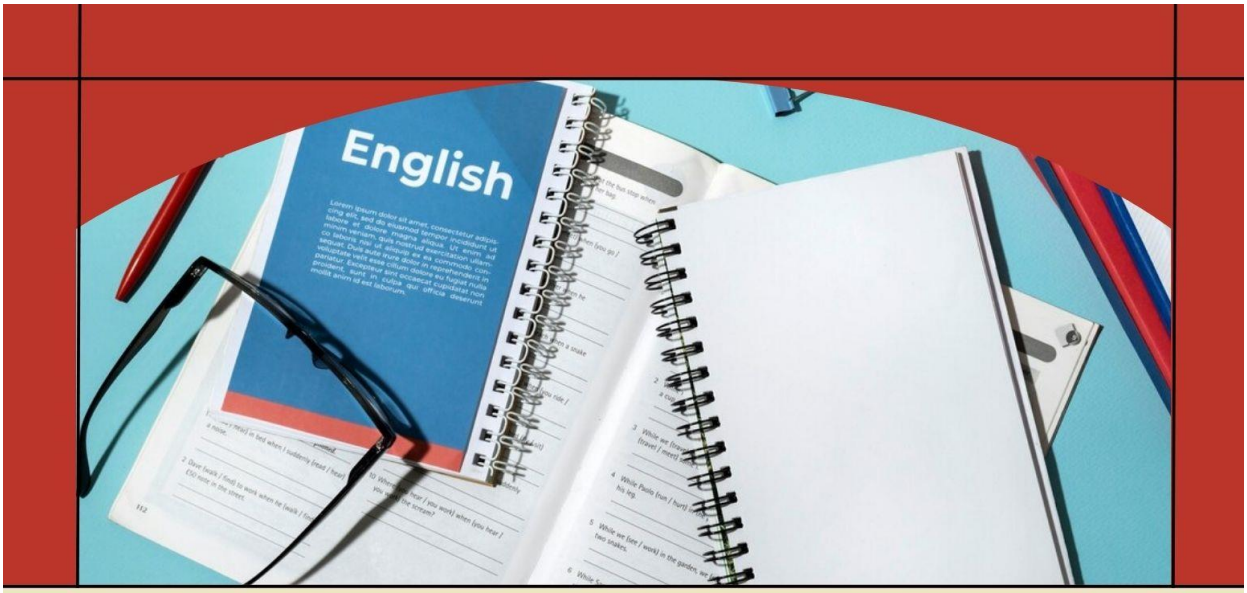

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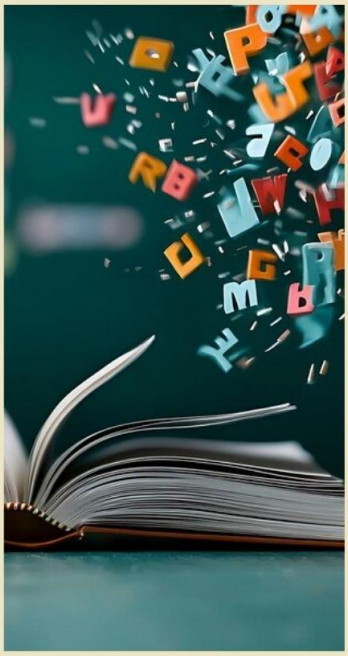

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Qualityoflifeintuberculosis:AreviewoftheEnglishlanguageliterature

