# Determinants of non-adherence to anti-tuberculosis treatment in high income, low incidence, settings: A scoping review

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## Online Supplement

**Supplementary material 1**

**Scoping review search example strategy from MEDLINE**

1.  Tuberculosis/

2.  (TB or tuberculo*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3.  1 or 2

4.  Drug Therapy/

5.  (medication* or medicine* or treatment* or therap*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

6.  4 or 5

7.  3 and 6

8.  Antitubercular Agents/

9.  7 or 8

10. Medication Adherence/ or "Treatment Adherence and Compliance"/

11. (adheren* or complian* or non-adheren* or non-complian* or nonadheren* or concordan* or non-concordan*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12. (LTFU or "los* to follow-up" or "los* to follow up" or LFU or default).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

13. Lost to Follow-Up/

14. 10 or 11 or 12 or 13

15. 9 and 14

16. limit 15 to (english language and humans)

**Supplementary material 2. Bibliometric data from included studies (n=25).**

| Year(s) of study | N | Country | Study population | Study design | Categories of determinants assessed | Adherence measure | Non-adherence definition | % Non-adherent | Citation information |
|---|---|---|---|---|---|---|---|---|---|
| *Prospective designs* | | | | | | | | | |
| Not given | 90 | Ireland | Patients being treated for pulmonary TB and discharged from a Dublin hospital. | Prospective cohort | Demographic Clinical | Urine sample, self-report or physician's impression from interview | Non-compliance: based on interview evidence and ≥1 negative urine sample(s). | 23.3 | Corcoran [38] |
| Not given | 113 | UK | Patients being treated at Leeds Chest Clinic receiving a rifampicin-containing regimen. | Prospective cohort | Demographic Clinical | Urine sample | Non-compliance: negative urine sample. | 7.0 | Wardman et al. [42] |
| 1988-1989 | 224 | USA | Patients being treated in Harlem Hospital Center, New York. | Prospective cohort | Demographic Clinical | State TB registry data and hospital records | Noncompliance: no follow-up treatment or LTFU. | 89.0 | Brudney & Dobkin [43] |
| 1995–1996 | 62 | USA | Patients being treated and residing within Georgia. | Prospective cohort | Psychosocial | Tuberculosis General Adherence Scale (TBGAS) | Lower scores on TBGAS scale | Not given (mean TBGAS score= 92.6%) | McDonnell et al. [35*] |
| 1999–2000 | 1515 | Spain | Patients being treated by a member of the Tuberculosis and Respiratory Infections Group of the Sociedad Española de Neumología y Cirugía Torácica (SEPAR). | Prospective cohort | Demographic Clinical Health systems | Epidemiological questionnaire completed by staff, including assessments of "appointment attendance, physician estimation, and patient confirmation" (data source not specified) | Default: no treatment received for >1 month or missed appointments. | 4.0 | Cayla et al. [49] |

| Year(s) of study | N | Country | Study population | Study design | Categories of determinants assessed | Adherence measure | Non-adherence definition | % Non-adherent | Citation information |
|---|---|---|---|---|---|---|---|---|---|
| 1998–2003 | 119 | Japan | Homeless patients or those in fragile living situations who received treatment in a Tokyo hospital (excluded patients with HIV/TB co-infection). | Prospective cohort | Demographic Clinical Health systems Psychosocial | Medical notes | Treatment interruption during outpatient care: no treatment for ≥2 consecutive months. | Not given (19.33 worked out from results) | Kizuki et al. [59] |
| 2000–2003 | 575 | UK | Patients being treated in the East of England. | Prospective cohort | Demographic Clinical | Patient notes (extracted by TB staff) | LTFU | 7.8 | Anyama et al. [37] |
| 2003 | 1941 | UK | Patients in Greater London who were or should have been on treatment. | Prospective cohort | Demographic Clinical Psychosocial | Self-report, pill counts, urine tests, medical records, case-manager "knowledge" of patient | Poor adherence: self-reported, inconsistent pill counts, negative urine test, or patients switched to DOT or hospitalised for poor adherence.<br><br>LTFU: being out of contact with services for at ≥2 months without medication during first 6 months of treatment. | Poor adherence: 46.0<br><br>LTFU: 15.0 | Story et al. [41] |
| 2006–2007 | 1490 | Spain | Patients being treated by a member of the Tuberculosis and Respiratory Infections Group of the Sociedad Española de Neumología y Cirugía Torácica (SEPAR) (excluded patients with known drug resistance or those not initiating standard treatment). | Prospective cohort | Demographic Clinical Health systems | Electronic diary completed by staff (no details regarding from where data obtained) | Poor adherence: including default (treatment interruption for >2 months, non-completion by 9-months on standard regimen, or <80% prescribed doses taken) and LFTU. | 6.2 | Cayla et al. [50] |

