

Bicycles	48	48		1.39(0.80-2.43)	0.244
Motocycles	13	47		0.87(0.48-1.59)	0.651
vehicles	30	7		2.53(0.93-6.87)	0.068
Is distance a challenge					
Yes	97	64		3.67(2.44-6.00)	0.0001
No	38	92		ref	
Paid for Transport					
Yes	92	93		1.64(1.01-2.66)	0.045
No	41	68		ref	
Disclosure of patient TB status					
Yes	115	150		ref	
No	20	9		2.90(1.27-6.60)	0.011
Household support					
Yes	89(45.18%)	108(45.82%)		ref	
No	42(47.73%)	46(52.27%)		1.11(0.67-1.83)	0.69
Taking drugs or substances					
Yes	46	27		2.37(1.37-4.20)	0.002
No	89	124		ref	

Health care and system-related factors

As shown in table 3, univariate analysis showed that those who paid for the service charge (OR, 2.93; 95%CI 1.24-6.94) were more likely to default relative to those who did not pay. Relative to those who resided <1Km from health facility, those from 1-6 Km (OR, 3.10; 95%CI 1.63-5.93) and those from more than 6 Km (OR, 5.06; 95%CI 2.05-12.49) were more likely to default on treatment. Analysis also revealed health staff attitude was an import determinant of default with those who agreed that staff had negative attitude (OR, 4.42; 95%CI 2.07-9.42) were more likely to default relative to those who disagreed. Further analysis revealed that those who agreed that staff in health facility were not skilled (OR, 2.97; 95%CI 1.52-5.77), health facility not well equipped (OR, 2.76; 95%CI 1.36-5.59), lack patient Support Structure (OR, 3.05; 95%CI 1.62-5.75) and lack of patient recognition(OR, 13.36; 95%CI 4.47-39.98) were more likely to default from treatment.

Characteristics	Cases (n = 135)	Controls (n = 162)		OR	p - value
	N(%)	N(%)	Total n(%)		
Waiting time at the facility					
Less than 30min	56(30.4)	128(69.6)	184(62.0)	0.15(0.0754 - 0.2958)	0.000
30min-1hr	41(74.6)	14(25.4)	55(18.5)	ref	
More than 1hr	39(67.2)	19(32.8)	58(19.5)	0.70(0.3094 - 1.5879)	0.394
Schedule for TB treatment					
Once Every week	102(44.7)	126(55.3)	228(78.9)	0.69(0.3900 - 1.2112)	0.194
Once Every Two Weeks	33(54.1)	28(45.9)	61(21.1)	ref	
Treatment Return date					
After one week	59(36.2)	104(63.8)	163(59.9)	0.24(0.1310 - 0.4580)	0.000
After fortnight	44(69.8)	19(30.2)	63(23.2)	ref	
After one month	16(66.7)	8(33.3)	24(8.8)	0.86(0.3162 - 2.3591)	0.775
I don't know	9(40.9)	13(59.1)	22(8.1)	0.30(0.1093 - 0.8174)	0.019
Frequency of taking drugs					
Once	124(45.3)	150(54.7)	274(94.2)	0.58(0.2140 - 1.5647)	0.281
More than Once	10(58.8)	7(41.2)	17(5.8)	ref	
Defaulting consequences					
Cured	7(87.5)	1(12.5)	8(5.3)	ref	
Dead	17(65.4)	9(34.6)	26(17.3)	0.27(0.0286 - 2.5491)	0.253
Resistance	49(67.1)	24(32.9)	73(48.7)	0.29(0.0339 - 2.5075)	0.262
Transmission to others	12(80.0)	3(20.0)	15(10.0)	0.57(0.0494 - 6.6062)	0.654