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Abstract

Introduction:Clinical outcomes have been the primary focus of tuberculosis (TB) research, with very few studies looking at how the disease affects patients' QOL. Methods: This is a comprehensive literature review that uses the following MESH terms: [TB] and 1–[Outcome], 2–[Outcome Assessment], 3–[Quality of Life], 4–[Mood Disorder], 5–[Cost and Cost Analysis], 6–[Religion], 7–[Perception], 8–[Social Support], 9–[Optimism], 10–[Stress], 11–[Signs and Symptoms], and 12–[Cost of Illness]. The process produced 1972 articles, out of which 60 were assessed and considered for inclusion. The implications on physical functioning and overall health perceptions have not been investigated, while tuberculosis somatic symptoms have been extensively researched. It is unclear how patients' mental well-being improves as a result of therapy, however patients often experience anxiety, frustration, or disappointment upon receiving a diagnosis. People who have a diagnosis have a harder time finding a job and are less capable of working while still taking care of their family. Among the impoverished, tuberculosis places the most financial strain. It is unclear how widespread tuberculosis (TB) stigma is in industrialised nations, but in poorer nations, both patients and their families face social exclusion. To sum up, studies examining TB quality of life have been few overall, and especially fewer in industrialised nations. Patients' ability to function and overall health, as well as their adherence to therapy, may all benefit from a deeper comprehension of tuberculosis (TB) treatment protocols.

Keywords:Qualityoflife,socialfunctioning,stigma,tuberculosis

Introduction

Tuberculosis (TB) is one of the greatest causes of mortality and morbidity around the world infecting approximately 8 billion people with a death rate of 1.7 million in the year 2000 [1]. In the US, despite available therapy, there continues to be a high prevalence of TB in certain populations, including foreign-born and HIV positive individuals [2]. In general, studies of TB have focused on outcomes such as mortality and biologic markersof cure. However, there has been increasing interest in the patient's perspective of disease, health,andmedicalcare;andqualityoflife(QOL) is recognized as a key outcome. It is recognized that chronic and subacute illnesses and their treatments alter peoples' perceptions of theirhealth and well-being, and that the social and emotionalburdenofdiseasecanequalandeven

exceedthephysicalimpactofillness[3].Although TB is considered to be an acute illness, therapy maytakeupto9–12 monthsandisassociatedwith multiple side effects [4]. Clinically, the burden of TB extends beyond its acute presentation. However, there has been little attention given to the burden of the illness and treatment or to quality of life (QOL) of people with TB. To better understand QOL in TB patients, we conducted a systematic review of published medical literature.

Methods

Searchstrategy

We conducted a systematic primary search of the literature resulting in a narrative literature review. UsingthePUBMEDdatabasefor1968–2000,we

employed the following MeSH terms: [Tuberculosis]and1–[Outcome],2–[OutcomeAssessment],3–[QualityofLife],4–[MoodDisorder], 5–[CostandCostAnalysis],6–[Religion],7– [Perception],8–[SocialSupport],9–[Optimism], 10–[Stress],11–[SignsandSymptoms],and12– [Cost of Illness]. A secondary search involved scanning the reference lists of articles identified from the primary search. Both searches were limitedtoarticlesinEnglishandadulthumansubjects (18 years or older).

Systematicreviewprocess

First, all article titles were examined by two researchers (BC and GBD) to see whether they were relevant to patient-reported quality of life in tuberculosis. Patient-reported physical and mental health, ability to carry out social and assigned responsibilities, and self-assessed health were the determinants of quality of life. We obtained and read abstracts of articles whose titles were deemed possibly relevant by at least one of the two investigators. Using the following criteria for exclusion, at least two researchers reviewed the abstracts: (1) research pertaining to diagnostic tests or aids, (2) studies without patient-reported outcomes or quality of life indicators, (3) studies including therapy or intervention, and (4) studies not primarily focused on tuberculosis. publications about medication or treatment side effects that omitted QOL, (5) broad reviews that failed to investigate QOL, (6) case reports, case series, literature reviews, or letters that failed to address QOL explicitly, and (7) publications concerning general reviews that failed to investigate QOL. Any quality of life (QOL) measure that needed to be gathered by patient interview, such as symptoms, emotional state, or sensations, was considered a patient-reported outcome. At least one reviewer was tasked with reading the paper and abstracting the quality of life data if both reviewers reached an agreement over inclusion status. It was customary to appoint a third reviewer to decide cases of abstract dispute. Somatic symptoms, physical functioning, psychological health, emotional functioning, role function, general health perceptions, and social functioning were the original categories into which the abstracts that were considered were categorised according to quality of life [5]. Reviewers of the abstracts were not informed of the feedback provided by the other reviewers. Of the articles that were included, 3/4 were reviewed by two-authors and the remaining 1/4 by one author (BC). Findings from the articles were categorized into the above stated QOL domains. It was anticipated that TB would have disease-specificdomains,whicheresubsequently added to categorize articles as noted in the Results Section.

