL-BREF	Cross-sectional	Mumbai, India	95	28	The psychological and physical health domains were the most affected. The social relations and environmental domain mean scores were 68.6 and 60.3, respectively. Loss of employment due to tuberculosis adversely affected the social relations and environmental domains. Qualitative analysis showed that support was the most important theme affecting QOL. Other themes were physical, psychological, social functioning and environmental factors.	HRQOL among study participants was lower, but higher than previously reported in tuberculosis patients. Encouragement is a key factor that has a positive impact on HRQOL, although both disease and treatment were physically and socially challenging.
10	International Multidisciplinary Research Journal Golden Research Thoughts ¹¹	Dr.Tukaram Narayan Shinde, Mrs.Laxmi Ashok Yakkaldevi, Dr.Rajani Dalvi, Mr.AshokYakkaldevi	2015	N/A	WHOQoL-BREF	N/A	Bihar, Andhra Pradesh and New Delhi, India	610	> 18	Young MDR-TB patients in the age group of 18 to 30 years had higher QOL than other age groups. In MDR-TB cases, the QOL of male patients is comparatively higher than female patients. The distribution of state-wise QOL was presented with four domains. The QOL for Andhra Pradesh patients was comparatively higher, except in the social domain aspects. The MDR-TB patients those who belonged to other faith had high mean score and except in social domain when compared to other religions.	The QOL in the four social domains of the MDR-TB patients remained much affected. Thus, there is a requirement to incorporate a systematic approach to the study of quality issues regarding tuberculosis and MDR-TB patients so that timely and relevant intervention can be provided for MDR-TB treatments.
11	Adverse events and patient' perceived health related quality of life at the end of multidrug-resistant tuberculosis treatment in Namibia ¹¹	Evans L Sagwa, Nunurairuswa, Farai Mavhunga, Timothy Rennie, Hubert GM Leufkens, Aukje K Mantel Teeuwisse	2016	2016	SF-8	Cross-sectional	Namibia	36	40	Overall, 36 patients aged 17-54 years responded to the questionnaire. The median HRQOL score for the physical component summary was 58.6, while the median score for the mental component summary was 59.3, indicating a moderately low self-rating of health. In all, 32 (89%) of the 36 patients experienced at least one adverse drug event of any severity during their treatment, none of which were life-threatening. The occurrence of adverse events was not related to HRQOL scores.	Treated MDR-TB patients in Namibia tended to have a moderately low HRQOL score. This result is not relevant to the occurrence of adverse events.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
12	The Functional Assessment of Patients With Pulmonary Multidrug-Resistant Tuberculosis ¹⁷	Marcos DP Godoy PT MSc, Fernanda CQ Mello MD PhD, Aginaldo J Lopes MD PhD, Walter Costa MD, Fernando S Guimaraes PT PhD, Antonio GF Pacheco MD PhD, Ivany A Castanho MD, and Sara LS Menezes PT PhD	2012	2008	AQ-20	Cross-sectional	University of the State of Rio de Janeiro, Rio de Janeiro, Brazil	18	43.7 ± 9.4	Spirometric evaluation showed that 78% of the subjects had abnormal patterns. The maximal respiratory pressures were significantly decreased in all subjects, despite the fact that their nutritional status was within the normal range. The distance completed in the six minute walk test was less than expected in 72% of the subjects. All of the subjects who were evaluated had residual lesions, and 78% reported a decreased QOL.	HRQOL among study participants was lower, but higher than previously reported in tuberculosis patients. Encouragement is a key factor that has a positive impact on HRQOL, although both disease and treatment were physically and socially challenging.
13	Individualized second line anti-tuberculous therapy for an extensively resistant pulmonary tuberculosis (XDR PTB) in East Malaysia ¹⁸	Muhammad Redzwan S Rashid Ali, MRCP, Anna P Ralph, FRACP PhD, Kunji Kannan Sivaraman Kannan, FCCP, Timothy William, FRCP	2015	2010	N/A	N/A	N/A	1	31	Multidisciplinary management (medical, surgical and supportive) has proven effective thus far in this very difficult case, which has had major QOL impacts for this young patient.	Tuberculosis risk among health-care workers in high tuberculosis-burden settings is considered highly. Obtaining upfront cultures and susceptibility results in all new tuberculosis cases is essential. The drug resistant problem during MDR-TB treatment, the value of surgical resection in refractory cases and the major QOL impact this disease can have on young individuals.
14	Quality of Life of Multi Drug Resistant Tuberculosis Patients: A Study of North India ⁸	Raman Sharma, Ravinder Yadav, Meenakshi Sharma, Varinder Saini, and Vipin Kousha	2014	N/A	WHOQOL-BREF	N/A	Multispecialty tertiary level hospital of North India	120	Unlimited	It was found that MDR-TB patients had worse QOL than PTB patients. In MDR-TB and PTB, psychology and environment domains (MDR-TB vs. PTB 17.46 vs. 15.23 and 22.00 vs. 18.91, respectively) were affected more than the physical and social (19.03 vs. 20.05 and 7.88 vs. 9.61, respectively). MDR-TB patients suffered greater financial damage compared to PTB because they were not covered under any program, while both patient types underwent social stigma because of their diseases.	It is essential to make an applicable, reliable measure to better identify quality issues methodologically, which would help health-care professionals and management to provide timely and relevant interventions for patient QOL improvement.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
15	Sequelae of pulmonary multidrug resistant tuberculosis at the completion of treatment ¹⁹	Rupak Singla, Manashree Mallick, Parullriggipuri, Neeta Singla, Amitesh Gupta	2018	N/A	SOLDQ	Cross-sectional	New Delhi, India	46	27.6 ± 10.5	At the completion of MDR-TB treatment 95.7% patients had residual symptoms; 100% patients had residual bilateral chest X-ray abnormality with 82.6% patients showing far advanced disease. PFT was abnormal in 97.6% patients with mixed pattern being the commonest abnormality. QOL was impaired with mean physical function of 46%	Significant numbers of MDR-TB patients still have sequelae after completing treatment. It is advisable to incorporate medical management and encouragement from the public for these patients in the national programs.
16	Residual lung damage after completion of treatment for multidrug-resistant tuberculosis ²⁰	S. de Vallière,*† R. D. Barker‡	2004	1997	N/A	N/A	Limpopo Province, South Africa	142	N/A	The mean zonal score was 6.5. Cavitation was present in more than half of the patients. Of 33 patients, 31 (94%) had abnormal lung function tests. Restrictive and combined restrictive/obstructive lung function patterns were the predominant abnormalities.	Despite the MDR-TB treatment being completed, residual lung damage was common and extensive. Such damage not only increases the risk of recurring tuberculosis, but also reduces the HRQOL of these patients. Early diagnosis and close follow-up of MDR-TB are essential to reduce the extent of residual lung damage and detect relapses.
17	Psycho-Socio-Economic Issues Challenging Multidrug Resistant Tuberculosis Patients: A Systematic Review ²¹	Thomas, B. E.; Shanmugam, P.; Malaisamy, M.; Oving, S.; Suresh, C.; Subbaraman, R.; Adinarayanan, S.; Nagarajan, K.	2016	2015	N/A	Extracting qualitative evidences and systematically organised	N/A	282 published articles	N/A	It was found that all studies had documented ranges of psychosocial and economic challenges experienced by MDR-TB patients. Depression, stigma, discrimination, drug side effects causing psychological distress and the financial constraints due to MDR-TB were some of the common issues reported in the studies. There were few intervention studies which addressed these psychosocial issues, most of which were small pilot studies. There was a dearth of large-scale randomized psychosocial intervention studies that could be scaled up to strengthen the management of MDR-TB patients, which is crucial for the tuberculosis control programme.	This review has defined the psychosocial and economic issues challenging MDR patients. However, there is urgent need for feasible innovative psychosocial and economic intervention studies to equip MDR-TB patients with coping mechanisms for their illness while improving treatment adherence, treatment outcomes and the overall QOL of MDR-TB patients.

