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**Table S1. Search strategy**

| OVID Database: EMBASE, MEDLINE, Global Health, PsycINFO, Social Work Abstracts |
|---|
| 1. exp tuberculosis, multidrug resistant/<br>2. (mdrtb or xdrtb).mp.<br>3. (mdr or xdr or ((multidrug or drug) adj resistan*)).mp.<br>4. (tuberculosis or tb).mp.<br>5. 3 and 4<br>6. 1 or 2 or 5<br>7. exp patient compliance/<br>8. (dropout* or drop out*).mp.<br>9. cash.mp.<br>10. reimburse*.mp.<br>11. refund*.mp.<br>12. reward*.mp.<br>13. incentiv*.mp.<br>14. voucher*.mp.<br>15. reminder*.mp.<br>16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15<br>17. (penal* or punish*).mp.<br>18. (nonadheren* or adheren* or abscond* or attrition* or complian* or noncomplian* or default* or fail* or stop* or refus* or incomplet* or interrupt*).mp.<br>19. 16 or 17 or 18<br>20. 6 and 19<br>21. limit 20 to yr="2000 -Current" |
| Cochrane CENTRAL |
| MeSH descriptor: [Tuberculosis, Multidrug-Resistant] explode all trees<br>(MDR or XDR)<br>(multidrug or drug) next (resistan*)<br>(#2 or #3) and (tuberculosis or TB)<br>#1 or #4<br>MeSH descriptor: [Patient Compliance] explode all trees<br>dropout or (drop out)<br>cash<br>reimburse*<br>refund*<br>reward*<br>incentiv*<br>voucher*<br>reminder*<br>#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14<br>penal* or punish*<br>nonadheren* or adheren* or abscond* or attrition* or complian* or noncomplian* or default* or fail* or stop* or refus* or incomplet* or interrupt*<br>#15 or #16 or #17<br>#5 and #18<br>#19 Publication Year from 2000 |
| Web of Science |
| 12. #11<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=2000-2017*<br>11. #5 AND #10<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*<br>10. #6 OR #7 OR #8 OR #9<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*<br>9. TS=(nonadheren* OR adheren* OR abscond* OR attrition* OR complian* OR noncomplian* OR default* OR fail* OR stop* OR refus* OR incomplet* OR interrupt*)<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*<br>8. TS=(reimburs* OR refund* OR reward* OR incentiv* OR voucher* OR reminder* OR monitor* OR penal* OR punish*)<br>*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years* |

7. TS=(cash)
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
6. TS= (dropout* or drop out*)
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
5. #1 OR #4
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
4. #2 AND #3
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
3. TS=(TB OR Tuberculosis)
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
2. TS=(mdr OR xdr OR ((multidrug OR drug) NEAR (resistan*)))
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
1. TS= (mdrtb OR xdrtb)
*Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*

Scopus

( ( TITLE-ABS-KEY ( droput* OR "drop out*" OR cash OR reimburs* OR refund* OR reward* OR incentiv* OR voucher* OR reminder* OR monitor* OR penal* OR punish* OR nonadheren* OR adheren* OR abscond* OR attrition* OR complian* OR noncomplian* OR default* OR fail* OR stop* OR refus* OR incomplet* OR interrupt* ) ) AND ( ( TITLE-ABS-KEY ( mdrtb OR xdrtb ) ) OR ( ( TITLE-ABS-KEY ( ( mdr OR xdr OR ( ( multidrug OR drug ) W/3 resistan* ) ) ) ) AND ( TITLE-ABS-KEY ( tb OR tuberculosis ) ) ) ) ) AND ( PUBYEAR > 2000 )

Table 2. Characteristics of included study cohorts in pooled analyses

| Author, Year (Cohort group/Trial arm) | Study period (years) | Country | N | HIV (%) | XDR (%) | Previously Treated (%) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Any | SLD |
| *Studies with two or more cohorts** | | | | | | | |
| Baral 2014 (Arm 1) | 2008 | Nepal | 33 | n/a† | n/a | n/a | n/a |
| Baral 2014 (Arm 2) | 2008 | Nepal | 42 | n/a† | n/a | n/a | n/a |
| Huerga 2017 (Homa Bay)^^ | 2006-2012 | Kenya | 28 | 17 (60.7) | 0 | 24 (85.7) | n/a |
| Huerga 2017 (Mathare)^^ | 2006-2012 | Kenya | 70 | 15 (21.4) | 0 | 63 (90.0) | n/a |
| Huerga 2017 (Nairobi)^^ | 2006-2012 | Kenya | 71 | 11 (15.5) | 0 | 67 (94.4) | n/a |
| Loveday 2015 (Site 1) | 2008-2010 | South Africa | 125 | 96/124 (77.4) | 0 | 87 (69.6) | 6 (4.8) |
| Loveday 2015 (Site 2 & 3) | 2008-2010 | South Africa | 350 | 235/333 (70.6) | 0 | 217 (62.0) | 33 (9.4) |
| Loveday 2015 (Site 4) | 2008-2010 | South Africa | 261 | 197/235 (83.8) | 0 | 107(41.0) | 14 (5.4) |
| Mohr 2017 (SAT)¥ | 2010-2014 | South Africa | 244 | 180 (73.8) | 0 | 146 (59.8) | 33 (13.5) |
| Mohr 2017 (SOC)¥ | 2010-2014 | South Africa | 160 | 112 (70.0) | 0 | 122 (76.3) | 19 (11.9) |
| Taneja 2017 (Control) | 2014 | India | 50 | 0 | 0 | 50 (100) | 0 |
| Taneja 2017 (Intervention) | 2014 | India | 50 | 0 | 0 | 50 (100) | 0 |
| *Studies with a single cohort* | | | | | | | |
| Alene 2017 | 2011-2014 | China | 481 | 0 | 10 (2.1) | 417 (86.7) | n/a |
| Bastard 2015 | 2002-2010 | Armenia/ Georgia | 393 | n/a† | 15/247 (6.1) | 304 (77.4) | 115 (29.3) |
| Cox 2007 | 2003-2005 | Uzbekistan | 87 | n/a† | 0 (0) | 87 (100) | 57 (65.5) |
| Escudero 2006øø | 1998-2000 | Spain | 25 | 0 | 1 (4.0) | 22 (88.0) | n/a |
| Gelmanova 2011§ | 2006-2008 | Russia | 38 | 0 | 2 (5.3) | 21 (55.3) | 10 (26.3) |
| Isaakidis 2011 | 2007-2011 | India | 58 | 58 (100) | 3/50 (6.0) | 51 (87.9) | 26 (44.8) |
| Joseph 2011 | 2006-2007 | India | 38 | 0 | 0 | 38 (100) | 0 |
| Keshavjee 2008 | 2000-2004 | Russia | 608 | 5/604 (0.8) | 29 (4.8) | 605 (99.5) | n/a |
| Kliiman 2009 | 2003-2005 | Estonia | 289 | 11 (3.8) | 54 (18.7) | 139 (48.1) | n/a |
| Meressa 2015 | 2009-2014 | Ethiopia | 612 | 133/612 (21.7) | 6/612 (1.0)# | 603 (98.5) | n/a |
| Mitnick 2003 | 1996-1999 | Peru | 75 | 1/65 (1.5) | 5 (6.7) | 75 (100) | n/a |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mitnick 2008§§ | 1999-2002 | Peru | 651 | 9/635 (1.4) | 48 (7.4) | 649 (99.7) | 420/648 (64.5) |
| Mohr 2015~ | 2008-2012 | South Africa | 853 | 605 (70.9) | 39 (4.6) | 576 (67.5) | 0 |
| Satti 2012ø | 2008-2009 | Lesotho | 134 | 94 (70.2) | n/a | 129 (96.3) | 18 (13.4) |
| Shin 2006 | 1998-2000 | Russia | 244 | 0 | n/a | 239 (98.0) | n/a |
| Suarez 2002 | 1997-1999 | Peru | 298 | n/a† | n/a | 298 (100) | n/a |
| Thomas 2007 | 1999-2003 | India | 66 | n/a† | 1/33 (3.0) | 66 (100) | n/a |
| Vaghela 2015 | 2009-2010 | India | 101 | 2 (2.0) | n/a | n/a | n/a |
| Yu 2015 ~ | 2007-2009 | Taiwan | 124 | n/a† | n/a | 60 (48.4) | n/a |

*Studies with more than one arm/cohort – each arm shown separately.

#Presumed XDR-TB

~Includes 190 patients with mono-RR-TB.

^^In the full sample (from all three study sites), resistance to second-line drugs were as follows: CPM 1/63 (1.6%), KM 1/63 (1.6%), and OFX 3/47 (6.4%).

¥ Includes unknown number of patients with mono-RR-TB. Of 244 in the SAT cohort, 67 patients had recorded outcomes before end of 6 months (16 LTFU; 33 died; 1 failure; 17 were transferred out). Of the 160 in the DOT cohort, 42 had recorded outcomes before end of 6 months (19 LTFU; 13 died; 2 failures; 8 were transferred out). These patients were excluded from analysis in the published study, however, they were included in this analysis (except those transferred out/not evaluated).

†The estimated prevalence of HIV among TB patients: 6.3% in Armenia; 3.5% in Uzbekistan; 6% in Peru; 2.2% in Georgia; 4.7% in Nepal; 3% in India (WHO 2017); and 2.4% in Taiwan.

Table S3. Treatment outcomes at end of study of cohorts included in pooled analyses*

| Author, Year (Cohort group) | Sample size (n) | Outcomes at end of study | | | | | |
|---|---|---|---|---|---|---|---|
| | | Lost to follow-up (%) | Success (%) | Failure (%) | Death (%) | Transferred out/not evaluated (%) | Still on treatment** (%) |
| *Studies with two or more cohorts* | | | | | | | |
| Baral 2014 (Arm 1) | 33 | 2 (6.1) | 28 (84.8) | 2 (6.1) | 1 (3.0) | 0 (0) | 0 (0) |
| Baral 2014 (Arm 2) | 42 | 6 (14.3) | 32 (76.2) | 2 (4.8) | 2 (4.8) | 0 (0) | 0 (0) |
| Huerga 2017 (Homa Bay) | 28 | 0 (0.0) | 16 (57.1) | 0 (0) | 5 (17.9) | 7 (25.0) | 0 (0) |
| Huerga 2017 (Mathare) | 70 | 6 (8.6) | 52 (74.3) | 0 (0) | 4 (5.7) | 8 (11.4) | 0 (0) |
| Huerga 2017 (Nairobi) | 71 | 6 (8.5) | 43 (60.6) | 1 (1.4) | 12 (16.9) | 9 (12.7) | 0 (0) |
| Loveday 2015 (Site 1) | 125 | 9 (7.2) | 90 (72.0) | 7 (5.6) | 17 (13.6) | 2 (1.6) | 0 (0) |
| Loveday 2015 (Site 2 & 3) | 350 | 70 (20.0) | 202 (57.7) | 23 (6.6) | 47 (13.4) | 8 (2.3) | 0 (0) |
| Loveday 2015 (Site 4) | 261 | 28 (10.7) | 135 (51.7) | 19 (7.3) | 69 (26.4) | 10 (3.8) | 0 (0) |
| Mohr 2017 (SAT) | 244 | 47 (19.3) | 99 (40.6) | 8 (3.3) | 48 (19.7) | 42 (17.2) | 0 (0) |
| Mohr 2017 (SOC) | 160 | 44 (27.5) | 66 (41.3) | 7 (4.4) | 19 (11.9) | 24 (15.0) | 0 (0) |
| Taneja 2017 (Control) | 50 | 21 (42.0) | 14 (28.0) | 3 (6.0) | 7 (14.0) | 5 (10.0) | 0 (0) |
| Taneja 2017 (Intervention) | 50 | 22 (44.0) | 20 (40.0) | 1 (2.0) | 6 (12.0) | 1 (2.0) | 0 (0) |
| *Studies with a single cohort* | | | | | | | |
| Alene 2017 | 481 | 130 (27.0) | 275 (57.2) | 63 (13.1) | 13 (2.7) | 0 (0) | 0 (0) |
| Bastard 2015 | 393 | 127 (32.3) | 171 (43.5) | 56 (14.2) | 39 (9.9) | 0 (0) | 0 (0) |
| Cox 2007 | 87 | 12 (13.8) | 54 (62.1) | 8 (9.2) | 13 (14.9) | 0 (0) | 0 (0) |
| Escudero 2006 | 25 | 2 (8.0) | 21 (84.0) | 0 (0) | 0 (0) | 2 (8.0) | 0 (0) |
| Gelmanova 2011 | 38 | 6 (15.8) | 27 (71.1) | 2 (5.3) | 2 (5.3) | 1 (2.6) | 0 (0) |
| Isaakidis 2011 | 58 | 7 (12.1) | 13 (22.4) | 2 (3.4) | 13 (22.4) | 0 (0) | 23 (39.7) |
| Joseph 2011 | 38 | 5 (13.2) | 25 (65.8) | 5 (13.2) | 3 (7.9) | 0 (0) | 0 (0) |
| Keshavjee 2008 | 608 | 119 (19.6) | 400 (65.8) | 58 (9.5) | 31 (5.1) | 0 (0) | 0 (0) |
| Kliiman 2009 | 289 | 48 (16.6) | 165 (57.1) | 35 (12.1) | 48 (16.6) | 0 (0) | 0 (0) |
| Meressa 2015 | 612 | 36 (5.9) | 481 (78.6) | 10 (1.6) | 85 (13.9) | 0 (0) | 0 (0) |
| Mitnick 2003 | 75 | 5 (6.7) | 55 (73.3) | 1 (1.3) | 14 (18.7) | 0 (0) | 0 (0) |
| Mitnick 2008 | 651 | 65 (10.0) | 429 (65.90) | 18 (2.8) | 134 (20.6) | 4 (0.6) | 1 (0.2) |
| Mohr 2015 | 853 | 227 (26.6) | 359 (42.1) | 48 (5.6) | 123 (14.4) | 96 (11.3) | 0 (0) |
| Satti 2012 | 134 | 1 (0.7) | 83 (61.9) | 1 (0.7) | 46 (34.3) | 3 (2.2) | 0 (0) |
| Suarez 2002 | 298 | 34 (11.4) | 136 (45.6) | 96 (32.2) | 32 (10.7) | 0 (0) | 0 (0) |
| Shin 2006 | 244 | 28 (11.5) | 188 (77.0) | 16 (6.6) | 12 (4.9) | 0 (0) | 0 (0) |
| Thomas 2007 | 66 | 16 (24.2) | 25 (37.9) | 17 (25.8) | 8 (12.1) | 0 (0) | 0 (0) |
| Vaghela 2015 | 101 | 7 (6.9) | 72 (71.3) | 4 (4.0) | 17 (16.8) | 1 (1.0) | 0 (0) |
| Yu 2015 | 124 | 0 (0.0) | 106 (85.5) | 2 (1.6) | 16 (12.9) | 0 (0) | 0 (0) |

*Results for studies with more than one patient cohort are shown separately for each study arm or cohort.

**These are patients who have not yet completed the study's standard treatment duration, and who do not have a final treatment outcome recorded by the end of study.

**Table S4. Summary of quality assessment of non-randomized studies (based on Robins-I Tool)**

| Author, Year | Overall risk of confounding bias | Overall Risk of selection bias | Overall risk due to intervention classification | Overall risk due to deviations from interventions | Overall risk of bias due to missingness | Overall risk of outcome measurement bias | Overall Risk of reporting bias | OVERALL BIAS |
|---|---|---|---|---|---|---|---|---|
| **Cohort studies without comparison groups** | | | | | | | | |
| Alene 2017 | n/a | Low | n/a | No information | Low | Low | Low | No information |
| Bastard 2015 | n/a | Low | n/a | No information | Moderate | Low | Low | No information |
| Cox 2007 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Escudero 2006 | n/a | Low | n/a | Low | Moderate | Low | Low | Moderate |
| Gelmanova 2011 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Isaakidis 2011 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Joseph 2011 | n/a | Low | n/a | No information | Low | Low | Low | No information |
| Keshavjee 2008 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Kliiman 2009 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Meressa 2015 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Mitnick 2003 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Mitnick 2008 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Mohr 2015 | n/a | Low | n/a | Low | Moderate | Low | Low | Moderate |
| Satti 2012 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Shin 2006 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Suarez 2002 | n/a | Low | N/a | Low | Low | Low | Low | Low |
| Thomas 2007 | n/a | Low | n/a | Moderate | Low | Low | Low | Moderate |
| Vaghela 2015 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| Yu 2015 | n/a | Low | n/a | Low | Low | Low | Low | Low |
| **Cohort studies with 2 or more interventions** | | | | | | | | |
| Mohr 2017 | Serious | Low | Low | Low | Low | Low | Low | Serious |
| Loveday 2015 | Serious | Low | Low | Low | Low | Low | Low | Serious |
| Cox 2014 | Serious | Low | Low | Low | Moderate | Low | Low | Serious |
| Huerga 2017 | Serious | Low | Low | Low | Moderate | Low | Low | Serious |

**Table S5. Summary of quality assessment of cluster randomized trials**

| Author, Year | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective outcome reporting? (reporting bias) | Other bias |
|---|---|---|---|---|---|---|---|
| Baral 2014 | Low | Low | High | Low | Low | Low | Serious risk of confounding bias |
| Taneja 2017 | Low | Low | High | Low | Low | Low | Serious risk of confounding bias |

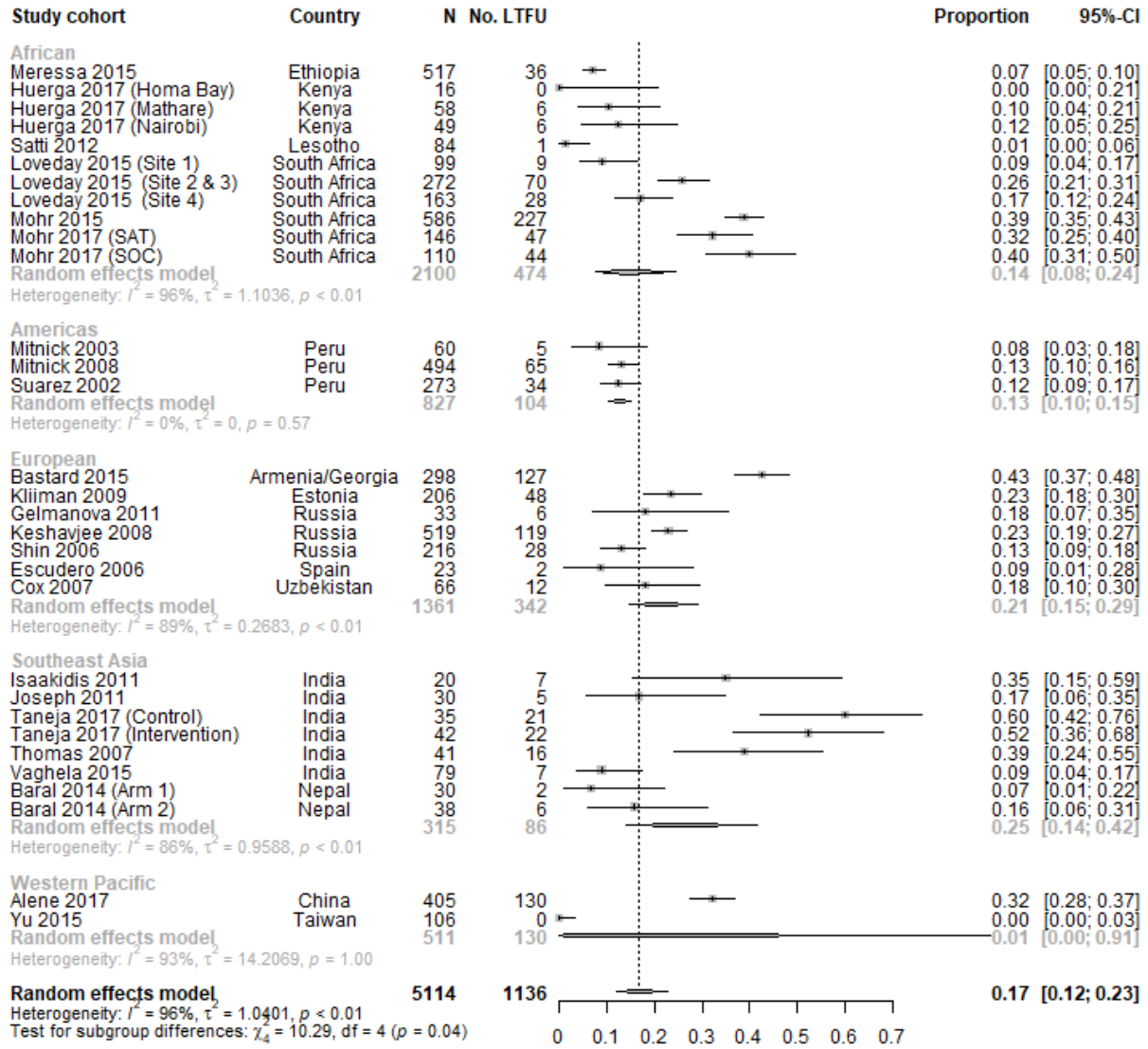


**Figure S1. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by WHO region.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

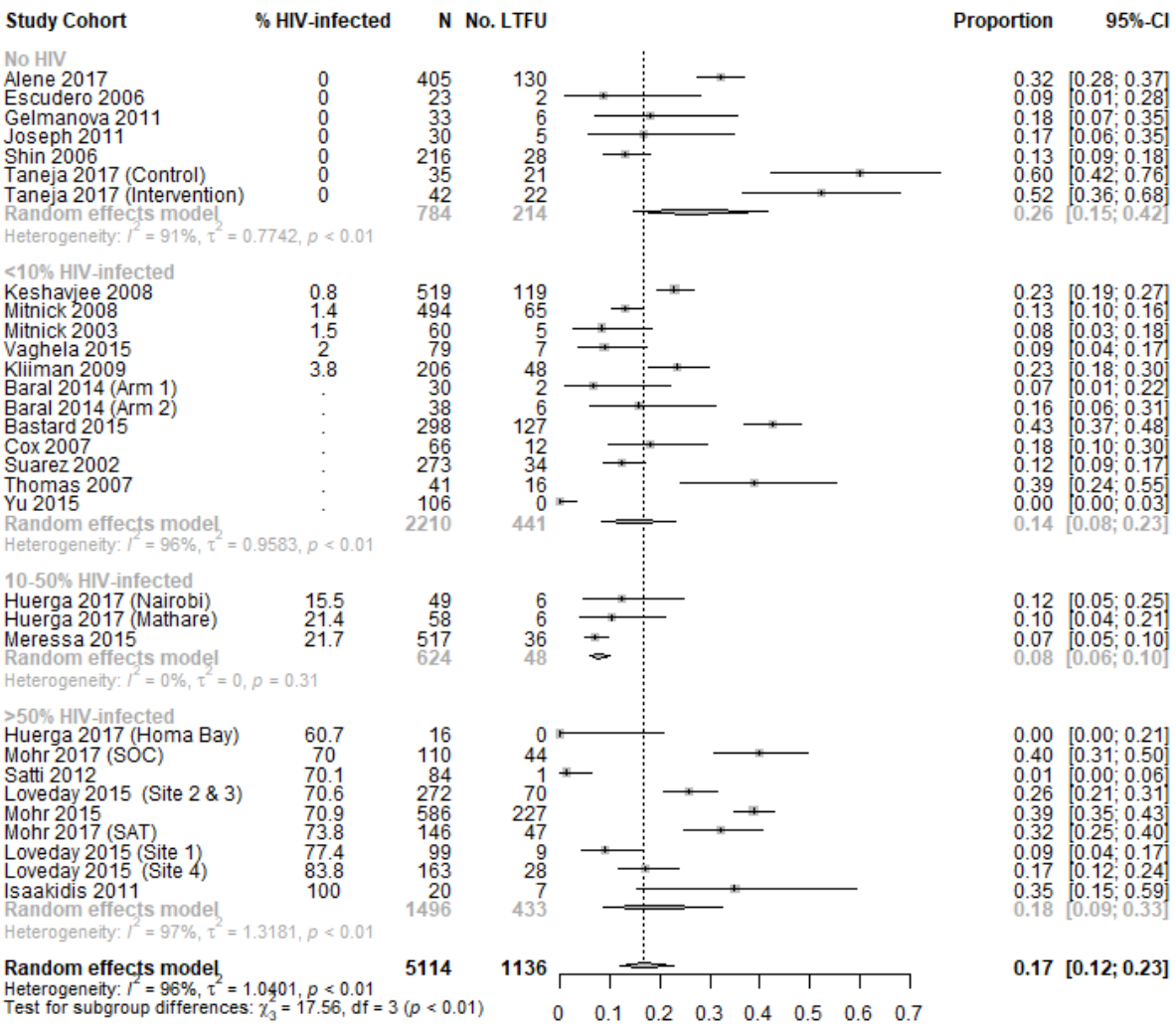


**Figure S2. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by HIV prevalence.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. For studies that did not report HIV prevalence, all were assumed to have <10% HIV prevalence according to country-level estimates of HIV prevalence among TB patients (see Table S3). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

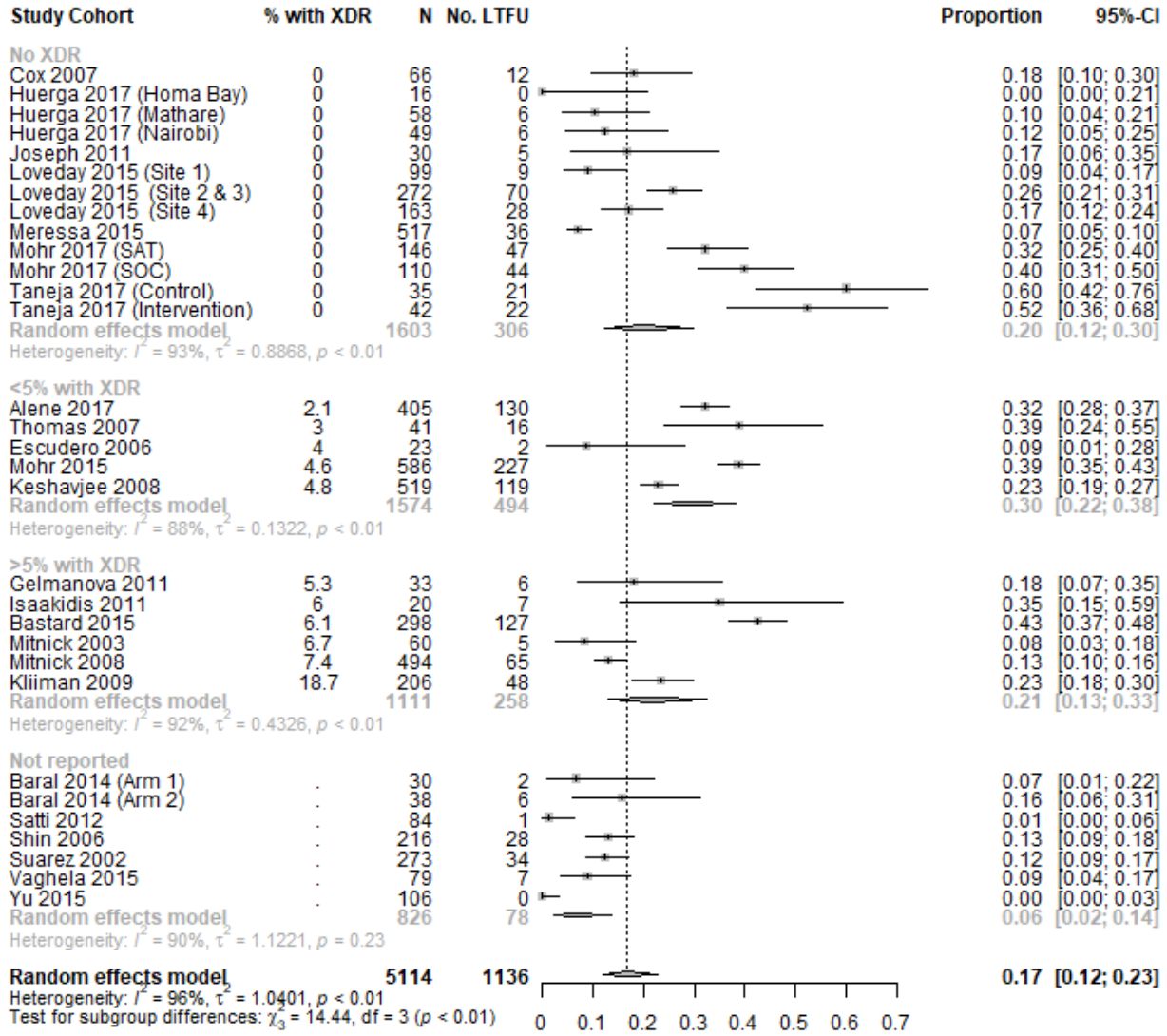


**Figure S3. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by XDR status.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; XDR = extensively drug-resistant TB.