| Year(s) of study | N | Country | Study population | Study design | Categories of determinants assessed | Adherence measure | Non-adherence definition | % Non-adherent | Citation information |
|---|---|---|---|---|---|---|---|---|---|
| 2006–2009 | 1490 | Spain | Patients being treated with culture-positive or smear-positive disease, extrapulmonary TB with caseating granuloma, identification by histology, or clinical, radiological, epidemiological or laboratory suspicion of TB (excluded patients with known drug-resistance or those with a contraindication to start standard treatment). | Prospective cohort | Demographic Clinical Health systems | Not specified | LFTU: treatment interruption (any reason) for ≥2 months, non-completion of treatment within 9 months for standard therapy, or taking <80% of prescribed dose. | 6.48 | Rodrigo et al. [51] |
| *Retrospective designs* | | | | | | | | | |
| 1988–1992 | 103 | Switzerland | Patients with bacteriologically confirmed pulmonary TB being treated in Vaud County. | Retrospective cohort | Demographic Clinical Psychosocial | Questionnaire completed by practitioners (using medical records) | Not adherent: not specified (adherence considered satisfactory if patient attended scheduled visits and requested prescriptions). | 18.4 | Zellweger & Coulon [54] |
| 1993 | 2576 | USA | Compared patients being treated in California who did and did not move during treatment to another health jurisdiction. | Retrospective cohort | Demographic Clinical Psychosocial | National TB surveillance data | Default: patients who refused treatment or were LTFU. | 5.5 | Cummings et al. [45] |
| 1991–1994 | 184 | USA | Patients with a first time, positive-culture being treated in New York City. | Retrospective cohort | Demographic Clinical | Contacting providers for clinic attendance and prescription information | Noncompliance: not attending clinic appointments for ≥2 months, or ≥3 months during 1 year. | 48.0 | Pablos-Mendez et al. [47] |
| 1993–1994 | 3520 | USA | Patients with culture-confirmed, rifampin- susceptible TB, starting a rifampin-containing regimen of at least 60 days, being treated in New York City. | Retrospective case-control | Demographic Clinical Health systems | State TB registry data and hospital records | Inappropriate treatment discontinuation: discontinuing rifampicin without experiencing serious adverse effects related to use. | 0.9 | Cook et al. [44] |

