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Title: The risk of multidrug or rifampicin-resistance in men versus women with TB

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Take-home message: Globally, the risk of drug-resistance, among those with TB, is the same for men as for women. However, local differences in high-burden risk groups lead to a need for a gender-differentiated approach to TB case-finding and care in some settings

Keywords:
Risk, Gender, Men, Women, Male, Female, Resistance, Burden, Prison, Migration, Foreign-born

Men are at an increased risk of Tuberculosis disease compared to women. Several risk factors for multidrug-resistant (MDR) or rifampicin-resistant (RR) TB disease are also more common in men, hence male TB patients may have a higher relative risk of MDR/RR-TB than female TB patients.

We used sex-disaggregated data of TB patients reported to the World Health Organization for 106 countries to calculate male-to-female (M:F) risk ratios of having MDR/RR-TB.

There was no evidence of either sex being more at risk of MDR/RR-TB in 81%(86/106) of countries, with an overall random-effects weighted M:F risk ratio of 1.04[95% confidence interval 0.97-1.11]. In 12%(13/106) of countries there was evidence that men were more at risk, while in 7%(7/106) women were more at risk. The risk of having TB that was MDR/RR increased for men compared to women as MDR/RR-TB incidence increased, and was higher for men than women in the Former Soviet Union, where the risk ratio was 1.16[1.06-1.28]. Conversely, the risk increased for women compared to men as GDP increased, and was higher for women than men in countries where the majority of TB burden was found in the foreign-born population, where the risk ratio was 0.84[0.75-0.94].

In general, the risk of MDR/RR-TB, among those with TB, is the same for men as for women. However, men in higher MDR/RR-TB burden countries, particularly the Former Soviet Union, face an increased risk that their infection is MDR/RR-TB, highlighting the need for a gender-differentiated approach to TB case-finding and care.

INTRODUCTION

Tuberculosis (TB) is the leading infectious cause of death globally, responsible for 1.5 million deaths in 2018. With around 214,000 of these deaths attributable to multidrug- or rifampicin-resistant (MDR/RR) TB disease,[1] TB contributes a third of all antimicrobial resistance (AMR) deaths globally, more than any other single infection.[2]

Of an estimated 10 million new cases of TB notified in 2018, 6.3 million were male and 3.7 million were female.[1] Men make up a greater proportion of undiagnosed prevalent TB, with over twice as many cases being missed among men as compared to women in low- and middle-income countries.[3] Furthermore, once diagnosed men have poorer treatment outcomes than women.[4] Despite clear evidence of substantial sex disparities in the burden of TB, whether these sex disparities extend to MDR/RR-TB is not well-understood.

Potential risk factors for drug-resistance may be more common in one sex, particularly men, than the other, which might be expected to further compound the known difference in risk in TB between sexes. Examples include a previous history of TB disease and treatment, reduced treatment adherence, longer duration of illness, imprisonment, smoking, and concurrent illnesses such as chronic obstructive pulmonary disease.[5,6] These risk factors will likely vary by setting. For example, in countries of the Former Soviet Union there have been high levels of past TB drug exposure combined with a degraded health system which may lead to reduced treatment support,[7] and hence high rates of MDR/RR-TB.

United Nations Member States have committed to addressing the global threats of both TB[8] and AMR.[9] To tackle these public health threats efficiently, groups at risk must be identified in order to ensure the most effective allocation of resources. Identifying groups with a higher burden of MDR/RR-TB is critical, particularly when empiric treatment is widely used, given the severe impact of the disease on health, increased mortality, long duration of treatment, potential toxicity of treatment and associated high costs.[7] In terms of the patient pathway, a lack of rapid drug susceptibility testing and the need to treat patients with the correct regimen quickly often results in empirical-evidence-based treatment.[10] It is therefore important to understand whether patient sex, including accompanying confounders, affects risk for drug-resistance.

We analysed country-level data on MDR/RR-TB reported to the World Health Organization (WHO) to calculate and compare risk ratios for MDR/RR-TB for men and women in this dataset. We compared male-to-female (M:F) risk ratios across settings and assessed the role of setting-specific risk groups in contributing to sex differences at a national level.