Others	7(25.0)	21(75.0)	28(18.7)	0.05(0.0050 - 0.4578)	0.008
Paid service charge					
Yes	19(70.4)	8(29.6)	27(9.5)	2.93(1.2386 - 6.9432)	0.014
No	115(44.7)	142(55.3)	257(90.5)	ref	
Distance of health facility					
<1Km	15	47		ref	
1-6 Km	96	97		3.10(1.63-5.93)	0.001
>6 Km	21	13		5.06(2.05-12.49)	0.0001
Staff have negative attitude					
Disagree	99	141		ref	
agree	31	12		4.42(2.07-9.42)	0.0001
Don't know	5	5		1.14(0.30-4.35)	0.849
Staff not skilled					
Disagree	100	139		ref	
agree	32	15		2.97(1.52-5.77)	0.001
Don't know	3	4		1.04(0.29-4.76)	0.957
Health facility not well equipped					
Disagree		46	58	ref	
agree		35	16	2.76(1.36-5.59)	0.005
Don't know				6.30(0.71-55.86)	0.098
Lack Patient Support Structure					
Disagree		95	137		

agree	37	17	3.05(1.62-5.75)	0.001
Don't know	3	5	0.58(0.11-3.04)	0.516
Staff Lack patient recognition				
Disagree	65	139	ref	
agree	25	4	13.36(4.47-39.98)	0.0001
Don't know	5	5	2.14(0.60-7.65)	0.242

Discussion

This study was carried out to identify the reasons and determinants default in a region with high HIV prevalence of western Kenya. We found that there are multiplicity of reasons for defaulting including distance from health facility, relocation, stigma, side effects of the drugs, period of treatment, ignorance, health facility factors and drug shortage suggesting that there context-specific issues influencing the rate of default and the treatment phase. This findings are in agreement with previous studies from Kenya (Muture et al., 2011), suggesting that although the Kenya, the government supports treatment of tuberculosis by availing free diagnostic services, drugs and direct observed therapy, there is a need of community targeted interventions to address these issues to ensure up-scaling of uptake of TB treatment in poor resource settings.

Previous studies have shown that within the settings of the settings were directly observed therapy has been implemented; there are several factors that lead to default from TB treatment default (Hascker et al., 2008; Muture et al., 2011; Culqui et al., 2012; Lackey et al., 2015). Contrary to previous studies that indicated that TB treatment default is associated with male gender (Muture et al., 2011; Lackey et al., 2015; Kigonzi et al., 2017), we found that males were less likely to default from TB treatment. Although the reasons for difference between our findings and the previous studies are not clear, it has been shown that in areas with high HIV-TB co-infection, male gender is protective against death in TB patients (Kigonzi et al., 2017). This has been attributed to gender-based barriers including financial dependence, lower general literacy and household stigma (Krishnan et al., 2014). In line with research conducted in Morocco and Northwest Ethiopia (Tessema et al., 2009; Cherkaoui et al., 2014) it was observed that younger older cases (<24 years) were more likely to default treatment compared to their older counterparts (≥ 20 years) and this is probably due to the fact that older patients do not face barriers such as financial dependence and stigma that may led to default or that they had superior strategies to help them cope with TB than their younger counterparts. Together, these data indicate that there is a need of programmatic intervention that target younger patients. Furthermore transport cost associated weekly collection of drugs from health facility can lead to

TB cases defaulting especially in households with limited resources (Muture et al., 2014). In line with this previous observation, our study reveals that TB patients who indicated that transport is a challenge or paid for transport were more likely default from TB treatment, indicating that there is need of programs that address issues of resources for transport and other opportunity costs to make the drugs easily available to TB patients. In poor resource settings such as our study area, patients have to choose between competing priorities like buying food for family members and paying for transport to get medication. It significant to note that our data also revealed that TB cases from households with ≤ 3 people were less likely to default compared to those with >4 people further suggesting that financial and opportunity cost are a major challenge to TB treatment and needs to be addressed in order to reduce the rate of default to TB treatment.