| Year(s) of study | N | Country | Study population | Study design | Categories of determinants assessed | Adherence measure | Non-adherence definition | % Non-adherent | Citation information |
|---|---|---|---|---|---|---|---|---|---|
| 1987–1996 | 1354 | Spain | Patients with HIV/TB co-infection, detected by the Active Epidemiological Surveillance System of the Barcelona Tuberculosis Prevention and Control Programme, being treated in Barcelona. | Retrospective cohort | Demographic Clinical | National TB surveillance data | Treatment abandonment: LTFU or failed medical controls and not found by public health surveillance nursing team. | 13.1 | Galdós Tangüis et al. [52] |
| 1993–1997 | 7529 | The Netherlands | Patients being treated in the Netherlands. | Retrospective cohort | Demographic Clinical Health systems | National TB registry data | LTFU (excludes patients reportedly continuing treatment elsewhere) | 8 | Borgdorff et al. [55] |
| 1998–2002 | 328 | USA | Patients who were culture-positive being treated in New York City (excluded patients with MDR-TB). | Retrospective case-control | Demographic Clinical Health systems Psychosocial | State TB registry data, patient interview forms, hospital records (including case manager notes) | Default (treatment interrupted for ≥60 days) with return to therapy<br><br>Default without return to therapy (including LTFU or treatment refusal) | 4.2 | Driver et al. [46] |
| 2001–2007 | 41,120 | UK | Patients being treated in England, Wales and Northern Ireland reported to the Enhanced Tuberculosis Surveillance (ETS) system. | Retrospective cohort | Demographic Clinical | National TB surveillance data | LTFU (before treatment completion, including patients who moved overseas) | 5.9 | Millet et al. [39] |
| 2000–2011 | 503 | Spain | Compares immigrant and native patients being treated in Catalonia. | Retrospective cohort | Demographic Clinical Psychosocial | Hospital records | Treatment abandonment: treatment interrupted for ≥2 months (without medical advice), or LTFU with no information available. | 1.8 | Ballesteros et al. [48] |
| 2009–2012 | 12,908 | UK | Patients being treated in London, England. | Retrospective cohort | Demographic Clinical | National TB surveillance and laboratory data (matched with national outreach data - "find and treat" registry) | Non-adherence (not specified) | 5.6 | Anderson et al. [36] |

| Year(s) of study | N | Country | Study population | Study design | Categories of determinants assessed | Adherence measure | Non-adherence definition | % Non-adherent | Citation information |
|---|---|---|---|---|---|---|---|---|---|
| 2000–2013 | 27,894 | Portugal | Patients with pulmonary TB being treated in continental Portugal, as identified through the national TB surveillance database (SVIG-TB). | Retrospective cohort | Demographic Clinical | National TB surveillance data | Default: treatment interrupted for >8 weeks after completing ≥1 month of treatment) | 4.9 | Nunes et al. [58] |
| 1995–2014 | 68 | Norway | Patients with MDR-TB being treated in Norway. | Retrospective cohort | Demographic Clinical | Hospital and laboratory records, TB registry data | LTFU: WHO 2013 definition (no treatment initiation, or treatment interrupted for ≥2 consecutive months). | 17.6 | Jensenius et al. [56] |
| 2006–2015 | 73,591 | Japan | Patients with pulmonary TB being treated in Japan. | Retrospective cohort | Demographic Clinical Health systems | National TB surveillance data | LTFU: definition from Japanese TB surveillance system (treatment interrupted for ≥2 consecutive months, or treatment duration <6 months). | 7.8 | Kawatsu et al. [57] |
| 1997–2017 | 190 | France | Patients diagnosed at Dron Hospital in Tourcoing (excluding those with MDR-TB or XDR-TB). | Retrospective cohort | Demographic Clinical | Not specified (appears to be medical and laboratory records) | LTFU: no treatment initiation or treatment interrupted for ≥2 consecutive months. | 15.0 | Tetart et al. [53] |
| *Mixed designs* | | | | | | | | | |
| 1978–1987 | 1009 | UK | Patients being treated in Blackburn, England. | Retrospective and prospective cohort | Demographic | Physician assessment, monthly health visitor reports (including pill counts) and clinic attendance | Poor compliance: ≥3 missed appointments or unfavourable assessments. | 3.0 | Ormerod & Prescott [40] |

*Note.* *determinants not extracted for this study. TB= Tuberculosis; LTFU= Loss to follow-up; MDR-TB= Multidrug-resistant tuberculosis; WHO = World Health Organization; XDR-TB= Extensively drug-resistant tuberculosis.

