S4 Table. Risk factors for acquired drug resistance examined

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| Randomised controlled trials |
| Reference | Potential risk factors for acquired drug resistance analysed |
| Algerian Working Group/British MRC 1991 Tubercle [16] | Rifampicin in regimen only during intensive phase \* |
| Baseline resistance to INH and STREP \* |
| Hong Kong TB Research Centre Madras/BMRC Am Rev Resp Disease 1991 [12] |  6 vs 8 months treatment including RHSZ throughout \* |
| Baseline drug resistance \* |
| Lienhardt JAMA 2011 [17] | Fixed dose combination in IP vs separate drug formulation \* |
| Swaminathan AJRCCM 2010 [10] | Baseline median CD4 count |
|  Baseline median HIV viral load |
| Nonadherence  |
| Baseline isoniazid resistance |
| 4 vs 7 month continuation phase |
| Baseline weight |
| Baseline Haemoglobin |
| Sputum smear grade  |
| TB Research Centre IJTLD 1997 [18] | Ethambutol in a twice weekly regimen \* |
| Frequency of dosing (twiceweekly or onceweekly) \* |
| Baseline drug resistance \* |
| Vernon Lancet 1999 [8] | Onceweekly isoniazid/rifapentine  |
| Baseline CD4  |
| Age Extrapulmonary + pulmonary disease  |
| Use of antifungal azoles  |
| Prospective cohort studies |
| Reference | Potential risk factors for acquired drug resistance analysed |
| Aung, IJTLD 2012 [19]# operational study with randomisation | Extension of intensive phase of treatment by 1 month for patients who are smearpositive after 2 months \* |
| Burman AJRCCM 2006 [9] | Age |
| Sex |
| Ethnicity |
| Foreign birth (immigrant) |
| Baseline BMI |
| Baseline resistance to INH/PZA |
| Extrapulmonary TB |
| Cavitatory disease |
| Extensive (bilateral) radiological disease |
| Receiving of both rifampin and rifabutin during intensive phase |
| Culture positivity at 2months |
| Concurrent drugs which reduce rifabutin levels |
| Concurrent drugs which increase rifabutin levels |
| Baseline HIV viral load  |
| Lack of use of ART during TB treatment |
| Lack of use of ART in first 2 months of TB treatment |
|  Baseline CD4 lymphocyte count |
| Cox, Clin Infect Dis 2007 [20] | Baseline drug resistance (polyresistance)  |
|  Strain type |
| El Sahly, J of Infect, 2006 [21] | HIV coinfection  |
| Ethnicity |
|  |  Smear positive |
| Disseminated TB (with pleural effusion)  |
| Murray SAMJ 2000 [22] | Baseline drug resistance \* |
|  HIV coinfection \* |
| Nettles, Clin Infect Dis 2004 [23] | HIV coinfection |
| Baseline median CD4 lymphocyte count  |
| Type of rifamycin used (rifampicin vs rifabutin) |
| Pasipanodya , J Inf Dis 2013 [24] | PK variability including peak and 24 hr area under the concentration time curve for drugs R,H,PZA \*statistical analyses only performed for a composite outcome of death, treatment failure and relapse, not for acquired drug resistance |
| Temple CID 2008 [14] | Baseline resistance |
| Age  |
| Sex |
| Baseline BMI |
| Nonadherence |
|  HIV coinfection |
| Baseline CD4 |
| ART use |
| Baseline extensive radiological disease |
| Baseline cavitatory disease  |
| Retrospective cohort studies |
| Reference | Potential risk factors for acquired drug resistance analysed |
| Chien, JAC 2013 [25] | Age group 45-64 |
|  |
| Smear positivity |
| Self-administration of treatment/lack of DOT |
| Cavitatory disease |
| Driver, Clin Infect Dis, 2001 [26] | HIV coinfection \* |
| Selfadministration of treatment/lack of DOT \* |
| Gelmanova, Bull WHO, 2007 [27] | Age |
| Gender |
| Non-adherence |
| Side effects |
| Substance abuse |
| Cavitatory disease |
| Previously incarcerated |
| Smear positivity |