This study showed that TB patients who had not disclosed their status were more likely to default from TB treatment. This can be attributed to the fact that in African societies TB patients are stigmatized due cultural factor associated with misinformation about the medical aspects of the disease and misinformation that TB is related to HIV (Muture et al., 2011; Kigonzi et al., 2017), this can influence patient health seeking behavior in terms of weekly collection of drugs since in areas with high HIV burden the patients are thought to be on antiretroviral drugs. This led the Kenyan Ministry of Health to integrate TB and HIV care where both the National tuberculosis control program (NTP) and the National AIDS and Sexually Transmitted Diseases (STD) Control Program (NASCOP) screen TB or HIV patients for both disease to enable early initiation to treatment and care (Lönnroth et al., 2010; Muture et al., 2011). Further our data reveal that TB cases that did not get household support were more likely to default and this can be attributed to household stigma (Krishnan et al., 2014). These data indicate that in order to reduce treatment default among TB patients there is need of advocacy programs against stigmatization directed at the community and at household levels to reduce stigma associated with TB. Several studies have shown that drug and alcohol use are associated with a higher risk of default (Culqui et al., 2011; Lackey et al., 2015; Kigonzi et al., 2017; Ramachandran et al., 2017). Consistent with these previous findings this study found that TB cases that were using drugs or substances were more likely to default. This is partly due to the fact that drug or substance use may lead to patients forgetting or failing to take drugs leading to default. More importantly, these drugs and substances can be cheaply obtained in poor resource setting and their combined effects with anti-tuberculosis drugs can liver damage (Muture et al., 2011). These exacerbated side effects can lead to TB treatment default. Of significance, behavior change intervention targeting reduction of patient alcohol has proven to be effective (Kaner et al., 2007).

With respect to health facility related factors associated with TB treatment default. our data indicates that waiting time at the facility before provision of services, patient knowledge about TB treatment schedule or return data and frequency of taking drugs, paying for service charges, distance to health facility, health provider negative attitude, lack of patient recognition, perception that staff are not well trained and the hospitals are not well equipped were important determinants of TB treatment default. This is in agreement with previous observation that Health system related factors such as service provider or patient attitudes, drug stock outs and access to health facility are important determinants of adherence or default to TB treatment (Daniel et al., 2006; Muture et al., 2011). Indeed it has been shown that health system barriers that impact on

TB treatment adherence including lack of adequate financing of health care programs and overstretched or overworked healthcare workers is a common phenomenon in poor resource countries like Kenya (Muture et al., 2011). However, these health facility factors can be mitigated through enhanced training of health care workers on communication and counseling, development of effective and patient centered materials that focus on adherence and self-monitoring, enhanced clinical follow up and surveillance of TB cases, provision of incentives like transport reimbursements, improved community participation in provision of based DOTS, integration of HIV and TB treatment and care, enhanced and efficient of TB programs and (adequate financial and human resources (Finlay et al., 2012). In addition, there is need to reduce waiting time, equip health facility and ensure that there are no drugs stock of TB drugs.

Conclusions

The main reasons for defaulting including distance from health facility, relocation, stigma, side effects of the drugs, period of treatment, ignorance, health facility factors and drug shortage suggesting that their context-specific issues influencing the rate of default and the treatment phase. In addition, being of younger age, taking substance or drugs, distance from the hospital, health workers attitude, lack of patient support structure was determinant of default.

References

- Allen S., (2006). *The Feasibility of Implementing brief Motivational Interviewing in the Context of Tuberculosis Treatment in South Africa* [Master's Thesis]. Stellenbosch (South Africa): University of Stellenbosch. pp 165.
- Barr R.G.; Diez-Roux, A.V.; Knirsch, C.A.; Pablos-Mendez, A. (2001). "Neighborhood Poverty and the Resurgence of Tuberculosis in New York City." *Am J Public Health* No. 91: pp1487–1493.
- (Muture, 2011)Carey, J.W. (2002). "Tuberculosis Beliefs among recent Vietnamese Refugees in New York State" *Public Health Reports*, Vol. 112, No.1: pp 66-72.
- Chakaya, J.M.; Kibuga, D.; Nganga, L.; Githui, W.A.; Mansoer, J.R.; Gakiria, G.; Kwamanga, D.; Maende, J. (2002). "Tuberculosis Re-Treatment Outcomes within Public Service in Nairobi, Kenya." *East African Medical Journal*, No. 79.
- Chang, K.C.; Leung, C.C.; Tam, C.M. (2004). "Risk Factors for Defaulting from Anti-Tuberculosis Treatment under Directly observed Treatment in Hong Kong." *International Journal Tubercle Lung Disease* No.8: pp1492–1498.