**Supplementary material 3. Frequency of determinants assessed by included studies.**

| Determinant category | Determinant grouping variable | Studies assessing determinant grouping variable: |
|---|---|---|
| Demographic | Age | n= 14<br>36 37 39 40 41 45 46 48 49 50<br>52 55 56 58 |
| | Sex | n= 14<br>37 39 41 42 43 47 49 50 52 54 55 56 57 58 |
| | Ethnicity | n= 5<br>39 41 44 45 47 |
| | Nationality/origin | n= 7<br>36 37 42 47 55 56 57 |
| | Residency/Immigration status | n= 9<br>39 48 49 50 51 53 54 55 58 |
| | Place of residence (e.g. homelessness, history of living in an institution or prison) | n= 16<br>36 41 43 45 46 47 48 49 50 51 52 54 55 57 58 59 |
| | Employment status | n= 4<br>50 53 57 59 |
| | Occupation | n= 2<br>45 57 |
| | SES indices (e.g. primary education only, living in low SES neighbourhood) | n= 5<br>37 38 42 52 57 |

| Determinant category | Determinant grouping variable | Studies assessing determinant grouping variable: |
|---|---|---|
| | Other (e.g. relationship status, receiving leave for appointments, place of residency, travelling behaviour, moved health jurisdiction during treatment) | n= 4<br>38 39 45 56 |
| Clinical | Disease site/presentation | n= 6<br>36 37 39 47 53 57 |
| | Smear & sputum culture result | n= 6<br>37 46 47 54 55 57 |
| | Treatment resistance | n= 3<br>45 47 59 |
| | TB history | n= 9<br>36 37 39 42 44 51 52 53 59 |
| | HIV status | n= 9<br>43 45 47 48 49 50 52 53 58 |
| | Substance use/issues | n= 17<br>36 38 41 43 44 45 46 47 49 50 51 52 53 54 56 58 59 |
| | Other (e.g. relapse (unspecified, diabetes co-morbidity) | n= 2<br>54 59 |
| Health systems | Route to care | n= 3<br>50 55 59 |
| | Treatment provider (e.g. treated at referral hospital, treated by private health provider) | n= 2<br>44 57 |

| Determinant category | Determinant grouping variable | Studies assessing determinant grouping variable: |
| --- | --- | --- |
| | HCP perceptions of patient knowledge | n=3<br>46 50 51 |
| | Other (e.g. hospitalisation, health insurance status, time from culture confirmation to presentation) | n= 3<br>46 49 57 |
| Psychosocial factors | Mental health problems | n= 3<br>41 46 54 |
| | Having close relationships | n= 1<br>59 |

Note. HCP= health care professional, SES= socioeconomic status, TB= tuberculosis

**Strength of evidence for demographic, clinical, health-systems and psychosocial factors associated with adherence to TB treatment**

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | | 1 | 2 | 3 | 4 |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| *Demographic Factors* | | | | | | | | | | |
| Age | Under 30 y/o | 36 [16-24] 50* [>50] 56 [≥40] 40* [30-44, 45-59, >60] | | | 41§,|| [30-59] | | | | | |
| | 25-34 y/o | | | | 37* [0-24] 55 [<25] | | | | | |
| | 30-65 y/o | | | 55¶ [<25] | 50* [>50] 52* [15-29] 55** [<25] | 30-65 y/o | | | 39 [15-44] 58 [15-34] | 36 [16-24] 37* [0-24] |
| | Over or equal 65 y/o | | | | 41§,|| [30-59] | Over or equal 65 y/o | 36 [16-24] 49* [≤17] | | 39 [15-44] 58 [15-34] | 37* [0-24] |
| | Other (e.g. unspecified, broad range) | 56 [≥40] 48 [<40] | 49* [≤17] | 52* [15-29] 55|||| | | Other (e.g. unspecified, broad range) | | | 46¶¶ [NS] | 37* [0-24] 46*** |

