#### Saudi Journal of Medicine

Abbreviated Key Title: Saudi J Med ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online) Scholars Middle East Publishers, Dubai, United Arab Emirates Journal homepage: https://saudijournals.com

# Original Research Article

# Assessment of Health-Related Quality of Life in Tuberculosis Treatment Centers in a Local Government Area in Southern Nigeria

Worgu Glory Ovunda<sup>1\*</sup>, Onotai Lucky Obukowho<sup>2</sup>, Asuquo Eme Olukemi<sup>3</sup>

<sup>1</sup>MBBS, MSc Public Health, FWACP, Department of Community Medicine, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria

<sup>2</sup>MBBS, MSc, FWACS, FICS, FACS, Department of Ear Nose and Throat Surgery, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria

<sup>3</sup>BSc, MSc, MPH, DHSM, Department Preventive and Social Medicine, University of Port Harcourt, Rivers State, Nigeria

**DOI:** 10.36348/sjm.2022.v07i09.010 | **Received:** 17.08.2022 | **Accepted:** 20.09.2022 | **Published:** 30.09.2022

\*Corresponding Author: Worgu Glory Ovunda

MBBS, MSc Public Health, FWACP, Department of Community Medicine, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria

# **Abstract**

Background: Studies from Rivers State have demonstrated high burden of drug resistance among pulmonary tuberculosis (PTB) patients and declining cure rate despite adequate treatment retention and highly effective directly observed treatment short-course. Aim: to explore the perception of clients on how PTB disease or its treatment affect their health (health-related quality of life), which could impact on TB treatment success rate among clients with PTB. Methods: A total of 225 adult clients with PTB were recruited by systematic random sampling method from each of the 8 randomly selected centers out of 40 active treatment centers in Obio/Akpor LGA of Rivers State. The SF 36 was used to collect responses which were grouped into 8 domains yielding 2 summary measures. Scores ≤49 were classified as poor, 50-74 relatively favourable and good for scores ≥75. Categorical data were presented as frequencies and proportions using tables and pie charts while quantitative data were presented as means and standard deviations. Results: Specific domains mean scores ranged from 34.9±33.7 (role physical) to 61.8±11.9 (general health) while physical component summary (PCS) and mental component summary (MCS) recorded 53.35±16.79 and 51.11±12.26 respectively. The overall HRQoL mean score for the study was 55.2 (± 3.6) with an undesirable score of 20.7%. Conclusion: Pulmonary tuberculosis patients in treatment centers in Obio / Akpor LGA had poor to relatively favourable HRQoL mean scores. Strengthening counselling practice may help improve support for the clients in coping with the disease and the effect of its treatment.

Keywords: Health-related Quality of life, pulmonary tuberculosis, treatment centers, DOTS, Nigeria.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

# Introduction

In the fight against tuberculosis, most attention has been paid to the clinical outcome of tuberculosis treatment and the achievement of a microbial cure, neglecting the patient-reported perception of health (or health-related quality of life) which has a significant impact on clinical treatment outcomes (Malik *et al.*, 2018). Treatment decisions based solely on the clinical expertise of the provider and best clinical evidence excluding the clients' perception of how the disease or its treatment affect their health (Prasad, 2013) may account for the declining cure rate in the face of the high-case holding (Nwidu *et al.*, 2015) and the efficacy of the directly observed treatment short-course (DOTS) (Dim & Dim, 2013) amongst others. Meanwhile, patient

preferences relate not only to their physical health (in terms of clinical outcomes) but also to their social and mental health (Sherbourne *et al.*, 1999); and their perception of how the disease or its treatment affects their health. Health-related quality of life (HRQoL) has been defined as "a subjective perception, influenced by current health status, of the ability to perform those activities that are important to individuals" (Naughton MJ *et al.*, 1996).

Poor HRQoL scores are found more with pulmonary tuberculosis (PTB) patients than the general population.(Salehitali *et al.*, 2019; Daniels *et al.*, 2019) Studies such as those conducted by Chikaodinaka, *et al.*, in TB patients have reported HRQoL levels as low

as 43.18, where 75 is the normative value (Chikaodinaka, 2018) while some other study in Nigeria have documented undesirable HRQoL scores among pulmonary tuberculosis patients specifically (Sule *et al.*, 2014) which are even more depressed at baseline before commencement of treatment (Chikaodinaka, 2018).