METHODS

Data

We used country-level sex-disaggregated data on new and previously treated cases collected by national TB programmes and reported to WHO. These data recorded the number of TB patients who underwent drug susceptibility testing (DST) before starting their current course of treatment, and had resistance results for rifampicin and isoniazid (MDR-TB, 2000-2015) or rifampicin (MDR/RR-TB, 2016-2018). Data were collected either through periodic, nationally representative drug-resistance surveys of a sample of patients, or through continuous surveillance by the routine collection of DST results for the majority of patients. We excluded data where drug resistance was not reported separately for men and women, or where data were not available for >80% of bacteriologically confirmed new TB cases.

Geographic segregation

To investigate any geographic differences, we compared WHO regions and two particular settings of interest; the Former Soviet Union, which has the highest proportions of MDR/RR-TB globally,[1] and low TB burden countries where most TB was found in the foreign-born population, such that the majority of MDR/RR-TB does not reflect local transmission.[11] In our dataset we identified Former Soviet Union countries as Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan. We identified selected low TB burden high-income countries were more than 50% of TB notifications were found in the foreign-born population as Australia, Austria, Belgium, Canada, Denmark, Germany, Israel, Italy, Luxembourg, Netherlands, New Zealand, Norway, Sweden, Switzerland, UK and USA, as well as Finland, Greece, Ireland and Slovenia where at least 25% of TB notifications were found amongst the foreign-born population.[11]

Analysis

We pooled data over time for countries with multiple years of available data, including pooling RR- and MDR-TB cases together, where these drugs were presumed to have the same M:F risk ratio. We calculated the ratio of the proportion of all male TB patients with a DST result that had MDR/RR-TB compared to the proportion of all female TB patients with a DST result that had MDR/RR-TB for each country separately. That is, the M:F risk ratio for each country. We conducted a random-effects meta-analysis on the country data to estimate the M:F risk ratio for MDR/RR-TB within TB patients globally, where we decided that high setting-specific variability in MDR/RR-TB burden and confounders warranted this approach over a fixed-effects meta-analysis as there was likely to be a distribution of true effects. We also conducted random-effects meta-analyses on country data by WHO geographic region, estimating heterogeneity using the I^2 statistic.[12]

We also compared M:F risk ratios for MDR/RR-TB across countries based on MDR/RR-TB burden and economic characteristics. We used WHO estimates[13] of the incidence of MDR/RR-TB per 100,000 population and the proportion of MDR/RR-TB among both new and retreatment pulmonary TB cases. We also used World Bank Group data[14] on country Gross Domestic Product Purchase Power Parity (GDP). We conducted weighted regression analyses (weighted by sample size) to identify any effect of MDR/RR-TB burden or GDP on the M:F risk ratio for MDR/RR-TB.

Using previously published data[15], we conducted a random-effects meta-analysis to identify the relative burden of MDR-TB compared to all TB in the foreign-born population in these selected low TB burden countries. We used United Nations data[16] on the foreign-born and foreign population to compare the sex of foreign-born individuals from high TB burden countries[1] in these selected low TB burden countries.

All analyses were conducted using the meta package[17] in the software R,[18] and results plotted using the ggplot2 package.[19] We considered there to be strong evidence of an association between sex and risk of MDR/RR-TB if the p-value for the M:F risk ratio was less than 0.01 and the strength of association was meaningful, in this case an effect size of >10%. We considered there to be some evidence of an association if the p-value was less than 0.05 and the effect size was >10%, and weak evidence (but cause for further investigation) if the p-value was less than 0.1 but the effect size was very large, in this case >25%. If the effect size was small (<10%) or the p-value large (>0.05 with a meaningful, but limited, effect size<25%), we considered that there was no evidence to conclude there was an association between sex and risk of MDR/RR-TB. We considered an I^2>25% to reflect an important level of heterogeneity[12], although we note that due to differences in confounding from surveillance and risk groups, a reasonable degree of heterogeneity is to be expected in our results.

Sensitivity analyses

We repeated the above analyses separately for data that were collected from drug resistance surveys versus through continuous surveillance, as the separate methods of data collection (representative samples of all notified cases compared to larger samples of only those notified patients receiving a DST) might have implications for gender bias. We also repeat the analyses separately for periods with data on MDR-TB (2000-2015) compared to RR-TB only (2016-2018).

We analysed how the M:F risk ratio changed according to the total proportion of all TB cases in the country (clinically or bacteriologically confirmed) who received a DST, conducting a weighted regression analyses (weighted by sample size). We used WHO estimates[13] of the total number of TB cases notified (including clinically diagnosed) and the number of notified TB cases tested for rifampicin resistance to characterise countries.

