#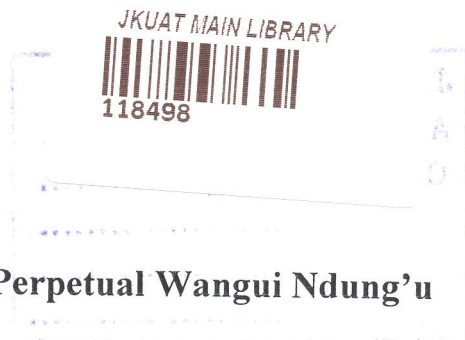 Recurrence of tuberculosis and its association with the emergence of multidrug resistant strains of Mycobacteria in Nairobi, Kenya 2010 to 2012

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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ABSTRACT

Tuberculosis (TB) is a major problem throughout the world posing enormous treatment challenges. Multidrug resistant (resistance to isoniazid and rifampicin) and extensively drug resistant (TB resistant to at least isoniazid and rifampicin as well as to floroquinolone and a second line injectable agent either kanamycin or amikacin or capreomycin) TB infections have greater mortality rate. Both types of resistance have been reported throughout the world including Kenya. There is limited information on the role played by recurrence, which is relapse of tuberculosis after completion of treatment, in occurrence of pulmonary tuberculosis. There is also limited information on risk factors associated with disease transmission and the different sub-types of *Mycobacterium tuberculosis* in circulation in the general population. Molecular typing allows a more rapid and precise species differentiation and is essential for investigating the spread of specific genotypes and any relationship with drug resistance. To study these factors and to understand the epidemiological features of recurrent TB, a cohort of 295 patients with pulmonary tuberculosis were recruited to the study at the start of treatment after giving informed consent. They were required to fill a structured questionnaire to determine known risk factors for transmission such as income, housing, level of education, employment, HIV status, smoking and alcohol consumption. They were followed for two years to detect recurrence. Sputa were collected and stained by Ziehl Nielsen method, then cultured in liquid and solid media and drug sensitivity tests done on grown cultures using first line drugs; isoniazid, streptomycin, rifampicin,

ethambutol and pyrazinamide. One hundred and thirty five isolates from individual patients were characterized by spoligotyping and MIRU-VNTR to determine their genetic diversity. There were 288 positive cultures from individual patients and eighty-six (30%) were resistant to at least one of five anti-tuberculosis drugs tested; 37 isolates (30.2%) were resistant to isoniazid; 15 (11.6%) to streptomycin; 13 (4.5%) to ethambutol; four (1.4%) to rifampin; and 30 (10.4%) to pyrazinamide. Four of the isolates (1.4%) had double resistance to isoniazid and pyrazinamide; four (1.4%) to streptomycin and isoniazid; and one (0.3%) to rifampin and streptomycin. Two isolates (0.7%) were multidrug resistant, and one was triple drug resistance. At least 77.7% of the patients who participated in the study were below the age of 40 years. One hundred and seventy one patients were tested for HIV and 26.9% were positive. There were significantly more males who were positive for TB than females ($\chi^2=0.963$; df=1; p<0.05). Monthly income was significant with 254 (86.1%) of the patients earning less than 100$ per month (p<0.05, 95% CI), while 198 (67.1%) were unemployed or were engaged in small businesses. Only 97 (32.9%) were in formal employment. There were 190(65%) patients living in single rooms with 110 (42.6%) living with more than two people in the room with a maximum of 10 people. Only 73 (28.3%) were living alone in a single room and only 8 families (2.7%) were living in houses with five or more rooms. Alcohol consumers and smokers were 117(39.7%) and 106 (36%) respectively. Half the patients 137 (46.4%) had not completed secondary education and only 18(6.4%) had