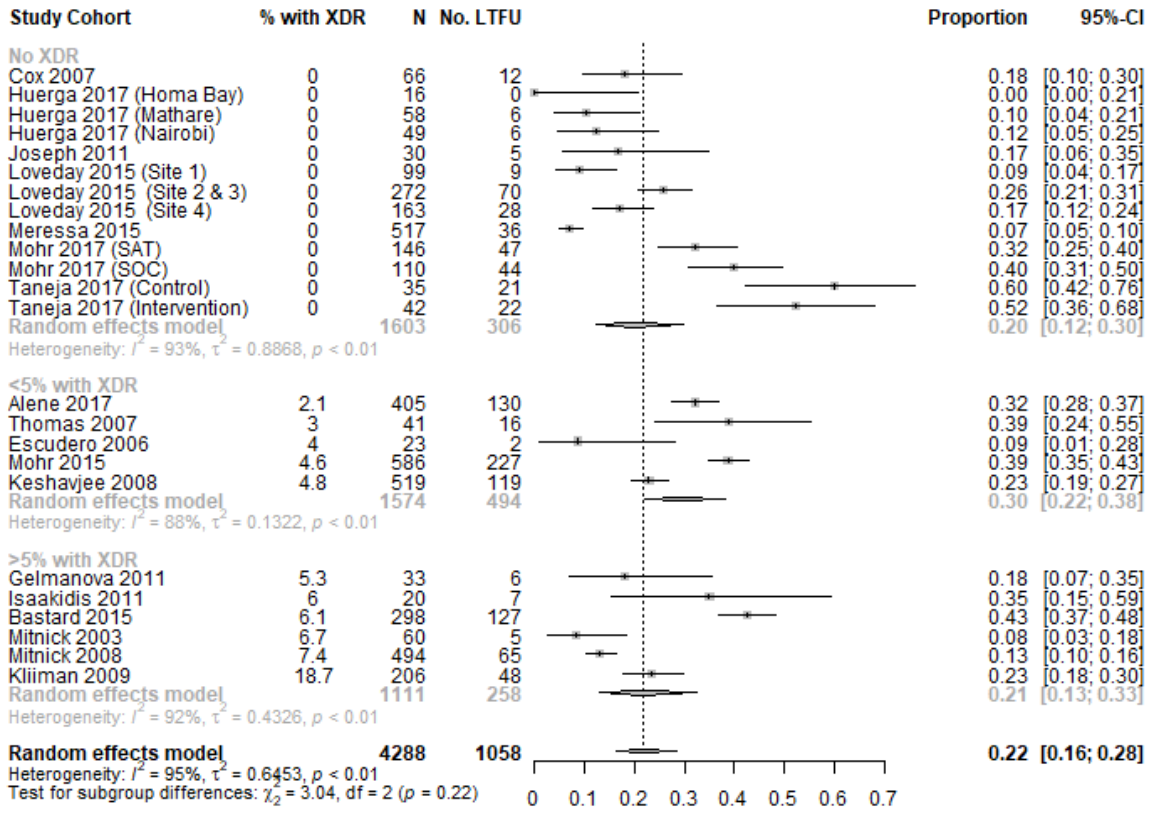


**Figure S4. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by XDR status, excluding studies that did not report XDR status.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Study cohorts that did not report XDR status among patients were excluded (n=7). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; XDR = extensively drug-resistant TB.

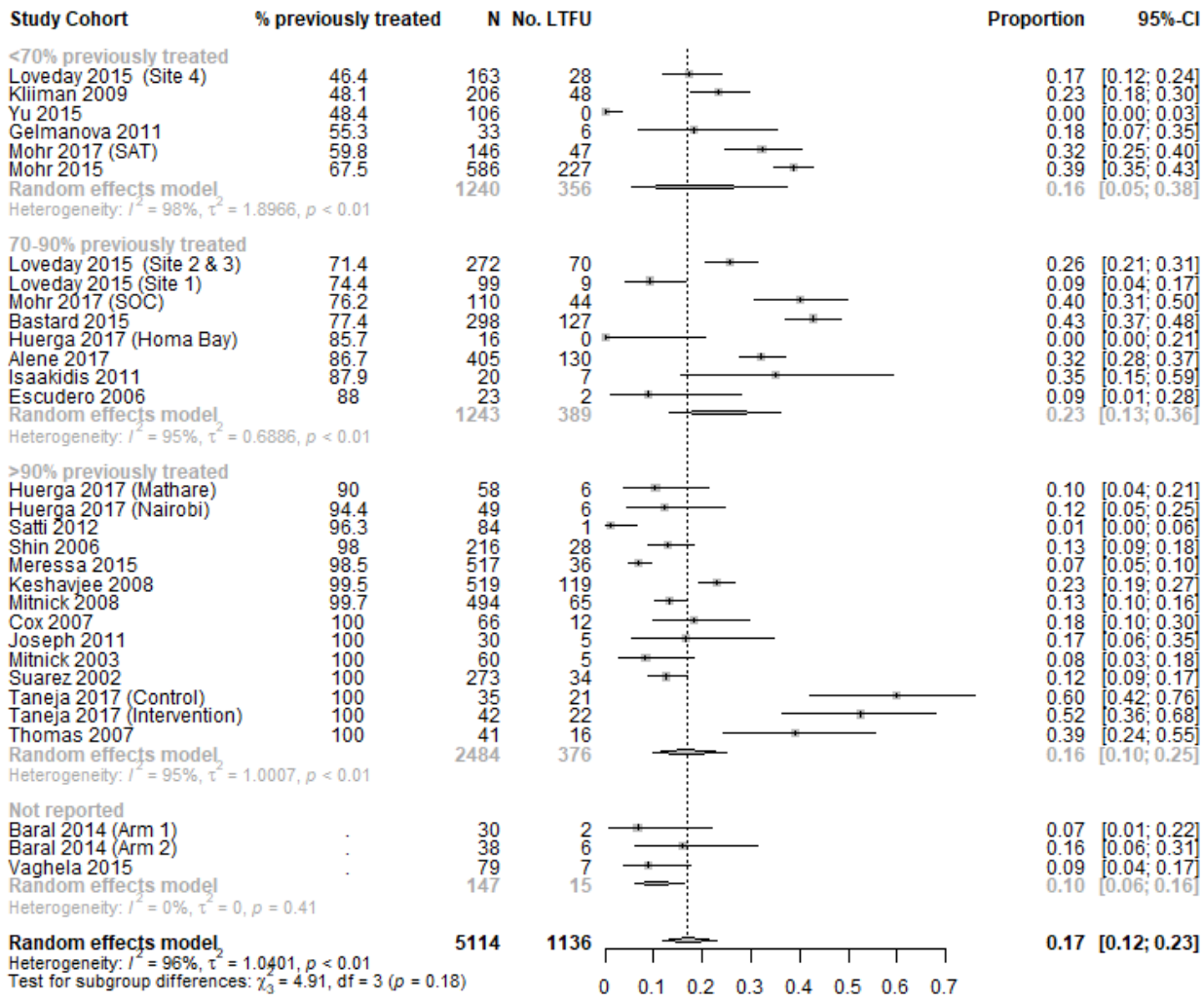


**Figure S5. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by proportion previously treated for any type of TB.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

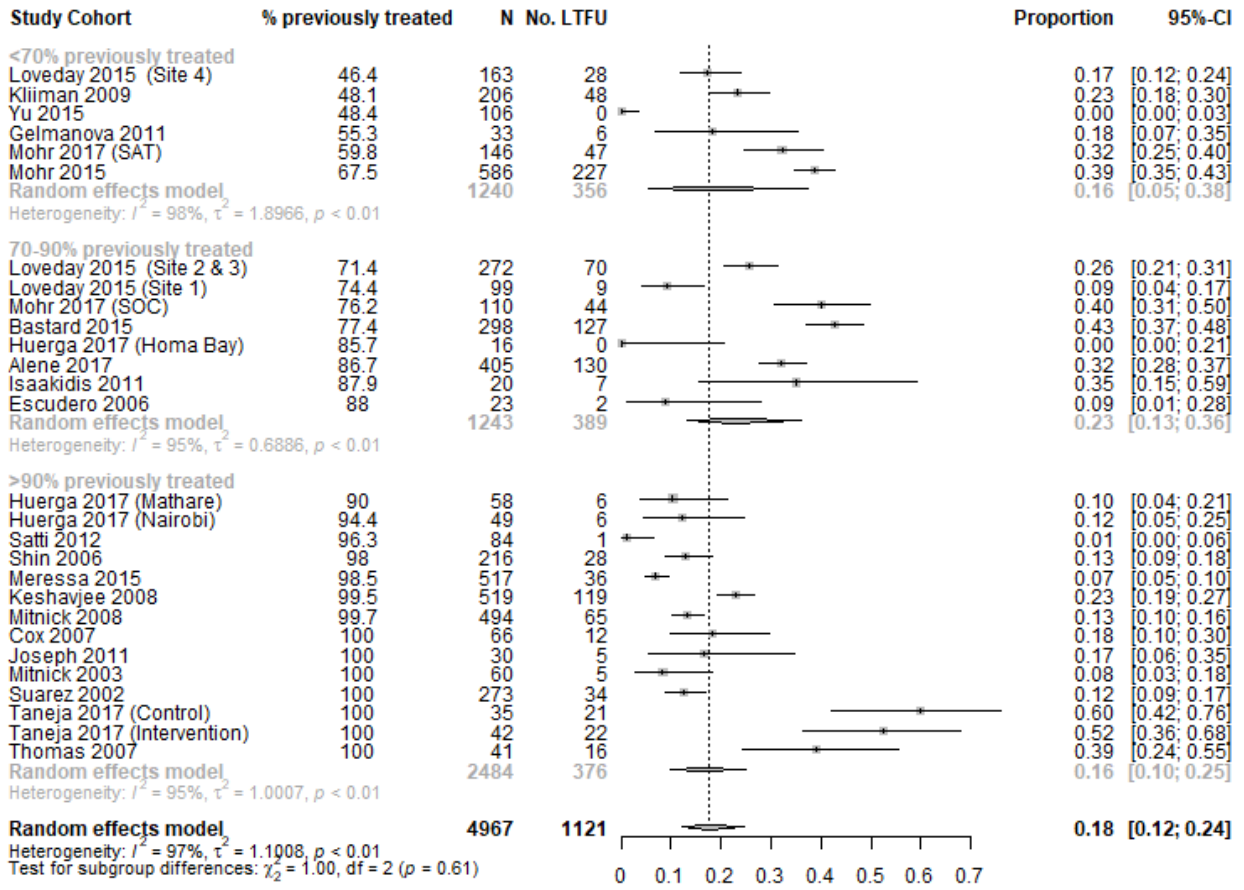


**Figure S6. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by proportion previously treated for any type of TB, excluding studies that did not report proportions previously treated.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Study cohorts that did not report proportions with any previous TB treatment were excluded (n=3). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

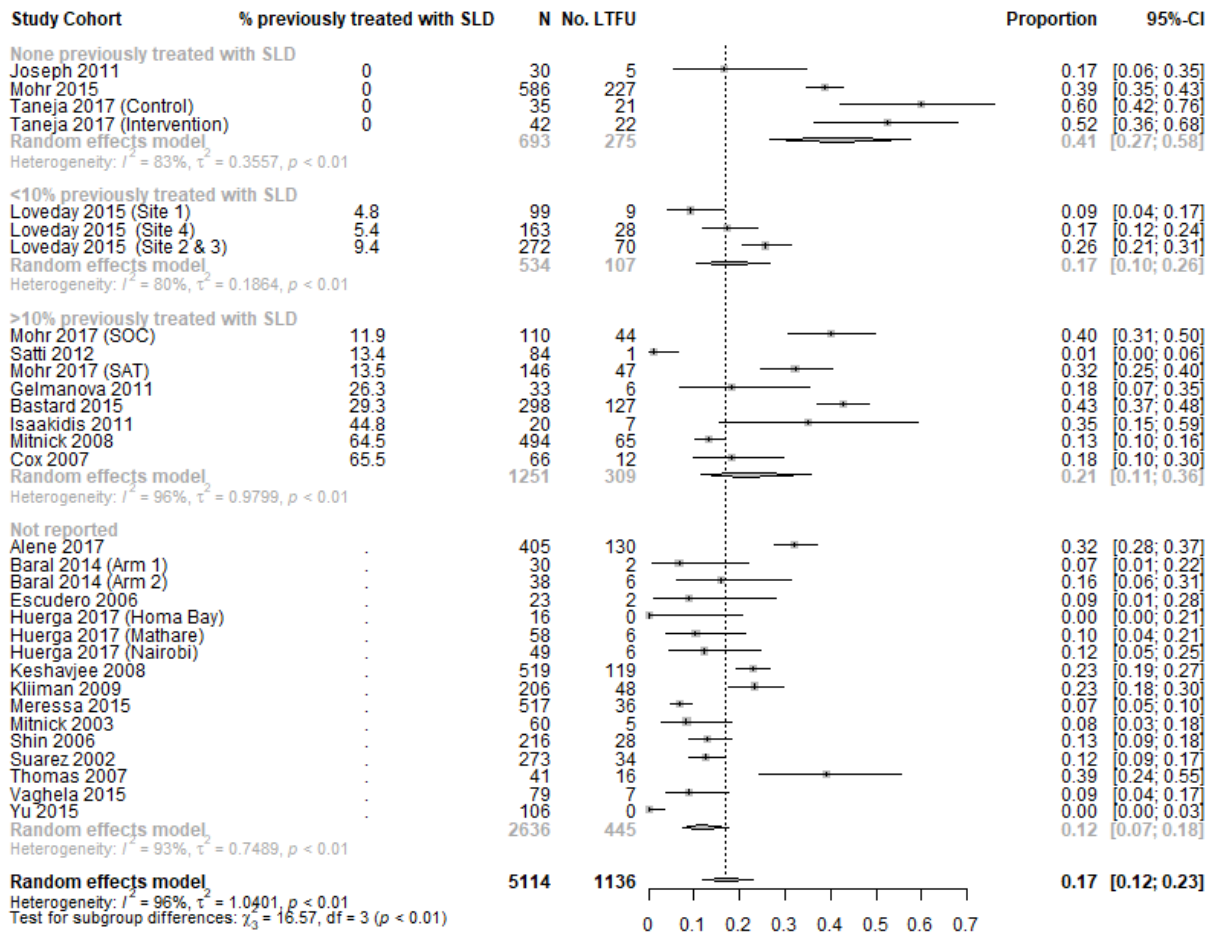


**Figure S7. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by proportion previously treated with second-line TB drugs.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; SLD = second-line drugs.

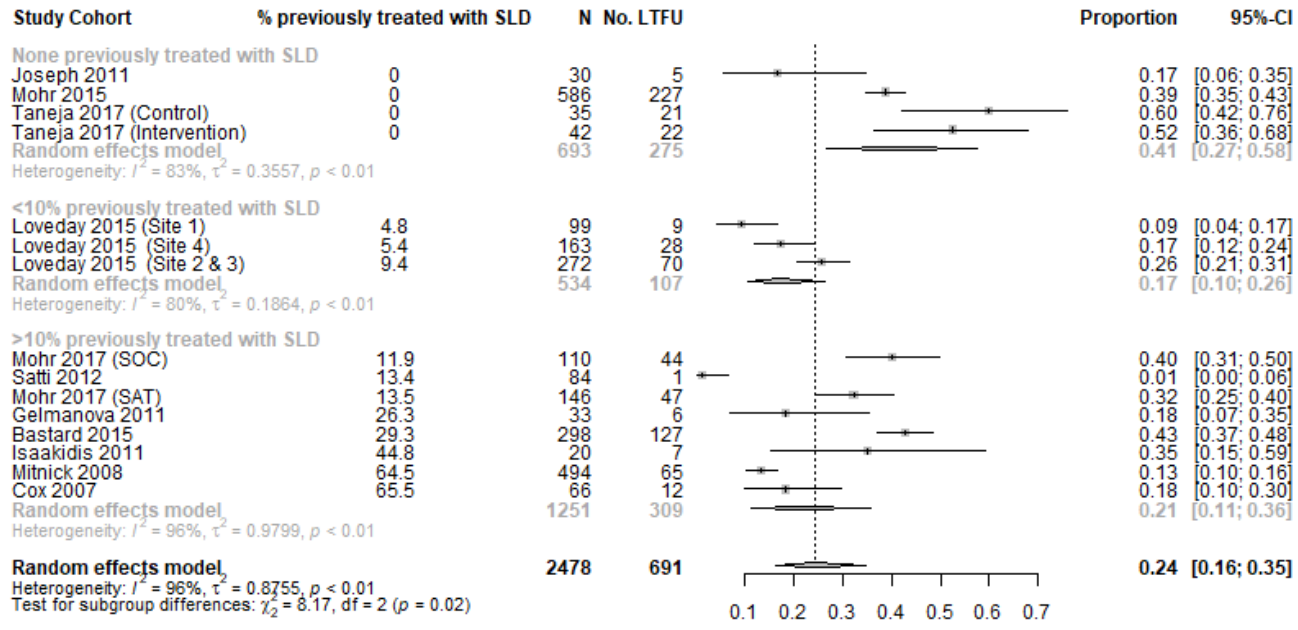


**Figure S8. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by proportion previously treated with second-line TB drugs, excluding studies that did not report proportions previously treated with SLD.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Study cohorts that did not report proportions with any previous treatment with second-line drugs were excluded (n=16). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; SLD = second-line drugs.

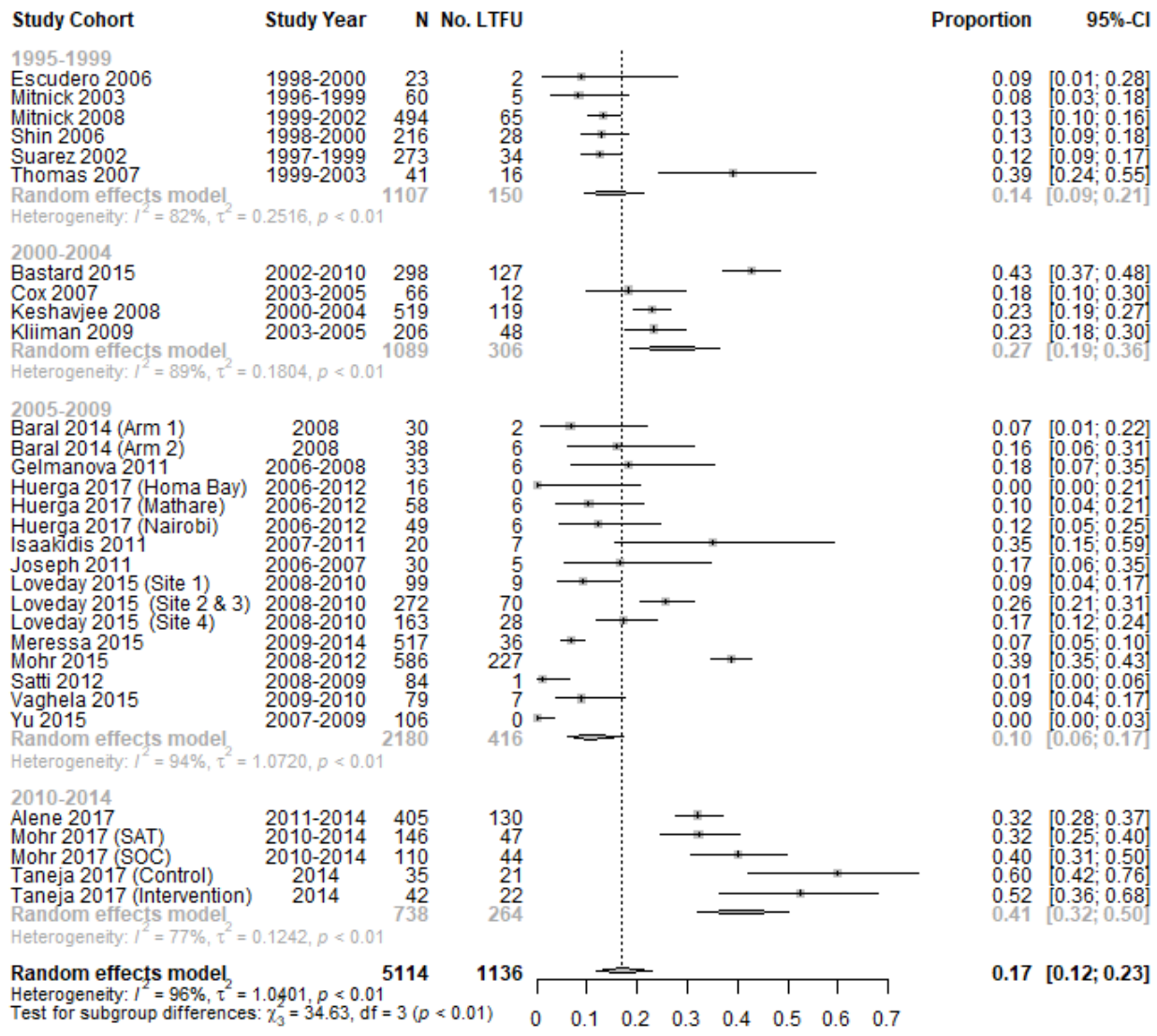


**Figure S9. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by the year study recruitment started.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Study cohorts that did not report proportions with any previous treatment with second-line drugs were excluded (n=16). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; SLD = second-line drugs.

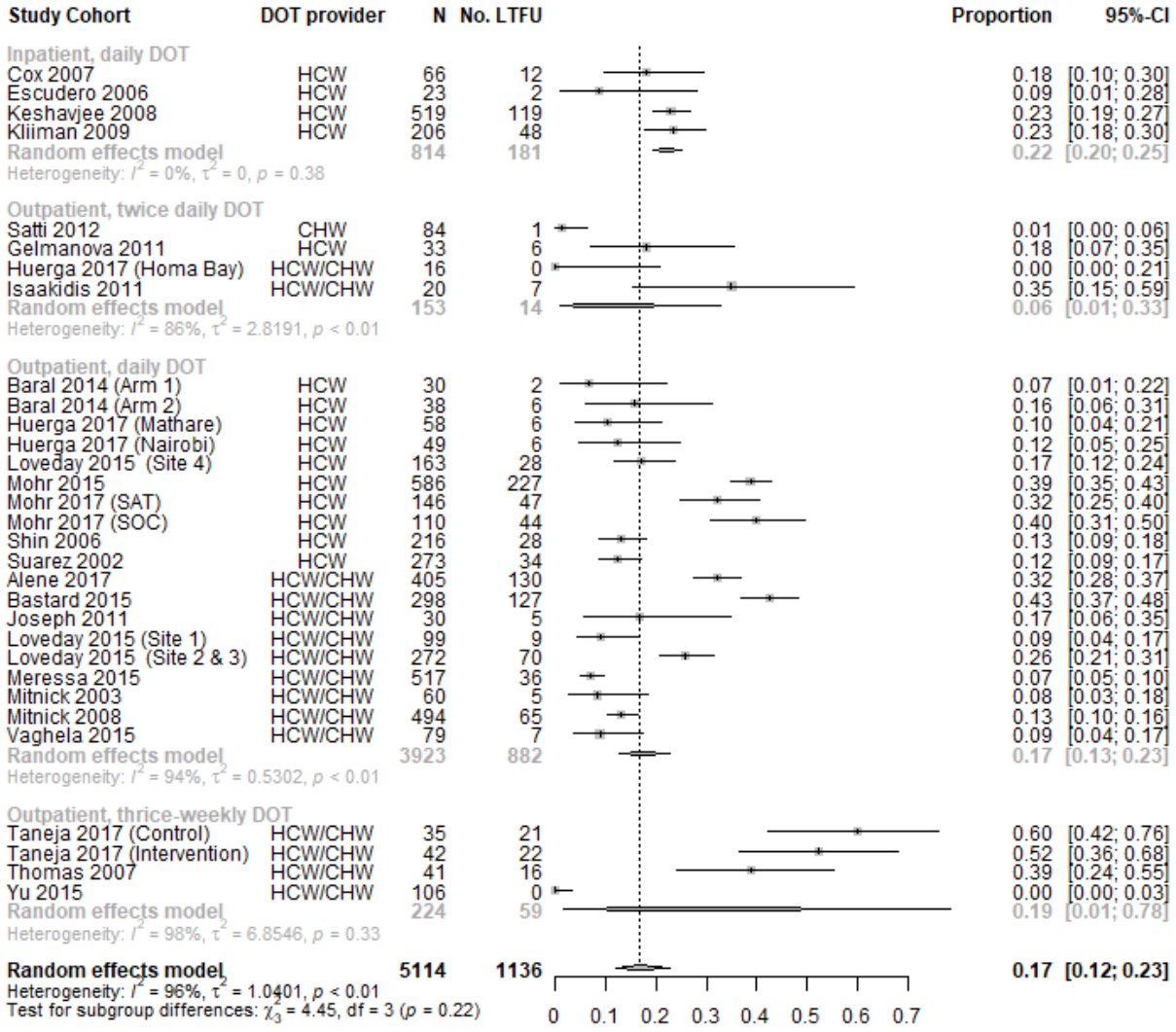


**Figure S10. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by DOT frequency method during the intensive phase.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; HCW = health care worker; CHW = community health worker; DOT = daily observed therapy.