We compared different approaches to pooling data from multiple years. Firstly, we repeated the above geographic random-effects meta-analysis for the M:F risk ratio, but considered each year of data as separate, for countries that had data from multiple years. Secondly, we conducted fixed-effects meta-analyses on data by year for each country that had data over multiple years, where the setting and population were presumed to be invariant enough over time to warrant this approach to determining the true effect. Thirdly, we considered results if we only used the most recent year of data for each country.

RESULTS

Sex-disaggregated data were available for 106 countries and territories, out of 164 that report drug-resistance TB data to WHO[1] (see Fig 1 and supplementary material Table S1), for 264,842 male and 137,374 female TB patients from 2002 to 2018. These data represented a total of 267 country-years, out of a total of 1422 reported; sex-disaggregated data were not available for the remaining country-years. In these data, at the global level, there was no evidence for an association between sex and MDR/RR-TB risk in TB patients (M:F risk ratio of 1.04 [95% confidence interval 0.97-1.11] and I^2=81%, see Fig 2). Nor was there evidence for an association between sex and risk in 86 (81%) countries (see Fig 1 and Supplementary Material Table S1 and Fig S1).

There was evidence of a M:F risk ratio greater than 1, i.e. men were more at risk of MDR/RR-TB than women, in 13 out of 106 (12%) countries - strong evidence of an association between sex and risk in Belarus, Georgia, Kazakhstan, Latvia, Lesotho, Lithuania, Malaysia, Peru, Poland, R. Moldova and Serbia and weak evidence in Eritrea and Jordan.

There was evidence of a M:F risk ratio less than 1, i.e. women were more at risk of MDR/RR-TB than men, in 7 out of 106 (7%) countries. The evidence of an association between sex and risk was strong in Eswatini, Netherlands, Namibia, Singapore and the USA, and weak in Pakistan and Oman).

Regional M:F risk ratios

There was strong evidence of an association between male sex and risk in the Former Soviet Union, where the M:F risk ratio was 1.16 (95% confidence interval [CI] 1.06-1.28, I^2=91%). Although 12 out of 13 countries had a risk ratio greater than 1, large sample sizes led to narrow confidence intervals with poor overlap.

There was strong evidence that in low TB burden countries where the majority of TB notifications occur in the foreign-born population[11] (see Table 1) there was an association between female sex and risk of MDR/RR-TB in women, with a M:F risk ratio of 0.84 (95% CI 0.75-0.94, I^2=31%). The strength of this evidence remained the same if we included countries where at least 25% of TB notifications were found in the foreign-born population (Finland, Greece, Ireland and Slovenia in our dataset), with a M:F risk ratio of 0.83 (95% CI 0.75-0.92, I^2=15%).

Trends in M:F risk ratios

There was evidence that the M:F risk ratio increased with increasing MDR/RR-TB incidence per 100,000 population, but no evidence of an increase with increasing proportion of MDR/RR-TB in either new and retreatment cases (see Fig 3).

There was strong evidence that the M:F risk ratio decreased with increasing GDP (see Fig 4). GDP was inversely correlated with the measures of MDR/RR-TB burden described above.

Foreign-born population

There was very strong evidence that, for selected high-income countries where the majority of notified TB cases occurred in the foreign-born population, the ratio of MDR-TB cases that were found in the foreign-born compared to general population (i.e. the number of cases in each population) was larger than the ratio for all TB cases.

The foreign-born population from WHO high TB burden countries in these selected countries were also consistently more likely to be women than men (see Table 1).

Sensitivity analysis

If we considered survey and surveillance data separately (54 countries each, where 2 countries had both forms of data available), neither group showed a M:F risk ratio different from 1. The above trend of changing risk with GDP and MDR/RR-TB incidence were present in the data from continuous surveillance (with reduced strength of evidence) but were not present in the survey data. This may be because few countries with a high GDP, or Former Soviet Union countries with a high MDR/RR-TB burden, rely on survey data. If we consider MDR-TB data and RR-TB data separately, only 5 countries reported RR-TB results: Eritrea, Lao PDR, Mongolia, Togo and UR Tanzania. Of these, only Mongolia had data for both MDR-TB and RR-TB, where separately analysing these data did not qualitatively change our conclusion that there was no evidence of an association between sex and risk of MDR/RR-TB in Mongolia.

There was no evidence in either the survey or surveillance data that the M:F risk ratio increased with an increase in the DST rate in the country in general.