With data demonstrating high burden of drug resistant TB (Otokunefor *et al.*, 2018) and declining TB cure rate in Rivers State despite adequate treatment retention (Nwidu *et al.*, 2015) and highly effective directly observed treatment short-course (DOTS) (Dim & Dim, 2013) it has become imperative to explore the perception of the clients on how pulmonary TB disease or its treatment affect their health (i.e., health-related quality of life), which could impact on TB treatment success rate among clients with pulmonary TB in treatment centers in Obio/Akpor LGA of Rivers State, South-South Nigeria.

# **MATEIALS AND METHODS**

# **Study Design**

A descriptive cross-sectional study design was used to study patients in tuberculosis treatment centers in Obio/Akpor LGA, Rivers State Nigeria.

## **Study Setting**

This study was carried out in selected tuberculosis treatment centers in Obio/Akpor LGA of Rivers State, South- South geopolitical zone of Nigeria. There are 57 tuberculosis treatment centers spread across the public and private health facilities in the LGA. Fifteen of these are in model primary healthcare centers (MPHC), three in medical centers, one in a tertiary hospital and 40 in private health facilities. However, only about 40 centers are actively reporting with private health facilities contributing to the bulk of inactive centers. Therefore, only facilities actively reporting were studied.

# Sample Size

Using Fisher's sample size formula for descriptive study (Fisher *et al.*, 1991), a minimum sample size of 180 participants was derived for the study based on the proportion of pulmonary

tuberculosis patients with relatively desirable healthrelated quality of life (86.5%) derived from a previous study (Chikaodinaka *et al.*, 2018). Anticipating a high non- response, minimum sample size was adjusted by 20% to give a sample size of 225 participants.

# **Eligibility Criteria**

Included in the study were adults 18 years and above with confirmed pulmonary TB patients in intensive or continuation phases of treatment. Patients with other co-morbid conditions were excluded from the study.

#### **Sampling Technique**

A two-stage sampling technique was used to recruit participants from TB treatment centers in Obio/Akpor LGA. Based on record from the State TB Coordinator, a total of 1,016 drug-susceptible cases were on management at the different centers in Obio/Akpor LGA in the first quarter of the previous year, giving an average of 25 cases per treatment center. Therefore, in the first stage, a total of 8 centers was selected by simple random sampling from the 40 active tuberculosis centers. Following proportional to size allocation, participants were selected by systematic simple random sampling from each of the selected centers as they come in for drug refill.

#### **Data Collection**

Data was collected using a self-administered semi-structured questionnaire. SF 36 was used to measure HRQoL (Ware & Gandek, 1998). The SF 36 is a standardized instrument designed to measure the effect of the disease on the multi-dimensional nature of health in a general sense and has been used extensively in most TB patient evaluations.

Two treatment centers not among those selected for the study were purposively selected for the pre-test. Purpose of the pre-test was to determine if the questions in the study are clear and easy to understand. A total of 23 patients (10% of sample size) were recruited and filled study tool. Following test and retest, some items in the study tool were modified (see Table 1 below).

**Table 1: Modification to Survey Tool** 

Item No	Original Item from SF-36	Modified Item Equivalent	
24	Moderate activities, such as moving a table,	Moderate activities, such as moving a table, pushing a	
	pushing a vacuum cleaner, bowling or playing	vacuum cleaner, mopping of floor or cleaning	
	golf	windows	
25	Lifting or carrying groceries	Lifting or carrying groceries or foodstuff	
43	Did you feel full of pep?	Did you feel full of energy?	
45	Have felt so down in the dumps that nothing	Have felt so depressed or sad that nothing could cheer	
	could cheer you up?	you up?	
48	Have you felt downhearted and blue?	Have you felt downhearted and moody?	

#### Variables

The HRQoL was measured using the selfadministered Short-Form 36 (SF 36) questionnaire designed by Ware & Gandek (1998). The SF 36 is a standardized instrument designed to measure the effect of the disease on all multi-dimensional health in a general sense and has been used extensively in most TB patient evaluations. The SF 36 instrument contains 36 questions which are grouped into 8 subscales or domains that are aggregated to yield 2 summary measures: mental component summary (MCS) and physical component summary (PCS). The domains of the PCS include physical functioning (10 questions), role-physical (4 question), bodily pains (2 questions) and general health (5 questions) while the MCS include vitality (4 question), social functioning (2 question), role-emotional (3 question) and mental health (5 question). The overall HRQoL score is then obtained from the mean of PCS and MCS scores.