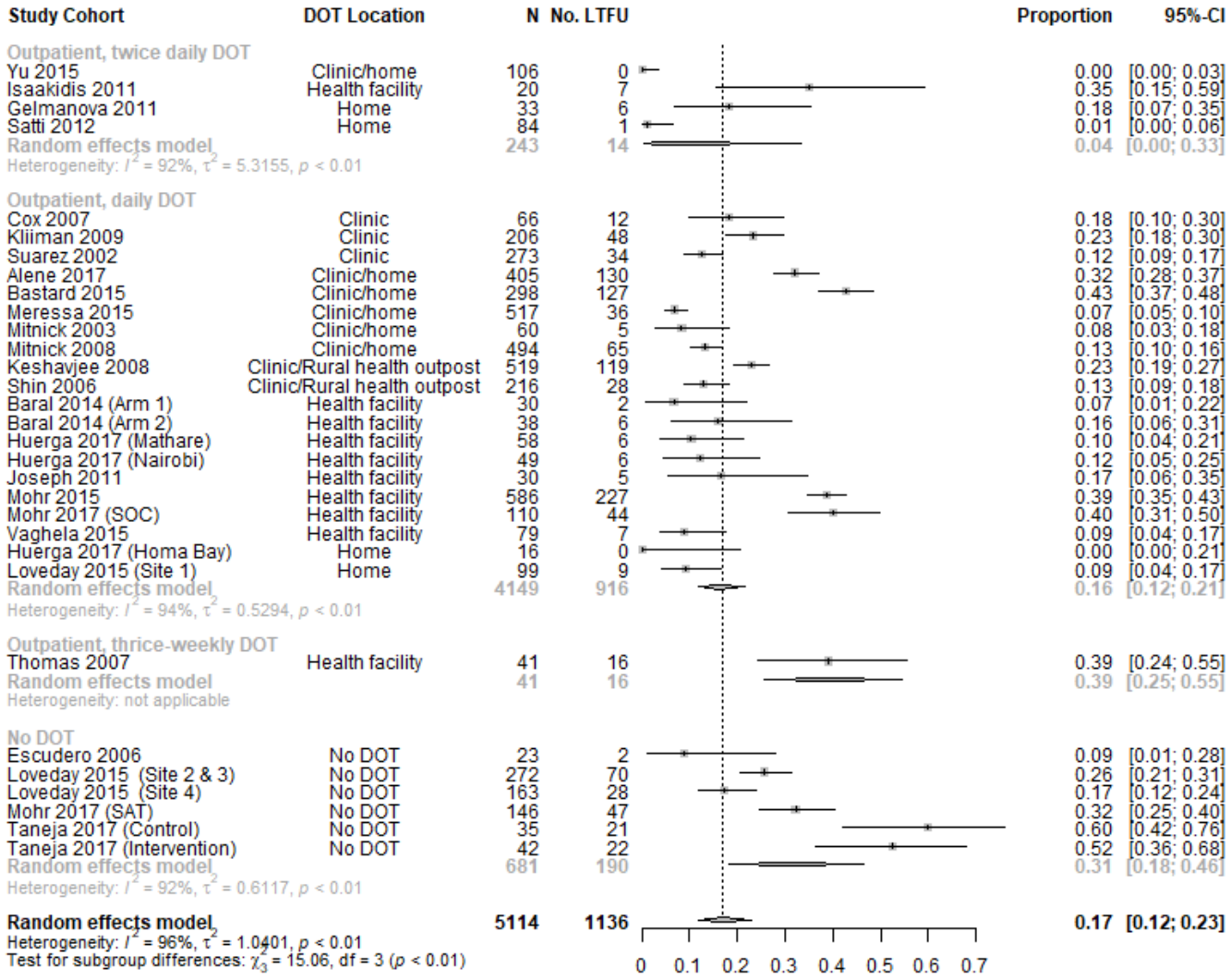


**Figure S11. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by DOT frequency during the continuation phase.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; HCW = health care worker; CHW = community health worker; DOT = daily observed therapy.

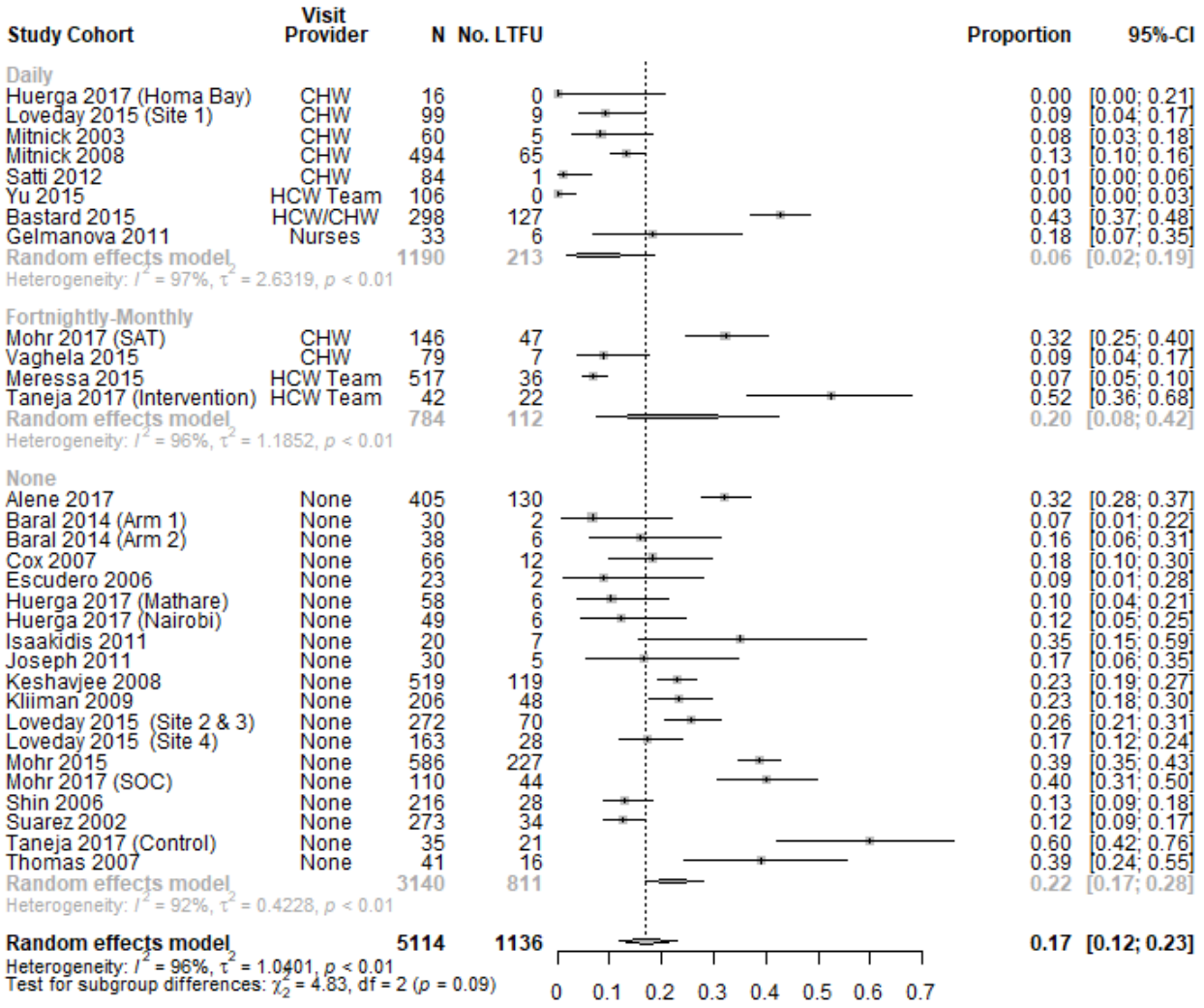


**Figure S12. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by frequency of home visits throughout treatment.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. The statistical heterogeneity in subgroup with daily home visits was decreased to $I^2$=90% when Bastard 2015 was excluded, with a pooled proportion LTFU of 4% (95%CI 1 to 13%), or when both Bastard 2015 and Gelmanova 2011 were excluded, with a pooled proportion LTFU of 3% (95% CI 1 to 12%). Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; HCW = health care worker; CHW = community health worker.

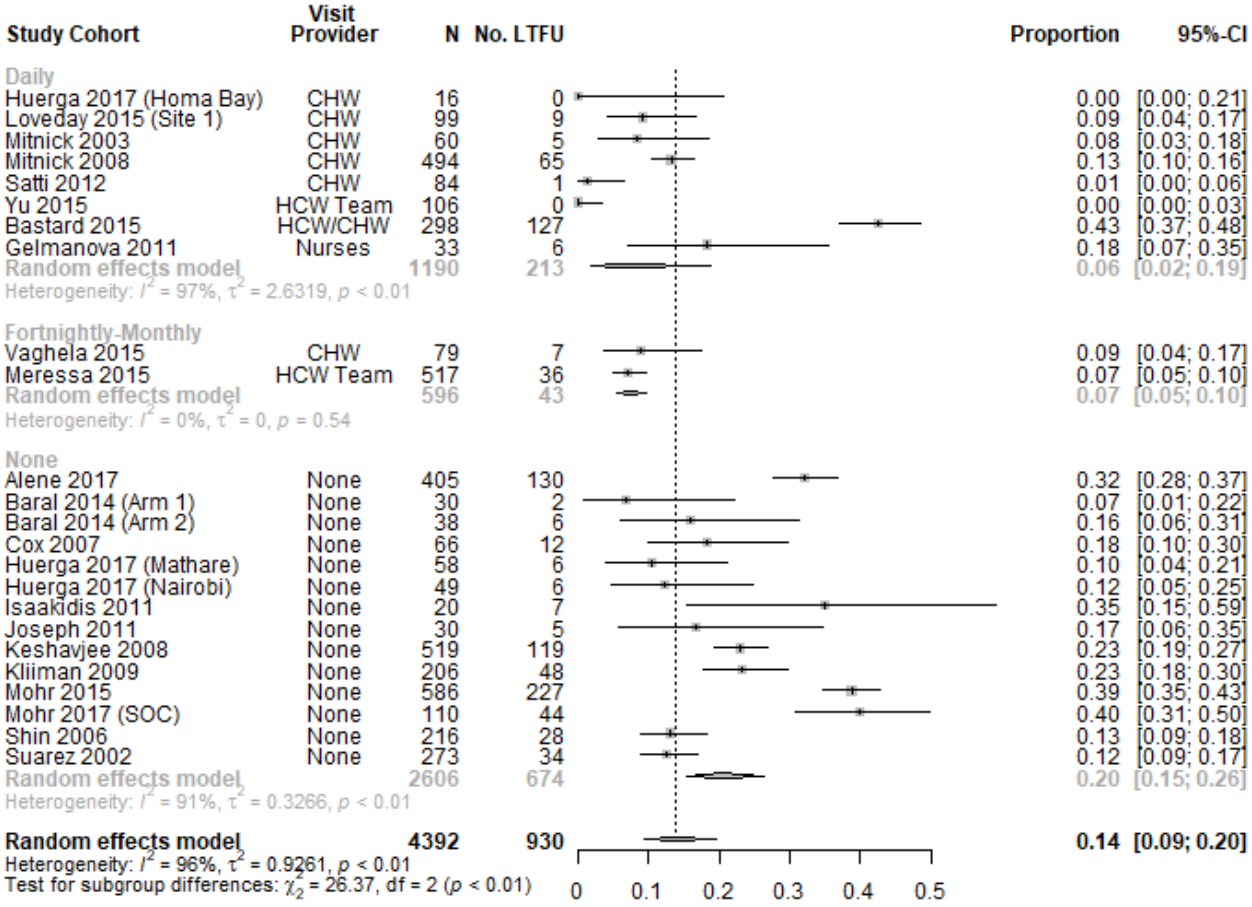


**Figure S13. Forest plot of proportions lost to follow-up (LTFU) stratified by frequency of home visits throughout treatment, among study cohorts that received twice-daily or daily DOT.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval; HCW = health care worker; CHW = community health worker.

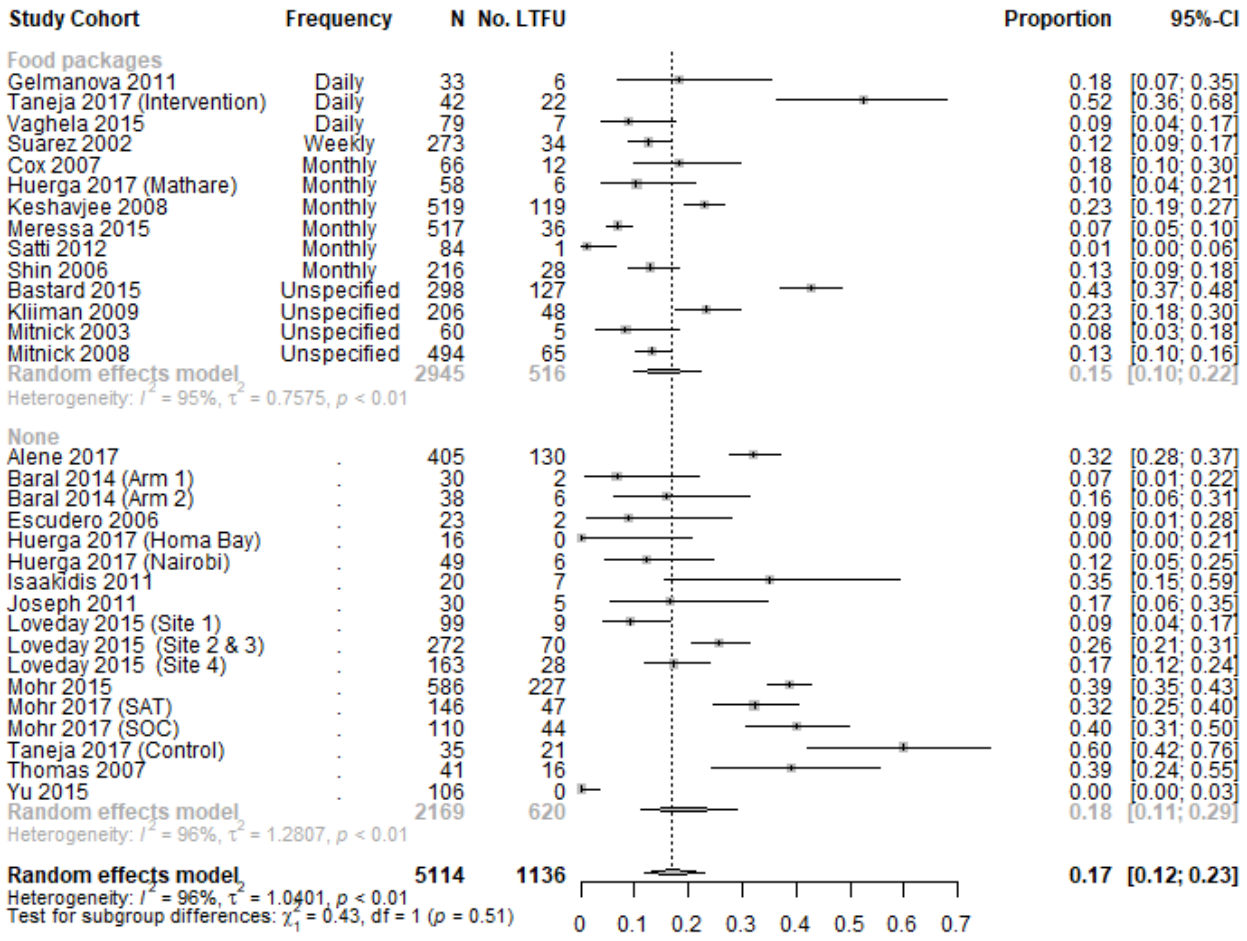


**Figure S14. Forest plot of proportions lost to follow-up (LTFU) across all study cohorts stratified by whether of food was provided during treatment.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

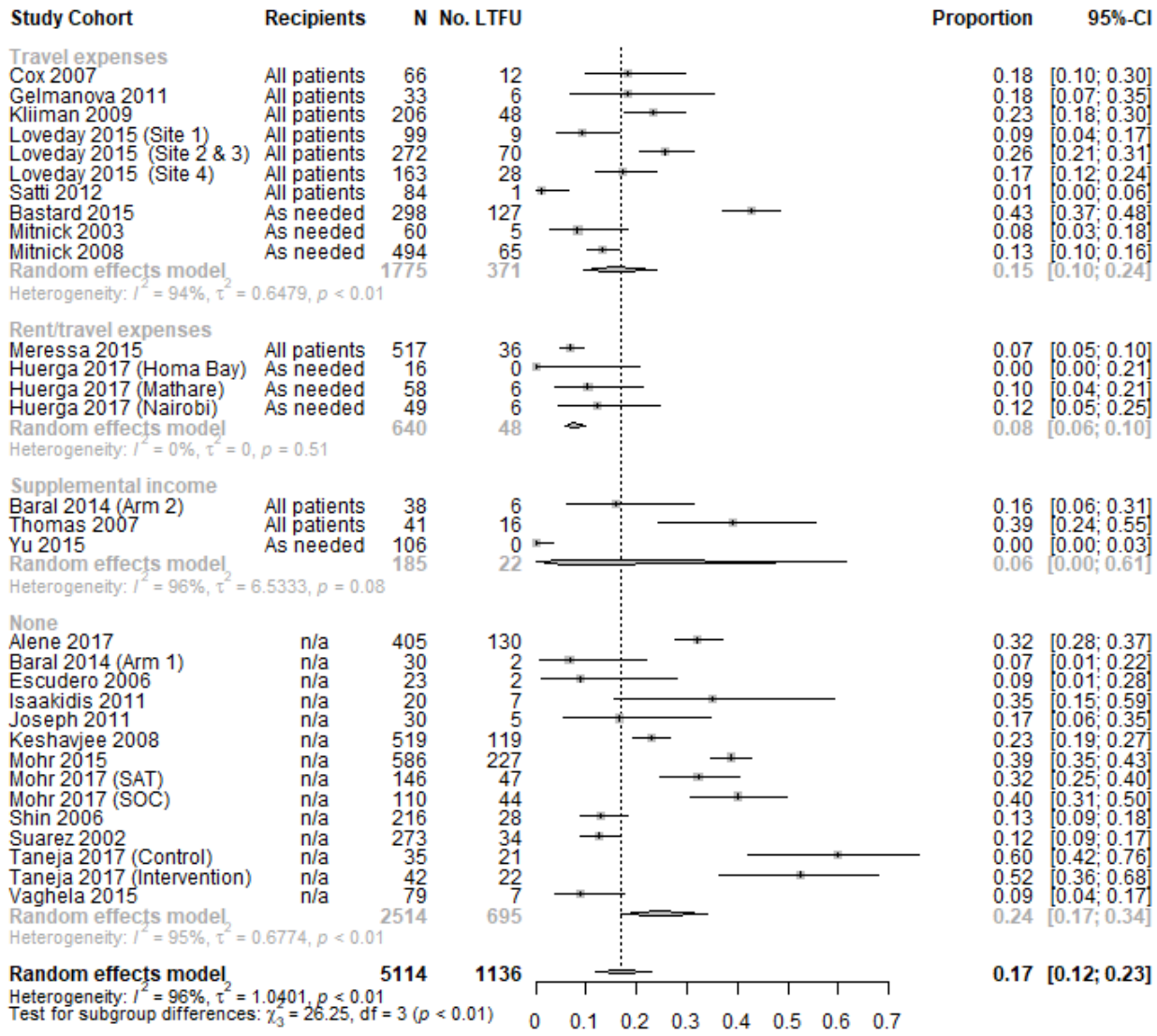


**Figure S15. Forest plot of proportions lost to follow-up across all study cohorts stratified by type of financial support provided during treatment.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

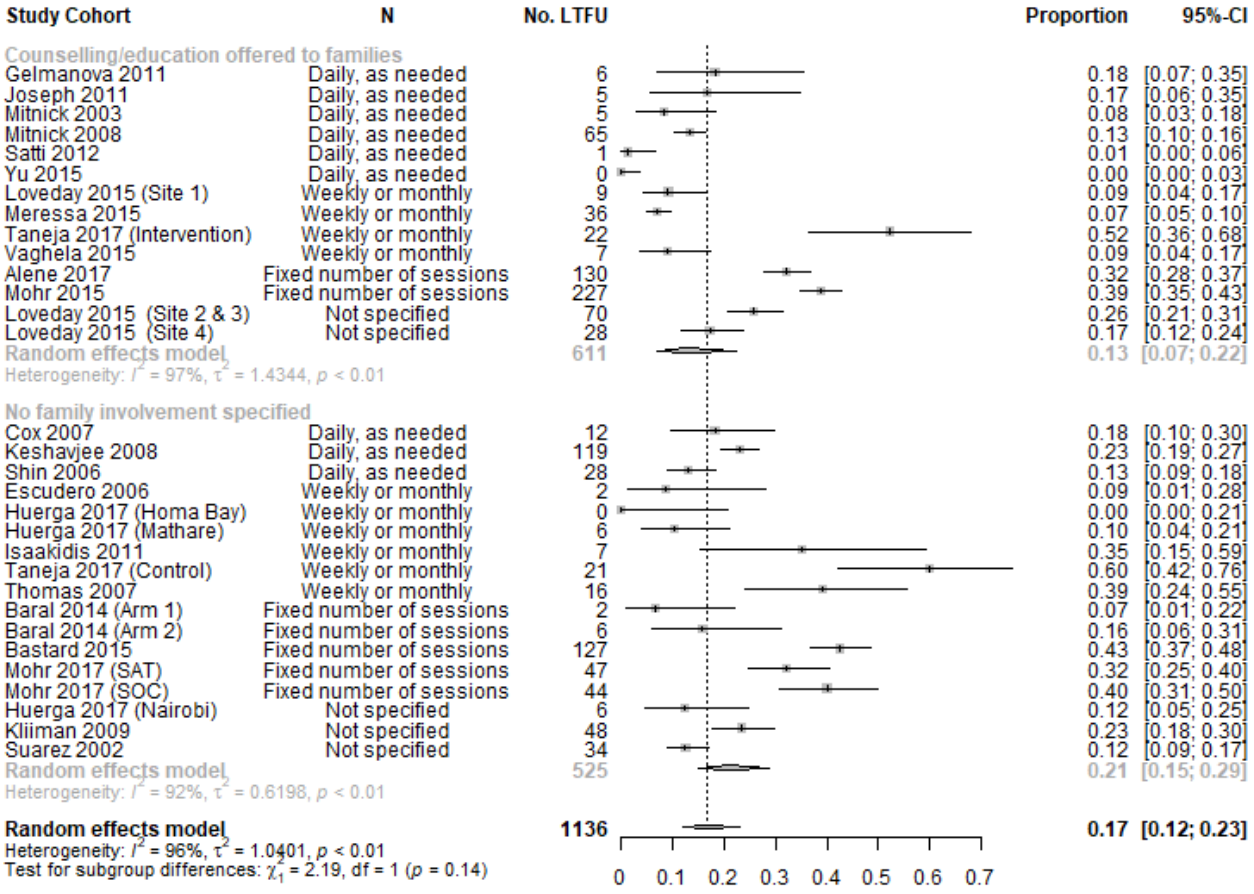


**Figure S16. Forest plot of proportions lost to follow-up across all study cohorts stratified by whether families were offered counselling and education.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

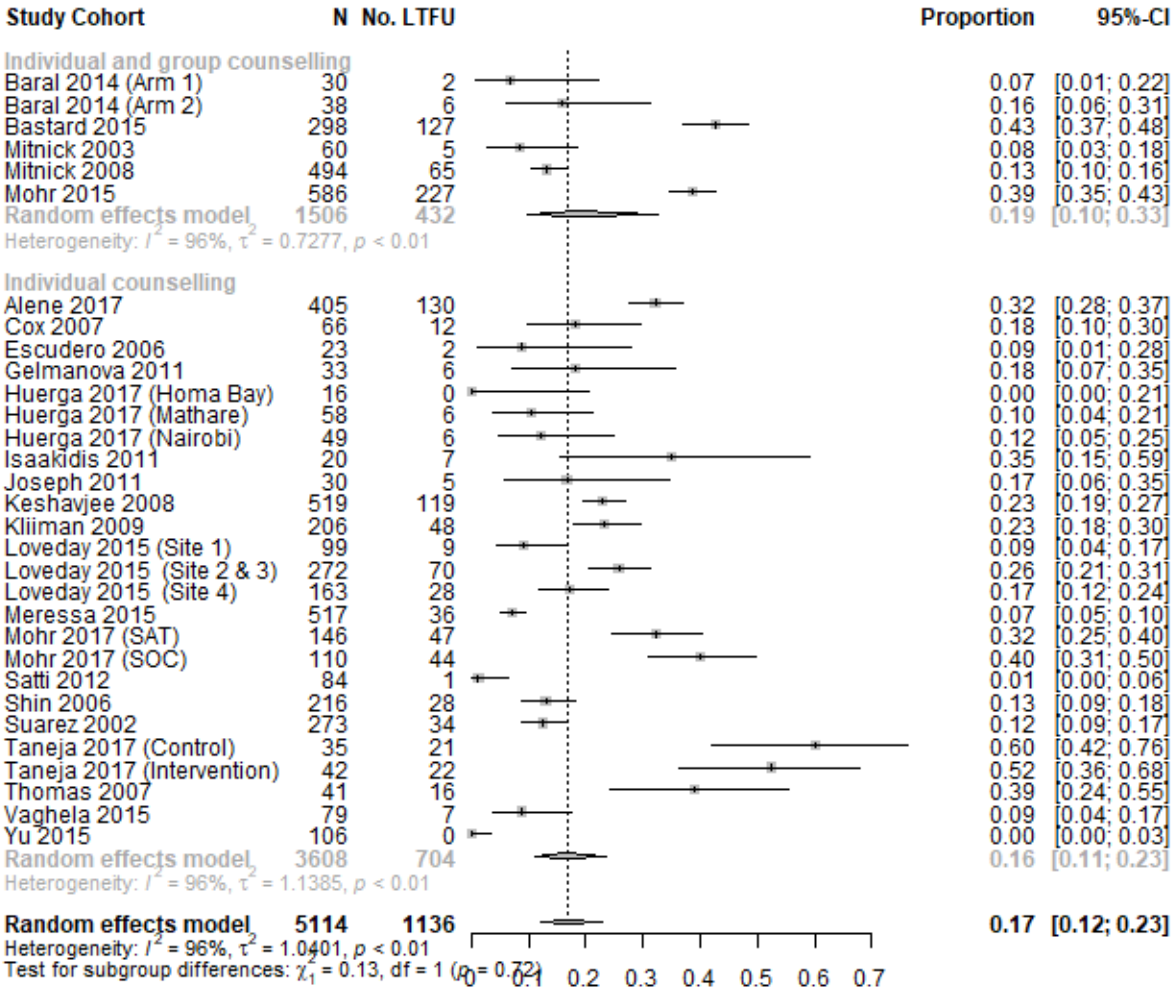


**Figure S17. Forest plot of proportions lost to follow-up across all study cohorts stratified by whether group counselling was offered in addition to individual counselling.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