If we considered each year of data for a country separately, there was still no evidence that the global M:F risk ratio was different to 1, with a M:F risk ratio of 1.03 (95% CI 0.98-1.09, I^2=75%). However, there was evidence of an association between female sex and risk in the Region of the Americas, and between male sex and risk in the European region (primarily as a result of inclusion of countries of the Former Soviet Union). There remained strong evidence of an association between male sex and risk in the Former Soviet Union. If we considered countries with multiple years of data and conducted a fixed-effects meta-analysis on each separate year, rather than simply pooling the data, our results were largely unchanged except in terms of the strength of evidence. If we considered only the most recent year of data, of those countries with multiple years of data only Kazakhstan and Georgia retained evidence of an association between sex and risk.

DISCUSSION

Our analysis showed that there was no evidence of an association between sex and risk of MDR/RR-TB in TB patients both globally and nationally in the majority (81%, 86/106) of countries, with an overall random-effects weighted M:F risk ratio of 1.04 [95% confidence interval 0.97-1.11]. However, the high level of heterogeneity in our results suggest that this association may vary significantly between settings. In 12% (13/106) of countries there was evidence that men were more at risk than women, while in 7% (7/106) there was evidence that women were more at risk than men. There was evidence that the risk of having TB that was MDR/RR increased for men compared to women as MDR/RR-TB incidence increased, and was higher for men than women in the Former Soviet Union where the M:F risk ratio was 1.16 [1.06-1.28]. Conversely, there was strong evidence that the risk of having TB that was MDR/RR increased for women compared to men as GDP increased, and was higher for women than men in countries where the majority of TB burden was found in the foreign-born population, where the M:F risk ratio was 0.84 [0.75-0.94].

Our analysis provides the most comprehensive analysis to date of the relationship between MDR/RR-TB and sex. While men are at greater risk than women of developing TB, men with TB are at no greater risk of MDR/RR-TB than women with TB. Men's excess of several risk factors that are associated with MDR/RR-TB, such as non-adherence and smoking,[5,6] do not result in an increased risk of MDR/RR-TB globally. Our results are consistent with previous global analyses suggesting that men with TB are no more at risk of MDR/RR-TB than women, while reinforcing the observation that this risk is strongly modified by setting.[5,20] Indeed, some setting-specific studies suggest an increased risk of MDR/RR-TB (in varying forms) amongst men,[21-26] while others suggest an increased risk amongst women,[27-32] and still others find no evidence that sex is a factor.[33-37]

Our results provide no evidence that there is a biological reason for either sex to be at a higher risk of MDR/RR-TB than the other, although this cannot be ruled out. However, heterogeneity in our results by setting suggests that there could be some role for gender (i.e. the role of males versus females in society) in determining either risk or detection of MDR/RR-TB. Specifically, variation between settings in the risk of MDR/RR-TB by sex may be due to differences in surveillance systems resulting in biases (such as coverage of DST or rates of clinical diagnosis) or a reflection of the local context (such as setting-specific differences in the M:F ratio among groups at risk, including prisoners, miners or foreign-born populations). In settings where there is evidence of a difference in risk of MDR/RR-TB between men and women, the interpretation depends on several considerations, and further investigation into confounding factors is required. We can only conclude that a particular group could be driving sex-related differences in MDR/RR-TB risk if there is simultaneously: (i) a higher rate of MDR/RR-TB as a proportion of all TB in the group than in the general population, (ii) a large enough fraction of TB in the population attributable to the group, and (iii) a large enough discrepancy in the sex ratio of the risk group.

Our results provided evidence that the risk of having TB that was MDR/RR increased for men compared to women as the MDR/RR-TB incidence, but not rate (in terms MDR/RR-TB as a proportion of all TB) increased. This was likely a result of the higher risk for men than women in the high MDR/RR-TB burden countries of the Former Soviet Union, which was consistent with previous results.[5,20] The high M:F risk ratios for MDR/RR-TB in these countries could be related to factors such as alcohol dependency or incarceration;[20,38] for example, high per capita rates of TB[39] as well as MDR/RR-TB[40] in prison populations in these countries, combined with a high proportion of TB cases attributable to prisons[41] could increase the M:F risk ratio given that prisoners are more often male than female.[42]

Conversely, there was strong evidence that the risk of having TB that was MDR/RR increased for women compared to men as GDP increased. The risk was also higher for women than men in countries where a high proportion of the national TB burden occurred in the foreign-born population, where countries with a high GDP are likely to see a greater proportion of TB in foreign-born populations. This could be due to the combined increased risk of MDR/RR-TB in foreign-born populations and the fact that women accounted for more than 50% of documented foreign-born individuals originating from high TB burden countries. MDR/RR-TB is also primarily a result of reactivation in these countries and may be influenced by poor living conditions and barriers to accessing care. In contrast to low and middle-income countries, this may affect women more than men amongst migrants in these countries as they are less likely to be active in the workforce.[43] However, these data do not take into account undocumented migrants, which may bias the findings.