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| Grouping variable | Potential risk factor | Strength of evidence 1 — OR/RR≥1.5, P≤0.05 | 2 — OR/RR≥1.5, P>0.05, n<154 | 3 — OR/RR>1.0 to <1.5, P≤0.05 | 4 — OR/RR<1.5, P>0.05 | Potential protective factor | Strength of evidence 1 — OR/RR≤0.5, P≤0.05 | 2 — OR/RR≤0.5, P>0.05, n<154 | 3 — OR/RR>0.5 to <1.0, P≤0.05 | 4 — OR/RR>0.5, P>0.05 |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 45[††,‡‡] *[>45]*<br>55[§§] *[<25]* | | | *[<25]* | | | | | *[NS]* |
| Sex | Male *[Female]* | 49* <br> 50* <br> 58* <br> 41[§,‖] <br> 54* | 56* | 39 <br> 55 | 43 <br> 47* <br> 52* <br> 37* | Male *[Female]* | | | | 43 <br> 42* <br> 57 |
| Ethnicity | Hispanic | 44* *[non-Hispanic Black]* <br> 45[††,‡‡] *[Asian]* | | | 47* *[White]* | | | | | |
| | Asian *[White]* | 39*,[†††] | | 39*,[‡‡‡] | 47* <br> 41[‖] | Asian *[White]* | | | | 39*,[§§§] <br> 41[§] |
| | Black African/ Caribbean/Black British/non-Hispanic black | 45[††,‡‡] *[Asian]* <br> 47* *[White]* <br> 39* *[White]* | | | 41§,[‖] *[White]* | | | | | |
| | Non-Hispanic White | 44* *[non-Hispanic Black]* | | | | | | | | |
| | Ethnicity category non-specific (e.g. White, Asian, or Hispanic) *[NS]* | 44 | | | | | | | | |
| | Other *[White]* | 39* | | | 41[‖] | Other *[White]* | | | | 41[§] |
| | | | | | | Black Caribbean *[White]* | | | | 41[‖] |
| Nationality/ origin‡ | Europe | 36[‖‖‖] *[South Asia]* <br> 55 *[Dutch]* | | 36[¶¶¶] *[South Asia]* | 36[****] *[South Asia]* | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** OR/RR≥1.5, P≤0.05 | **2** OR/RR≥1.5, P>0.05, n<154 | **3** OR/RR>1.0 to <1.5, P≤0.05 | **4** OR/RR<1.5, P>0.05 | | **1** OR/RR≤0.5, P≤0.05 | **2** OR/RR≤0.5, P>0.05, n<154 | **3** OR/RR>0.5 to <1.0, P≤0.05 | **4** OR/RR>0.5, P>0.05 |
| | Asia | | 42* *[British]* | | 36 *[South Asia]* <br> 55 *[Dutch]* | | | | | |
| | North America and Oceania *[Abroad]* | | | | 47* *[Dutch]* | North America and Oceania *[South Asia]* | | | | 36 |
| | Africa | 55†††† *[Dutch]* | 56 *[NS]* | | 36 *[South Asia]* <br> 55‡‡‡‡ *[Dutch]* | | | | | |
| | East Mediterranean *[Dutch]* | 55 | | | | East Mediterranean *[South Asia]* | | | | 36 |
| | Foreign-born *[UK born]* | 37* | | | | Foreign-born *[Japan born]* | | | | 57 |
| | Other/country of birth unknown *[Dutch]* | 55 | | | | Other/Country of birth unknown *[Japan born]* | | | 57 | |
| | Latin, South, Central America or Caribbean | | | | 36 *[South Asia]* <br> 55 *[Dutch]* | | | | | |
| | | | | | | North Africa *[South Asia]* | | | | 36 |
| Residency/ immigration status | Immigrant or migrant *[native]* | 48 <br> 49 <br> 50 <br> 58 <br> 51 <br> 54* | | | | Immigrant or migrant *[native]* | | | | 53* |
| | Recent migrant (under 4 years) | 39* *[UK born}* | | | 55 *[other]* | | | | | |
| | Migrant 5+ years *[UK born]* | | | | 39* | | | | | |
| | Illegal immigrant *[not in category]* | 55 | | | | | | | | |
| | Asylum seeker *[not in category]* | | | | 55 | | | | | |
| | Time in resident country unknown *[UK born]* | 39* | | | | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | | **1** | **2** | **3** | **4** |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| Place of residence | Living alone | 50<br>*[with family]*<br>51<br>*[NS]* | | | | | | | | |