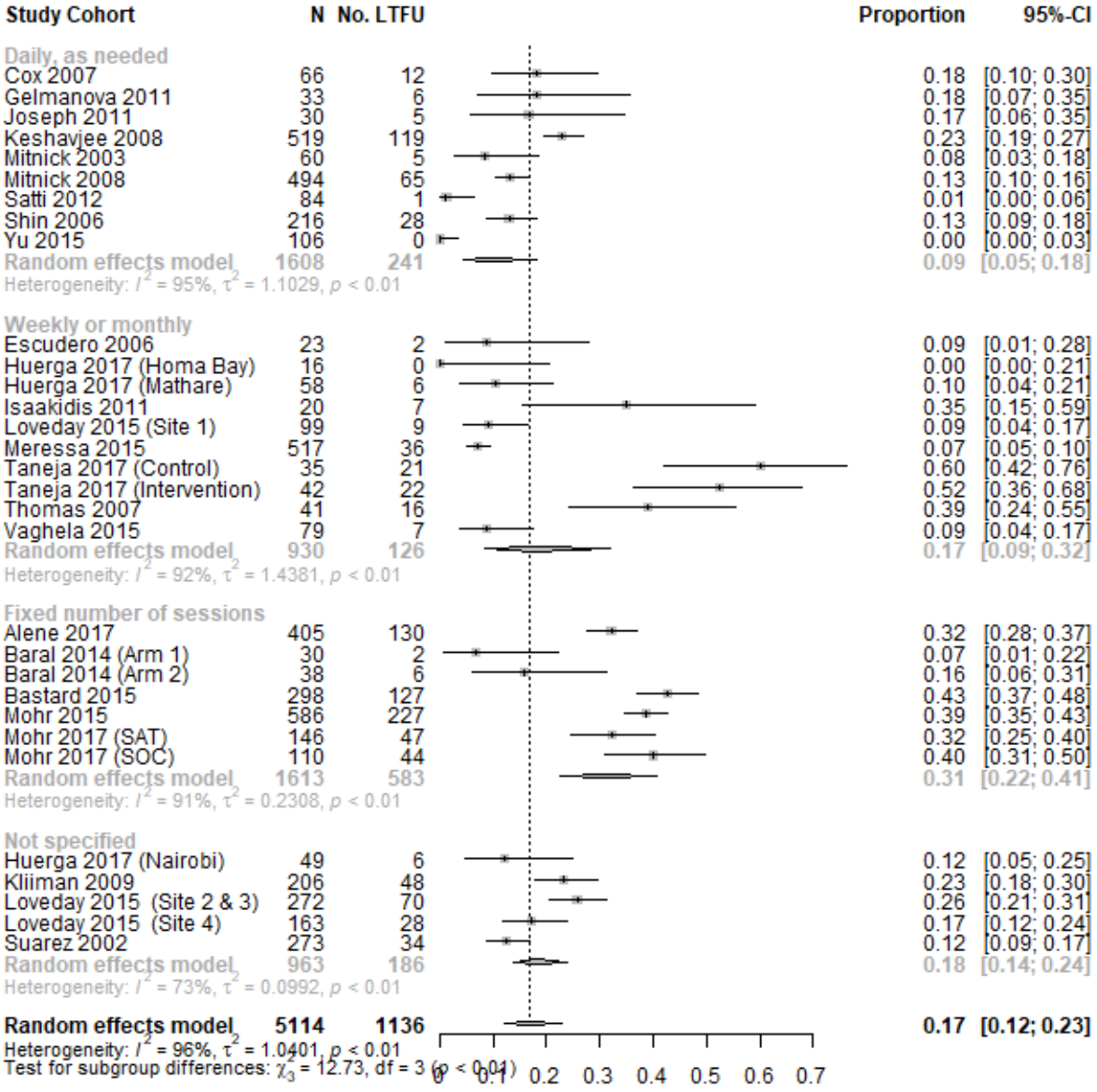


**Figure S18. Forest plot of proportions lost to follow-up across all study cohorts stratified by frequency of individual counselling provided during treatment.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

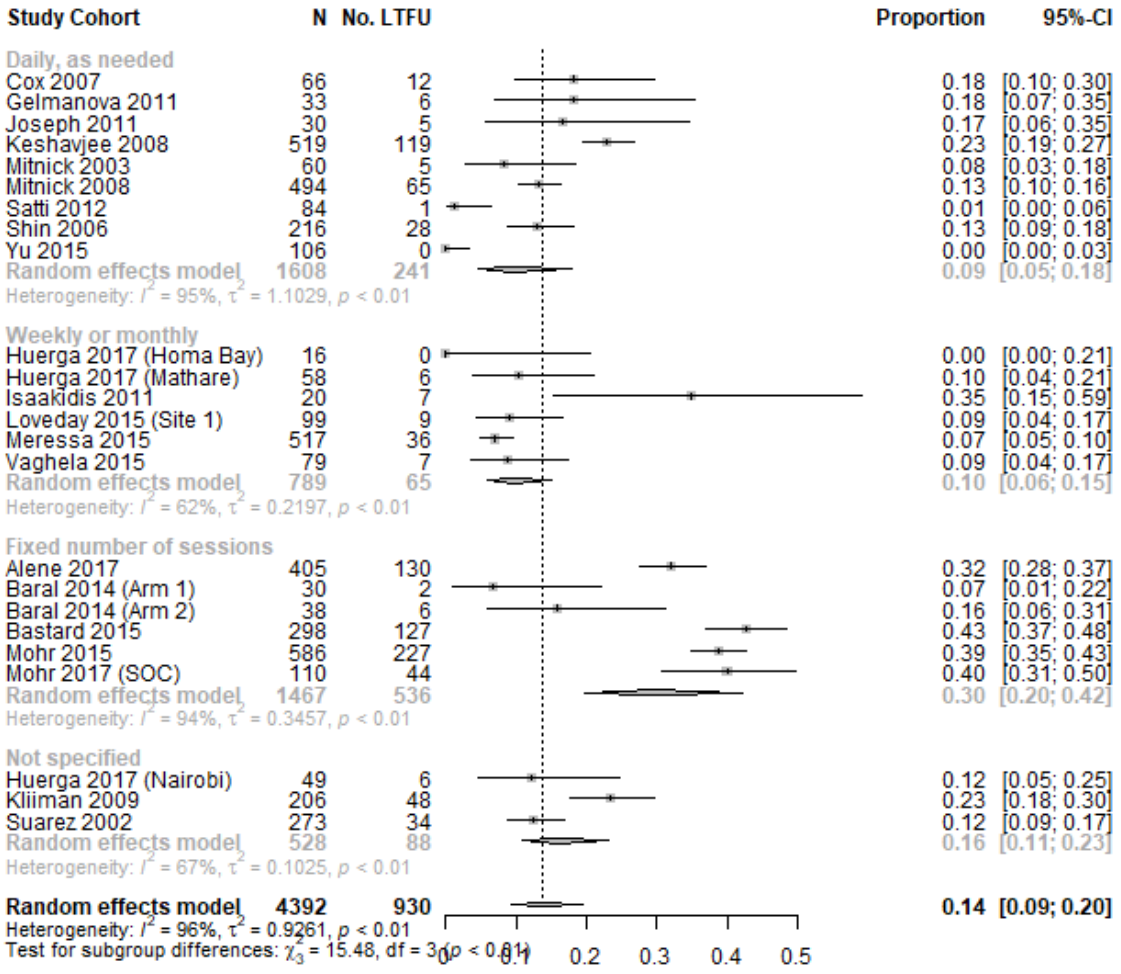


**Figure S19. Forest plot of proportions lost to follow-up stratified by frequency of individual counselling provided during treatment, among study cohorts that received twice-daily or daily DOT.** Patients who died, failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

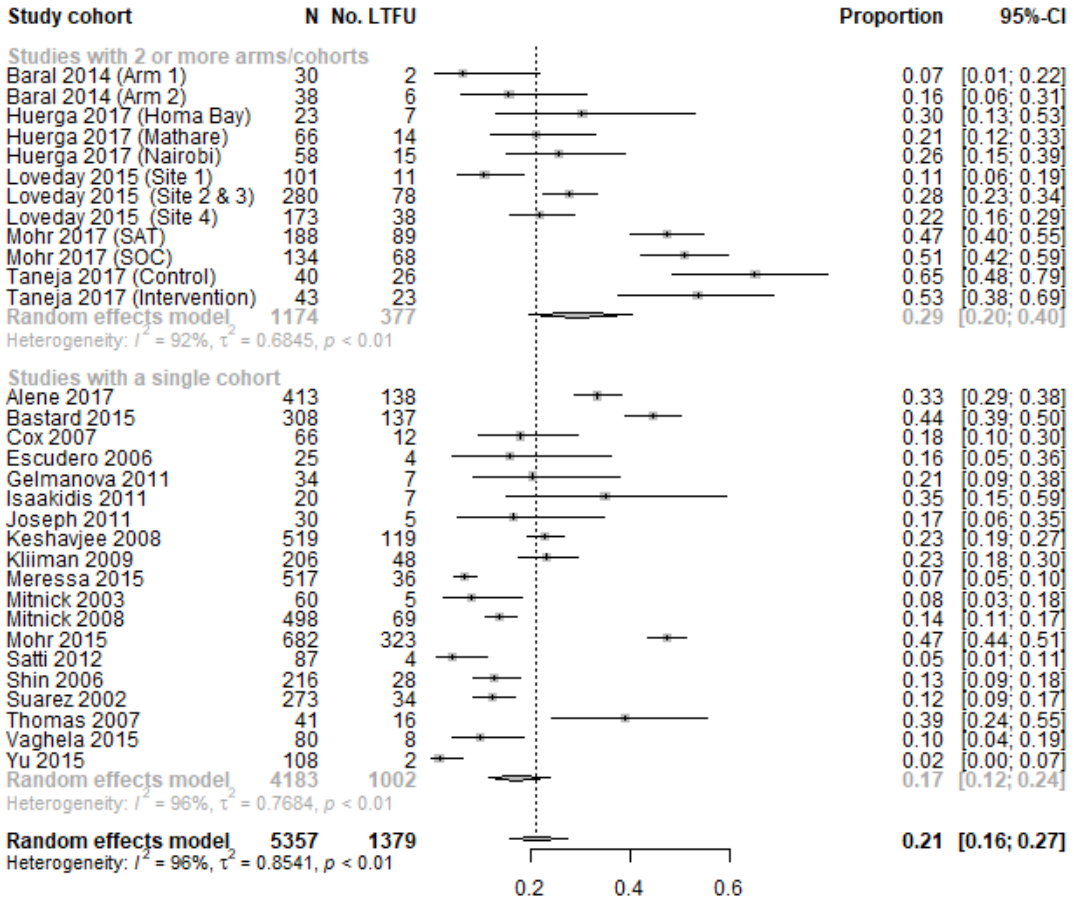


**Figure S20. Forest plot of proportions lost to follow-up (LTFU), including those who transferred out or without reported final outcomes, across all study cohorts.** Patients who died or failed treatment were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

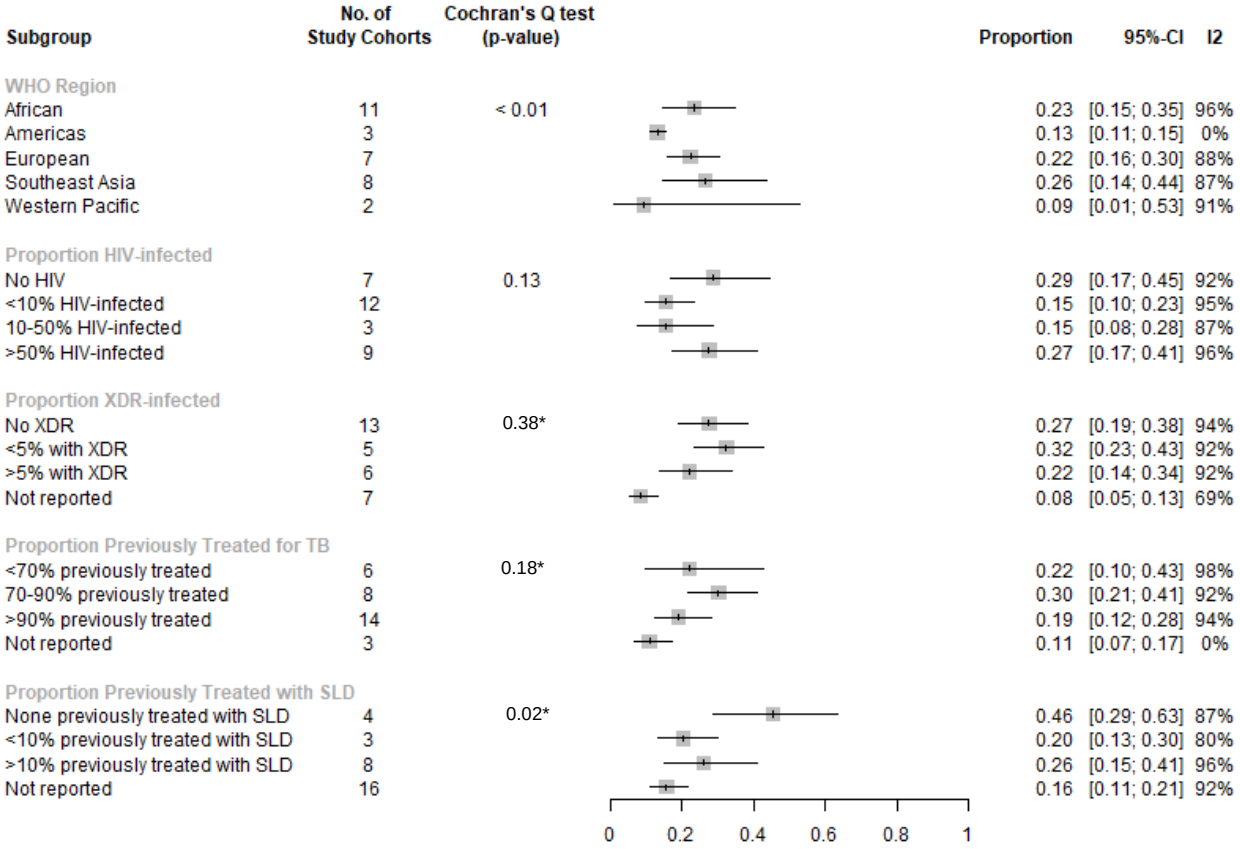


**Figure S21. Forest plot of pooled proportions lost to follow-up, including those who transferred out or whose treatment outcome was not evaluated, across all study cohorts, stratified by study cohort characteristics.** Patients who died or failed treatment were excluded. *Study cohorts that did not report this parameter were excluded from the Cochran's Q test for subgroup differences.

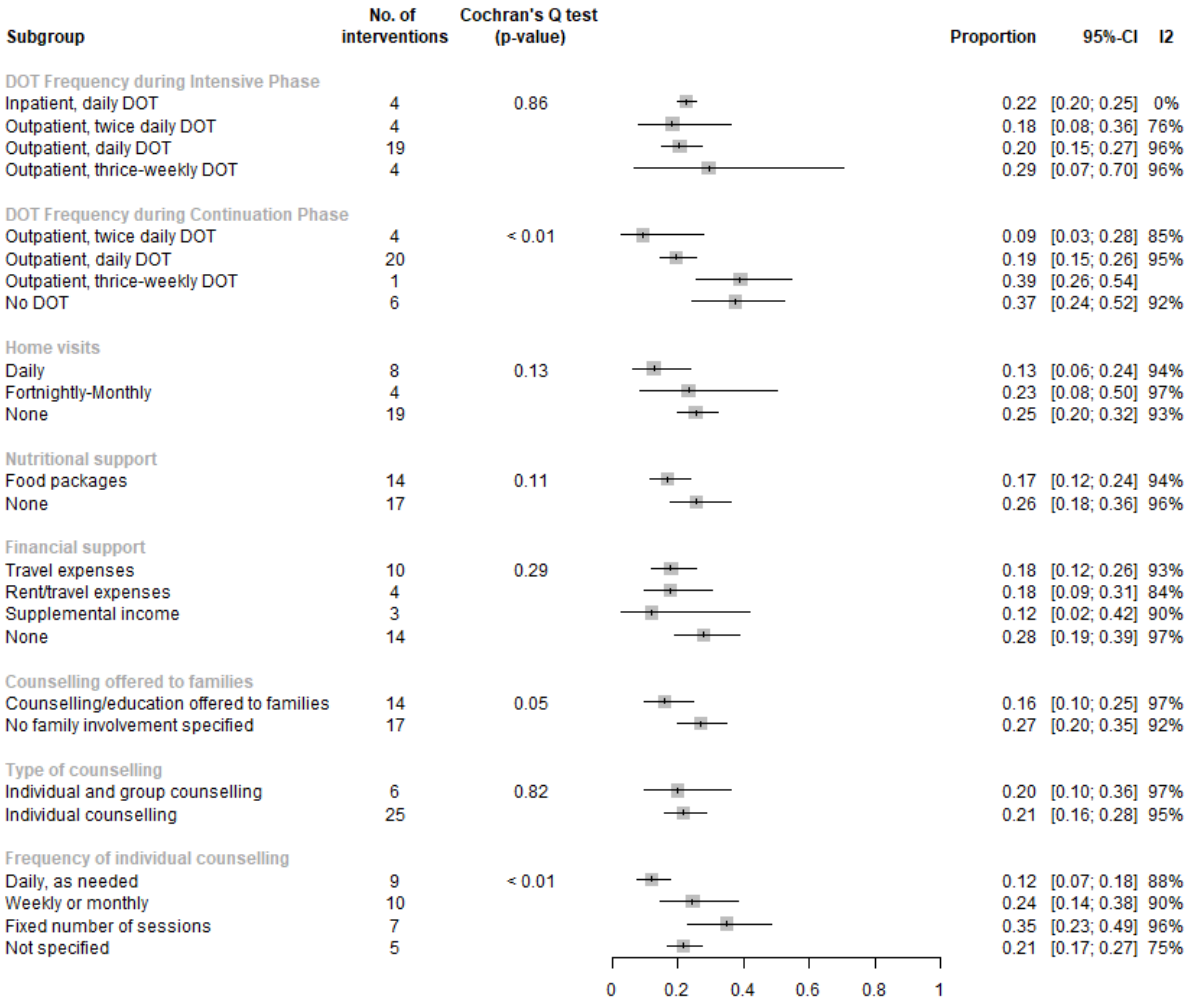


**Figure S22. Forest plot of pooled proportions lost to follow-up, including those who transferred out or whose treatment outcome was not evaluated, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died or, failed treatment were excluded.

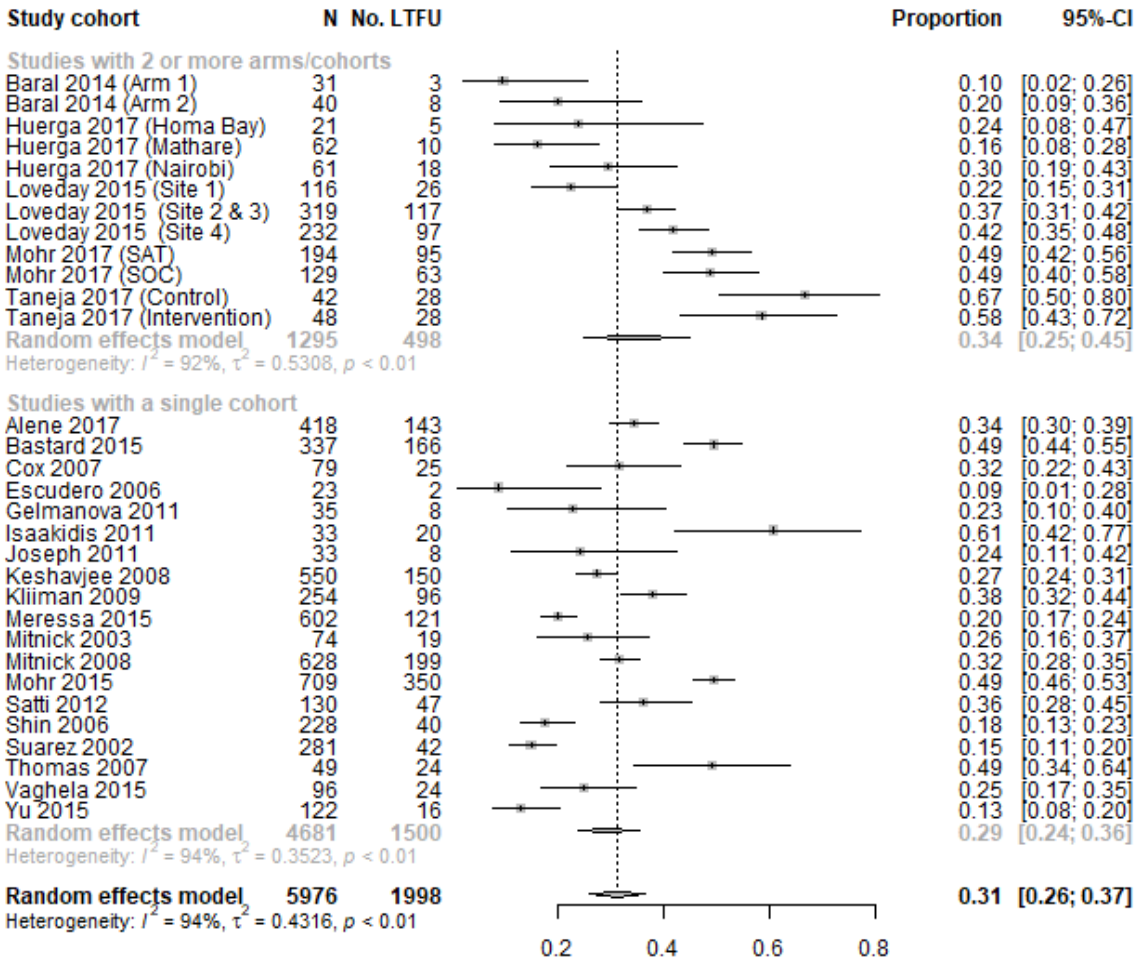


**Figure S23. Forest plot of proportions lost to follow-up (LTFU), including those who died, across all study cohorts.** Patients who failed treatment, transferred out or whose treatment outcome was not evaluated, were excluded. Abbreviations: SAT = self-administered therapy; SOC = standard of care; CI = confidence interval.

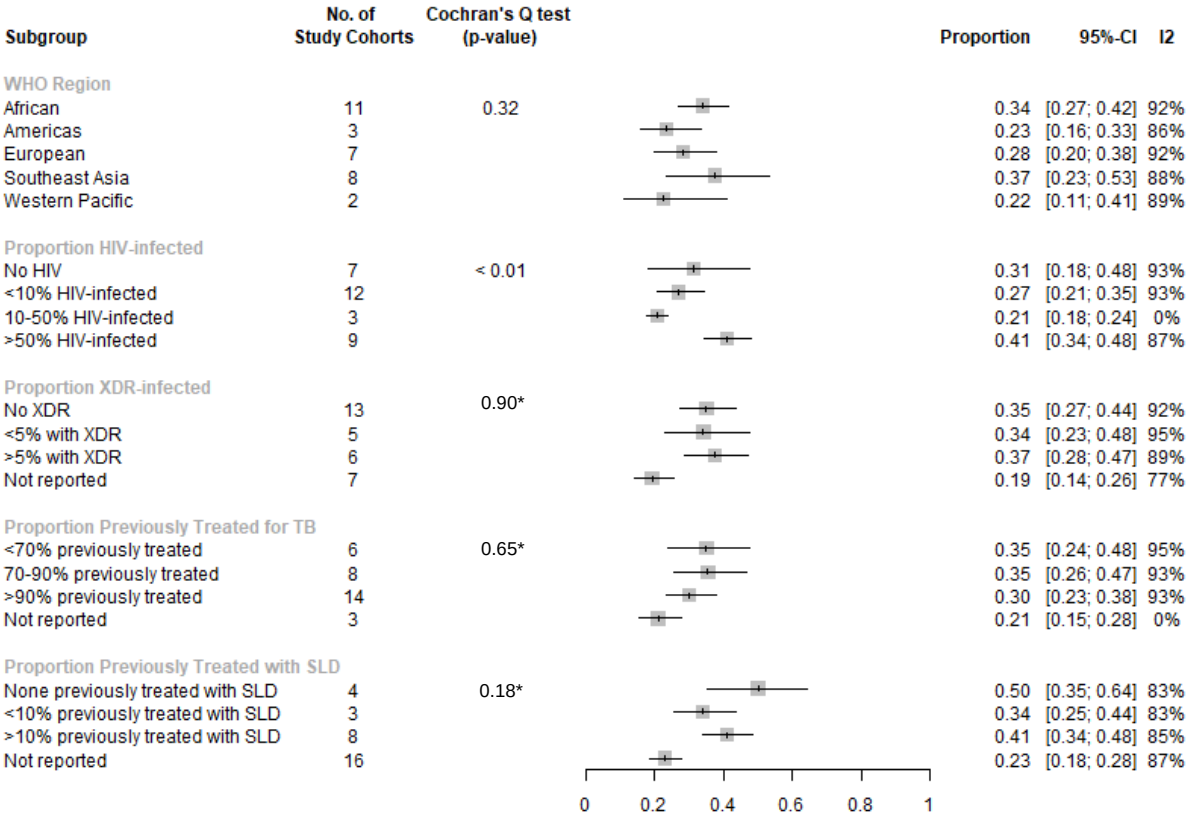


**Figure S24. Forest plot of pooled proportions lost to follow-up, including those who died, across all study cohorts, stratified by study cohort characteristics.** Patients who failed treatment, who transferred out or whose treatment outcome was not evaluated, were excluded. *Study cohorts that did not report this parameter were excluded from the Cochran's Q test for subgroup differences.

