



Treatment outcomes in Pulmonary Tuberculosis and associated factors worldwide: a systematic review and meta-analysis

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Introduction The increasing of TB burden is usually related to inadequate case detection, diagnosis and cure. Global targets for TB control, adopted by the World Health Organization (WHO), are to detect 70% of the estimated incidence of sputum smear-positive TB and to cure 85% of newly detected cases of sputum smear-positive TB (WHO, 2003).

Factors associated with unsuccessful treatment outcomes are closely related to TB risk factors.

Objectives To describe treatment success rates in pulmonary TB cases and to identify factors associated with unsuccessful treatment outcomes, according to *ad-hoc* studies.

Methods A systematic review of articles published between 2000 and 2012 was made, following the MOOSE guidelines (Meta-analysis of Observational Studies in Epidemiology Group). Online bibliographic databases PUBMED and WEB OF KNOWLEDGE were searched to identify relevant papers. Successful outcomes included patients who were cured or who completed treatment. Unsuccessful outcomes included died, failed, defaulted and transferred out (corresponding to WHO categories). Random-effect meta-analysis was used to estimate combined success rates and pooled odds ratios (OR), as studies did not share a common effect size.

Results

The 24 articles included (Figure 1) reported treatment outcomes on study populations from 17 countries. Seven studies approached determinants for successful outcomes and 17 for unsuccessful (Table 1).