- Comolet, T.M.; Rakotomalala, R.; Rajaonarivoa, H. (1998). "Factors Determining Compliance with Tuberculosis Treatment in an Urban Environment, Tamatave, Madagascar:"*International J Tubercle Lung Disease*.
- De Vos, P.F. (2002). *Tuberculosis, Adherence Behavior the Inner City* [Master's Thesis]. Edmonton (Alberta): University of Alberta. pp 221.
- Demissie, M.; Getahun. H.; Lindtjorn, B. (2003). "Community Tuberculosis Care through "TB Clubs" in Rural North Ethiopia." *Social Science Medicine*, No.56: pp 2009-2018.
- Diaz de Quijano, E.; Brugal, M.T.; Pasarin, M.I.; Galdos-Tanguis, H.; Cayla, J.; Borrell, C. (2001). "Influence of Social Inequality, Social Unrest and Extreme Poverty on Tuberculosis Morbidity in the City of Barcelona." *Rev Esp Salud Publica*; No. 75: pp 517-527.
- Dick, J.; Schoeman, J.H.; Mohammed, A.; Lombard, C. (1996). "Tuberculosis in the Community: Evaluation of Volunteer Health Worker Program to Enhance Adherence to Anti Tuberculosis Treatment." *Tubercle & Lung Disease*, Vol. 77, No3: pp 274-279.
- Dye Christopher, Catherine J. Watt, & Daniel Bleed, (2002). "Low Access to a Highly Effective Therapy, A Challenge for International Tuberculosis Control". *International Journal of Tuberculosis and Lung Disease*, No.; 4: pp146-52.
- Edginton, M.E.; Sekatane, C.S.; Goldstein, S.J. (2002). *Patients' Beliefs: Do they affect Tuberculosis Control? A Study in a Rural District of South Africa*. *Int J Tuberc Lung Dis* 6: 1075-1082.
- Enos, M.; Sitienei, J.; Ongango, J.; Mungai, B.; Kamene, M.; Wambugu, J.; Kipruto, H.; Manduku, V.; Mburu, J.; Nyaboke, D.; Ngari, F.; Omesa, E.; Omale, N.; Mwirigi, N.; Okallo, G.; Njoroge, J.; Githiomi, M.; Mwangi, M.; Kiraithe, D.; Kiplimo, R.; Ndombi, A.; Odeny, L.; Mailu, E.; Kandie, T.; Maina, M.; Kasera, K.; Mulama, B.; Mugi, B. and Weyega, H. (2016). Kenya Tuberculosis Prevalence Survey 2016: Challenges and Opportunities of Ending TB in Kenya.
- Ellis, J.H.P.; Beyers, N.; Bester, D.; Gie, R.P.; Donald, P.R. (1997). "Sociological and Anthropological Factors related to the Community Management of Tuberculosis in the