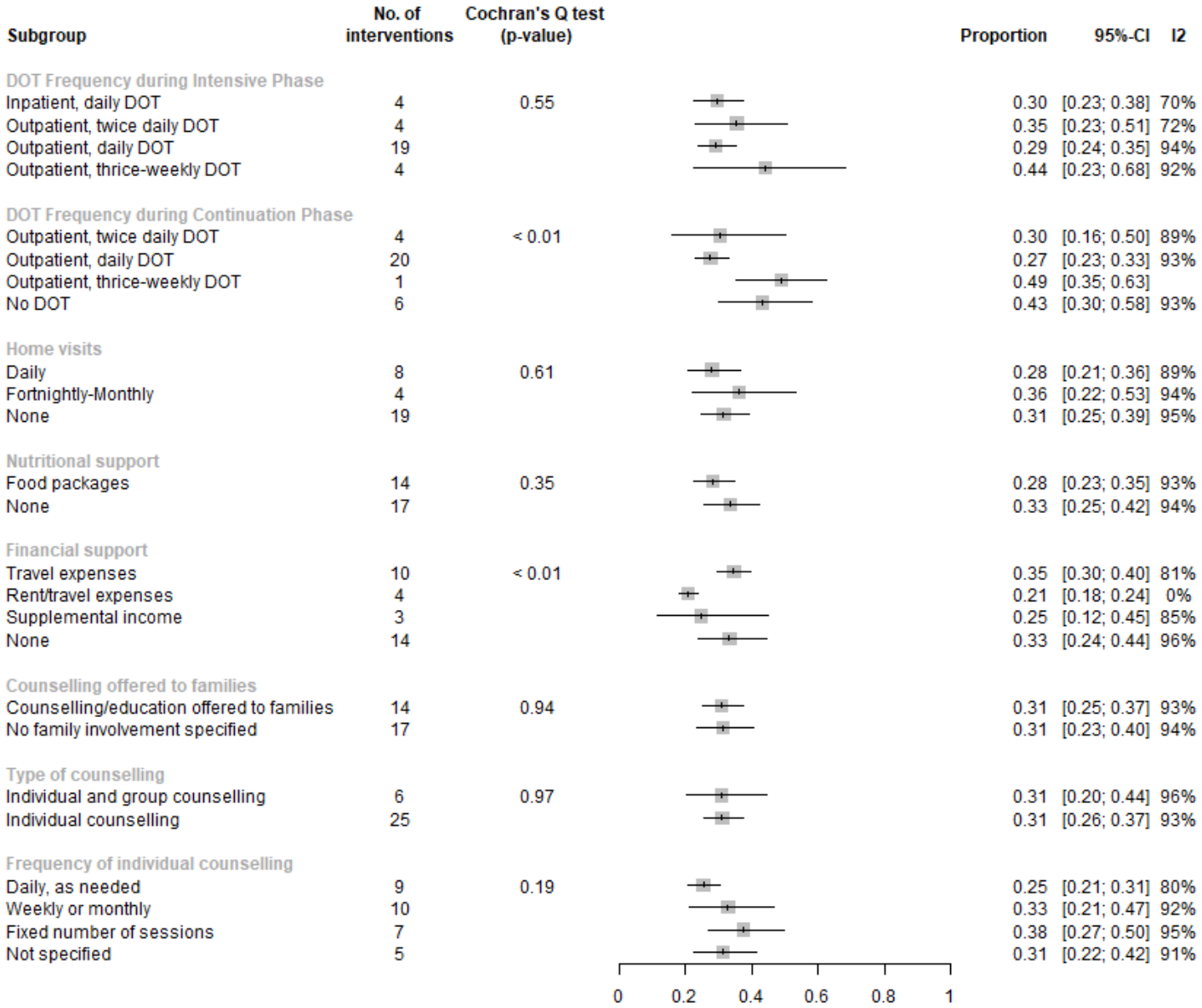


**Figure S25. Forest plot of pooled proportions lost to follow-up, including those who died, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

**No HIV**

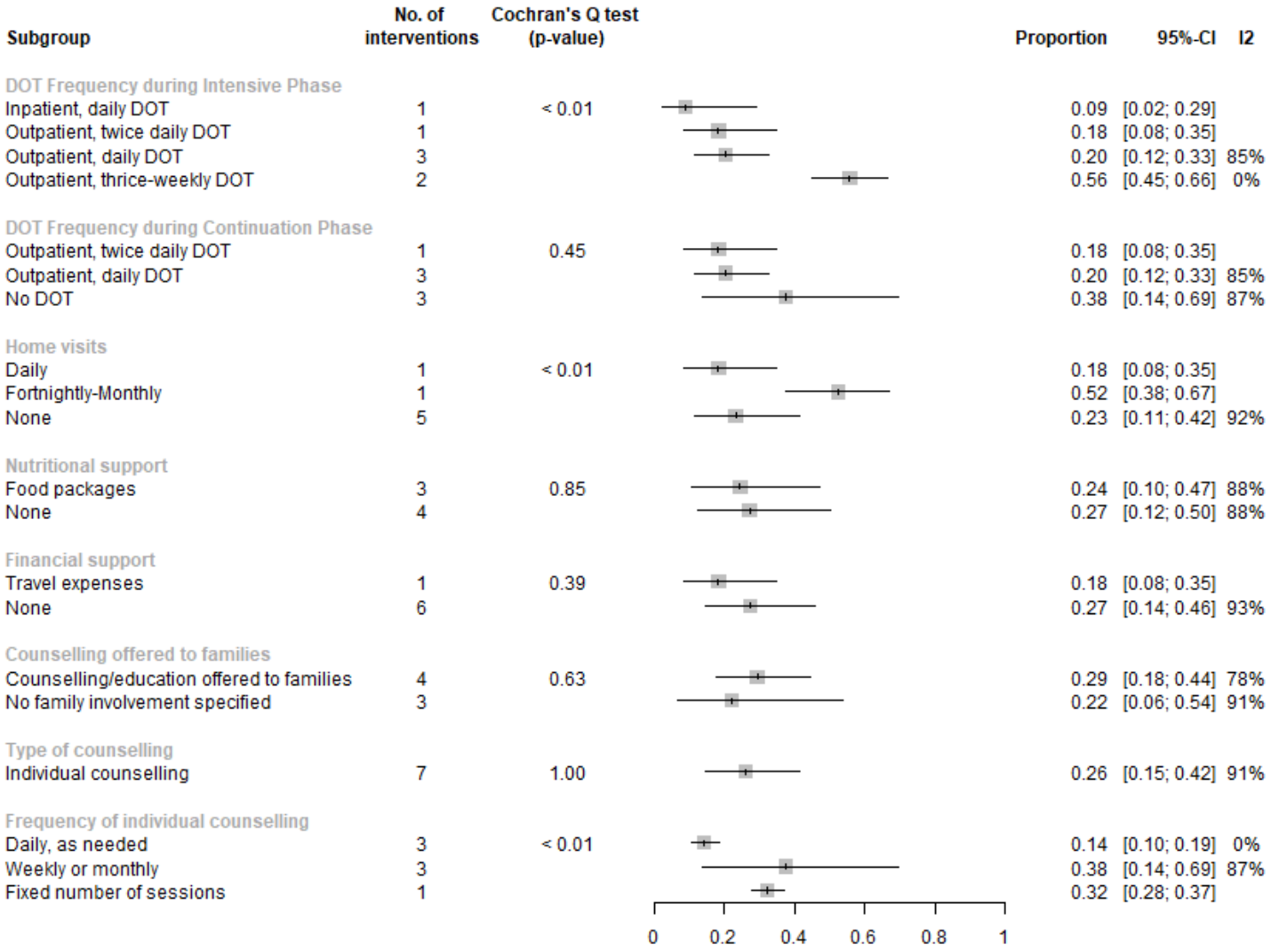


**Figure S26. Forest plot of pooled proportions lost to follow-up among study cohorts with no reported HIV, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

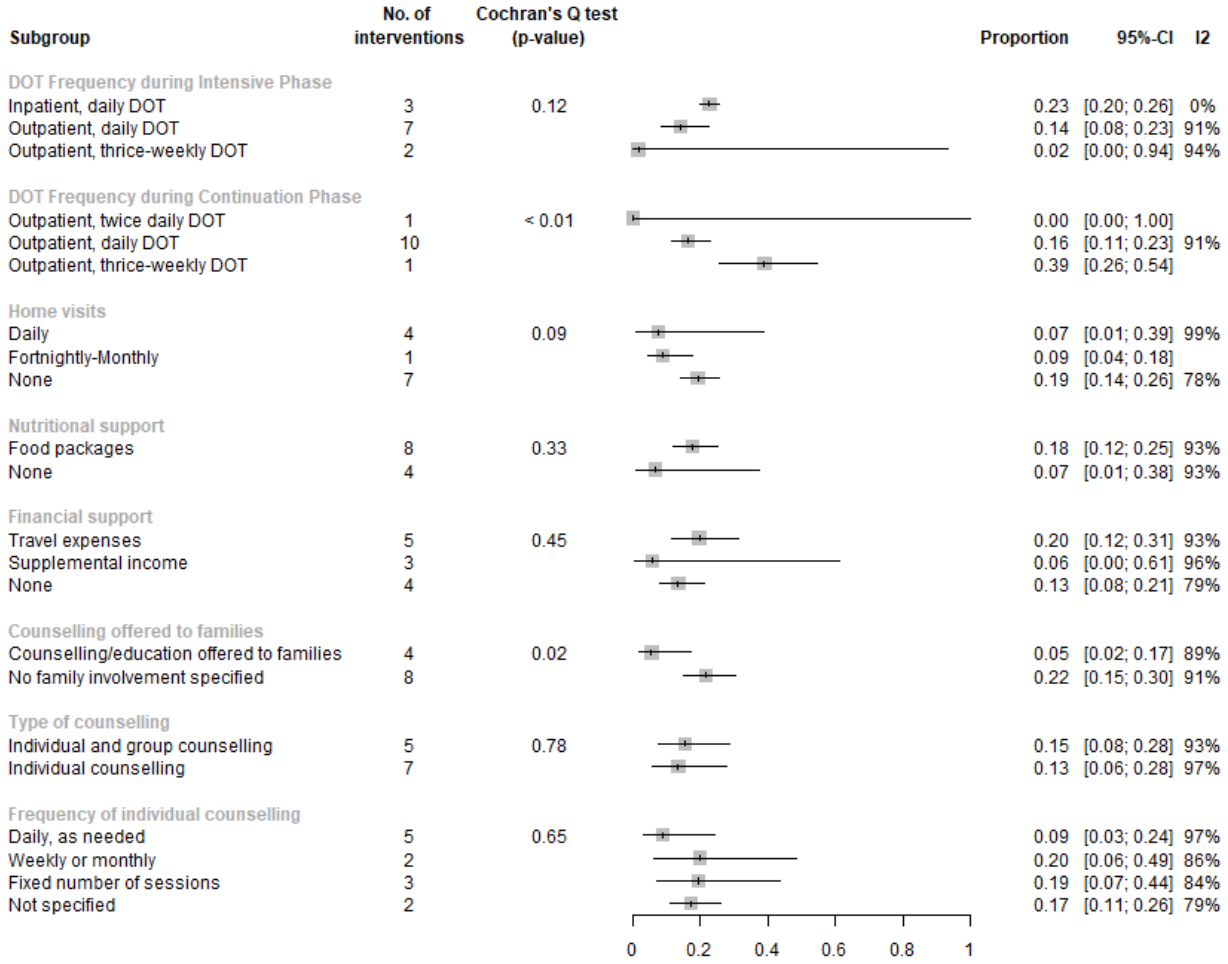


**Figure S27. Forest plot of pooled proportions lost to follow-up among study cohorts with less than 10% HIV prevalence, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

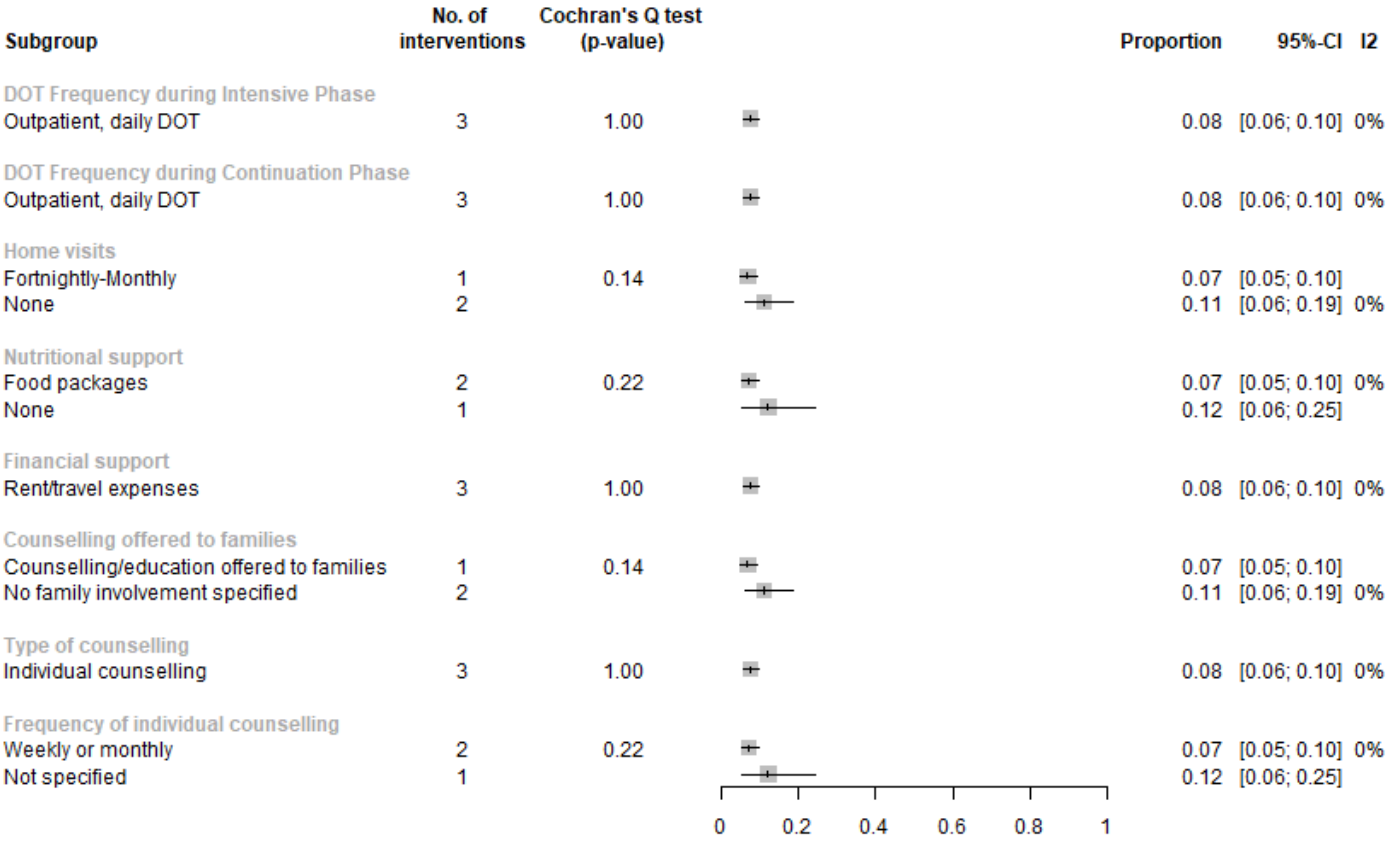


**Figure S28. Forest plot of pooled proportions lost to follow-up among study cohorts with 10 to 50% HIV prevalence, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

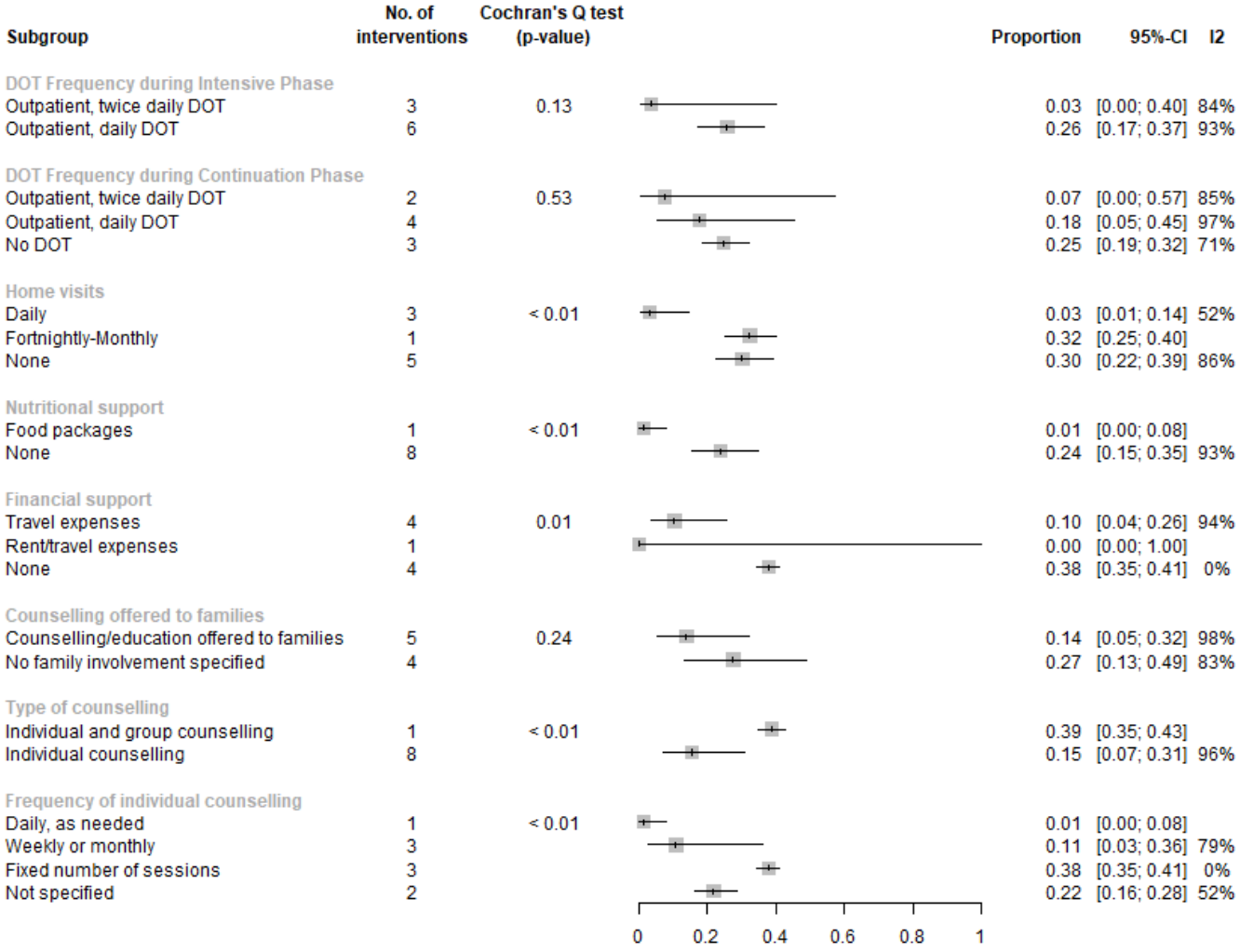


**Figure S29. Forest plot of pooled proportions lost to follow-up among study cohorts with greater than 50% HIV prevalence, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

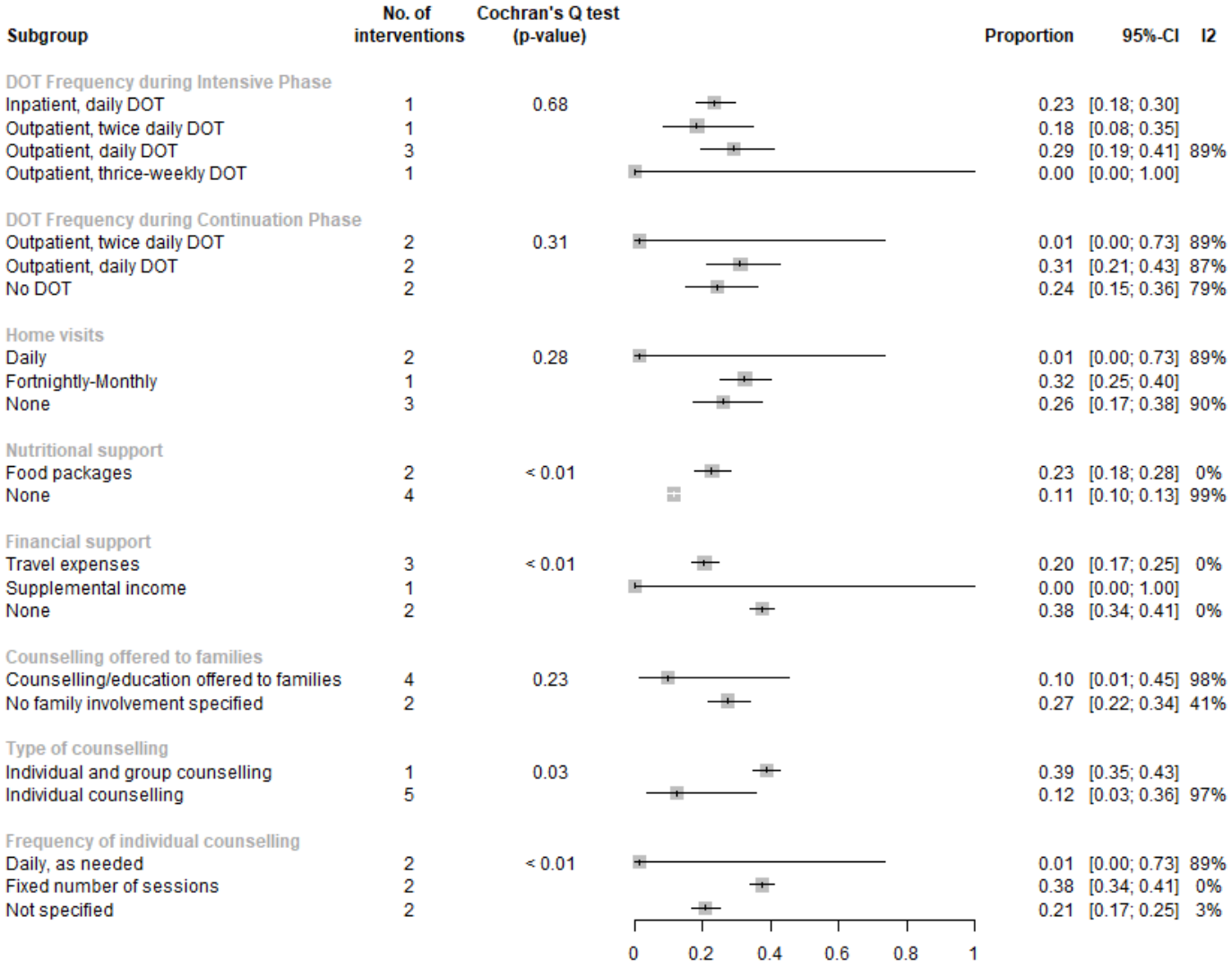


**Figure S30. Forest plot of pooled proportions lost to follow-up among study cohorts with less than 70% previously treated patients, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

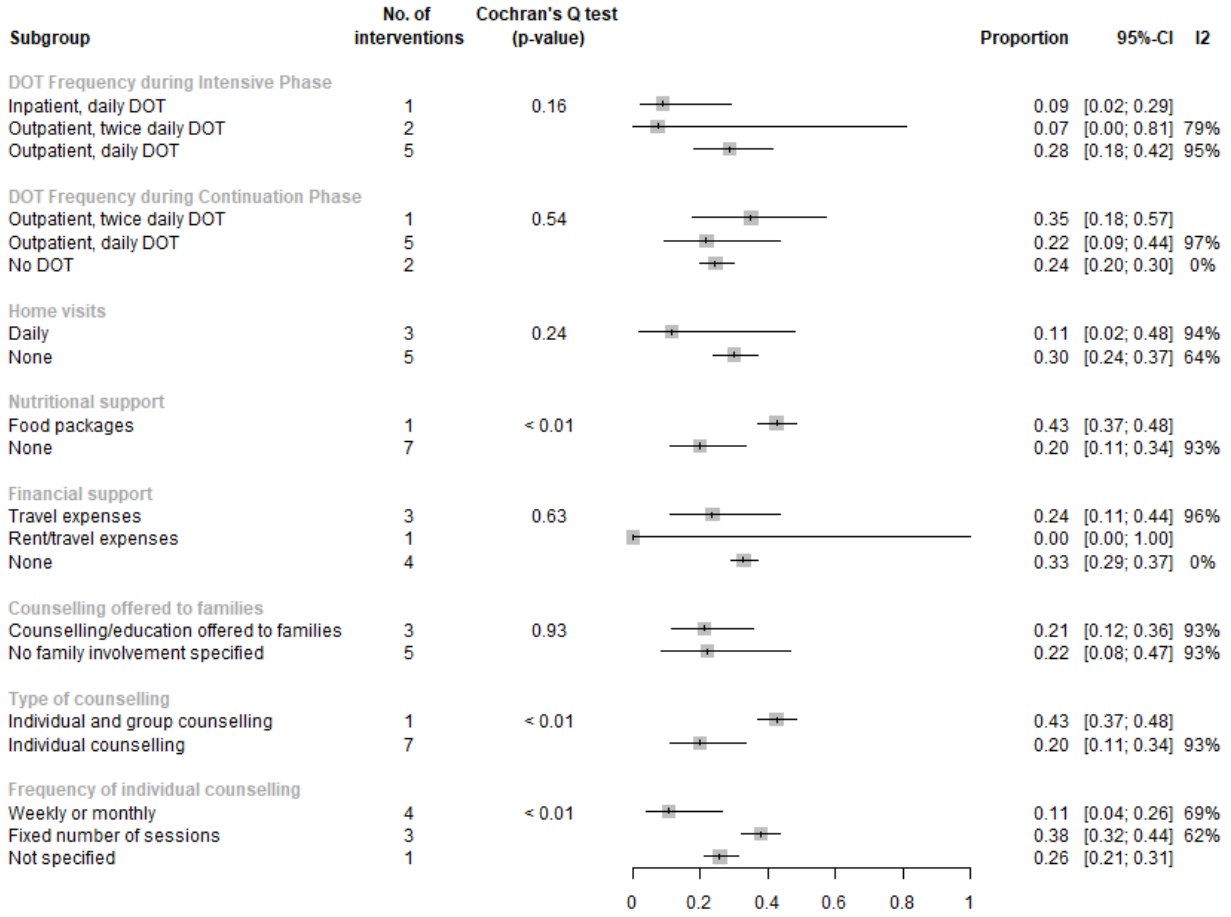


**Figure S31. Forest plot of pooled proportions lost to follow-up among study cohorts with 70% to 90% previously treated patients, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