Scoring the SF 36 ensures that all items are scored such that favourable health state has a higher score. Therefore, all items are on a 0-100 range with 0 representing the lowest score and 100 represent the highest possible scores achieved. Means of items on the same scale are taken together to create the 8 domain scores. Scores  $\leq$ 49 were classified as poor (undesirable), 50-74 fair (relatively favourable) and good (desirable) for scores  $\geq$ 75 (Salehitali *et al.*, 2019).

#### **Data Analysis**

Data from the questionnaires were extracted, coded and entered into Microsoft Excel ® 1997-2003 Version and imported into International Business Machines (IBM) Statistical Package and Service Solution (SPSS), Version 25 for analysis. Categorical data were presented as frequencies and proportions in tables and pie charts while quantitative data were presented as mean and standard deviations.

#### **Ethical Clearance**

Ethical approval to conduct this study was obtained from the University of Port Harcourt's Ethical Committees while the Rivers State Ministry of Health (RSMOH) gave permission for this study. Respondents received information about the study and only those who provided written consent were allowed into the study.

## **RESULTS**

A total of 208 (92.4%) of administered questions were properly completed, of which 128 (61.5%) were from 5 model primary healthcare centers, 46 (22.1%) from 1 tertiary hospital, 30 (14.4%) from 1 medical center while 4 (1.9%) from 1 private health facilities.

The characteristics of the respondents are shown in Table 2 below.

**Table 2: Characteristics of respondents** 

Variable	Category	Frequency (n=208)	Percent
Age	18-27	56	26.9
	28-37	65	31.3
	38-47	55	26.4
	48-57	15	7.2
	58 and Above	17	8.2
Sex	Male	107	51.4
	Female	101	48.6
Marital Status	Single	94	45.2
	Married	98	47.1
	Widowed	11	5.3
	Separated/Divorced	5	2.4
<b>Educational Level Completed</b>	None	13	6.3
	Primary	25	12.0
	Secondary	101	48.5
	Tertiary	69	33.2
<b>Employment Status</b>	Employed	116	55.8
	Unemployed	92	44.2
Residence	Urban	123	59.1
	Rural	85	40.9
Phase of Treatment (n=208)	≤2 Months	116	55.8
	> 2 Months	92	44.2
Sputum Status (n=208)	Productive	168	80.8
	Unproductive	40	19.2
Result of Sputum Test (n=168)	Positive	149	88.7
	Negative	19	11.3

The mean age of respondents was 36.3 (SD 9.4) years, gross majority of the respondents (65,

31.3%) were in the age group 28-37 years, males constituted more than half (107, 51.4%) of respondents

while majority (98, 47.1%) of respondents were married. Respondents who have tertiary education (69, 33%) constituted the second largest group following those with secondary education. Gross majority (116, 55.8%) of respondents were in a current employment and reside in the urban area (123, 59.1%). Respondents

in intensive phase (2 months or less) of treatment contributed 116 (55.8%) of the study population with vast majority of respondents (168, 80.8%) having productive cough at diagnosis while 71.6% of the respondents were bacteriologically diagnose.

Table 3: HRQoL mean scores of respondents

HRQoL measure	Variable	Mean	Standard Deviation
Specific HRQoL Domains	General Health	61.8	11.9
	Pains	59.6	18.6
	Physical Functioning	57.1	22.6
	Social Functioning	56.7	13.9
	Vitality (Energy/Fatigue)	52.6	14.9
	Mental (Emotional)	54.3	12.7
	Role Emotional	40.9	38.4
	Role Physical	34.9	33.7
<b>Summary Measures</b>	Physical Component Summary	53.4	16.8
	Mental Component Summary	51.1	12.3
Overall HRQoL		55.2	3.6

The mean scores of the 8 specific HRQoL domains ranged from 34.9 to 61.8 with General Health domain having the highest mean score (61.7  $\pm$  11.9) while the lowest mean score (34.9  $\pm$  33.7) was recorded in the Role Physical domain. For the summary

measures, Physical Component Summary had a higher mean score (53.4  $\pm$  16.8) than Mental Component Summary (51.1  $\pm$  12.3). The overall HRQoL mean score for the study was 55.2 ( $\pm$  3.6) (see Table 3above).