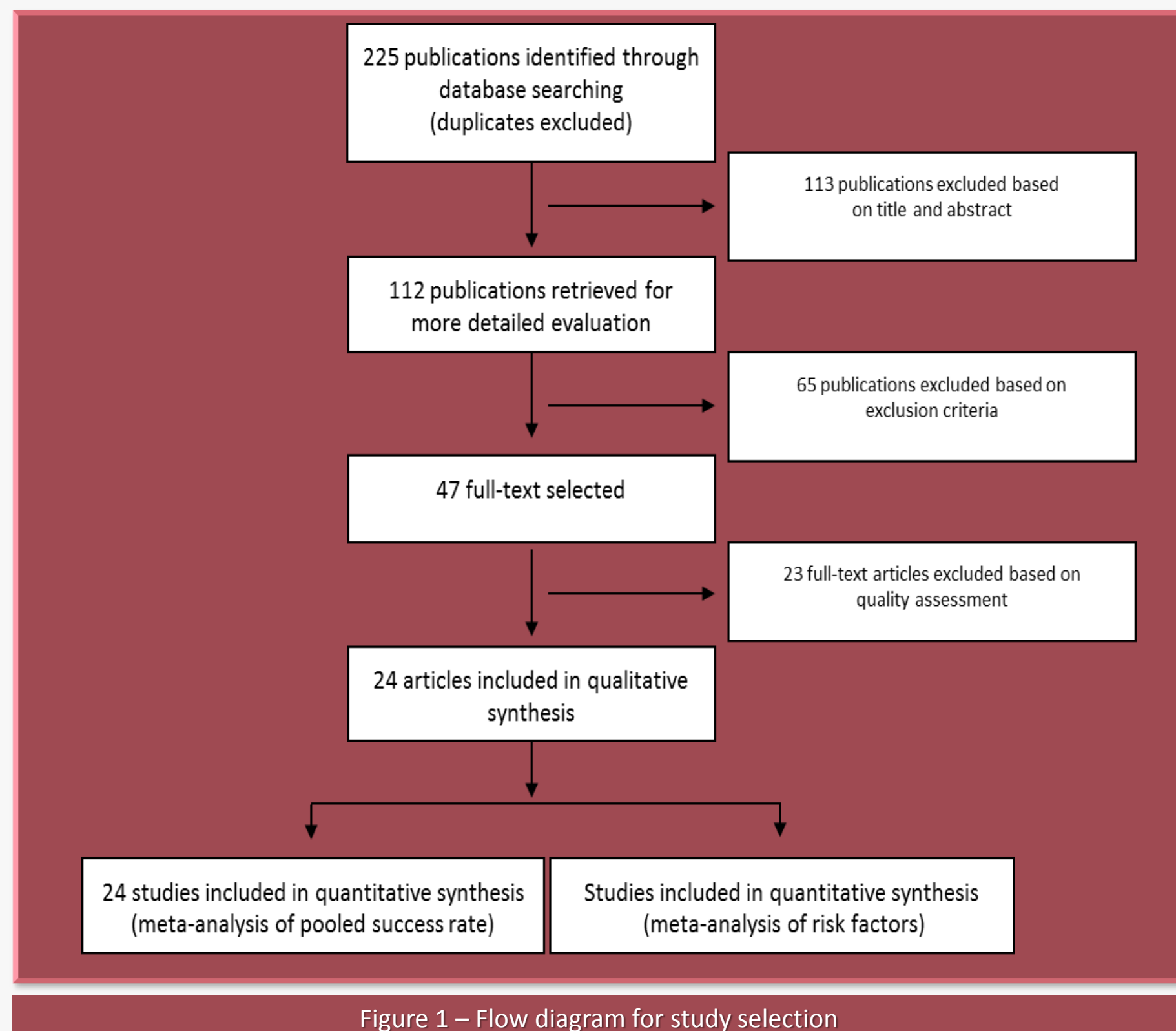
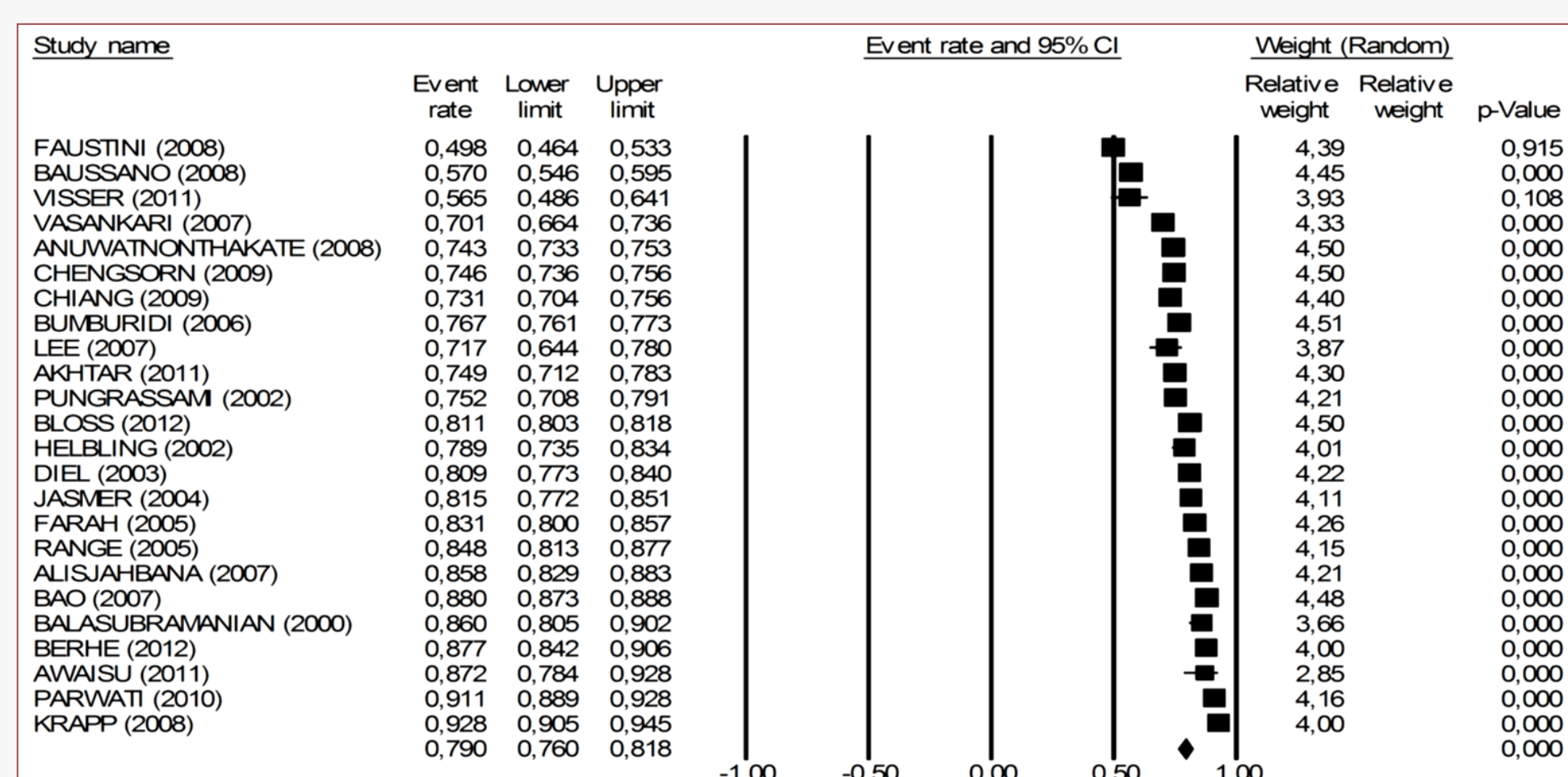