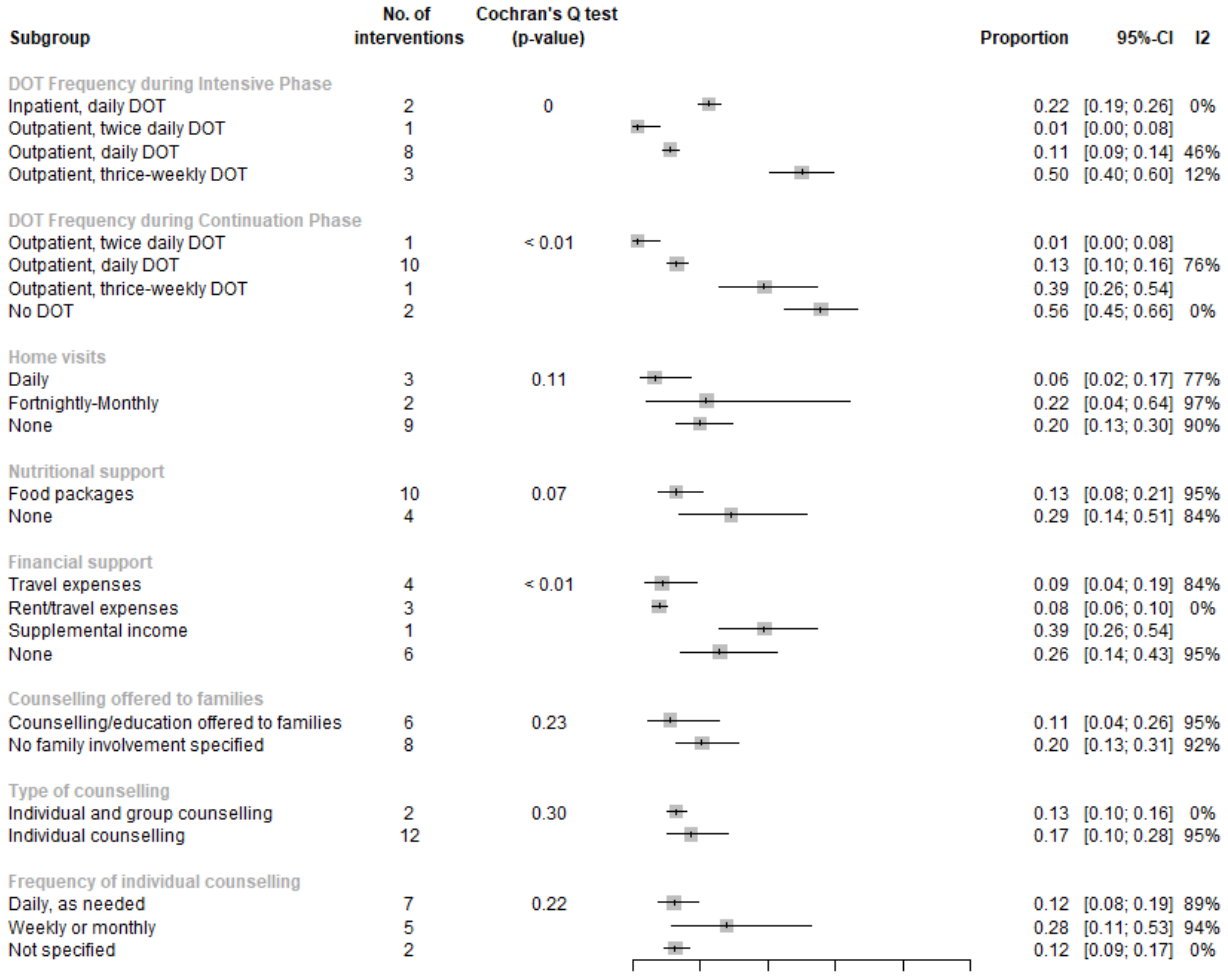


**Figure S32. Forest plot of pooled proportions lost to follow-up among study cohorts with greater than 90% previously treated patients, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

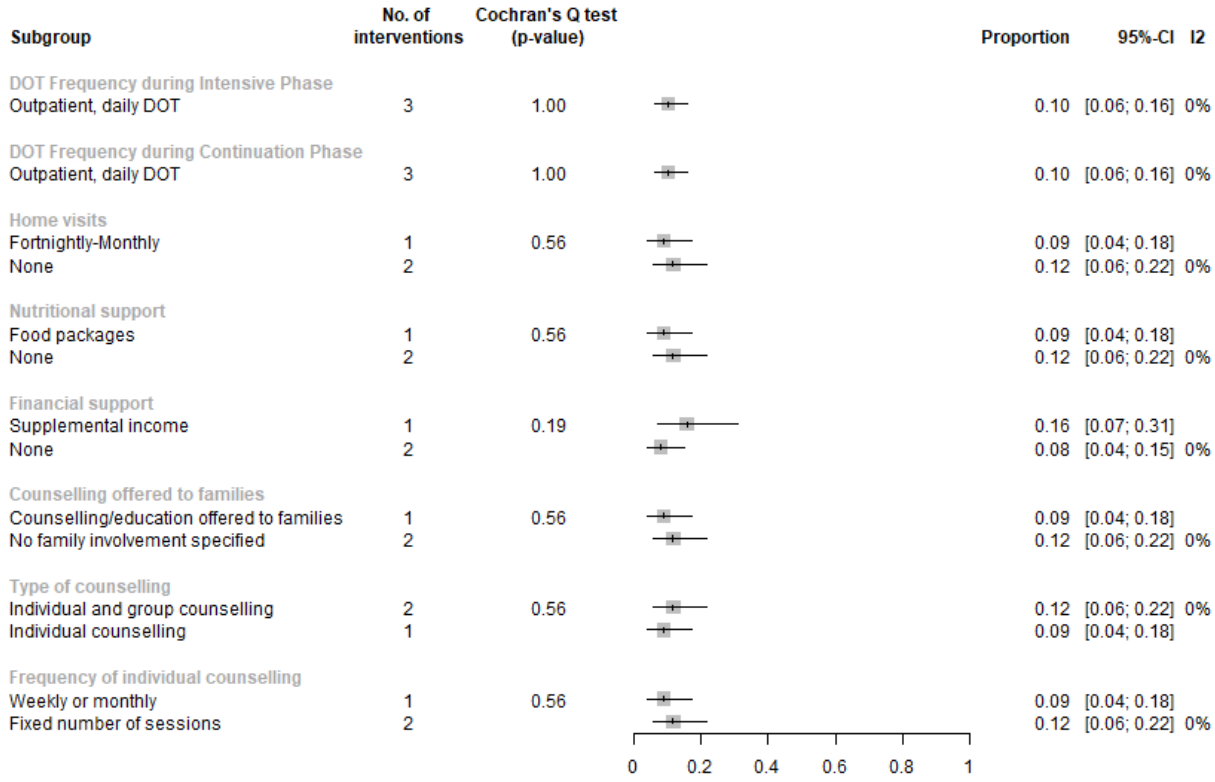


**Figure S33. Forest plot of pooled proportions lost to follow-up among study cohorts that did not report the proportion of patients who were previously treated for TB, stratified by frequency of directly observed therapy (DOT) during the intensive and continuation phase, and by type of adherence support provided during treatment.** Patients who died, failed treatment, transferred out or whose treatment outcome was not evaluated were excluded.

**Table S6. Additional treatment adherence outcomes reported by study cohorts**

| Study (sample size, n) | Outcome | Result |
|---|---|---|
| **Gelmanova 2011 (n= 38)** | % Adherence (proportion of prescribed doses taken), mean (SD) | 79.0 (16.9) |
| **Bastard 2015 (n=323)** | Overall duration of interruptions (days) | Median: 3 (IQR 2-7) |
| | Max duration of interruptions per patient (days) | Median: 18 (IQR 8-27) |
| | Time to first interruption, median (IQR), days | 95 (42-205) |
| | Time to first interruption, No. (%) | |
| | ≤ 3 months | 155 (48.0) |
| | 3 to <6 months | 75 (22.2) |
| | 6 to 12 months | 50 (15.5) |
| | >12 months | 43 (13.3) |
| | Incidence of interruptions due to patient, median (IQR) | 1.03 (0.39-2.05) |
| | Incidence of interruptions due to adverse effects median (IQR) | 0 (0-0.17) |
| | Duration of gaps between interruptions, median (IQR), days | 13 (5-37) |
| | Interruptions of >2 days, No. (%) of patients | 272 (84.2) |
| | Gaps between interruptions >10 days, No. (%) | 194 (60.1) |
| | Adherence ≥ 80%, No. (%) | 127 (39.3) |
| **Shin 2006 (n=244)** | % missed doses (of all prescribed doses), median (range) | 5 (0-45) |
| | <2% missed doses | 52 (21.3) |
| | ≥2% and <5% missed doses | 68 (27.9) |
| | ≥5% and <11.0% missed doses | 62 (25.4) |
| | ≥11% missed doses | 62 (25.4) |

**Table S7. Summary of feasibility and implementation issues reported by included studies**

| Study ID | Feasibility of intervention |
|---|---|
| Gelmanova 2011 | The authors estimated an average per patient cost enrolled in the Sputnik program of approximately US$6.50/day, compared to the alternative of in-patient care for the duration of treatment, ranging from US$9.30/day to as high as US$35.00/day. |
| Loveday 2015 | During the implementation and expansion of decentralized care, the four decentralized sites included in the study varied in number of days of hospitalization (from an average of 96 to 180 days), which suggested there were site differences in interpreting and implementing guidelines. The authors concluded that this highlighted "the importance of regular monitoring and support during service expansion, to ensure health systems are functional and new programmes implemented in accordance with guidelines." Many patients were hospitalized longer than the study planned (80 days vs. 2 weeks). Furthermore, the intensity and fidelity of the intervention delivery varied by site: at site 1 where there was more financial resources and ownership/support from the district leadership, there were 16 mobile injection teams – compared to 2 each at sites 2 and 3, and none at site 4 – as well as "additional staff at the out-patient clinic who established systems, implementation of a locally developed patient treatment literacy programme and home assessment by a multidisciplinary team before patient discharge. These programme components were partially implemented at other decentralised sites. Additionally, authors from an earlier study under the same intervention (Brust 2012) concluded, "This illustrates the difficulty in changing a long-standing practice in MDR-TB treatment, where the hospital staff was reluctant to discharge patients who were still culture positive due to concerns that they could transmit the disease to family and/or friends in the community." The authors estimated "the operational costs of the home-based treatment model are approximately 25% those of the centralized in-patient model (B Margot, personal communication), suggesting that the home-based program is both effective and less expensive." |
| Meressa 2015 | The authors provided a gross estimate of program costs, exclusive of second-line drugs, at approximately $2000 per patient over the 2-year treatment period. These costs included: ancillary medications, laboratory monitoring (e.g. cultures, DST and other routine labs), food supplementation, transportation and accommodation for patients, home visits, capacity building, programme management, personnel training, salaries for dedicated staff, salary supplementation of national staff and some infrastructure improvements. These estimates do not include the overhead costs associated with hospital-based care. |
| Mitnick 2003 | The therapy costs per patient ranged from $504 to $32,383 (mean of $15,681 per patient), which were approximately 10 percent of those for hospitalized patients. In a qualitative study (Acha 2007) exploring the social support groups provided under this intervention, the authors found participation varied widely: average of 6 sessions per patient. There were undocumented activities related to participation (spillover effects, such as: "mutual home visits, weekend socialization, and significant friendships among group members", which could contribute to overall treatment adherence. There were logistical challenges to organizing the support groups, including: "finding adequate and low-cost meeting places, ensuring attendance, tardiness and delays (in large part due to Peruvian custom), finding willing facilitators, securing the resources to finance the sessions and excursions, and subsidising transportation costs in necessary cases." Also difficult to find willing facilitators due to TB-related stigma, and lack of prior experience. |
| Mohr 2017 | There was initial reluctance from some care providers to endorse the pilot intervention, as such, some eligible patients in pilot clinics were never offered SAT. |
| Suarez 2002 | The study showed second-line treatment for TB was feasible and cost-effective: "The total programme cost was affordable in the context of the National Tuberculosis Programme's budget, and the mean cost per DALY gained was around US$150-200." |
| Thomas 2007 | Finding DOT providers who could give intramuscular injection to the patients in rural areas was difficult. As such, rural patients received their injections from the village health worker when possible, otherwise either from a private provider by paying a fee or from the primary health center. The authors concluded, "all efforts should be taken before starting treatment to identify a |

| | |
|---|---|
| | DOT provider nearer to the patient's residence, who could administer injections, possibly by involving network of private providers available in most villages." |

**Table S8. Summary of Included Studies.**

| **INCLUDED COHORTS** | |
|---|---|
| **Author, Year:** | Alene 2017 |
| **Study period:** | Jan 2011 to Dec 2014 |
| **Study setting:** | The study was conducted in Hunan Province, in central-south China. Hunan Chest Hospital in Changsha, is the province's only chest hospital. The hospital has 610 beds, and treats and diagnoses patients with chest and lung diseases including TB, MDR-TB, and XDR-TB, referred from throughout the province. The MDR-TB treatment centre was established at the hospital in 2011 and serves as a referral hospital for all HIV-negative persons with presumptive drug resistant TB in the province. The national treatment success rates for people with MDR-TB and XDR-TB in 2013 were 55% and 22%, respectively. |
| **Description of Intervention:** | Patients were initially hospitalized for 1 to 2 months during the intensive phase and received DOT by trained medical staff, as well as free nutritional meals, and psychological support and counselling from nurses. After discharge, patients received daily DOT and psychosocial support from trained family members or trained community-based supervisors, and returned to the hospital monthly to collect medication. Education and counselling was routinely provided to patients and families. |
| **Patient eligibility:** | All bacteriologically-confirmed MDR-TB patients registered at the treatment centre during the study period were included. Exclusion criteria included: patients who were diagnosed with MDR-TB but did not start treatment (n=8); patients who were transferred out (n=8); and patients co-infected with HIV. |
| **Sample size:** | 481 (471 MDR-TB; 10 XDR-TB) |
| **Treatment regimen:** | Individualized regimen containing four drugs based on DST results and previous TB treatment, usually includes: an injectable agent (kanamycin, amikacin or capreomycin), a fluoroquinolone (i.e. levofloxacin, ofloxacin or moxifloxacin), PAS, prothionamide, pyrazinamide, clarithromycin, ethambutol, or cycloserine). |
| **Treatment duration:** | 24 months for MDR-TB; 30 months for XDR-TB |
| **Duration of injectable:** | 6+ months for MDR-TB; 12+ months for XDR-TB |
| **Hospitalization period:** | 1 to 2 months |
| **Funding source:** | Reported no specific funding from public, commercial or not-for-profit organizations |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Bastard 2015 |
| **Study period:** | Jun 2002 to Jul 2010 |
| **Study setting:** | Drug-resistant TB programs supported by MSF in Yerevan, Armenia and Abkhazia, Georgia. The programs covered the entire city of Yerevan in Armenia and the autonomous region of Abkhazia in Georgia. |

| | |
|---|---|
| **Description of Intervention:** | Patients were hospitalized initially and discharged after 2 smear-negative sputum samples. After discharge, DOT 6 days a week at closest health facility, or at home from health personnel or trained community member. Psychological support was provided, individually and in group sessions, together with socioeconomic support (financial and nutrition support and transport reimbursement). |
| **Patient eligibility:** | All DST-confirmed MDR-TB patients who started treatment during the study period and who had a treatment outcome (24+ months follow-up) by 31 July 2010. Patients who were transferred out or still on treatment at the end of study were excluded from analysis. |
| **Sample size:** | 393 |
| **Treatment regimen:** | Individualized regimens based on DST results, including at least 4 effective drugs, including 2nd-line drugs (ofloxacin, levofloxacin and moxifloxacin, kanamycin and capreomycin, para-aminosalicylic acid, ethionamide, cycloserine). |
| **Treatment duration:** | 18 to 24 months |
| **Duration of injectable:** | 6+ months (4+ months past culture conversion) |
| **Hospitalization period:** | Until 2 smear-negative sputum samples |
| **Funding source:** | Funding support from MSF. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Cox 2007 |
| **Study period:** | Oct 2003 to Jan 2005 |
| **Study setting:** | Nukus City and Chimbay in Karakalpakstan, a semiautonomous region in western Uzbekistan, with high levels of poverty, environmental degradation and slow reform of health services. |
| **Description of Intervention:** | The pilot program is a collaborative effort between MSF, the Ministries of Health in Karakalpakstan and Uzbekistan and the National Reference Centre for Mycobacteria in Germany. Patients received counselling, reimbursement for treatment-related transport costs during outpatient care, four meals daily during hospitalization, and monthly food parcels. |
| **Patient eligibility:** | Inclusion criteria were: residents of Nukus City and Chimbay; culture positive pulmonary TB; previously been treated in the DOTS program; and no concomitant medical conditions that precluded anti-TB treatment, which included cirrhosis, uncontrolled seizure disorder, significant psychiatric disease and known allergies to second-line anti-TB drugs. |
| **Sample size:** | 87 |
| **Treatment regimen:** | A standardized empiric regimen of pyrazinamide, ofloxacin, ethionamide, p-aminosalicylic acid (PAS), cycloserine and either capreomycin or kanamycin, was provided until DST results become available, after which the regimen is adjusted accordingly. |
| **Treatment duration:** | Minimum 18 months after culture conversion |
| **Duration of injectable:** | 6 months |

| | |
|---|---|
| **Hospitalization period:** | Patients were generally hospitalized for the first six months. The total duration depended on the use of an injectable, availability of family support, and clinical condition. |
| **Funding source:** | Funding support from Médecins Sans Frontières, and contributions in kind from the Ministry of Health in Karakalpakstan and the National Reference Center for Mycobacteria in German.y |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/ab |
| **Author, Year:** | Cox 2014 (*Note: Patients in the pilot program were excluded from main analyses because they formed part of the larger, and more up-to-date, sample in Mohr 2015. However, this study was retained for the analysis of comparative studies.)* |
| **Study period:** | Jan 2005 to Dec 2011 (treatment outcomes not available for patients initiating treatment in 2011) |
| **Study setting:** | Khayelitsha, a township near Cape Town, South Africa, with high rates of HIV, TB and DR-TB. There are approximately 200 cases of DR-TB diagnosed in Khayelitsha each year, with a HIV infection rate of 72%. Eleven health facilities in Khayelitsha provide integrated HIV and TB services for patients. HIV-infected TB patients are started on antiretroviral therapy shortly after initiating TB treatment. In early 2007, MSF and the City of Cape Town Health Department conducted a review of DR-TB diagnosis and treatment in Khayelitsha, of the 181 patients identified up to the end of 2006, 30% of patients were successfully treated and 70% suffered a poor treatment outcome (including LTFU, failure or death). |
| **Description of Intervention:** | A pilot program to provide community-based DR-TB diagnosis and treatment was introduced in late-2007.<br><br>*Before pilot program (hospital-based):* Hospitalization during intensive phase (6 months) followed by clinic-based DOT without additional support.<br><br>*Pilot program (community-based):* After diagnosis at a primary care clinic, patients are counselled by a dedicated DR-TB counsellor and treatment is started by the clinic TB medical officer. Patients who are severely ill and requiring hospitalisation, or who have XDR-TB, are referred directly to the tertiary TB hospital for admission. Also includes social assistance and support groups, routine home visit at start of treatment by trained community health worker, and daily DOT at local clinic. |
| **Patient eligibility:** | Rifampicin-resistant TB adult patients who resided in Khayelitsha or were diagnosed in one of 10 primary care facilities in the subdistrict. Excluded patients transferred to Khayelitsha after starting treatment elsewhere and those restarted on treatment after previous default or treatment failure. |
| **Sample size:** | 970 started treatment between 2005 to 2011. Excluding those initiating treatment in 2011: 787 with treatment outcomes available (216 before pilot program; 571 after pilot program). |
| **Treatment regimen:** | *Before pilot program*: Standardized treatment regimen.<br>Intensive phase: 5 drugs for 4 months (kanamycin, ethionamide, ofloxacin, ethambutol and pyrazinamide)<br>Continuation phase: 3 drugs (ethionamide, ofloxacin and ethambutol) for 12 to 18 months. Pyrazinamide was continued for extensive cavitary disease. If ethambutol resistance was diagnosed, then ethambutol was replaced with terizidone.<br><br>*Pilot program*: Standardized regimen adapted based on DST results.<br>Intensive phase: five drugs (kanamycin, ethionamide, pyrazinamide, ofloxacin, and |

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| | either terizidone or cycloserine)<br>Continuation phase: four drugs (ethionamide, pyrazinamide, ofloxacin, and either terizidone or cycloserine). |
| **Treatment duration:** | *Before pilot program*: 16 to 24 months.<br>*Pilot program*: 24+ months |
| **Duration of injectable:** | 6 months, and at least 4 months after culture conversion. |
| **Hospitalization period:** | *Before pilot program*: Minimum 6 months [183/216 (84.7%)]<br>*Pilot program*: Patients were hospitalized only if they were clinically unstable and unable to attend their clinic daily [145/571 (25.4%)] |
| **Funding source:** | Program implementation was funded by Medecins Sans Frontieres (MSF Belgium). Programme evaluation was supported by MSF and the University of Cape Town. |
| **Potential conflicts of interest:** | The funders were involved in study design, data collection and analysis. However, final preparation of the manuscript and the decision to publish rests with the first author. |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Escudero 2006 |
| **Study period:** | Jun 1998 to Dec 2000 |
| **Study setting:** | Hospital La Fuenfría, Madrid. |
| **Description of Intervention:** | Psychological support and counselling was provided by repeated clinical interviews during hospitalization and during out-patient follow-up. The clinician and a psychologist focused on the need for optimal treatment adherence and explored the main difficulties patients found in achieving these goals. Patients could be contacted by phone by the medical team after discharge. |
| **Patient eligibility:** | Confirmed adult MDR-TB patients without HIV enrolled for treatment at the hospital. |
| **Sample size:** | 25 |
| **Treatment regimen:** | Individualized regimen containing one injectable drug plus at least three oral drugs, adjusted based on prior anti-tuberculosis treatment and DST results. |
| **Treatment duration:** | 18 months or 12 months after first two negative cultures |
| **Duration of injectable:** | 6 months (5 days/week for months 1-2, 3 days/week for months 3-4, and 2 days/week for months 5-6) |
| **Hospitalization period:** | Until first negative sputum culture. Mean 65 days (range 9–483 days). |
| **Funding source:** | Not stated |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Gelmanova 2011 |
| **Study period:** | Dec 2006 to Nov 2008 |

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| **Study setting:** | Tomsk City metropolitan area (population: 526 000) has a high burden of MDR-TB. The area's DOTS TB program expanded to include MDR-TB treatment in 2000. |
| **Description of Intervention:** | The 'Sputnik' program was implemented in Dec 2006 jointly by the Tomsk Oblast Tuberculosis Services (TOTBS) and Partners In Health (PIH). The program goal is to improve treatment adherence among patients with adherence problems in the standard ambulatory care TB program. Most smear-positive patients initiate treatment in hospitals. After discharge, patients are provided with transportation passes, daily food sets and monthly hygiene sets. The program is staffed by a team of two nurses who visit patients at their convenience and provide twice-daily DOT. A physician joins the team every 10 days for home visits and clinical follow-up. Patients also receive clothing and assistance through state social services. Sputnik has a high nurse-to-patient ratio, and includes provision of cellphones to nursing staff, patient access to specialists and social/psychological support (a psychologist visited patients at home and also worked with family members), and provides additional training to program nurses for addressing patients' biosocial challenges. |
| **Patient eligibility:** | MDR-TB patients treated under the Sputnik program. Patients who were referred to the Sputnik program from standard care by a clinical committee included: those who refused to start treatment or stopped taking medications; those missing more than 25% of prescribed doses; those with a history of loss to follow-up in the previous 6 months; and those considered to be at high risk for loss to follow-up for other medical, social or economic reasons. Due to limited program capacity, patients are only referred to the Sputnik program after all standard options are exhausted. |
| **Sample size:** | 38 |
| **Treatment regimen:** | Standardized regimen.<br>Intensive phase (6-9 months): 6 drugs- kanamycin, ofloxacin (levofloxacin), ethionamide, pyrazinamide, ethambutol and cycloserine<br>Continuation phase (18 months): 4 drugs- ofloxacin (levofloxacin), ethionamide, ethambutol and cycloserine. p-aminosalicylic acid (PAS) is included in the regimen as a substitute drug if any bactericidal drug (K, Ofl, Z and Eto) or 2 bacteriostatic (E and Cs) drugs are not tolerated. |
| **Treatment duration:** | 24+ months |
| **Duration of injectable:** | 6 to 9 months |
| **Hospitalization period:** | Initial hospitalization until smear-negative |
| **Funding source:** | Not reported |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | The Sputnik program cost per patient was approximately US$6.50/day. This is compared to average in-patient care of US$9.30/day to US$35.00/day. |
| **Author, Year:** | Huerga 2017 |
| **Study period:** | May 2006 to May 2012 |
| **Study setting:** | The study took place at three sites in Kenya: Mathare Green House Clinic, which provides free outpatient HIV/TB care to people living in the Mathare slum (population of 340,000); Homa Bay County Hospital, serving a rural area of Western Kenya (population of 360,000); and Kenyatta National Hospital in Nairobi, the largest referral facility in East Africa. |
| **Description of Intervention:** | All patients received DOT 6 days a week. Patients at the Mathare and Nairobi sites received clinic-based outpatient care throughout treatment. In Homa Bay, the majority of patients received twice-daily DOT: at the nearest health facility in the |

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| | morning and by CHWs at patient homes in the evening during the intensive phase, and DOT was provided by CHWs at patient homes during continuous phase.<br><br>TB education and psychosocial counselling were provided at all sites. At the Mathare and Homa Bay sites, counselling sessions were provided by a counsellor following a standardized guide, weekly during the first month of intensive phase, bi-weekly thereafter, followed by monthly during continuation phase. At the Nairobi site, counselling was provided by nurses on request by the doctor available [from email correspondence with H Huerga].<br>A multi-disciplinary team provided medical, psychological and social care to the MDR-TB patients. The team is composed of a medical doctor, a clinical officer, a nurse, and a counsellor. In addition, there was a full-time social worker available in Mathare due to the magnitude of the social problems in a slum context. Furthermore, in Homa Bay, for each patient treated at home, two community health workers were identified and trained. Financial support was provided to all patients to cover income losses due to treatment and transport fees to attend the clinic. Patients at the Mathare site also received a daily hot meal at the day-care unit, and a monthly food basket. |
| **Patient eligibility:** | All patients who started MDR-TB treatment at the study sites. |
| **Sample size:** | 169 (70 in Mathare; 28 in Homa Bay; 71 in Nairobi) |
| **Treatment regimen:** | Standardized regimen, individualized based on DST results once available. The intensive phase (minimum 6 months) consisted of an injectable agent (kanamycin or capreomycin) and 3 or 4 oral drugs (levofloxacin, prothionamide, cycloserine, or para-aminosalicylic acid). Patients at the Nairobi site were treated with ethambutol or PZA instead of PAS, and until 2009 ofloxacin (OFX) was used instead of LVX. The continuation phase (18 months) included the same drugs as in the intensive phase minus the injectable agent. |
| **Treatment duration:** | 24+ months |
| **Duration of injectable:** | 6+ months |
| **Hospitalization period:** | None required |
| **Funding source:** | Not stated |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Isaakidis 2011 |
| **Study period:** | May 2007 to May 2011 |
| **Study setting:** | An urban, overpopulated slum setting in Mumbai, India. MSF started treating MDR-TB among HIV-infected individuals in May 2007. MDR-TB treatment became available in Mumbai's public sector in late 2010, prior to which it was only available in the private sector. |
| **Description of Intervention:** | Patients in stable clinical conditions started treatment on an ambulatory basis, otherwise they were hospitalized under the supervision of the MSF clinical team. Twice-daily DOT by trained DOT provider at a facility no more than 10 minutes walking distance from patients' home, including public health posts, private practitioners and local NGOs. Patients attended the MSF clinic monthly for medical and psychosocial follow-up. |