| | Homelessness/no fixed abode *[has fixed abode]* | 36<br>43<br>49∗<br>45††,‡‡<br>46¶¶,∗∗∗<br>59§§§§<br>47<br>52<br>41§,‖ | 59‖‖‖‖‖‖‖<br>54∗ | | 55<br>48 | Homelessness/no fixed abode [has fixed abode] | | | 58 | 57 |
| | History/living in institution or prison | 51<br>*[NS]*<br>55<br>*[no history]*<br>58∗<br>*[no history]*<br>46¶¶<br>*[not incarcerated]*<br>41§<br>*[no imprisonment during current treatment]*<br>36<br>*[NS*<br>50<br>*[with family]* | | 52∗<br>*[no history]* | 49∗<br>*[NS]*<br>45††<br>*[not in category]* | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence 1 OR/RR≥1.5, P≤0.05 | 2 OR/RR≥1.5, P>0.05, n<154 | 3 OR/RR>1.0 to <1.5, P≤0.05 | 4 OR/RR<1.5, P>0.05 | Potential protective factor | Strength of evidence 1 OR/RR≤0.5, P≤0.05 | 2 OR/RR≤0.5, P>0.05, n<154 | 3 OR/RR>0.5 to <1.0, P≤0.05 | 4 OR/RR>0.5, P>0.05 |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 45‡‡ *[not in category]* | | | | | | | | |
| | Shared accommodation *[with family]* | | | | 50 | | | | | |
| | Living in a county jail at diagnosis | 45††,‡‡ *[not in category]* | | | 50 *[with family]* | | | | | |
| Employment status | Active occupational status *[retired]* | 50* | | | | | | | | |
| | Unemployed | 50* *[retired]* | 59* *[employed]* | | | Unemployed *[Full/part- time employed]* | | | | 57 |
| | Disabled occupational status *[retired]* | 50* | | | | | | | | |
| | | | | | | Temporary/self employed | 53* *[NS]* | | | 57 *[Full/part- time employed]* |
| Occupation | HCP *[Full/part- time employed]* | | | 57¶¶¶¶ | 57***** | HCP *[Full/part- time employed]* | | | | 57††††† |
| | Housemaker *[Full/part- time employed]* | | | | 57 | | | | | |
| | Job/employment unknown *[Full/part- time employed]* | | | 57 | | | | | | |
| | Migrant agricultural work *[NS]* | 45††,‡‡ | | | | | | | | |
| | | | | | | Student *[Full/part- time employed]* | | | | 57 |
| SES indices | Receiving social welfare benefit *[not in category]* | | | | 57 | | | | | |
| | Low SES level neighbourhood *[any other SES level neighbourhood]* | 52 | | | | | | | | |
| | Townsend score high deprivation *[Townsend score least deprivation]* | | | | 37* | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | | **1** | **2** | **3** | **4** |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| | Primary education only *[2nd/3rd level education only]* | 38* | | | | | | | | |
| | SES Level 4/5 (high deprivation) *[SES Level 1,2, or 3]* | 42* | | | | | | | | |
| | Having medical card *[no medical card]* | 38* | | | | | | | | |
| | | | | | | Townsend score between low and high deprivation *[Townsend score least deprivation]* | | | | 37* |
| Other | Living outside of London *[living in London]* | | | 39* | | | | | | |
| | Living in Oslo *[NS]* | | 56 | | | | | | | |
| | Single/separated or widowed *[married]* | 38* | | | | | | | | |
| | Moved health jurisdiction within state during T$_x$ *[not moving during Tx]* | 45* | | | | | | | | |
| ***Clinical Factors*** | | | | | | | | | | |