Figure 1 – Flow diagram for study selection

Success Rate

Success rates ranged from 49.6% to 92.8% and their pooled estimate was of 79.0% (95% CI: 76.0%–81.8%) (Figure 2). 7 showed success rates above 85%, and only 5 presented a success rate above 87%, 3 of which were institution-based. Studies with the highest rates (>87%) included new pulmonary patients only.



Random-effect model parameters: $Q=1550.81$; $p=0.000$; $I^2=98.5\%$. No possible effect of publication bias was found (Begg's test, $p=0.206$; Egger's tests, $p=0.744$).

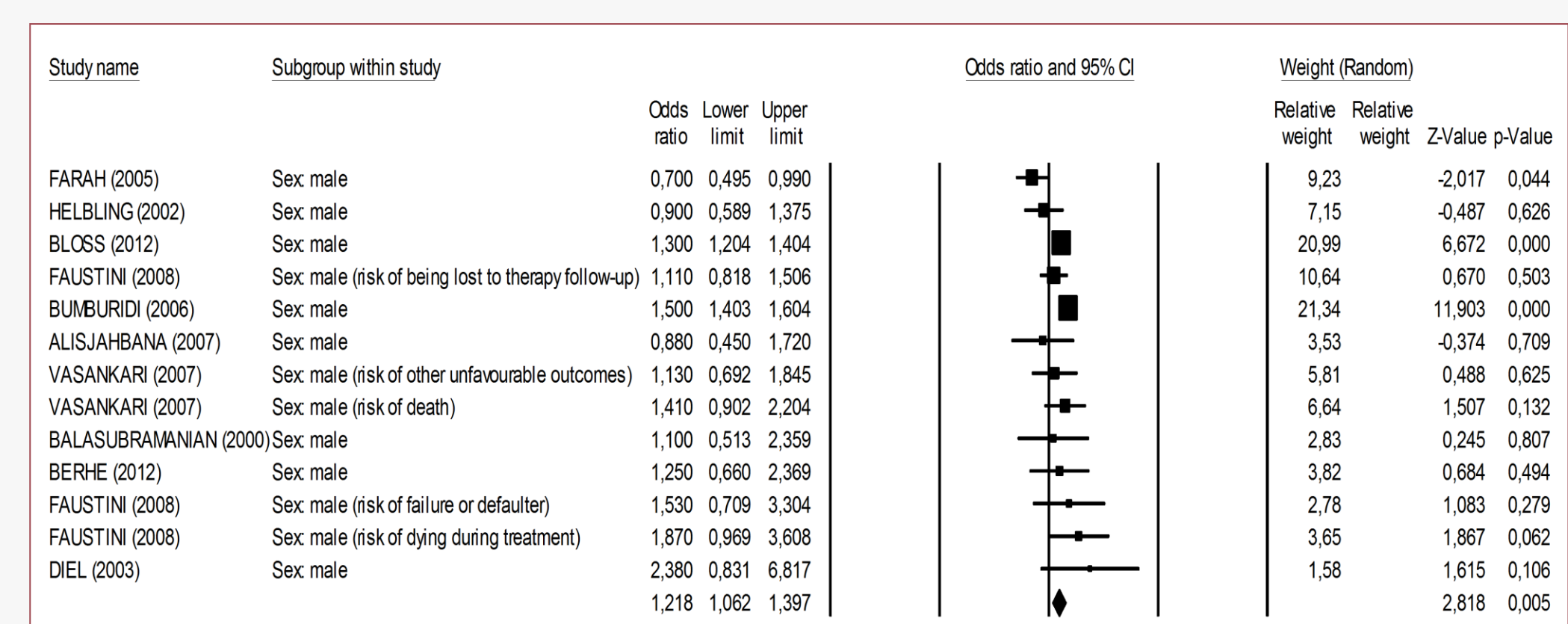
Figure 2 – Percentage of successful TB treatment outcomes and 95% confidence interval. The centre of the diamond represents the combined success rate.