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| **Patient eligibility:** | All HIV-infected patients treated for MDR-TB (bacteriologically confirmed or suspected based on clinical findings and treatment history) at the clinic during the study period. |
| **Sample size:** | 58 |
| **Treatment regimen:** | Standardized regimen modified based on DST results, included six drugs: pyrazinamide, capreomycin, moxifloxacin, ethionamide, cycloserine and PAS. |
| **Treatment duration:** | 18+ months |
| **Duration of injectable:** | 6+ months |
| **Hospitalization period:** | Only if patient was clinically unstable for outpatient care. |
| **Funding source:** | No external funding sources. |
| **Potential conflicts of interest:** | This is an MSF study. |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Joseph 2011 |
| **Study period:** | Jun 2006 to Sep 2007 |
| **Study setting:** | Tiruvallur district and the Chennai Corporation area (with a combined population of almost 7.5 million) in southern India, in Chennai, Tamil Nadu. Previous reports from the TB Research Centre (TRC) in Chennai have shown MDR-TB treatment success rates of 37% to 50%. |
| **Description of Intervention:** | Hospitalization was recommended for the first two to four weeks of treatment. After discharge, patients attended the nearest health centre of their choice for DOT by trained DOT providers, which included government health care providers, private medical practitioners, and friends and relatives staying close by. DOT providers received one-on-one training from the TRC to administer drugs, counsel patients for drug regularity, identify and refer patients to the medical officer in case of any adverse drug reactions, and send patients to the TRC for monthly follow-ups. Patients were given emergency contact details for the medical officer and TRC field workers. |
| **Patient eligibility:** | Patients with DST-confirmed MDR-TB in the study district were traced and enrolled into the study. Exclusion criteria were: under 18 years of age; pregnancy; concurrent major psychiatric illness or serious medical illness; previous treatment (>1 month) with any second line anti-TB drugs; and HIV infection. |
| **Sample size:** | 38 |
| **Treatment regimen:** | The standardized regimen consisted of: an intensive phase (6 to 9 months) with 6 drugs (Km, Ofx, Eto, Z, E abd Cs); followed by a continuation phase (18 months) with 4 drugs (Ofx, Eto, E and Cs). |
| **Treatment duration:** | 24+ months |
| **Duration of injectable:** | 6 months, or 9 months if culture conversion occurred after the 4$^{th}$ month. |
| **Hospitalization period:** | 2 to 4 weeks recommended |
| **Funding source:** | WHO and the United States Agency for International Development (Model DOTS Project) |
| **Potential conflicts of interest:** | Not stated |
| **Issues with implementation (if reported):** | n/a |

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| **Economic information (if reported):** | n/a |
| **Author, Year:** | Keshavjee 2008 |
| **Study period:** | Sep 2000 to Nov 2004 |
| **Study setting:** | Tomsk Oblast in western Siberia, Russia, which has about 1·1 million inhabitants, approximately half of whom live in remote villages. |
| **Description of Intervention:** | Patients are routinely hospitalized during intensive phase, and discharged for the continuation phase, unless there is an underlying condition that precludes discharge (such as a psychiatric disorder, alcoholism or homelessness). TB physicians routinely assessed all patients initiating treatment for possible alcohol or substance use disorders. Daily DOT was provided by feldshers, who are often nurses at very rural outposts, to supervise the TB and Naltrexone medications, or at TB clinics, TB hospital or day hospital. Supplementary nutritional support is provided to prisoners and in-patients, and monthly food packages and/or free meals are given to fully adherent out-patients. |
| **Patient eligibility:** | Patients who started MDR-TB treatment and had documented MDR-TB during the study period. |
| **Sample size:** | 608 |
| **Treatment regimen:** | The individualized treatment containing at least 5 drugs, based on DST or drugs thought to be sensitive, including: any first-line oral agent to which isolate is sensitive; an injectable to which an isolate is sensitive; a quinolone; other second-line drug (usually ethionamide or cycloserine or PAS). |
| **Treatment duration:** | 18 months after culture conversion |
| **Duration of injectable:** | 6+ months after culture conversion |
| **Hospitalization period:** | Routinely hospitalized for the duration of injectable use, between 6 to 9 months. |
| **Funding source:** | Financial and travel support from Bill & Melinda Gates Foundation and Eli Lilly Foundation, the Frank Hatch Fellowships in Global Health Equity at the Brigham & Women's Hospital, Infectious Disease Society of America, the Heiser Foundation, and the US National Institutes of Health, and the John D and Catherine T MacArthur Foundation. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Kliiman 2009 |
| **Study period:** | Jan 2003 to Dec 2005 |
| **Study setting:** | Estonia, a republic of the former Soviet Union, which has a high burden of MDR-TB and XDR-TB. |
| **Description of Intervention:** | Daily DOT at clinics after discharge. Patients received nutritional support and transportation reimbursement for clinic visits. |
| **Patient eligibility:** | MDR-TB patients with culture-confirmed pulmonary TB with a recorded treatment outcome. |
| **Sample size:** | 235 MDR-TB and 54 XDR-TB patients |

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| **Treatment regimen:** | Individualized regimen based on DST results, containing at least four oral drugs used daily and an injectable daily until culture conversion, and three to five times weekly for another 2 to 3 months after. |
| **Treatment duration:** | 12 to 18 months after culture conversion |
| **Duration of injectable:** | Two to three months after culture conversion |
| **Hospitalization period:** | Until culture conversion |
| **Funding source:** | None stated |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Loveday 2015 |
| **Study period:** | Jul 2008 to Jun 2010 |
| **Study setting:** | A community-based model of MDR-TB treatment was piloted in 2008 at four community-based sites attached to purposively selected rural hospitals in areas with high reported incidence of MDR-TB, in Kwazulu-Natal, South Africa. Treatment outcomes at the four sites are compared to those at a centralized hospital. Approximately 76% of MDR-TB patients in KwaZulu-Natal are HIV-infected. |
| **Description of Intervention:** | Directly observed therapy (DOT) was not consistently implemented and most patients self-administered oral treatment with limited adherence monitoring.<br><br>*Hospital site*: Patients were initially hospitalized at a centralized, specialist TB hospital, followed by monthly outpatient visits to the same hospital. Patients were often discharged before the completion of the injectable phase and were not provided intensive education (as done at the community-based sites).<br><br>*Community-based sites 1-4*: Patients were initially hospitalized at rural hospitals attached to community-based sites. Monthly outpatient visits to community-based sites after discharge. Home-based care was available for patients discharged from the community-based sites during the intensive phase of treatment, where injections were administered daily at the local clinic or by mobile injection teams (at sites 1 to 3 only). Education was provided to patients and their families about MDR-TB and HIV. There was some variability in delivery of intervention at the four sites (see Table S4 for details). Additionally at Site 1 (only): Weekly education sessions were held, led by a clinic assistant and a nurse, on MDR-TB and HIV treatment with patients and their treatment supporters (family or friend). After the intensive phase, CHWs replaced nurses in making home visits and providing DOT. Travel expenses incurred by patients and their treatment supporters for clinic visits were reimbursed. |
| **Patient eligibility:** | Adult patients (>18 years) with laboratory-confirmed MDR-TB were enrolled. Patients with resistance to any second-line drug, or who received care at both the hospital and a community-based site, or who were participating in an MDR-TB clinical trial, were excluded.<br><br>*Hospital site*: All eligible MDR-TB patients, excluding those from the catchment areas of the community-based sites.<br><br>*Community-based sites*: All eligible MDR-TB patients in the catchment areas of the sites. |
| **Sample size:** | 1549 (813 from hospital; 736 from community-based sites) |
| **Treatment regimen:** | Standardized regimen<br>Intensive phase: kanamycin (KM), PZA (Z), EMB (E),ethionamide (ETH), ofloxacin |

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| | (OFX) and cycloserine (CS)<br>Continuation phase: Z, E, ETH, OFX and CS. |
| **Treatment duration:** | 22+ months |
| **Duration of injectable:** | 4 to 6 months |
| **Hospitalization period:** | Median 144 days (IQR 83 to 185) |
| **Funding source:** | Funding support from the Medical Research Council of South Africa (Cape Town, South Africa), Izumi Foundation (Boston, MA, USA) and a United Way Worldwide grant from the Lilly Foundation/Lilly MDR-TB Partnership (Indianapolis, IN, USA). Additional funding from the Columbia University- Southern African Fogarty AIDS International Training and Research Program (AITRP), Implementation Science Traineeship Program funded by the United States President's Emergency Plan for AIDS Relief (PEPFAR) through the Fogarty International Center, National Institutes of Health (grant # D43TW00231), Bethesda, MD, the National Institute of Allergy and Infectious Diseases (K23AI083088), Bethesda, MD, USA. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | Treatment success rates across community-based sites varied widely. This could be due to different interpretation and implementation of guidelines. For instance, the hospitalization period varied from 96 to 180 days. |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Meressa 2015 |
| **Study period:** | Feb 2009 to Dec 2014 |
| **Study setting:** | St. Peter's Hospital in Addis Ababa, Ethiopia and the University of Gondar Hospital (UoG) in Gondar, northwestern Ethiopia. Ethiopia is a high MDRTB-burdened country. The national MDR-TB treatment program was established in 2009, and is based on a multidisciplinary HIV/TB care model developed in Cambodia. This study reports the treatment outcomes from the first four years of the program. |
| **Description of Intervention:** | As outpatients, monthly visits to hospital outpatient clinic and daily DOT at local health centres by health staff or at home by family DOT supporter. Family treatment supporters trained on adherence monitoring. Monthly home visits by outpatient team in Addis Ababa and Gondar. Monthly food basket provided to all patients. Economic assistance, if needed, for transportation and housing. Patients who were initiated on therapy as outpatients were followed by the GHC (Global Health Committee) outpatient team, including roving nurses who provided them with daily injections of the injectable agent (5–6 days per week). |
| **Patient eligibility:** | All MDR-TB patients who initiated treatment before December 2012 (with at least 24 months of follow-up by December 2014) at two hospital-based study sites. MDR-TB was presumed for 61 (10.0%) patients, who had documented unsuccessful cure by first-line treatment, but without microbiological confirmation. |
| **Sample size:** | 612 |
| **Treatment regimen:** | Standardized second-line drug regimen:<br>(1) at least three oral agents to which the patient was presumed to have susceptibility (eg, levofloxacin, ethionamide, cycloserine or para-aminosalicyclic acid (PAS)), (2) pyrazinamide and (3) an aminoglycoside (amikacin or kanamycin) or polypeptide (capreomycin) injectable agent. |
| **Treatment duration:** | 18 months after bacteriological conversion |
| **Duration of injectable:** | Minimum 8 months. Median 9.6 months (IQR 8.1-11.0 months). |

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| **Hospitalization period:** | Until smear conversion or clinically stable. A subset of healthier patients was initiated on therapy as outpatients beginning in 2010. |
| **Funding source:** | Funding support from the Jolie-Pitt Foundation, the Annenberg Foundation, Lilly MDR Partnership, and Lilly Foundation, the Ethiopian Federal Ministry of Health, The Stanford Center for Innovation in Global Health, the National Institutes of Health (K01 AI104411) and Children's Hospital Boston. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | Gross estimate of programme costs, exclusive of second-line drugs, is approximately $2000 per patient over the 2-year period of treatment. Costs include: ancillary medications, laboratory monitoring, food supplementation, transportation and accommodation for patients, home visits, capacity building, programme management, personnel training, salaries for dedicated staff and salary supplementation of national staff and some infrastructure improvements. Excludes overhead costs for infrastructure and personnel associated with hospital-based care. |
| **Author, Year:** | Mitnick 2003 |
| **Study period:** | Aug 1996 to Feb 1999 |
| **Study setting:** | Resource-poor setting, Northern Lima (Carabayllo, Comas, and Independencia districts), Peru. |
| **Description of Intervention:** | Patients received limited nutritional, financial, and social support through Socios En Salud. A team of specially trained community health workers, nurses, and physicians provided treatment on an outpatient bases. Daily DOT at homes or local health centres. |
| **Patient eligibility:** | Patients who initiated supervised, individualized treatment for MDR-TB before 1 Feb 1999 under a community-based treatment program (joint initiative of an NGO (Socios En Salud) and the Peruvian Ministry of Health). Inclusion criteria were: residence in the government-approved catchment area in northern Lima (Carabayllo, Comas, and Independencia districts); referral to the program by a collaborating health center after the failure of at least one course of directly observed, standardized short-course chemotherapy; laboratory-documented multidrug-resistant tuberculosis; survival until the results of drug-susceptibility testing became available; and provision of written informed consent. |
| **Sample size:** | 75 |
| **Treatment regimen:** | Individualized regimens containing a minimum of 5 first and second-line drugs based on DST results. First-line drugs were preferred if susceptible. An injectable was given for at least six months after culture conversion. |
| **Treatment duration:** | 18+ months (12 consecutive negative cultures) |
| **Duration of injectable:** | 6+ months after culture conversion |
| **Hospitalization period:** | None |
| **Funding source:** | Supported by Thomas J. White, the Massachusetts State Laboratory Institute, the National Institute of Allergy and Infectious Diseases, Eli Lilly, and the Bill and Melinda Gates Foundation. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | Cost of therapy ranged from US$504 to $32,383 per patient. Mean of $15,681 was approximately 10% of costs for hospitalized patients. |

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| **Author, Year:** | Mitnick 2008 |
| **Study period:** | Feb 1999 to Jul 2002 |
| **Study setting:** | Metropolitan Lima, Peru. A comprehensive individualized MDR-TB treatment program was introduced in 1996. |
| **Description of Intervention:** | Comprehensive supervised outpatient treatment, free of charge to patients. All patients received DOT through local hospitals, health clinics, and daily home visits by community health workers. Patients with emotional and psychosocial difficulties, who had weak social support, or with adherence problems were invited to participate in a social support group that included weekly, and later bi-monthly support groups/group therapy, recreational excursions, symbolic celebrations and family workshops (Acha 2008). Limited nutritional and financial support and opportunities for income generation were provided, as needed. Hospitalization was available, if medically indicated. |
| **Patient eligibility:** | All MDR-TB patients who initiated individualized treatment under the program, with baseline DST results for at least four drugs: isoniazid, rifampicin, one fluoroquinolone, and one second-line injectable (kanamycin, capreomycin, or amikacin). |
| **Sample size:** | 651 (48 XDR-TB patients; 603 MDR-TB patients) |
| **Treatment regimen:** | Individualized treatment based on DST results, containing at least five drugs likely to be effective, including a fluoroquinolone and an injectable agent. |
| **Treatment duration:** | 18+ months |
| **Duration of injectable:** | 8+ months after culture conversion |
| **Hospitalization period:** | Only if medically indicated. Overall, 29 (4.5%; 3/48 XDR-TB patients and 26/603 MDR-TB patients) initiated treatment in hospital. Duration depended on when the patient became clinically stable and ready for discharge. |
| **Funding source:** | Supported by grants from the Bill and Melinda Gates Foundation, Thomas J. White, Partners in Health, the Peruvian Ministry of Health, the David Rockefeller Center for Latin American Studies at Harvard University, the Francis Family Foundation, the Pittsfield Anti-tuberculosis Association, the Eli Lilly Foundation, and the Hatch Family Foundation and by career development awards from the National Institute of Allergy and Infectious Diseases (5 K01 A1065836, to Dr. Mitnick) and the National Heart, Lung, and Blood Institute (5 K01 HL080939, to Dr. Becerra). |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Mohr 2015 |
| **Study period:** | Aug 2008 to Jan 2012 |
| **Study setting:** | Khayelitsha, a township near Cape Town, South Africa, with high rates of HIV, TB and DR-TB. There are approximately 200 cases of DR-TB diagnosed in Khayelitsha each year, with a HIV infection rate of 72%. Eleven health facilities in Khayelitsha provide integrated HIV and TB services for patients. HIV-infected TB patients are started on antiretroviral therapy shortly after initiating TB treatment. |

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| **Description of Intervention:** | Individual-specific DR-TB counselling (four sessions throughout treatment – three in the first month of treatment, including a home visit with counselling and education for families by the DR-TB counsellor and a social worker/peer educator/nurse, and one during the continuation phase). Patients are invited to attend weekly peer support groups conducted at the clinics, moderated by a DR-TB counsellor or peer educator. Daily DOT at local clinic. A dedicated social assistant is available in Khayelitsha to assist patients in accessing disability/social grants, and refer patients to other support services. Hospitalization only if patients were clinically unstable and unable to attend their clinic daily. |
| **Patient eligibility:** | All DR-TB (resistance to at least Rifampicin) patients registered in Khayelitsha during the study period with known HIV status, and without previous treatment with second line drugs. Patients who transferred from facilities outside the sub-district and those with bacteriologically unconfirmed DR-TB (mostly children aged ≤5 years) were excluded. |
| **Sample size:** | 853 |
| **Treatment regimen:** | Standardized regimen adapted to DST results.<br>Intensive phase: 5 drugs (kanamycin, ethionamide, pyrazinamide, ofloxacin, and either terizidone or cycloserine)<br>Continuation phase: 4 drugs (ethionamide, pyrazinamide, ofloxacin, and either terizidone or cycloserine). |
| **Treatment duration:** | 24+ months |
| **Duration of injectable:** | 6 months |
| **Hospitalization period:** | No mandatory hospitalization |
| **Funding source:** | Funding support from MSF and Wellcome Trust. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Mohr 2017 |
| **Study period:** | Jan 2010 to Dec 2014 |
| **Study setting:** | Khayelitsha is a peri-urban township outside of Cape Town, South Africa, most of the 450,000 residents in informal settlements. There are approximately 200 newly diagnosed RR-TB patients each year, with a case notification rate of 55/100,000 and an HIV co-infection rate of 70%. Progressive implementation of SAT took place from 2012 to 2015 at 5 of 10 primary care clinics in Khayelitsha. These initial pilot clinics were chosen based on available resources, functionality, and willingness of staff to participate. The national LTFU rate among RR-TB patients ranges from 20% to 31%. |
| **Description of Intervention:** | *Standard of care (SOC) cohort*: Patients attended the clinic 5 days per week for DOT for the entire treatment. Patients received four standardized counseling sessions provided by trained RR-TB counselors: upon diagnosis; at treatment initiation; during the intensive phase; and upon completion of intensive phase. Patients lost to follow-up were traced telephonically or via home visits from local community health workers or counselors.<br><br>*Self-administered therapy (SAT) cohort*: The same care is received during the intensive phase. After completion of the intensive phase, patients received tailored counselling from an RR-TB counsellor, which includes discussing the option of SAT. Prior to enrollment into SAT, local community health workers conduced home visits |

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| | to assess the social situation, identify a treatment supporter, and determine adherence barriers. After enrollment patients received an adherence counseling session by a dedicated MSF counselor, where medications were reviewed, a pillbox was issued and adherence barriers were addressed. Patients received weekly or monthly supply of medications, depending on clinic and patient preference. Community health workers visited weekly initially and monthly as soon as patients were deemed to be doing well in the programme, during which they provided support and addressed adherence barriers. |
| **Patient eligibility:** | All RR-TB patients who initiated treatment during the study period, and who had a final treatment outcome before 1 Jan 2017, at the 5 pilot clinics were considered for study enrollment. Patients were excluded if they had a treatment outcome within 6 months of treatment initiation (42 in SOC cohort; 67 in SAT cohort).<br><br>*SOC cohort*: Eligible RR-TB patients who initiated treatment at least 6 months prior to SAT implementation at their respective clinics. Treatment initiation times for inclusion in the SOC cohort ranged from January 2010 to July 2013.<br><br>*SAT cohort*: Eligible RR-TB patients who initiated treatment at least 6 months after SAT implementation at their respective clinics were considered for SAT. Treatment initiation times for patients included in the SAT cohort ranged from Jan 2012 to Dec 2014. Patient eligibility for SAT was assessed based on: treatment adherence history (for RR-TB and concomitant diseases); and clinical status and any adverse events requiring ongoing monitoring. Enrollment decisions were made at weekly clinic meetings attended by community health workers, doctors, RR-TB professional nurses and MSF counsellors. Eligible patients, who gave verbal consent, and who were no longer receiving an injectable agent (including those who were already in the continuation phase) were enrolled. |
| **Sample size:** | 295 RR-TB patients who completed at least 6 months of treatment (118 in SOC cohort; 177 in SAT cohort); of which 292 had final treatment outcomes by 1 Jan 2017 (118 in SOC cohort; 174 in SAT cohort) |
| **Treatment regimen:** | Patients from both cohorts received a standard RR-TB treatment regimen provided to patients contained all or most of the following drugs: kanamycin, moxifloxacin, pyrazinamide, ethambutol, terizidone, ethionamide and high dose isoniazid. The initial phase (6 months, and at least 4 months after culture conversion) consisted of kanamycin, ethionamide, pyrazinamide, ofloxacin, and either terizidone or cycloserine. The continuation phase (at least 18 months) consisted of ethionamide, pyrazinamide, ofloxacin, and either terizidone or cycloserine. |
| **Treatment duration:** | 24+ months |
| **Duration of injectable:** | 6+ months, at least 4 months after culture conversion |
| **Hospitalization period:** | None |
| **Funding source:** | The pilot SAT program was funded by MSF and Cape Town City Health, and the study was funded by MSF. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | Among patients enrolled in the SOC cohort (n=118), 17 (14.4%) were later considered for and received SAT (due to the phased implementation of SAT at the clinics), with a median time to SAT-enrollment of 14.8 months (IQR 12.8-20.3). In addition to these patients, other patients in the SOC cohort might have received an informal version of SAT as facilities occasionally provided a supply of medications for self-administration to relieve pressure on the clinic. These patients however did not receive the specialized counseling and community support integral to the SAT pilot programme.<br><br>Some eligible patients were never offered SAT due to the slow, phased implementation of the pilot program, reluctance from some providers to provide SAT, and limited resources. |

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| **Economic information (if reported):** | n/a |
| **Author, Year:** | Satti 2012 |
| **Study period:** | Jan 2008 to Sep 2009 |
| **Study setting:** | All 10 districts in Lesotho under the national MDR-TB program. |
| **Description of Intervention:** | A team of community nurses assessed the home situation, educated families, and arranged for a community health worker to provide twice-daily DOT in the patient's home, who also accompanied the patients for monthly clinic visits. Community health workers received regular training on HIV and MDR-TB, and in psychological support. They were reimbursed for all costs incurred and compensated with performance-based payment. Treatment was provided free-of-charge. All patients received a food package and reimbursement for travel expenses incurred during treatment. |
| **Patient eligibility:** | All adult patients (15 years or older) with DST-confirmed MDR-TB, who received second-line TB treatment between Jan. 1, 2008 and Sep. 29, 2009 in the national MDR-TB program. |
| **Sample size:** | 134 |
| **Treatment regimen:** | Patients were initiated on a standardized regimen of six drugs –pyrazinamide, kanamycin, levofloxacin, prothionamide (or ethionamide), cycloserine, and para-aminosalicylic acid – until DST results are available, after which it is adjusted accordingly. |
| **Treatment duration:** | Median duration of 22.9 months (IQR, 21.6–24.0) |
| **Duration of injectable:** | 6 months |
| **Hospitalization period:** | Not mandatory; patients who were critically ill or who had severe adverse events were hospitalized. |
| **Funding source:** | Support received from the Department of Global Health and Social Medicine Research Core at Harvard Medical School |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Shin 2006 |
| **Study period:** | Jun 1998 to Dec 2000 |
| **Study setting:** | The Tomsk Oblast in western Siberia, where there is a very high burden of MDR-TB. Half of the population lives Tomsk, the capital city, and the remainder lives in remote rural villages, which are often inaccessible for parts of the year. |
| **Description of Intervention:** | Patients are routinely hospitalized during intensive phase, and discharged for the continuation phase, unless there is an underlying condition that precludes discharge (such as a psychiatric disorder, alcoholism or homelessness). TB physicians routinely assessed all patients initiating treatment for possible alcohol or substance use disorders. Daily DOT was provided by feldshers, who are often nurses at very rural outposts, to supervise the TB and Naltrexone medications, or at TB clinics, TB hospital or day hospital. Supplementary nutritional support is provided to prisoners and in-patients, and monthly food packages and/or free meals are given to fully adherent out-patients. |

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| **Patient eligibility:** | Confirmed or suspected MDR-TB (based on history of previous treatment failures) who were receiving DOTS-Plus treatment from the civilian sector (n=134, 54.9%) and prison sector (n=110, 45.1%) |
| **Sample size:** | 244 |
| **Treatment regimen:** | The individualized treatment containing at least 5 drugs, based on DST or drugs thought to be sensitive, including: any first-line oral agent to which isolate is sensitive; an injectable to which an isolate is sensitive; a quinolone; other second-line drug (usually ethionamide or cycloserine or PAS). |
| **Treatment duration:** | 18+ months |
| **Duration of injectable:** | 6+ months after culture conversion |
| **Hospitalization period:** | Routine hospitalization in the civilian sector during the intensive phase (i.e. duration of injectable). Among civilian patients, 98 (73.1%) started treatment in the hospital (median duration of 7.9 months), the remainder started as outpatients in the day hospital. |
| **Funding source:** | Funding for medications and patient care was provided by the Bill & Melinda Gates Foundation and the Open Society Institute. Funding for physician and health care worker training was provided by the Eli Lilly foundation. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Suarez 2002 |
| **Study period:** | Oct 1997 to Mar 1999 |
| **Study setting:** | Peru, a middle-income country where TB treatment is provided free of charge. |
| **Description of Intervention:** | Daily DOT by nurses and monthly medical check-up by doctors. Patients were provided appointment cards and weekly food parcels. |
| **Patient eligibility:** | Patients with confirmed MDR-TB who were enrolled in the second-line treatment programme in Peru. |
| **Sample size:** | 298 |
| **Treatment regimen:** | Standardized regimen consisting of kanamycin (1 g injectable), ciprofloxacin (1 g orally), ethionamide (750 mg orally), pyrazinamide (1500 mg orally), and ethambutol (1200 mg orally). Kanamycin was administered for the first 3 months. |
| **Treatment duration:** | 18 months |
| **Duration of injectable:** | 3 months |
| **Hospitalization period:** | None |
| **Funding source:** | Not declared |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | The average cost per patient for those who completed the full course of treatment was US$2381, with the second-line drugs, at US$824 per patient, being the most expensive item. |
| **Author, Year:** | Thomas 2007 |
| **Study period:** | Jan 1999 to Dec 2003 |