Our dataset did not allow a comparison of whether men or women were more likely to have DST performed. These data are not routinely collected, and few studies report DST rate by sex (although see, for example, [44]). However, In countries where the coverage of TB patients with DST was lower (which are more likely to be those with data from only periodic surveys) the higher likelihood for women compared to men to be clinically diagnosed rather than bacteriologically confirmed could affect the M:F risk ratios we observed. This, in turn, could be influenced by factors relating to access to appropriate diagnostics services. With an increasing number of countries recommending Xpert MTB/RIF for all TB cases,[45] any previous difference in access to DST according to sex (if such a difference exists) should be overcome. However, practical implementation of these policies is of course challenging and achieving 100% coverage of DST will take some time.

The dataset also did not distinguish new and previously treated cases by sex, which may have allowed the identification of factors that increased risk for either sex for acquiring MDR/RR-TB through direct transmission or during treatment of a drug-susceptible strain. However, we note that sex is not known to modify the association between previous treatment and MDR-TB[21].Due to a lack of sex-disaggregated data, we were also not able to assess sex disparities in risk of extensively drug-resistant TB, where there has been some suggestion that women might be at an increased risk.[46-50]

Finally, sex-disaggregated data were not available for 11 of the 30 high MDR/RR-TB burden countries, including Angola, DPR Korea, DR Congo, Ethiopia, India, Indonesia, Kyrgyzstan, Papua New Guinea, Russian Federation, South Africa and Zimbabwe. It is vital that laboratory networks and case recording and reporting systems in these and other high MDR/RR-TB burden countries be strengthened.

Conclusions

At a global level, the risk of MDR/RR-TB among TB patients is the same for men as for women, unless directly linked to a particular risk group, despite men having a known higher risk of TB. However, men in higher MDR/RR-TB burden countries, particularly the Former Soviet Union, face not just an increased risk of TB disease, but also a further increased risk that their infection is multidrug- or rifampicin-resistant. This highlights the need for a gender-differentiated approach to TB case-finding and care. Access to rapid, universal DST at the time of TB diagnosis is required to inform an appropriate treatment regimen, improve the outcomes of treatment, reduce costs faced by patients and those associated with health systems, and prevent onward transmission for both men and women.

CONTRIBUTORS

CFM and KCH conceived and designed the study. CFM performed all the data analysis and wrote a first draft of the article. CFM, KCH, ASD, GMK, and RGW designed the methodology and critiqued the results. All authors contributed to editing the final draft.

DECLARATION OF INTERESTS

We declare no competing interests.

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FIGURES AND TABLES

Table 1: Foreign-born and foreign population from high TB burden countries by sex in 2015 based on official statistics,[16] as well as number of TB and MDR-TB cases,[15,51-54] for selected countries where >50% of TB incidence is in the foreign-born population.[11]

Country	Men	Women	MDR/RR-TB MF ratio	TB cases (foreign-born in [])	MDR-TB cases (foreign-born in [])
Australia	931,365	1,036,116	0.90		
Austria	63,034	78,322	0.80	583 [364]	12 [12]
Belgium	72,608	78,592	0.92	988 [519]	15 [13]
Canada	1,352,339	1,549,093	0.87	1,639 [1,169]	22
Denmark	48,809	69,886	0.70	357 [242]	6 [4]
Germany	1,481,691	1,843,541	0.80	5,864 [3969]	120 [109]
Israel	207,640	253,145	0.82	280 [233]	11
Italy	679,994	920,734	0.74	3,769 [1,764]	70
Luxembourg	1,329	1,602	0.83	30 [20]	0 [0]
Netherlands	201,321	252,283	0.80	867 [625]	10 [10]

New Zealand	153,171	163,564	0.94	253 [217]	2 [2]
Norway	74,313	109,176	0.68	318 [282]	5 [5]
Sweden	131,461	172,289	0.76	821 [735]	22 [21]
Switzerland	91,695	151,948	0.60	564 [428]	11
United Kingdom	1,591,934	1,759,494	0.90	6,240 [4,312]	49 [42]
USA	5,301,978	6,052,656	0.88	9,557 [6,350]	73 [63]