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No	Title	Author(s)	Publication Year	Conducting Year	Instrument	Study Design	Location	Number of sample	Age of sample (years)	Results	Conclusion
18	Health Related Quality of Life among Patients with Tuberculosis and HIV in Thailand ⁷	Wanitchaya Kittikraisak, Pritaporn Kingkaew, Yot Teerawattananon, Jomkwan Yothasamut, Supalert Natesuwan, Weerawat Manosuthi, Virasakdi Chongsuvivatwong, Sara J. Whitehead	2012	2009	EQ-5D, EQ-VAS	Cross-sectional	Chiang Rai Regional Hospital and Bamrasnaradura Infectious Diseases Institute, Thailand	222	35-47	The median age among patients was 40 years and the average monthly household income was 6,000 Baht. In Tobit regression analysis, factors independently predictive of UEQ-5D included age and monthly household income. The UEQ-5D of 740 year old patients was considerably lower compared to younger persons. Higher UEQ-5D was significantly associated with higher monthly household income in a dose response fashion. The median UEQ-5D was highest among patients who had been successfully treated for tuberculosis and lowest among MDR-TB patients who were on treatment.	The measured utilities were overvalued by UCAL for two co-morbidity patients, which led to the need for a more precise method to estimate the utility of patients with such conditions. Despite tuberculosis and MDR-TB treatments affecting the self-cognitive health status of these patients, it will gradually decrease after successful treatment.