- Western Cape Communities of Ravensmead and Uitsig”. *South Africa Med. Journal* No. 87: pp1047-1051.
- Fong, C. (2004). *Gender and Access to DOTS in a Poor Rural and Minority Area of Gansu Province, China* [PhD Dissertation]. Baltimore (MD): Johns Hopkins University. 138 p.
- George, L.J. (2003). *Compliance with Medication and Directly observed Therapy in the Treatment of TB in Lesotho* [PhD Dissertation]. Philadelphia (PA): Faculty of the School of Social Work, University of Pennsylvania. 300p.
- Gleissberg, V.G. (2001). *Patient Views on Tuberculosis: Is Compliance with Treatment the Key to Success or beside the point?* [MSC Thesis.] Uxbridge (United Kingdom): Department of Anthropology. Brunel University. 55 p.
- GoK (2009-2010). Siaya District Health Sector AOP, DMOH, Siaya.
- Gopi, P.G.; Vasantha, M.; Muniyandi, M.; Chandrasekaran ,V.; Balasubramanian, R. (2007). “Risk Factors for Non-Adherence to Directly observed Treatment (DOT) in a Rural Tuberculosis Unit, South India.” *India Journal Tububacle.*;Vol.54, No.2: pp 66–70.
- Greene, J.A. (2004). “*An Ethnography of Non-Adherence: Culture, Poverty, and Tuberculosis in Urban Bolivia.*” *Cult Med Psychiatry* No.28:pp 401-425.
- Hane, F.; Thiam, S.; Fall, A.S.; Vidal, L.; Diop, A.H. (2007). “ *Identifying Barriers to Effective Tuberculosis Control in Senegal; An Anthropological Approach.*” *Int J Tubercle Lung Disease.* Vol.11,No.5: pp 539–543.
- Harper, M.; Ahmadu, F.A.; Ogden, J.A.; McAdam, K.P.; Lienhardt, C. (2003). “*Identifying the Determinants of Tuberculosis Control in Resource-Poor Countries: Insights from a Qualitative Study in The Gambia.*” *Trans R Soc Trop Med Hyg*No.97:pp 506-510.
- Holmes, C.B.; Hausler, H.; Nunn, P. (1998). “A Review of Sex Differences in the Epidemiology of Tuberculosis”. *International Journal Tubercle LungDis.*No.2:pp96–104.
- Holtz, T.H.; Lancaster, J.; Laserson, K.F. (2006). “Risk Factors associated with Default from Multidrug-Resistant Tuberculosis Treatment, South Africa,” 1999-2001. *International Journal Tubercle Lung Dis.* No.10:pp649–655.

- Jaiswal, A.; Singh, V.; Ogden, J.A.; Porter, J.D.H.; Sharma, P.P. (2003). "Adherence to Tuberculosis Treatment: Lessons from the Urban setting of Delhi," *India. Trop Med Int Health*, No.8: pp 625-633.
- Johansson, E.; Long, N.H.; Diwan, V.K.; Winkvist, A. (1999). "Attitudes to Compliance with Tuberculosis Treatment among Women and Men in Vietnam." *International Journal Tubercle Lung Disease*, No.3, pp 862-868.
- Johansson, E.; Diwan, V. K.; Huong, N.D. & Ahlberg, B.M. (1999). "Staff and Patient Attitudes to TB and Compliance with Treatment: An Exploratory Study in a District in Vietnam." *International Journal Tubercle and Lung Disease*, No. 77, pp178-183.
- Joseph, H.A.; Shrestha-Kuwahara, R.; Lowry, D.; Lambert, L.A.; Panlilio, A.L. (2004). "Factors Influencing Health Care Workers' Adherence to Work Site Tuberculosis Screening and Policies." *Am J Infect Control*, No.32, pp 456-461.
- Kaona, F.A.; Tuba, M.; Siziya, S.; Sikaona, L. (2004). "An Assessment of Factors Contributing to Treatment Adherence and Knowledge of TB Transmission among Patients on TB Treatment." *BMC Public Health*, No. 4, pp 68.
- Khan, A.; Walley, J.; Newell, J.; Imdad, N. (2000). "Tuberculosis in Pakistan: Socio-Cultural Constraints and Opportunities in Treatment Pakistan." *Social Science and Medicine*, No.50, pp 247-254.
- Khan, M.A.; Walley, J.D.; Witter, S.N.; Shah, S.K.; Javeed, S. (2005). *Tuberculosis Patient Adherence to Direct Observation: Results of a Social Study in Pakistan. Health Policy Plan* No.20, pp 354-365.
- Khanna, B.K.; Srivastava, A.K.; Ali, M. (1977). "Drug Default in Tuberculosis India" *India Journal. Tubercule*, Vol.24, No.3, pp 121.
- Kolappan, C.; Subramani, R.; Karunakaran, K.; Narayanan, P.R., (2006). "Mortality of Tuberculosis Patients in Chennai, India." *Bull World Health Organ*, No.84 pp 555-60.
- Matebesi, Z. (2004). *Living with TB: The Career of the Tuberculosis Patient in the Free State, SA* [PhD Dissertation]. Bloemfontein (South Africa): Department of Sociology, University of the Free State. 216 p.