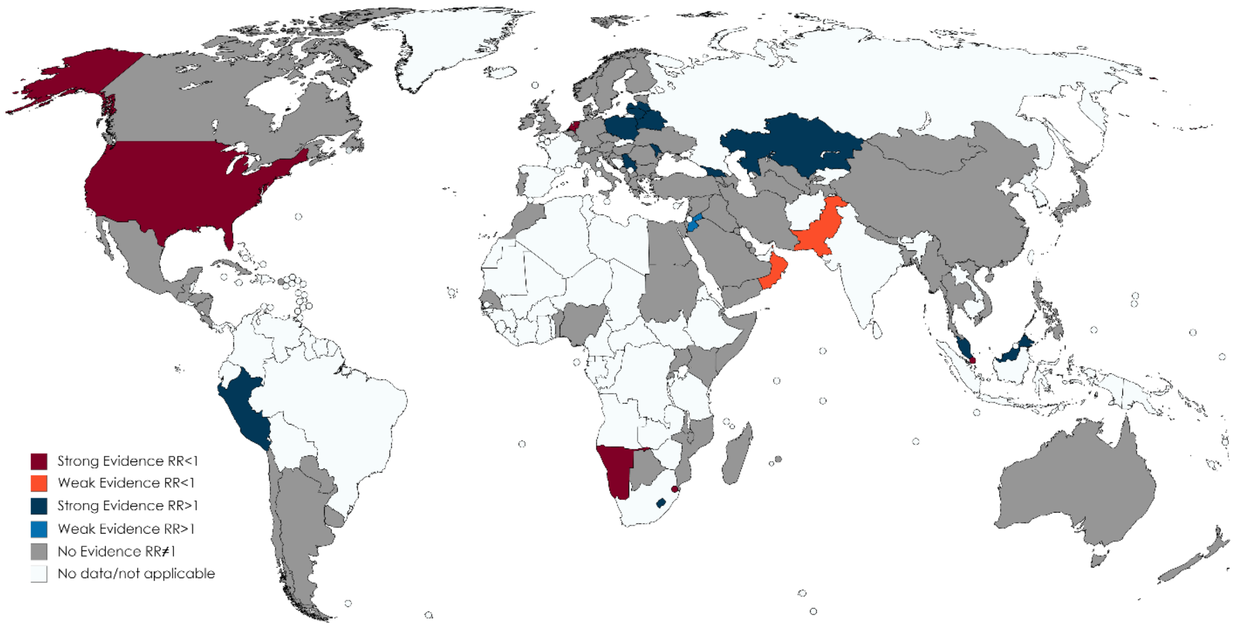


Figure 1: Countries with WHO-reported drug resistance survey/surveillance data disaggregated by sex, showing those with strong evidence (p-value<0.01 and effect size>10%), or weak evidence (0.05<p-value<0.1 and effect size>25%) for an association between sex and risk of MDR/RR-TB amongst TB patients. In blue, there is evidence of an association between male sex and risk, in red between female sex and risk. Countries in grey have sex disaggregated data but no evidence of an association.