| Disease site/ presentation | Pulmonary *[extra-pulmonary]* | 36 53* | | 39 | | Pulmonary *[extra-pulmonary]* | | | | 37* |
| | Extra-pulmonary *[not in category]* | | | | 47* | | | | | |
| | | | | | | With cavity | | | 57 *[no cavity]* | 47* *[no cavitary disease]* |
| Smear & sputum culture | Smear +ve and/or culture +ve | | | | 37* *[-ve]* | Smear +ve and/or culture +ve | 46*** *[not +ve in first 30 days of initial sputum collection]* | | 57 *[-ve]* | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | | **1** | **2** | **3** | **4** |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| | | | | | 46¶¶ *[not +ve in first 30 days of initial sputum collection]* 54* *[NS]* | | 55 *[no bacteriological confirmation]* | | | |
| | Culture/smear unknown/not done | | | 57‡‡‡‡ *[-ve]* | 47* *[+ve]* 57§§§§ *[-ve]* | | | | | |
| | | | | | | Smear -ve and/or culture –ve *[+ve]* | | | | 47* |
| $T_x$ resistance | MDR | 45††,‡‡ *[NS]* | | | 47* *[No resistance]* | | | | | |
| | Other resistance *[no resistance]* | | | | 47* | Other resistance *[no resistance]* | | | | 59* |
| TB history | Previous TB | 36 *[NS]* | 59* *[no history]* | | 39 *[no history]* | Previous TB *[no history]* | | | | 37* |
| | Previous TB $T_x$ *[no previous Tx]* | 44 51 52 42* | | | | | | | | |
| | Unknown previous TB status *[no history]* | | | 39 | | | | | | |
| | Previous TB $T_x$ default *[no previous default]* | 42* | | | | First episode of TB *[NS]* | 53 | | | |
| HIV status | HIV infection *[HIV negative]* | 49* 50* 58 | | | 47* | HIV infection *[HIV negative]* | | | | 48* |
| | HIV status known/missing *[HIV negative]* | | | | 50* 47* | | | | | |
| | HIV negative *[NS]* | 53 | | | | | | | | |
| | AIDS *[HIV negative]* | | | | 47* | AIDS (or AIDS related | 43 | | | 45‡‡ |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | | 1 | 2 | 3 | 4 |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| | | | | | | complex) [NS] | 45†† | | | |
| | HIV infection via IDU transmission [sexual transmission] | 52* | | | | | | | | |
| Substance use/misuse | Alcohol use [NS] | 36 | | | | | | | | |
| | Alcohol misuse/addiction | 43 [NS] <br> 58 [not in category] <br> 53* [NS] | 38* [0 drinks per week] <br> 54* [NS] | | 47* [no history of alcoholism] <br> 52* [No alcoholism] | | | | | |
| | Illicit drug use | 36 [NS] <br> 41‖ [NS] <br> 56 [NS] | 54* [NS] | | 47* [No cocaine use] <br> 46¶¶ [NS] | Illicit drug use [NS] | | | | 46*** |
| | Illicit drug misuse/addiction | 50 [No IDU] <br> 58 [NS] <br> 47 [no IDU] <br> 51 [NS] <br> 49 [not drug addict] | | | | | | | | |
| | Drug use unknown | 50 [No IDU] <br> 51 [NS] | | | | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | | 1 | 2 | 3 | 4 |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| | Any substance misuse (including IDU, non-IDU, and alcohol) [NS] | 45††,‡‡ | | | | | | | | |
| | Being treated with methadone [NS] | 44 | | | | | | | | |
| | Alcohol problems in hospital [Not in category] | | 59* | | | | | | | |
| Other | Relapse (unspecified) [NS] | 54* | | | | | | | | |
| | | | | | | Diabetes co-morbidity [not in category] | | | | 59* |