Results

From the primary literature search, 1972 articles were identified initially (Figure 1 describes the review process); after the review of titles, 396 abstracts were examined by at least tworeviewers. A total of 102 abstracts were identified as potentially relevant; 22 could not be obtained locally or by inter-library loan. Thirty-nine articles were includedinthereview.Inthesecondarysearchofthe reference lists from these articles, another 21 articles were identified. A total of 60 articles are reviewed in this paper. During the course ofliterature review, TB specific QOL domains of spiritual well-being, and financial well-being were identified and added to the generic domains noted above [5]. The following sections include results and relevant experts from the articles organized by domainsofQOL(Table 1forcitedarticles).When articles failed to clarify how data was obtained (physician elicited or spontaneously reported), all QOL relevant was included in our review; when obvious spontaneous patient reported data was preferentially cited.

Somaticsymptoms

Somatic symptoms are the patient's physical sensationsresultingfromillnessortreatment.Somatic symptoms were the most extensively studied QOL domain; however,ingeneral,itwasnotclearifthe symptoms described were reported spontaneously bypatientsorelicitedbyphysicians. The spectrum of TB symptoms is wide, ranging from no symptoms, to a fulminant process, to specific single organ complaints. The most commonly reported symptom was fever (60%). Cough presented commonly in sputum-positive cases with an abnormal chest radiograph (69%) with severity proportional to radiographic abnormality [6–7]. Symptomsweremorecommoninmenandmiddle

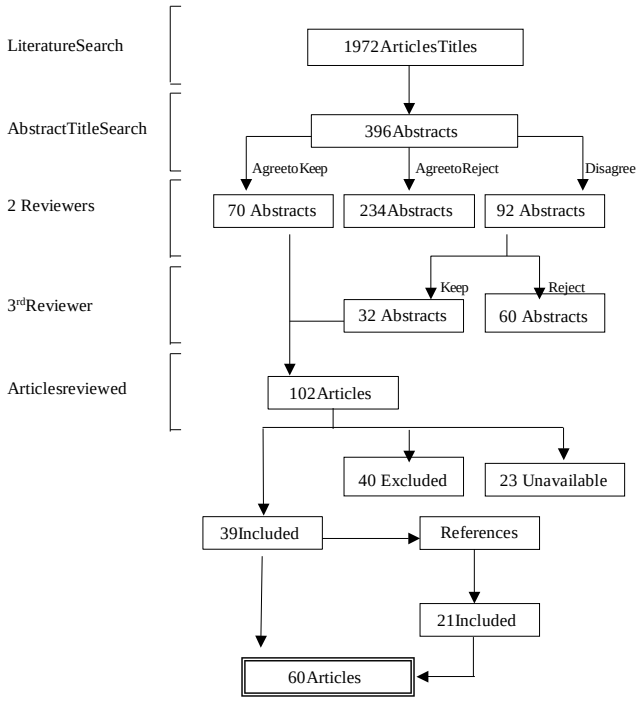

Figure1.ResultsofthescreeningprocesstoselectarticlesonQOLinTB.

aged individuals [6, 8]. With treatment, symptomatic improvement began in 2–3 weeks.

Physicalfunctioning

Physical functioning is the ability of the patient to perform basic activities of daily living. Our search only revealed that TB arthritis was associated with long-term disability [9]. No study specifically examined how symptoms or disease impacted the patient's physical functioning.