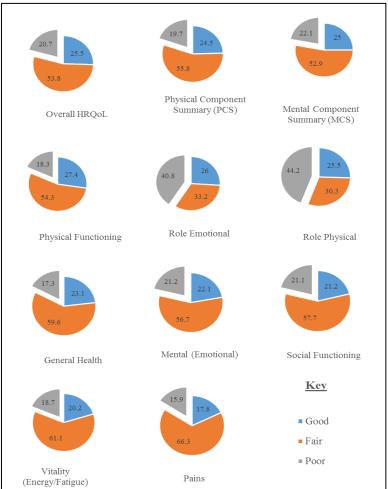


Fig. 1: HRQoL Outcomes of Respondents in Various Domains

Overall, 43 (20%) of respondents had poor or undesirable HRQoL scores. For the summary measures, more respondents had poorer HRQoL scores in the Mental Component Summary (46, 22.1%) compared to the Physical Component Summary (41, 19.7%). In the HRQoL specific domains, majority of respondents had poor or undesirable HRQoL scores in the Role Physical domain (92, 44.2%) and Role Emotional domain (85, 40.8%) (See Figure 1 above).

#### **DISCUSSION**

In developing an evidence-based approach to the management and evaluation of tuberculosis control programmes, HRQoL measures the third part in the evidence triad by adding the perspective of the patient (on how the disease affects them) to the mix of best clinical evidence and the experience of the clinician (Prasad, 2013; Sule *et al.*, 2014). This study found that clients with pulmonary tuberculosis receiving treatment from TB treatment centers in Obio/Akpor LGA of Rivers State, South-South Nigeria had poor to fair HRQoL mean scores across all domains, in component summary measures and in overall scores (Salehitali *et al.*, 2019).

In this study, the role physical domain was the most adversely affected, followed by the role emotional domain. The low score recorded in these two domains can be attributed to emotional and physical stress due to illness that may have affected respondents in carrying out various tasks. The score recorded in the role physical (worst affected) domain was attributed to physical stress as a result of the disease that may have affected the respondents in performing their daily life activities agrees with results of previous local studies (Sule et al., 2014; Chikaodinaka et al., 2018) but differed with the work done in India which recorded a score of 91.91 (SD 14.91), much higher score than the reference point (Salehitali et al., 2019) The difference in the result of the Indian study from this study may be attributed to the age of the study participants, whereas the Indian study had an older population (mean age 51±21.25 years) compared to this study which had a younger group (36.31±9.94 years). Younger persons who are in the active age group may have more demand on them by their work compared to older persons who may be retired and occupy less physically demanding physical roles. In this study, the second-worst affected domain was the role emotional, which is attributed to emotional stress as a result of the disease that may have affected the respondents in carrying out various tasks. This finding agrees with other studies (Atif et al., 2014; Salehitali et al., 2019) and explained by the mean age of respondents as younger people have the need to relate to others in their daily activities that may have been affected by the disease especially when they are actively coughing.

However, this study found the general health domain as the least affected and followed closely by the

body pain domain. The impact of tuberculosis on the level of current and future states of health relative to other people is assessed by the general health domain. This finding was not consistent with the results of a Malaysian study that also used the SF- 36 tool among 216 smear-positive PTB patients and recorded the general health domain as the second-worst affected after the role emotional domain (Atif et al., 2014). Unlike the Malaysian study which took the reading at the baseline before the commencement of therapy, this study measured HRQoL at least one month into the treatment and it is expected that because of relief from treatment, respondents had less severe problems and rated their overall health better and even expected improvement in their health. This finding agrees with other studies (Marra et al., 2008; Kruijshaar ME et al., 2010). This was followed closely by the body pains domain, which assessed how body pains as a result of the disease interfered with normal work and the degree of pain being experienced. This finding agrees with some previous local studies (Sule et al., 2014; Chikaodinaka et al., 2018). This also agrees with the works of Koohi et al., (2017) and Salehitali et al., (2019).