**Health-Systems Factors**

| Grouping variable | Potential risk factor | 1 | 2 | 3 | 4 | Potential protective factor | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|---|---|---|---|
| Route to care | Source – emergencies [primary care] | 50* | | | | | | | | |
| | Source – specialist [primary care] | | | 50* | | | | | | |
| | Source – other [primary care] | | | 50* | | | | | | |
| | Collapsing on street [other reason] | | 59* | | | | | | | |
| | Detection of TB by screening [other detection] | | | 55 | | | | | | |
| Tx provider | Tx started in OP department [initial hospitalisation] | | | 57 | | | | | | |
| | Private health provider [provider was DOH] | 44* | | | | | | | | |
| | Private health provider with low volume of patients [private health provider with high volume] | 44* | | | | | | | | |
| | Tx by low volume provider [NS] | 44 | | | | | | | | |
| HCP perception of patient's | Had previous Tx comprehension† [no previous Tx comprehension] | 50 | | | | | | | | |

| Grouping variable | Potential risk factor | Strength of evidence | | | | Potential protective factor | Strength of evidence | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | | 1 | 2 | 3 | 4 |
| | | OR/RR≥ 1.5, P≤ 0.05 | OR/RR≥ 1.5, P> 0.05, n< 154 | OR/RR> 1.0 to <1.5, P≤ 0.05 | OR/RR< 1.5, P> 0.05 | | OR/RR≤ 0.5, P≤ 0.05 | OR/RR≤ 0.5, P> 0.05, n< 154 | OR/RR> 0.5 to <1.0, P≤ 0.05 | OR/RR> 0.5, P> 0.05 |
| knowledge | Had difficulty with previous T$_x$ comprehension† *[easy previous Tx comprehension]* | 50 | | | | | | | | |
| | Poor understanding *[NS]* | 51 | | | | | | | | |
| | Lack of awareness of TB severity *[NS]* | 46¶¶,*** | | | | | | | | |
| Other | Hospitalised (includes IP care) *[not hospitalised]* | | | | 49* | | | | | |
| | Months from +ve culture to DOH interview† *[NS]* | | | 46¶¶ | | Months from +ve culture to DOH interview *[NS]* | | | | 46*** |
| | No health insurance *[has health insurance]* | | | | 57 | | | | | |
| ***Psychosocial Factors*** | | | | | | | | | | |
| Mental health issues | Mental health problems *[NS]* | 41§,‖ | | | | Mental health problems *[NS]* | 46*** | | | 46¶¶ / 54* |
| Having close relationships | | | | | | Having close relationships *[no close relationships]* | | | 59* | |

*Note.* Where variable levels are non-binary, baseline comparator is given italicised in square brackets, either next to variable level or individual study reference where this differs between studies. No data was extracted from [35]. Some variables could not be extracted from [55] (urban residence, previous default from TB Tx, homelessness, alcohol addiction, drug addiction, occupation, travel to endemic areas, disease site, HIV co-infection), [54] (age), [42] (age, nationality (other)), [59] (sex, age, disease site, cavitary disease, sputum smear result), and [38] (drinking (moderate drinking)). +ve= positive, -ve= negative, DOH= Department of Health, HCP= healthcare professional, IDU= intravenous drug use, IP= inpatient, MDR= multidrug-resistant, NS=not specified, OP= outpatient, SES= socioeconomic status, TB= tuberculosis, T$_x$= Treatment *=univariate/ bivariate analysis. †=Determinants were not further defined. ‡=nationality: studies [36], [47], and [37] comparator is not the study country, for studies [55], [56], [42] and [57], comparator is study country. §=outcome: outcome: non-adherent in first 2 months, ‖= outcome: loss to follow-up within 6 months, ¶= age: 35-44, **= age: 55-64, ††= outcome: excludes patients who moved during study, ‡‡= outcome: includes patients who moved during study, §§= age: 75, ‖‖= age: 45-54, ¶¶= outcome: default with return to therapy, ***= outcome: default without return to therapy, †††= ethnicity: Indian, ‡‡‡= ethnicity: Pakistani, §§§= ethnicity: Bangladeshi, ‖‖‖= nationality/origin: born in Central Europe, ¶¶¶= nationality/origin: born in West Europe, ****= nationality/origin: born in East Europe, ††††= nationality/origin: Somalian and other

African, ‡‡‡‡= nationality/origin: Moroccan, §§§§= place of residence: staying in transient hostel after discharge, ‖‖‖‖‖‖‖= place of residence: homeless prior to admission, ¶¶¶¶= HCP: Nurse, *****= HCP: Physician, †††††= HCP: Other HCP, ‡‡‡‡‡= Smear: culture/smear not done, §§§§§= Smear: culture/smear unknown.