Psychologicalhealthandemotionalfunctioning

Psychological health includes aspects of the individual's mood and emotional well-being. Khan found that 72.2% of patients were worried, frustrated, or disappointed by the diagnosis, and27.8% did not initially accept their diagnosis, arisk factor for delay or refusal of therapy [10, 11]. Distress about spreading the disease to others and the economic impact of illness have been reported [12, 13]. We found no longitudinal studies of psychological health during and beyond completion of required therapy.

Rolefunction

Role functioning includes a person's ability to function in designated roles at work, society, and home [14]. The mean number of work days lost because of TB and its treatment ranged from 28 to 68 days, irrespective of occupation [13, 15, 16]. Patients expressed fear of informing their employers about their diagnosis because of potential jobs loss [17]. In Pakistan,although 83% of patients workedat the time of diagnosis, only 36% were still working by the time directly observed therapy (DOT) was initiated [10].

The diagnosis of TB in the family increased the workload on the family primary caregivers (wives and mothers), and diminished the caregiver's ability to generate income and care for the remainder of the family [18]. A few studies suggested TB's impact on QOL may be greater for women than men. Women were less able to perform household activities and care for their children; therefore, women did not seek medical care until their illness became very serious [13, 19]. In India, female patients, were rejected by their husbands andsentawayuntilcured[19]. Therearen o

Table1.Summaryofthepaperscitedincludingfirstauthor,countryofstudy,year(s)ofstudy,studydesign,QOLdomains,andkeyfindingsrelated toQOL Reference no. Author Country; Year

		Design sample #	Domains	Key findings
15	M.Aoki Japan;1980–1985	Surveystudy	SS, RF	1.54%ofconfirmedTBcasesthoughttheirsymptomswere'maybea cold'
6	D.Banerji India;1960–1961	Case–controlstudy	SS	1.Coughisthemostcommonsymptominsputumpositivecases
				2. Superficial probing of symptoms is insufficeint to explore the patient's awareness of symptoms
				3. Men and younger patients reported more symptoms Case–
23	F. Barnhoorn India; 1988–1989	control study	RF, SF, SWB, FWB	1. Treatment compliers report more symptoms
				2.Socialsupportcorrelatedwithtreatmentcompliance
				3.Satisfactionwithhealthcareprovidercontributedpositivelyto treatment compliance
		Caseseries	PF	1.17/30withTBofthekneehadsomemilddeformity
9	S.P.Chow P.R.China;1956–1980	Cross-sectionalstudy	GHP	1.Patientsidentifiedtheopportunitytoreceivegoodmedicalcareasthe
20	H.Davidson USA;1995			mostimportantaspectofDOT
				2.PatientsfeltincentivesimportantinDOT
				3. Half of patients surveyed reported being better offwith DOT thanself- supervised care
		Case–controlstudy	SS, PF	1.SymptomsaresimilarforHIVandnon-HIVpatients
8	P.Hongthiam-thong Thailand;1993			2. Symptomsweremorelikelytobereportedbymenandmiddleage individuals than the young or old
		Literaturereview	RF	1.WomenwithTBgenerallyfareworsethanmen
19	P. Hudelson Not applicable; Not applicable			2.Barrierstocarearegreaterandcomplianceislowerforwomen
				3.Fearandstigmahadagreaterimpactinwomenwithgreater repercussions for families and children.
		Focusgroup	PHEF,RF,SF,FWB	1.Insufficientknowledgeandfinanceswerethemajorobstaclesto complianceamongmen
22	E.Johansson Vietnam;1991–1993			2. Interaction with health staff and social stigma were the main obstacles among women
		Focusgroup	PH,EF,RF	1.Tuberculosisisa'dirty'diseaseaffectingpoorpeople
				2.TBsocialstigmaledtodelaysinseekingmedicalcare
17	E.Johansson Vietnam;1991–1993			3. Thepatient'seconomicsituationwasanimportantdeterminantof compliance
10	A.Kahn Pakistan;2000*	Open-endedinterviewse ries	PH,EF,RF,SF,SWB	1.Patientsweredissatisfiedwithhealthcareprovided
				2. BecauseofageneralbeliefthatTBisincurable,patients,fearing societal rejection, avoid treatment
18	P. KamolratanakulThailan d;1996–1997	Cross-sectional study	RF	1. Illness-related costs particularly affect patientswith incomes below the poverty line