The study also found that the mental component summary (MCS) (which assesses mental health, role emotional, social functioning and vitality) faired worst compared to the physical component summary (PCS) (which assesses bodily pains, general health, physical functioning and role physical). This finding is not consistent with some other studies (Chamla, 2004; Chikaodinaka et al., 2018) but agrees with the findings of Sule et al., (2014) and Salehitali et al., (2019). Lower MCS scores found in this study shows that the respondents experienced more emotional problems resulting in psychological distress and role limitations compared to physical problems (Atif et al., 2014). This may be explained by the possible improvement of physical problems over the mental aspect by anti-TB medications.

The HRQoL scores recorded in this study for the overall HRQoL, component summaries and the domains were undesirable (poor) to relatively favourable (fair) though similar to other studies conducted in countries with poor socio- economic states (Sule *et al.*, 2014; Li *et al.*, 2017) and consistent with other studies on TB, which suggest that HRQoL scores in TB diseases are much lower than the general population (Balgude & Sontakke, 2012; Kastien-Hilka *et al.*, 2017; Salehitali *et al.*, 2019).

This study noted a lag in the mental component summary behind the physical component which obviously improved on treatment leaving the mental component summary behind. This demonstrates the need to provide support via counselling to the clients as treatment progresses to ameliorate emotional and physical role impairment. The process of contact

tracing affords the providers with ample opportunity for family counselling which will in turn strengthen the TB treatment support system. Provider training and retraining would also help providers support the clients with targeted counselling to address emotional and physical distress due to the disease and its treatment that hamper fulfilment of daily roles.

#### **CONCLUSION**

Clients with pulmonary tuberculosis receiving treatment from TB treatment centers in Obio/Akpor LGA of Rivers State, South-South Nigeria had poor to fair HRQoL mean scores across all domains, summary measures and overall scores. Mental component summary was more affected than the physical component summary. In improving the national TB Control Programme to check and reverse the current trend of drug-resistant tuberculosis and the declining TB cure rate, policymakers, programme managers and providers should factor in the impact of the disease on the various dimensions of the client's health and thus the need to train and retrain providers in counselling to strengthen system. Policymakers, program managers, and providers should consider the impact of the disease on the various dimensions of the client's health and the need to train and retrain providers in counselling to strengthen the system. This could help to reverse the current trend of drug resistance and declining TB cure rate among patients with pulmonary TB in treatment centers.

# **AUTHORS' CONTRIBUTIONS**

All authors were involved in conceptualization, planning and implementation of the study. Data collection team was led by WGO. All authors contributed to the interpretation of the results, read, and approved the final manuscript.

#### CONFLICT OF INTEREST

The authors declare that there was no conflict of interest at any stage of this study and have not received any type of funding or grant to conduct this study.

# **ACKNOWLEDGEMENT**

We are grateful to the staff and patients of the various tuberculosis treatment centers for their cooperation during the period of data collection for this study.

## **REFERENCES**

- Atif, M., Syed Sulaiman, S., Shafie, A., Asif, M., Sarfraz, M., Low, H., & Babar, Z.-U.-D. (2014). Impact of tuberculosis treatment on health-related quality of life of pulmonary tuberculosis patients: a follow-up study. *Health and Quality of Life Outcomes*, 12(1), 19. https://doi.org/10.1186/1477-7525-12-19
- Balgude, A., & Sontakke, S. (2012). Study of