MDR-TB and XDR-TB patients.¹³

India and Africa are two locations that have the most people being affected by this infectious disease. In total, nearly 10 studies (Table-5) performed their research in these locations (around 50% for each one). Many reasons can explain this preference, but the most prominent are hygiene and health-care systems. Mycobacterium tuberculosis can easily spread from one person to another through air and both India and Africa have large developing populations. As a result, hygiene and health-care conditions may be of little concern to the citizenry. The results are summarised in greater detail in Table-6.

Discussion

This review indicated the effects on QOL for MDR-TB and XDR-TB patients. There were four domains assessed among the reviewed studies: physical, psychological, social and environmental. The HRQOL of MDR-TB and XDR-TB patients became worse mainly due to physical and psychological problems after completing treatment. Financial damage, social functioning and environmental factors also affected the QOL of MDR-TB and XDR-TB patients. Nevertheless, HRQOL differed regarding gender and age among those patients. HRQOL was higher in the age group of 18 to 30 years¹¹ while QOL in patients 40 years old or older was significantly lower.⁷ Male patients also had a higher QOL when compared to female patients.¹¹

Ten studies focused on the QOL of MDR-TB patients, but

different tools were used among these studies (WHOQOL-BREF, EQ-5D, SOLDQ, SF-8, SF-36v2, SOLDQ). Despite the heterogeneity of measurement tools, evidence showed that MDR-TB patients had moderately low HRQOL scores. Five studies compared the HRQOL between MDR-TB patients and other patients, such as PTB, DS-TB, non-DR-TB and TB-cured subjects. These studies also used different measurement tools yet visibly indicated that MDR-TB received greater effect on HRQOL from alternative methodology than other groups. Moreover, there was a relation between contracting MDR-TB and being older, less educated, smoking and unemployed.⁵ However, a conflict remained between two findings about the effects of ADRs on the QOL of MDR-TB patients. One article stated that an increase in total ADRs was considerably associated with a decrease in HRQOL¹⁴ while another study disclaimed this statement.¹⁵ This may be due to the influence of heterogeneity in measurement instruments, time and execution areas (EQ-5D vs SF-8, 2015 vs 2016, South Africa vs Namibia respectively).

On the other hand, we still encountered some limitations while conducting this review. Firstly, our theme is the QOL of MDR-TB and XDR-TB patients, however, most of the studies only researched MDR-TB patients. In particular, we only have one study about the QOL of one XDR-TB patient,¹⁶ which makes it difficult to provide a proper overview and represent the QOL for international XDR-TB patients. Secondly, many different measurement instruments were used among the reviewed articles, so there was a high level of heterogeneity when pooling the

results. We did not possess guidelines for assessing these scores equivalently, which caused summarisation and comparison difficulties. Based on this review, greater attention is recommended for the QOL of MDR-TB and XDR-TB patients. There is also a need for a specific tuberculosis HRQOL tool to standardise finding interpretation.

Conclusion

In conclusion, this review provides an overview for HRQOL of MDR-TB and XDR-TB patients. Those patients had lower QOL compared to other types of tuberculosis patients. Despite the positive impact of MDR-TB treatment on patients, their physical and mental health remain compromised at the end of treatment. Social functioning, economic and financial challenges also considerably affect their QOL. Further, there is a lack of research that focuses on assessing the HRQOL of MDR-TB patients and XDR-TB patients in particular. The limited number of published studies on this vital topic emphasises a need for greater investment in research concentrating on HRQOL for those patients. Only with such study can health-care professionals and management provide timely, applicable, reliable, and relevant interventions to improve the overall QOL of those patients.

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