				2. Outofpocketexpensesarefinancedfromhouseholdsavings,loans,sale of property
21	Kelly-RossiniUSA;1994	Interview	PH,EF,SF,FWB	1.Feelingsofisolation,abandonment,andboredomarecommon 2.Medicalstaffbehaviorsthatfosterhumanconnectionsmayenhancethe patient's QOL and promote treatment adherance
11	R.Liefooghe Pakistan;1995	Focus group	SS,PH,EF,RF, SF, SWB	1. TBisperceivedasaverydangerous,infectious,andincurabledisease 2. Socialstigmatizationandisolationleadstodiagnosisdenalandtreatment rejection 3. Socialconsequenceshaveagreaterimpactonwomen 4. PregnancyisacommonreasonforstoppingTBtreatment
12	J.I.Mata Honduras;1983	Focusgroupstudy	SS, PHEF,SF	1.MostpatientsfearthattheirfamiliesandfriendswillrejectthembecauseTBstigma 2. Individualsstoppedtreatmentprematurelybecauseofsymptomsimprovement
25	K.Ndeti EastAfrica;1969	Focus group; Patient interviews	SS, RF, SF, SWB, FWB	1. Traditional beliefs about TB still exist and modify the seeking of medical attention, compliance with TB therapy, and social stigmatization of TB patients 2. Financial limitation affects the ability to seek care; and the need towork may supercede the need for continued treatment
16	D.Pocock SouthAfrica;1995	Surveystudy	RF,FWB	1.Hospitalizationfortreatmentinitiationleadstofinancialdifficulties which must be weighed against need for supervised drug treatment
13	R.Rajeswari India;1999*	Focus group	PHEF, RF, SF, FWB	1. Rural and urban women face familial rejection 2. Theabilityofwomentocareforfamilyandchildrensignificantly decreases after a TB diagnosis 3. Eleven percent of children must discontinue school, and 8% took upemployment because of a TB diagnosis in the family
24	A.J. Rubel Worldwide;1992*	Literaturereview	SS,RF,SF,SWB	1.Socialstigmatizationexistsinmanycultures 2.Financialburdensofillnessmayleadtotreatmentbarriers
27	E.M. Thomson SouthAfrica;1986*	Cross-sectionalstudy	RF,FWB	1.Insufficientattentionisgiventothesocio-economicfactorsassociated withTB 2.Centralized health servicesdecreases health careaccess for patients
7	T.C.Y.Tsao PeoplesRep. China; 1989	Cohortstudy	SS	1.Feveristhemostcommonsymptom
26	T.S.vander WerfGhana;1985–1987	Cohortsurveystudy	SS,RF,FWB	1.Manypatientsseekreligionandtraditionalhealerswhendiagnosed withTB 2.Educationleveldidnotaffecttreatmentcompliance

SS – Somatic symptoms; PF – physical functioning; PHEF – psychological health and emotional functioning; RF – role functioning; GHP – general health perceptions; SF – social functioning; SWB – spiritual well-being, and FWB – financial well-being.
*Nodateofstudyinarticle;therefore,dateofpublicationontable.

studies of whether role functioning at home and in society return to baseline after treatment and clinical improvement.

Generalhealthperceptions

General health perceptions includes perceptions of current and future health, health relative to others, and satisfaction with one's health [14]. There have been no studies of the general health perceptions outside the perception of DOT. Patients enrolledin a DOT program reported treatment incentives (e.g. transporation tokens and food vouchers) improved the acceptability of TB diagnosis, treatment satisfaction, and overall QOL [20].