- impact of antitubercular therapy on quality of life. *Indian Journal of Medical Sciences*, 66(3–4), 71-77. https://doi.org/10.4103/0019-5359.110911
- Chamla, D. (2004). The assessment of patients health-related quality of life during tuberculosis treatment in Wuhan, China. *The International Journal of Tuberculosis and Lung Disease*, 8(6).
- Chikaodinaka, A. A. (2018). Health-Related Quality of Life (HRQoL) scores vary with treatment and may identify potential defaulters during treatment of tuberculosis. *Malawi Medical Journal*, 30(4), 283. https://doi.org/10.4314/mmj.v30i4.12
- Daniels, K. J., Irusen, E., Pharaoh, H., & Hanekom, S. (2019). Post-tuberculosis health-related quality of life, lung function and exercise capacity in a cured pulmonary tuberculosis population in the Breede Valley District, South Africa. South African Journal of Physiotherapy, 75(1). https://doi.org/10.4102/sajp.v75i1.1319
- Dim, C., & Dim, N. (2013). Trends of tuberculosis prevalence and treatment outcome in an underresourced setting: The case of Enugu state, South East Nigeria. *Nigerian Medical Journal*, 54(6), 392. https://doi.org/10.4103/0300-1652.126292
- Fisher, A. A., Taing, J., Stoe\_El, J., & Townsend, J. (1991). *Handbook for Family Planning Operations Research Design SecondEdition*.
- Kastien-Hilka, T., Rosenkranz, B., Sinanovic, E., Bennett, B., & Schwenkglenks, M. (2017). Healthrelated quality of life in South African patients with pulmonary tuberculosis. *PLOS ONE*, 12(4), e0174605.
  - https://doi.org/10.1371/journal.pone.0174605
- Koohi, F., Nedjat, S., Yaseri, M., & Cheraghi, Z. (2017). Quality of Life among General Populations of Different Countries in the Past 10 Years, with a Focus on Human Development Index: A Systematic Review and Meta-analysis. *Iran J Public Health*, 46(1), 12–22.
- Kruijshaar ME, Lipman M, Essink-Bot ML, Lozewicz S, Creer D, Dart S, Maguire H, & Abubakar I. (2010). Health status of UK patients with active tuberculosis. *Int J Tuberc Lung Dis.*, 14(3), 296-302.
- Li, C.-T., Chu, K.-H., Reiher, B., Kienene, T., & Chien, L.-Y. (2017). Evaluation of health-related quality of life in patients with tuberculosis who completed treatment in Kiribati. *Journal of International Medical Research*, 45(2), 610-620. https://doi.org/10.1177/0300060517694491
- Malik, M., Nasir, R., & Hussain, A. (2018). Health Related Quality of Life among TB Patients: Question Mark on Performance of TB DOTS in Pakistan. *Journal of Tropical Medicine*, 2018, 1-7. https://doi.org/10.1155/2018/2538532
- Marra, C. A., Marra, F., Colley, L., Moadebi, S., Elwood, R. K., & Fitzgerald, J. M. (2008). Healthrelated quality of life trajectories among adults with

- tuberculosis: Differences between latent and active infection. *Chest*, 133(2), 396-403. https://doi.org/10.1378/chest.07-1494
- Naughton, M. J., Shumaker, S. A., Anderson, R. T.,
  & Czajkowski, S. M. (1996). Psychological Aspects of Health-Related Quality of Life Measurement: Tests and Scales. In: Quality of Life and Pharmacoeconomics in Clinical Trials. In Spilker B (Ed.), infona.pl. Lippincott-Raven.
- Nwidu, L. I., Blessing, O., & Abanee, P. S. K. (2015). The Prevalence of Tuberculosis and Leprosy in Primary Health Care Levels in Rivers State, Nigeria. *Biomedical and Pharmacology Journal*, 1(2), 265-274.
- Otokunefor, K., Otokunefor, T. V., & Omakwele, G. (2018). Multi-drug resistant Mycobacterium tuberculosis in Port Harcourt, Nigeria. African Journal of Laboratory Medicine, 7(2). https://doi.org/10.4102/ajlm.v7i2.805
- Prasad, K. (2013). Fundamentals of evidence based medicine. In *Fundamentals of Evidence Based Medicine*. Springer India. https://doi.org/10.1007/978-81-322-0831-0\_1

- Salehitali, S., Noorian, K., Hafizi, M., & Dehkordi, A. H. (2019). Quality of life and its effective factors in tuberculosis patients receiving directly observed treatment short-course (DOTS). *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, 15, 100093. https://doi.org/10.1016/j.jctube.2019.100093
- Sherbourne, C. D., Sturm, R., & Wells, K. B. (1999). What outcomes matter to patients? *Journal of General Internal Medicine*, 14(6), 357-363. https://doi.org/10.1046/j.1525-1497.1999.00354.x
- Sule, A., Odeigah, L., Alabi, K., Issa, B., Shittu, R., Joseph, A., Abiola, O., & Natie, B. (2014). Quality of Life of Patients with Tuberculosis in a Nigerian Teaching Hospital. *Turkish Journal of Family Medicine* & *Primary Care*, 8(2), 39. https://doi.org/10.5455/tjfmpc.46982
- Ware, J. E., & Gandek, B. (1998). Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *Journal of Clinical Epidemiology*, 51(11), 903-912. https://doi.org/10.1016/S0895-4356(98)00081-X