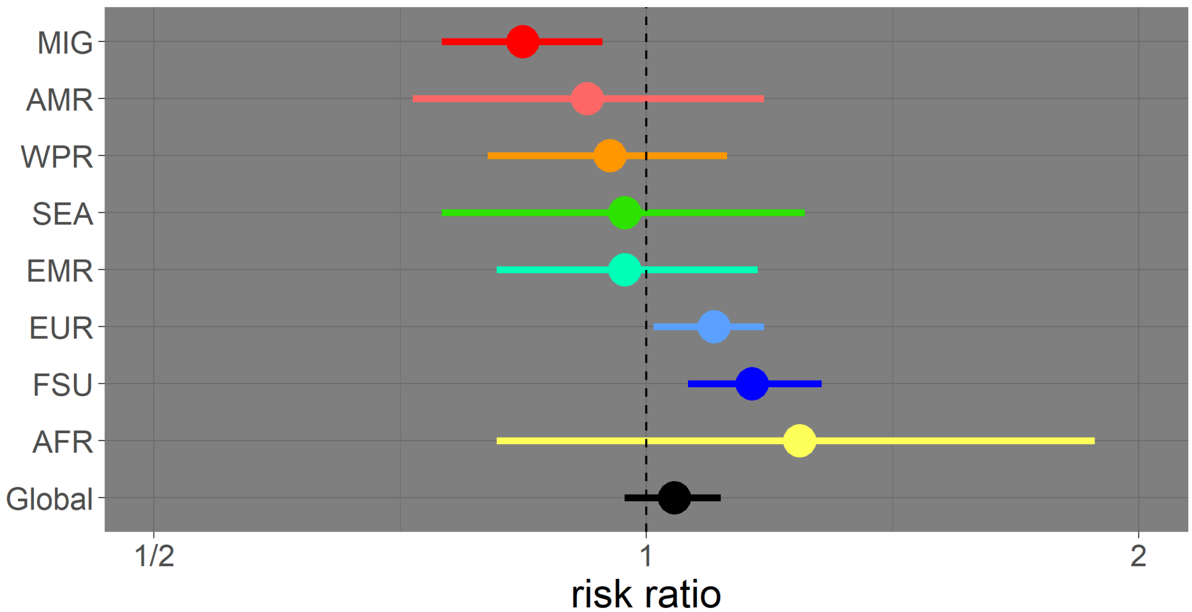
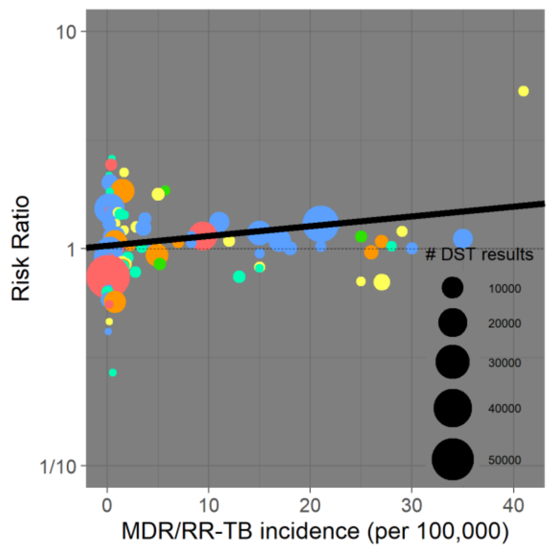


Figure 2: Forest plot showing MDR/RR-TB M:F risk ratio and 95% confidence interval for by WHO region or setting of interest (countries where the majority of TB is found in the foreign-born population MIG, Region of the Americas AMR, Western Pacific Region WPR, South-East Asia Region SEA, Eastern Mediterranean Region EMR, European Region EUR, Former Soviet Union FSU and African Region AFR). Data among all (new and retreated) cases are presented.