Socialfunctioning

Social functioning includes the patient's interaction with those individuals around them at home, work, and society [14]. In the hospital setting, some patients found respiratory isolation peaceful, but many felt lonely, confined, and abandoned [21]. A focus group study found patients who felt well received by the health facility were more adherent with therapy [22]. Unfriendly health care workers made some patients feel 'threatened, uncomfortable, unwelcome, and unwilling' to return [23].

Prior to discharge from the hospital, 15% of patients in Mexico City believed that they would be rejected by their families; on discharge, 52% were not received back into their homes [24]. In a Vietnamese study, discrimination against TB patients led to non-adherence with therapy [22]. In PakistanpatientsgavefalseaddressestoTBclinics fearing identification that would lead to stigmatizationofthewholefamily[10,11].ATBdiagnosis made sons and especially daughters undesirable as spouses, husbands and wives divorced, or husbands took second wives. The extent of social stigma in the developed world has received little formal study.

Spiritualwell-being

Spiritual well-being includes the connection one feels with a deity, nature, or others; it may or may not be related to the individual's religion [14]. In manycultures,itisbelievedthatTBisGod-given for 'sins' as a 'punishment'; many asked 'God for forgiveness' to attain a cure [10, 11]. The Zulu culture, the TB patient is considered a witch with the power to spread disease; since witchcraft passes through familial lines, all family members are implicated [24, 25]. Patients, who believed that witchcraft caused TB, were more likely to pray to God for a cure, and significantly less likely to adhere with TB therapy [23]. In many cultures, it is difficult to separate spirituality, culture, and religion; a patient's acceptance of their disease may stemfromculturalacceptabilityofthedisease.We found no studies that examined the impact of TB on spiritual well-being itself or belief in God.

Financialwell-being

When people are sick, it may have a significant impact on their family's financial stability, which is typically related to how effectively they are able to carry out their job responsibilities. Even though tuberculosis treatment is often covered by the government, patients and their families still had to pay for things like missed wages and transportation to medical appointments [22]. Due to financial concerns, patients may have to decide whether to return to work or discontinue treatment, which may contribute to non-adherence [23]. Because to tuberculosis, a large percentage of patients (31-50%) face financial hardships. 16 and 26. Eighty percent of families had financial hardships when the tuberculosis patient was the main earner. Among Thai patients, 14.4% to 21.9% used savings, 17.3% to 22.9% borrowed from relatives, 7.4% to 15.9% sold family assets, and 8.8% to 11.8% took out loans from banks [18]. Due to the high expense of tuberculosis treatment, low-income patients often appear at a later stage of the illness, when a cure is both more expensive and less certain. A third of Indian patients said they couldn't afford to provide their kids with enough to eat, clothes, or school supplies [13]. Because their parents were sick with tuberculosis, 11% of the children affected stopped going to school and 8% got jobs.

Discussion

It is evident from this review that TB can affect QOL both directly andindirectly. Surprisingly, we foundnostudiesthathadutilizedstandardized

generic or disease-specific QOL instruments in patients with TB. Moreover, there are many gapsin our knowledge base both with regard to theQOL of TB patients, and how QOL changes with treatment and cure. Physical symptoms have been well-described, both prior to diagnosis and overthe course of treatment. The pill burden for stan- dard therapy averages 9 pills/day and higher for drug resistant TB. Side effects increase with num- ber of medications and concomitant illnesses such as Hepatitis B and C and HIV [27–29]. TB medications have multiple drug–drug interactions furthercomplicating thetreatment [30].Despiteallof this, no study describes the impact of TB symptoms, diagnosis, or treatment on functional status or on general health perceptions.