| Treatment commenced in hospital setting |
|  Hospitalisation later in treatment  |
|  Self-administration of treatment/lack of DOT |
| Jasmer, AJRCCM, 2004 [28] |  Self-administration of treatment/lack of DOT |
| Kim BMC ID 2008 [13] | Age \* |
| Sex \* |
| Comorbidity \* |
| Previous TB treatment \* |
| Length of RE in continuation phase \* |
| Extensive radiological disease \*  |
| Smear positivity \* |
| Li CID 2005 [29] | HIV coinfection  |
| CD4 count in the HIV coinfected cohort |
| Baseline drug resistance in the HIV cinfected cohort  |
| Change in type of rifamycin (rifampin to rifabutin or vice versa) during treatment |
| Intermittent dosing of rifampin or rifabutin during intensive phase  |
| Matthys, PLoS ONE, 2009 [11] | Baseline drug resistance \* |
| Moulding IJTLD 2004 [30] | Separate drug formulation (as opposed to fixed dose combination) \* |
| Private sector management \* |
| Porco CID 2012 [31] | Age |
| Ethnicity |
| Gender |
| Foreign birth |
| Previous TB |
| Extrapulmonary TB |
| Smear positivity |
| Private sector care |
| Baseline drug resistance |
| HIV coinfection |
|  Cavitatory disease  |
| Quy IJTLD 2003 [32] | Age |
| Sex |
| Baseline drug resistance |
| Seung CID 2004 [33] | Baseline drug resistance \* |
| Spellman 1988 AIDS [34] | HIV coinfection \* |
| Baseline drug resistance \* |
| Weis, NEJM 1994 [35] | Selfadministration of treatment (lack of DOT) |
| Yoshiyama IJTLD 2004 [15] | Previous treatment failure \* |
| Baseline resistance \* |
| HIV coinfection \* |
|  Strain type \* |
| Yuen, PLoSONE 2013 [36] | Age |
| Ethnicity |
| Country of birth |
| Region of birth |
| In correctional facility at time of diagnosis |
| Injecting drug use |
| Noninjecting drug use |
| Alcohol |
| Strain type |
| HIV coinfection |
| Homelessness |
| Baseline drug resistance |
| Smear positivity  |
| Cavitatory disease |
| Extrapulmonary only disease |
|  Self-administration of treatment/lack of DOT |
| Case control studies |
| Reference | Potential risk factors for acquired drug resistance analysed |
| Bradford Lancet 1996 [37] | Ethnicity |
| Foreign birth |
| Unemployment |
| Homelessness |
| Alcohol excess |
| Baseline AIDS |
| Self-administration of treatment/lack of DOT |
| ART use |
| Previous TB treatment |
| Initial 4 drug regimen |
| GI symptoms |
| Azole use |
| Non-adherence |
| CD4 lymphocyte count |
| Fixed dose RH tablet |
| Munsiff, Clin Infect Dis 1997 [38] | Age |
| Gender |
|  Country of birth |
|  Recreational drugs |
|  Homelessness |
|  Self-administration of treatment/lack of DOT |
| Non-adherence  |
| Baseline AIDS  |
| Baseline smear positivity  |
| Weiner CID 2005 [39] | Age |
| Gender |
| Ethnicity |
| Baseline BMI |
| Site of TB involvement |
| Extensive (bilateral) radiological disease |
| Cavitatory disease |
| Rifabutin area under curve (AUC024hrs) and maximal concentration |
| Deacetylrifabutin under curve (AUC024hrs) and maximal concentration |
| Isoniazid AUC and maximal concentration |
| Birth in Mexico |
| Baseline CD4 lymphocyte count |
| Baseline HIV viral load |
| Deacetylrifabutin AUC and maximal concentration |
| Nacetyltransferase type 2 genotype |
| Abbreviations: DOT directly observed therapy NTM nontuberculous mycobacteria MDR multidrug resistant ART antiretroviral therapy BMI body mass index INH/H isoniazid PZA pyrazinamide R rifampin E thambutol IP intensive phase CP continuation phase Hb haemoglobin ART antiretroviral therapy BMI body mass index . \* No statistical analysis was performed in the study and therefore the risk factor for ADR was reported as per trend noted |