Mazonde, G.N. & Steen, T.W., Ngakayasetwana, NgakayaMazonde, G.N. & Steen, T.W. (2005). "Health seeking Behaviour in Bostwana with Pulmonary Tuberculosis" *Journal of Social Science and Medicine*. Vol. 48, No.2 pp163-172.

Messmer, P.R.; Jones, S.; Moore, J.; Tagart, B.; Parchment, Y.; Holloman, F. & Quintero, L. (1998). "Knowledge, Perceptions and Practice of Nurses towards HIV/AIDS Patients Diagnose with Tuberculosis." *Journal of Continuing Education in Nursing*, Vol. 29 No. 3 pp 117-25.

Mitnick, C.; Bayona, J.; Palacios, E, *et al.*, (2003). "Community-Based Therapy for Multidrug-Resistant Tuberculosis in Lima, Peru." *National Engl J Med*, No. 348, pp119–128.

MOH. NLTP Annual Report. 2007.

Molly, F.; Franke, Sasha, C.; Appleton, Jaime Bayona Fernando Arteaga; Eda Palacios, KarimLlaro Sonya, S; Shin, Mercedes ,C.; Becerra, Megan, B.; Murray and Carole, D. Mitnick. (2008). *Risk Factors and Mortality Associated with Default from Multidrug-Resistant Tuberculosis Treatment in Peru*.

Mweemba, P.; Haruzivishe, C.; Siziya, S.; Chipimo, P.J.; Cristenson, K.; Johansson, E. (2008). "Knowledge, Attitude and Compliance with Tuberculosis Treatment", Lusaka, Zambia" *Medical Journal of Zambia*, Vol. 35, No. 4 pp 2008.

NASCOP (2018). Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya.

Nair, D.; George, A.; Chacko, K. (1997). *New Insights from Poor Urban Patients Tuberculosis in Bombay*. *Health Policy Plan*, No.12, pp77-85.

Nyurebda, T.E.; Harries, A.D.; Gausi, F. (2003). "Decentralization of Tuberculosis Services in a Urban Setting, Lilongwe, Malawi." *International Journal Tubercle Lung Disease*, pp21–29.

Orem, D.E. (1990). *Nursing Concepts of Practice* (4th Ed.). St. Louis: Mosby Year Book.

Pablos- Mendez, A.; Knirsch, C.A.; Barr, R.G. Lerner, B.H.; Frienden, T.R.L. (1997). "Non-Adherence in Tuberculosis Treatment: Predictors and Consequences in New York City". *American Journal of Medicine*. No.10, pp164–170.

Public Health Report (1992). *Social and Cultural Factors in the Successful Control of Tuberculosis*.

Reyes-Guillén, I.; Sánchez-Pérez, H.J.; Cruz-Burguete, J.; Izaurieta-de Juan, M. (2008). "Anti-Tuberculosis Treatment Defaulting. An Analysis of Perceptions and Interactions in Chiapas, Mexico." *Salud Publica Mex* No.50 pp 251-257.

Declarations

Ethical Consideration

The study was approved by the ethical review board of University of East Africa Baraton (REC: UEAB/17/02/2016). All the study participants parents and legal guardians gave their written

Competing interest

The authors declare they have no competing interests.

Authors' contributions

KF, JOA and ASA conceived of the study and participated in its design; KF and AO carried out laboratory assays; ASA carried out statistical analysis. KF and AJO drafted the manuscript. All authors read and approved the final manuscript

Acknowledgements

We would like to thank the Health Department team of Rachuonyo North sub county for their technical support.