PsychologicaldistressiscommoninTBandcan decrease treatment adherence, but there are no studies of the long-term psychological effects of TB and/or TB treatment [11].Given theprolonged treatment course, treatment side effects, and the stigma attached to the diagnosis, one might expect psychological impact to extend well beyond the acute illness. Although a few studies have examined patients' perceptions of directly observed therapy (DOT), there are none on how DOT affects QOL [21, 30].

TBaffectstheabilitytoworkbothduringillness and after treatment [13, 16, 31]. In addition, the presence of the sick individual alters the family functioning and can affect the entire family [13, 18]. We found that because of the need to suspend education, uninfected children may suffer lifelong effects of a family member's TB infection. The social stigmatization of TB leads to isolation by community, friends, and family, denial of the diagnosis, and rejection of treatment [22]. It is unclear the extent stigma affects patient outcomes, and there is little data on the impact of stigma in industrialized countries.

Our study had some limitations. First, we restricted our review to the English language literature. Thus, we failed to capture information from non-English language journals. As TB is more prevalent in developing countries, it is possiblethat we may have missed part of the literature on QOL and TB. Weighing against this is that the large majority of QOL research has been con- ducted in English and Western European languages.Second,weutilizedreviewoftitlesand abstracts to findrelevant articles.It ispossible that we missed papers in which QOL comprised a minor portion of the results. Since most of the studies found in the search were conducted in developing countries, the results may be less generalizable, but our search revealed little literature from the industrialized regions. Because 1/4 of the articles reviewed were reviewed by only one author, there may be a bias introduced lack of a second reviewer.

There are many unanswered questions. Is the social isolation world-wide? Do DOT incentives decrease the financial impact of TB? How does QOL at diagnosis affect medication adherence? Does QOL improve with treatment? Do shorter treatmentregimensimproveQOLfaster?Istherea difference in QOL for individuals with multi-drug resistant TB? Are there any positive effects of TB diagnosis?

More specifically, women and children of patientswithTBneedtobestudiedgivenpreliminary resultsthatwomenaremoresignificantlyimpacted than men and that children may suffer secondarily [13, 18, 19]. Long term follow up of patients on standard therapy may provide insight into whether QOL plays a role in the development of resistant disease. While DOT is standard of care in many countries, it is not used in many others because of lack ofaccess tomedical care, insufficient medical staff, and insufficient infrastructure [30]. Therefore, TB therapy still relies to some extent on patient centered issues, hence the importance ofQOL.

Relatively little is known about the relationship between QOL and adherence in chronic disease in general, and nearly nothing is known in TB. Similar to other illnesses, it is probable that adherence will be affected by the combination of adverse effects of disease and treatment, aswell as the beneficial effects of treatment. Patients and providers could benefit from learning about the expected effects and course of both disease and treatment in terms of impact on their QOL. This could help set expectations, and direct interventions to improve both adherence and patient functioning and well-being.

What advice can we provide to investigators interestedinincludingqualityoflifeinstrumentsin their research? Until disease-specific instruments areavailable,itwouldseemreasonabletouse

generic QOL instruments or batteries of available instruments. Our review suggests that in additionto generic aspects of health-related quality of life, the domains of financial and spiritual well-being are likely to be important, particularly in resource limited settings.

To date, clinical studies of TB have addressed mycobacteriologic cure, and rather than amelioration of the patient's illness which encompasses more than physical signs and symptoms; psychological distress, alteration in role function, economic status deterioration, changes in spirituality and perceptions of the world surrounding the personwithTB alsorequireinvestigation.Abetter understanding of the QOL impact of treatments may lead to more pallatable therapies, better treatment adherence, and better patient and public health outcomes.

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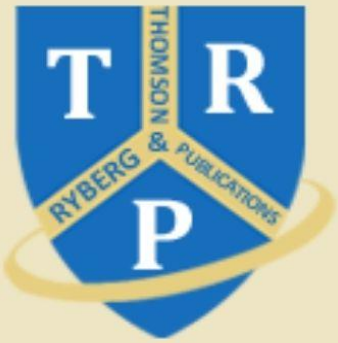

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