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| **Study setting:** | Predominantly rural sub-district of Tiruvallur district, in south India, and nearby Chennai Sity. The Revised National TB Control Programme (RNTCP) was implemented in Triuvallur district in 1999, the area has 17 governmental health care facilities, including 7 designated microscopy centers. |
| **Description of Intervention:** | After discharge, patients attend primary health centres or NGO for thrice-weekly DOT. Monthly clinical assessment and sociological counselling. Reminders were sent one week prior to monthly check up. Financial assistance was provided at the monthly visits for all patients to compensate for loss of wages and travel expenses. |
| **Patient eligibility:** | All culture-confirmed MDR-TB patients who were referred to the Tuberculosis Research Centre during the study period from the study area in Tiruvallur district, and from an NGO working in nearby Chennai city. |
| **Sample size:** | 66 |
| **Treatment regimen:** | Individualized regimen based on DST results. The regimens used were:<br>Group I: $6Sm_3(Km_3)OfxEtoZE$ daily followed by 12OfxEtoZE daily<br>Group II: Other combinations. E.g.: $6Sm_3(Km_3)OfxEtoZH_{high\ dose}$ daily followed by 12OfxEtoZH daily; or $6Sm_3(Km_3)OfxZE$ with Cs/PAS/High dose INH daily followed by 12 months of oral drugs; etc. |
| **Treatment duration:** | 18+ months |
| **Duration of injectable:** | 6 months |
| **Hospitalization period:** | Recommendation of 1 month. 30 (45%) were not hospitalized, and 10 (15%) hospitalized for <10 days. |
| **Funding source:** | Funding support from the World Health Organization and the United States Agency for International Development under the Model DOTS Project. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Vaghela 2015 |
| **Study period:** | Aug 2009 to Mar 2010 |
| **Study setting:** | Northeast, East, Central and West districts of Delhi, India – large metropolitan area with a high burden of TB and MDR-TB. |
| **Description of Intervention:** | Daily DOT by a DOT Provider at a DOTS-plus centre or hospital. Mobile multi-disciplinary teams, consisting of one male and one female trained community health workers, made home visits every 15 days during intensive phase and every 45 days in continuation phase. The home visits included psychosocial support and counselling for patients and their families, hygiene and nutrition counselling, and nursing care. Patients from very poor socioeconomic backgrounds were provided free multigrain biscuits and an egg per day. Patients were given the mobile numbers for the team members such that in case of an adverse drug reaction or early warning symptoms, they can get immediate attention. Teams assisted patients in registering for financial support under the government TB scheme. |
| **Patient eligibility:** | All new MDR-TB patients registered at clinics in the selected districts |
| **Sample size:** | 101 |
| **Treatment regimen:** | Standardized regimen.<br>Intensive phase: kanamycin, ofloxacin (levofloxacin), ethionamide, pyrazinamide, ethambutol and cycloserine |

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| | Continuation phase: ofloxacin (levofloxacin), ethionamide, ethambutol and cycloserine<br><br>P-aminosalicylic acid (PAS) is included in the regimen as a substitute drug if any bactericidal drug (K, Ofl, Z and Eto) or 2 bacteriostatic (E and Cs) drugs are not tolerated. |
| **Treatment duration:** | 24 to 29 months |
| **Duration of injectable:** | 6 to 9 months |
| **Hospitalization period:** | Not reported |
| **Funding source:** | Funded by Eli Lilly and Company (India) Pvt. Ltd. |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **Author, Year:** | Yu 2015 |
| **Study period:** | Jan 2007 to Jun 2008 [updated to 2012 using unpublished data (Yu 2018, accepted manuscript: https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciy066/4831095?redirectedFrom=fulltext)] |
| **Study setting:** | Northern Taiwan, where the government established a new patient-centred MDR-TB treatment program in May 2007 to standardize MDR-TB care, named Taiwan MDR-TB Consortiums (TMTC). Prior to its establishment, MDR-TB patients had to visit either prescribed hospitals or a contracted out-patient clinic for daily injections, and public health nurses were not familiar with the complicated regimens for MDR-TB or the related adverse effects. Between 1992 and 1996, the national lost to follow-up rate among MDR-TB patients was approximately 30%. |
| **Description of Intervention:** | Hospitalization was encouraged at treatment initiation. Designated observers and nurses provided DOT and injections to patients, typically at their home. Taiwan CDC also provided NTD 1 million for every patient (a maximum of NTD 2 million for the 2-year treatment period, excluding the cost of medicine) to be used flexibly by the medical team for incentives and enablers to improve adherence. Education and counselling provided by the medical team during home visits to patients and their families. When patients attended out-patient clinics for refills or check-ups, they were accompanied by team members from the TMTC to address hospital affairs and have examinations done in regards of infection control. |
| **Patient eligibility:** | All pulmonary, bacteriologically confirmed MDR-TB cases who received treatment with second-line drugs, during the study period. MDR-TB patients with positive culture results after January 2007 were informed and consented to participate in the Consortium program. |
| **Sample size:** | 126 |
| **Treatment regimen:** | Individualized regimens based on DST results. Four susceptible drug, including EMB, PZA, a fluoroquinolone, an injectable, and other oral 2$^{nd}$-line drugs. |
| **Treatment duration:** | 18 to 24 months (18 months after sputum conversion) |
| **Duration of injectable:** | 6 months |
| **Hospitalization period:** | 2 weeks to 2 months |
| **Funding source:** | Centers for Disease Control, Taiwan |
| **Potential conflicts of interest:** | None declared |

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| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |
| **INCLUDED TRIALS** | |
| **Author, Year:** | Baral 2014 (mixed methods) |
| **Study period:** | Jan 2008 to Dec 2008 |
| **Study setting:** | Nepal, a mid-TB burden country where TB is highly stigmatised. MDR TB treatment is provided from 10 treatment centres and 34 sub-centers throughout the country. There is a well-functioning national TB programme but management is complicated by the country's terrain. A national DOTS-Plus program for MDR-TB was piloted in November 2005. The reported non-completion rates under the program were 22%, 15% and 18% in 2005, 2006 and 2007 respectively. This study was conducted at the 7 DOTS-Plus centres in the Kathmandu Valley. |
| **Randomization:** | The seven DOTS-Plus centres were randomized to 3 types of care by randomly selecting from the numbers 1 to 7 (representing each centre): 2 to standard care (controls); 2 to standard care plus counselling; and 3 to standard care plus counselling and financial support. Individual randomization could not be done due to the certainty of contamination among patients within a centre. |
| **Trial arms:** | Control arm (standard care): Each patient nominated someone (usually a family member) as a treatment supporter. Daily DOT at the clinic.<br><br>Intervention arm 1: Standard care plus individual (2 to 5 sessions) and small-group counselling (every 2-3 weeks) by trained Public Health Nurse. Counselling sessions were between 15 to 30 minutes, and were tailored to issues identified in previous sessions. The general content was information about disease, drugs and treatment, curability, treatment continuation, social barriers such as stigma, support from health workers, community and family members, financial hardship due to MDR TB etc.<br><br>Intervention arm 2: Standard care plus counselling sessions (as in Intervention arm 1), and additionally, patients received financial support (2000 Nepali Rupees (~28USD) per month). |
| **Patient eligibility:** | All MDR-TB patients starting treatment at the DOTS-plus centres in 2008 were eligible for study inclusion. |
| **Sample size:** | 156 (control: 81; intervention 1: 33; intervention 2: 42) |
| **Treatment regimen:** | Standardized regimen.<br><br>Intensive phase: five drugs (pyrazinamide, kanamycin, ofloxacin, ethionamide, and cycloserine) for eight months, but is extended to twelve months if the patient is smear- or culture-positive at six months (8Z-Km-Ofx-Eto-Cs/16Z-Ofx-Eto-Cs).<br><br>Continuation phase: same as intensive phase, but without kanamycin. |
| **Treatment duration:** | 16 months, extended by up to 8 months if culture conversion occurred between 12 and 18 months of treatment |
| **Duration of injectable:** | 8 to 12 months |
| **Hospitalization period:** | Hospitalization only for severe side effects. |
| **Funding source:** | Funded by UK Aid from the UK Department for International Development (DFID). |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |

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| **Economic information (if reported):** | n/a |
| **Author, Year:** | Taneja 2017 |
| **Study period:** | Apr 2014 to May 2014 |
| **Study setting:** | This pilot study was conducted at two sites (Malviya Nagar Government Hospital and Nehru Nagar Chest Clinic, both in New Delhi) randomly selected from a list of 20 hospitals in Delhi, India, at which a cluster trial was being plan. |
| **Randomization:** | Cluster randomization by hospital site |
| **Trial arms:** | Control arm (Nehru Nagar site): The control arm received regular treatment and investigations as per RNTCP guidelines. During the intensive phase, patients visited the DOTS centre thrice weekly for DOT provided by health workers. During the continuation phase, patients received weekly supplies of drugs from the DOTS centre to be consumed at home. Health education and counselling was given at each visit to the DOTS centre. DOTS health workers were given incentives from program funding for every patient that successfully completed treatment.<br><br>Intervention arm (Malviya Nagar site): In addition to standard care (as in control arm), a team of two trained homecare providers provided comprehensive home-based care to MDR-TB patients and their family members, which included counselling on the importance of treatment adherence, on their emotional needs, as well as health education on coughing etiquettes, avoiding risk to family members, etc. Additional support included: nursing care and referral to other higher centres in case of illness or mental health issues; physical, mental and vocational rehabilitation; assistance in obtaining Government financial support; support for obtaining or returning to work and school; and nutritional support (eggs and nutritious multigrain provisions) and counselling. The homecare team visited patients fortnightly during the intensive phase and every 45 days during the continuation phase. In addition to providing counselling and education, the team also recorded body weight, side-effects of medicines and complications of the disease. The team also motivated the patients to go for routine sputum microscopy, X-Ray, sputum culture and other relevant investigations. |
| **Patient eligibility:** | MDR-TB patients who received treatment for more than 6 months. Exclusion criteria were: any form of disability and comorbidities; and pregnancy. |
| **Sample size:** | 100 (50 in each arm) |
| **Treatment regimen:** | Standardized regimen, adjusted based on DST results, consisting 6 drugs (Kanamycin, Levofloxacin, Ethionamide, Pyrazinamide, Ethambutol and Cycloserine) during the intensive phase (6 to 9 months), and 4 drug (sLevofloxacin, Ethionamide, Ethambutol and Cycloserine) during continuation phase (18 months). |
| **Treatment duration:** | 24 to 27 months |
| **Duration of injectable:** | 6 to 9 months |
| **Hospitalization period:** | None |
| **Funding source:** | None stated |
| **Potential conflicts of interest:** | None declared |
| **Issues with implementation (if reported):** | n/a |
| **Economic information (if reported):** | n/a |

**Table S9. Detailed quality assessment of non-randomized studies (based on Robins-I Tool)**

| **Author, Year** | Alene 2017 |
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| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No information – unclear on whether counselling continued after hospital discharge |
| Overall risk due to deviations from interventions | No information |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | 8/489 (1.6%) patients were not included because their outcomes were not available (i.e. transferred out or not assessed) |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – treatment outcomes were obtained from an internet-based TB Management Information System in the Tuberculosis Control Institute of Hunan Province, and from MDR-TB medical records and the DST registration book at Hunan Chest Hospital. |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | No information |

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| **Author, Year** | Bastard 2015 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No information – unclear how frequent or for how long were individual and group counselling provided for, and whether this was routinely provided to all patients |
| Overall risk due to deviations from interventions | No information |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 22/415 (5.3%) were excluded from analysis because they did not have an outcome at the administrative censoring date (12 were still receiving treatment and 10 had transferred out). |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Moderate |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – treatment outcomes obtained from routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | No information |
| **Author, Year** | Cox 2007 |

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| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No, this was a pilot program with a small sample that appeared to adhere to the protocol. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – treatment outcomes obtained from routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Escudero 2006 |
| **Bias in selection of participants into the study** | |

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| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – provided clear details of intervention implementation and delivery. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Most – 2/25 (8%) patients transferred to other hospitals |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Moderate |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – used routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | Low |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Moderate |
| **Author, Year** | Gelmanova 2011 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No - clear details of intervention implementation and delivery. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes, except 1/38 (2.6%) patient who was transferred out |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Isaakidis 2011 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – clear details of intervention implementation and delivery. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 23/58 (39.7%) were still on treatment at the end of the observational period, all initiated treatment <24 months before end date. Thus, although they were censored, their exclusion does not affect results. |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Joseph 2011 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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|---|---|
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No information – the intervention required a network of trained DOT providers to deliver treatment, and also weekly delivery of the TB drugs to the DOT providers by research staff, it was not reported whether this was done successfully and that treatment was consistently delivered without interruptions. |
| Overall risk due to deviations from interventions | No information |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | No information |
| **Author, Year** | Joseph 2011 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | Low |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Meressa 2015 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – detailed description of intervention delivery |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Mitnick 2003 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data. However, this study used a non-standard definition for lost to follow-up: "Withdrawal from therapy was defined by one or more months of missed therapy during the first year, and two or more months missed during the second year." Of the 5 patients lost to follow-up, it is not clear how many were lost during the first year. If many were lost in the first year, *and* interrupted treatment for less than 2 months, then the lost to follow-up rate would be overestimated in this study compared to other studies. However, this seems unlikely to be true. |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |

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|---|---|
| **Author, Year** | Mitnick 2008 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – unlikely given the type of intervention provided was flexible. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes, except 5/651 (0.8%) who were transferred out (n=4) or still on treatment at end of study (n=1). |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – however, the definition for lost to follow-up was not done according to the same WHO standard as other studies: "Treatment default was a physician-defined end point assigned upon the failure of attempts to return to therapy those patients who had not been adhering to their treatment regimen." Therefore, there is a possibility that among 18/651(2.8%) patients who failed, there could be a proportion who in fact would have been classified as lost to follow-up if they had interrupted therapy for 2 or more consecutive months. However, this would be a small proportion and have little influence on the results. |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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|---|---|
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Mohr 2015 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | Not beyond what would be expected: "In the earlier years of the programme, DR-TB counselling was less structured and focused primarily on treatment initiation." |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 96/853 (11.3%) were transferred out of the study clinics, therefore their outcomes were not recorded. |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | Yes – 14 patients were included due to unknown HIV status. However, unlikely to affect results. |
| Overall risk of bias due to missingness | Moderate |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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|---|---|
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Moderate |
| **Author, Year** | Satti 2012 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – very clear description of intervention development and implementation |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Most – 3/134 (2.2%) of patients were transferred out. |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – used routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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|---|---|
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Shin 2006 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – detailed description of intervention implementation and delivery |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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|---|---|
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Shin 2006 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – detailed description of intervention implementation and delivery |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Thomas 2007 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | Yes – the study reported difficulties identifying DOT providers near patients (as planned in the intervention), therefore patients often travelled further than expected for treatment, or had to pay a fee to receive treatment from a private provider. |
| Overall risk due to deviations from interventions | Moderate |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Moderate |
| **Author, Year** | Vaghela 2015 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – clear implementation and delivery description |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes – 1/101 (1%) patients transferred out |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |

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| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Author, Year** | Yu 2015 |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No – the study intervention had a flexible adherence support component. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes – 2/126 (1.6%) patients transferred out |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No – routinely collected data |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Low |
| **Cohort studies with 2 or more interventions** | |
| **Author, Year** | Mohr 2017 |
| **Bias due to baseline confounding** | |
| *Did the authors use an appropriate analysis method that controlled for all the important confounding domains?* | No – one important potential confounder that was unbalanced at baseline between the SOC and SAT cohorts was history of previous TB treatment. A smaller proportion of patients in the SAT cohort had a TB treatment history (59.8% in SAT cohort vs 76.3% in SOC cohort) – this could confound the relationship between the intervention and the outcome of lost to follow-up, likely biasing the effect of intervention away from the null. |
| *Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?* | N/A |

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| *Did the authors control for any post-intervention variables that could have been affected by the intervention?* | No |
| Overall risk of confounding bias | Serious |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No – patients were selected to receive self-administered therapy (SAT) based on an assessment by the care team made after the intensive phase of treatment, however, the authors did an intention-to-treat analysis where cohort group assignment depended on time of treatment initiation relative to implementation of intervention, and not on whether the patient actually received SAT or not. |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall Risk of selection bias | Low |
| **Bias in classification of interventions** | |
| *Were intervention groups clearly defined?* | Yes |
| *Was the information used to define intervention groups recorded at the start of the intervention?* | Yes |
| *Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?* | No |
| Overall risk due to intervention classification | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |

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| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | Yes – Due to the staggered recruitment of patients based on the timing of implementation of the intervention (SAT – self-administered therapy), there were some patients in the control (SOC- standard of care) cohort who received the intervention (n=17). However, they tended to only be placed out for SAT late in treatment (median time to SAT-enrollment was 14.8-months (IQR 12.8±20.3)), thus the bias would be minimal and towards the null. Additionally, patients in the SOC-cohort might have received an informal version of SAT as facilities occasionally provided a supply of medications for self-administration to relieve pressure on the clinic, despite clinic DOT being the SOC. This would so slightly bias the estimated effect of SAT towards the null. These patients however, did not receive the specialized counseling and ongoing community support integral to the intervention. Similarly, the |
| *If yes, were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?* | Yes – the estimated effect was likely biased towards the null due to contamination and slight deviations in the SOC group. |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 42/244 (17.2%) and 24/160 (15.0%) in the SAT and SOC cohorts were transferred out/not evaluated for final treatment outcomes. The proportions were similar across two groups. |
| *Were participants excluded due to missing data on intervention status?* | No |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No |
| *Were outcome assessors aware of the intervention received by study participants?* | Yes |
| *Were the methods of outcome assessment comparable across intervention groups?* | Yes |
| *Were any systematic errors in measurement of the outcome related to intervention received?* | No |
| Overall risk of outcome measurement bias | Low |

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| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall Risk of reporting bias | Low |
| **OVERALL BIAS** | Serious |
| **Author, Year** | Loveday 2015 |
| **Bias due to baseline confounding** | |
| *Did the authors use an appropriate analysis method that controlled for all the important confounding domains?* | No - there was no multivariate adjusted analysis for confounders. Some important confounders that were unbalanced at baseline between the two groups included: previous TB treatment (96% among patients at the centralized hospital vs. 60% among patients at the decentralized sites); and sputum smear-positivity (54% among patients at centralized hospital vs. 73% among patients at the decentralized sites). Unclear what direction this would bias the effect estimates. |
| *Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?* | N/A |
| *Did the authors control for any post-intervention variables that could have been affected by the intervention?* | No |
| Overall risk of confounding bias | Serious |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall risk of selection bias | Low |
| **Bias in classification of interventions** | |

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|---|---|
| *Were intervention groups clearly defined?* | Yes |
| *Was the information used to define intervention groups recorded at the start of the intervention?* | Yes |
| *Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?* | No |
| Overall risk due to intervention classification | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No |
| *If yes, were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?* | N/A |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | Yes – 2.7% among those at the decentralized sites and 0.2% of those at the centralized site were transferred out or were not evaluated for final treatment outcomes. |
| *Were participants excluded due to missing data on intervention status?* | No |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Low |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No |

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|---|---|
| *Were outcome assessors aware of the intervention received by study participants?* | Yes |
| *Were the methods of outcome assessment comparable across intervention groups?* | Yes |
| *Were any systematic errors in measurement of the outcome related to intervention received?* | No |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall risk of reporting bias | Low |
| **OVERALL BIAS** | Serious |
| **Author, Year** | Cox 2014 |
| **Bias due to baseline confounding** | |
| *Did the authors use an appropriate analysis method that controlled for all the important confounding domains?* | No - the paper had a multivariate adjusted model for estimating the effect of intervention on 'time to death', but not for lost to follow-up (our primary outcome of interest). The final treatment outcomes were available as stratified by HIV-status in the intervention (community-based model) group, but not for the control (hospital-based model) group. Limited data available on important potential confounders such as additional resistance to second-line drugs, and severity of disease. |
| *Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?* | N/A |
| *Did the authors control for any post-intervention variables that could have been affected by the intervention?* | N/A |
| Overall risk of confounding bias | Serious |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |

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|---|---|
| *Do start of follow-up and start of intervention coincide for most participants?* | Yes |
| Overall risk of selection bias | Low |
| **Bias in classification of interventions** | |
| *Were intervention groups clearly defined?* | Yes |
| *Was the information used to define intervention groups recorded at the start of the intervention?* | Yes |
| *Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?* | No |
| Overall risk due to intervention classification | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No |
| *If yes, were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?* | N/A |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 10.3% and 4.6% of the community-based and hospital-based cohorts were transferred out or not evaluated for final treatment outcomes. |
| *Were participants excluded due to missing data on intervention status?* | No |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Moderate |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No |
| *Were outcome assessors aware of the intervention received by study participants?* | No |
| *Were the methods of outcome assessment comparable across intervention groups?* | Yes |

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|---|---|
| *Were any systematic errors in measurement of the outcome related to intervention received?* | No |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall risk of reporting bias | Low |
| **OVERALL BIAS** | Serious |
| **Author, Year** | Huerga 2017 |
| **Bias due to baseline confounding** | |
| *Did the authors use an appropriate analysis method that controlled for all the important confounding domains?* | No –there was a multivariate analysis for the "unfavourable outcomes", not for lost to follow-up. Did not report on many potential confounders, however, among those reported, proportions infected with HIV were not balanced at baseline across the three groups (21.4% in Mathare; 60.7% in Homa Bay; and 15.7% in Nairobi), and was associated with unfavourable outcomes in both univariate and multivariate analyses. |
| *Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?* | N/A |
| *Did the authors control for any post-intervention variables that could have been affected by the intervention?* | No |
| Overall risk of confounding bias | Serious |
| **Bias in selection of participants into the study** | |
| *Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?* | No |
| *Do start of follow-up and start of intervention coincide for most participants?* | N/A |
| Overall risk of selection bias | Low |
| **Bias in classification of interventions** | |
| *Were intervention groups clearly defined?* | Yes |
| *Was the information used to define intervention groups recorded at the start of the intervention?* | No |

| | |
|---|---|
| *Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?* | No |
| Overall risk due to intervention classification | Low |
| **Bias due to deviations from intended interventions (assessing effect of assignment to intervention)** | |
| *Were there deviations from the intended intervention beyond what would be expected in usual practice?* | No |
| *If yes, were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?* | N/A |
| Overall risk due to deviations from interventions | Low |
| **Bias due to missing data** | |
| *Were outcome data available for all, or nearly all, participants?* | No – 25.0% in Homa Bay, 11.4% in Mathare and 12.7% in Nairobi sites were transferred out or not evaluated for final treatment outcomes. This is likely associated with both the intervention and lost to follow-up. |
| *Were participants excluded due to missing data on intervention status?* | No |
| *Were participants excluded due to missing data on other variables needed for the analysis?* | No |
| Overall risk of bias due to missingness | Moderate |
| **Bias in measurement of outcomes** | |
| *Could the outcome measure have been influenced by knowledge of the intervention received?* | No information |
| *Were outcome assessors aware of the intervention received by study participants?* | Yes |
| *Were the methods of outcome assessment comparable across intervention groups?* | N/A |
| *Were any systematic errors in measurement of the outcome related to intervention received?* | N/A |
| Overall risk of outcome measurement bias | Low |
| **Bias in selection of the reported result** | |
| *Multiple outcome measurements within the outcome domain?* | No |

| | |
|---|---|
| *Multiple analyses of the intervention-outcome relationship?* | No |
| *Bias in selection of the reported result [different subgroups?]* | No |
| Overall risk of reporting bias | Low |
| **OVERALL BIAS** | Serious |

**Table S10. Detailed quality assessment of cluster randomized trials**

| | |
|---|---|
| **Author, year** | Baral 2014 |
| Random sequence generation (selection bias) | Low |
| Support for judgement | "Prior to the start of the formative study, we randomly allocated the DOTS-plus centres to 3 types of care – 2 to counselling, 3 to combined support, and 2 to usual care – by selecting randomly from the numbers 1 to 7" |
| Allocation concealment (selection bias) | Low |
| Support for judgement | Cluster randomized trials – all patients at each randomized site received the same treatment. There is low risk of selection bias (of sites) due to lack of allocation concealment. |
| Blinding of participants and personnel (performance bias) | High |
| Support for judgement | Site staff likely knew they were randomized to an intervention site or not due to changes in treatment delivery practices. This could have caused better performance in non-intervention duties as well, which could lead to bias. |
| Blinding of outcome assessment (detection bias) | Low |
| Support for judgement | Assessment of final treatment outcomes are objective and unlikely to vary based on intervention status. |
| Incomplete outcome data (attrition bias) | Low |
| Support for judgement | Final treatment outcomes were reported for all enrolled patients. |
| Selective outcome reporting? (reporting bias) | Low |
| Support for judgement | All treatment outcomes were reported. |
| Other bias | Not enough clusters for randomization to eliminate confounding bias. Likely residual confounding, especially given some baseline imbalances. There was multivariate analysis for loss to follow-up outcome to adjust for age or sex, separately, but not for other important confounders, such as severity of disease. |
| Author, Year | Taneja 2017 |
| Random sequence generation (selection bias) | Low |
| Support for judgement | "Cluster trial was being planned in twenty hospitals in Delhi, therefore this pilot study was planned to be conducted with two hospitals. Among the hospitals two |

| | |
|---|---|
| | hospitals- Malviya Nagar Government Hospital and Nehru Nagar Chest Clinic were selected by simple random sampling using lottery method." |
| Allocation concealment (selection bias) | Low |
| Support for judgement | Use of simple random sampling to assign sites to cluster trial, unlikely to induce bias due to lack of concealment |
| Blinding of participants and personnel (performance bias) | High |
| Support for judgement | Site staff likely knew they were randomized to an intervention site or not due to changes in treatment delivery practices. This could have caused better performance in non-intervention duties as well, which could lead to bias. |
| Blinding of outcome assessment (detection bias) | Low |
| Support for judgement | Assessment of final treatment outcomes are objective and unlikely to vary based on intervention status. |
| Incomplete outcome data (attrition bias) | Low |
| Support for judgement | Final treatment outcomes were reported for all enrolled patients. |
| Selective outcome reporting? (reporting bias) | Low |
| Support for judgement | All treatment outcomes were reported. |
| Other bias | There were only two sites included in the study, which is a small sample size and susceptible to confounding. Also cluster design means site-specific characteristics could introduce confounding. There were baseline difference in important covariates such as religion, death of family member due to TB, family members with TB, that could have confounded results. However, there was no multivariate analyses done. |