Table 1 – Main characteristics of the studies.

| First author (year) | Country | PTB incidence 2011 (x10 ⁵) | *MDR-TB burden | *HIV burden | Study type | Study population | Success definition | Data collection |
|------------------------|-----------------------------|--|----------------|-------------|-----------------------------|------------------|-----------------------------|---|
| AKHTAR (2011) | Pakistan | 231 | High | - | cohort study | clinic-based | Cured + Treatment completed | Medical/Treatment records and questionnaire |
| ALISJAHBANA (2007) | Indonesia | 187 | High | High | cohort study | clinic-based | Cured | Medical/Treatment records |
| ANUWATNONTAKATE (2008) | Thailand | 124 | - | High | cohort study | clinic-based | Cured + Treatment completed | Medical/Treatment and laboratory records |
| AWAISU (2011) | Malaysia | 81 | - | - | cohort study | clinic-based | Cured + Treatment completed | Medical/Treatment records |
| BALASUBRAMANIAN (2000) | India | 181 | High | High | cohort study | clinic-based | Cured | Medical/Treatment records and questionnaire |
| BAO (2007) | China | 75 | High | High | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| BAUSSANO (2008) | Italy | 3 | - | - | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| BERHE (2012) | Ethiopia | 258 | High | High | cohort study | population-based | Cured + Treatment completed | Medical/Treatment records and questionnaire |
| BLOSS (2012) | China | 75 | High | High | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| BUMBURIDI (2006) | Kazakhstan | 129 | High | - | cohort study | population-based | Cured | Monitoring system |
| CHENGSORN (2009) | Thailand | 124 | - | High | cohort study | population-based | Cured + Treatment completed | Medical/Treatment and laboratory records |
| CHIANG (2009) | China | 75 | High | High | cohort study | population-based | Cured + Treatment completed | Medical/Treatment records |
| DIEL (2003) | Germany | 5 | - | - | cohort study | population-based | Cured + Treatment completed | Medical/Treatment records and questionnaire |
| FARAH (2005) | Norway | 6 | - | - | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| FAUSTINI (2008) | Italy | 3 | - | - | case-control study | population-based | Cured + Treatment completed | Monitoring system |
| HELBLING (2002) | Switzerland | 5 | - | - | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| JASMER (2004) | United States of America | 4 | - | - | cohort study | population-based | Cured + Treatment completed | Monitoring system |
| KRAPP (2008) | Peru | 101 | - | - | cohort study | clinic-based | Cured | Medical/Treatment records |
| LEE (2007) | China | 75 | High | High | cohort study | clinic-based | Cured + Treatment completed | Medical/Treatment records |
| PARWATI (2010) | Indonesia | 187 | High | High | cohort study | clinic-based | Cured | Medical/Treatment records |
| PUNGRASSAMI (2002) | Thailand | 124 | - | High | cohort study | clinic-based | Cured | Medical/Treatment records and questionnaire |
| RANGE (2005) | United Republic of Tanzania | 169 | - | High | randomized controlled trial | clinic-based | Cured | Medical/Treatment records and questionnaire |
| VASANKARI (2007) | Finland | 8 | - | - | cohort study | population-based | Cured + Treatment completed | Medical/Treatment records |
| VISSER (2011) | South Africa | 993 | High | High | randomized controlled trial | clinic-based | Cured | Medical/Treatment records |

Risk factors

Meta-analysis for risk factors was conducted only for age and sex, due to the limited number of studies focusing on other factors. Unsuccesses were significantly associated with male sex (OR=1.22, 95%CI: 1.06–1.40, $p=0.005$) (Figure 3). Age did not appear as a relevant factor.



Random-effect model parameters: $Q=33.56$; $p=0.001$; $I^2=64.3\%$. Begg's test, $p=0.127$; Egger's tests, $p=0.172$.

Figure 3 – Odds ratio for unsuccessful treatment outcomes for male sex. Estimates and 95% confidence intervals for each study together with the pooled estimate.

Conclusions Treatment success varied widely among studies and only 1/5 of them evinced success rates above the 85% WHO recommended threshold. The heterogeneity of studies focusing on success factors made it difficult to analyze their possible effects on outcomes; male sex was the most commonly identified risk factor, although this association was not strong. Most programs performance need to be closely monitored and improved.

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