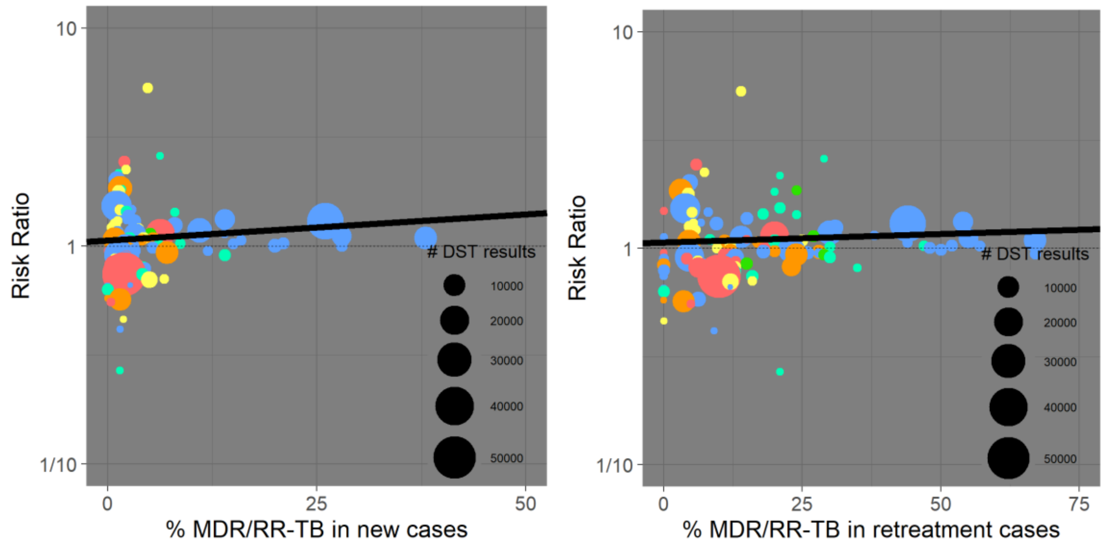


Figure 3: MDR/RR-TB burden compared to MDR/RR-TB M:F risk ratio by country. Data among all (new and retreated) cases are presented, where each circle represents a country where the size is scaled to the number of sex-disaggregated DST results available. Black lines indicate the weighted linear regression best-fit. Colours indicate the WHO region for each country (African Region in yellow, Region of the Americas in red, Eastern Mediterranean Region in turquoise, European Region in blue, South-East Asia Region in green and Western Pacific Region in orange). A risk ratio greater than 1 suggests that, among those with TB, men were more at risk of MDR/RR-TB than women, while a risk ratio less than 1 suggests that, among those with TB, women were more at risk of MDR/RR-TB than men.

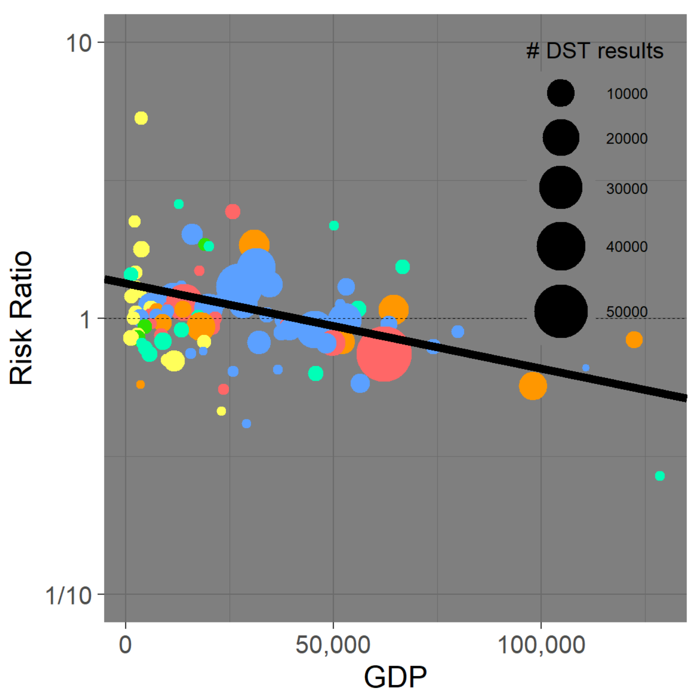


Figure 4: Gross Domestic Product Purchase Power Parity compared to MDR/RR-TB M:F risk ratio by country. Data among all (new and retreated) cases are presented, where each circle

represents a country where the size is scaled to the number of sex-disaggregated DST results available. The black line indicates the weighted linear regression best-fit. Colours indicate WHO region for each country (African Region in yellow, Region of the Americas in red, Eastern Mediterranean Region in turquoise, European Region in blue, South-East Asia Region in green and Western Pacific Region in orange). A risk ratio greater than 1 suggests that, among those with TB, men were more at risk of MDR/RR-TB than women, while a risk ratio less than 1 suggests that, among those with TB, women were more at risk of MDR/RR-TB than men.

country	iso3	region	year	dr_m	dr_f	total_m	total_f	burden_inc
Albania	ALB	WER	2011	4	1	151	54	0.53
Argentina	ARG	AMR	2005	22	14	507	322	1.2
Armenia	ARM	FSU	2007	171	28	758	134	8.3
Australia	AUS	WPR	2002	6	6	361	347	0.16
Australia	AUS	WPR	2003	6	1	421	363	0.16
Australia	AUS	WPR	2004	7	5	417	368	0.16
Australia	AUS	WPR	2005	3	8	427	383	0.16
Australia	AUS	WPR	2007	10	14	48	50	0.16
Australia	AUS	WPR	2008	7	14	50	46	0.16
Australia	AUS	WPR	2010	18	15	606	504	0.16
Australia	AUS	WPR	2011	13	10	408	315	0.16
Australia	AUS	WPR	2012	10	8	514	382	0.16
Australia	AUS	WPR	2013	7	7	364	239	0.16
Australia	AUS	WPR	2014	5	10	380	306	0.16
Austria	AUT	WER	2008	10	4	311	176	0.22
Austria	AUT	WER	2010	8	8	290	184	0.22
Austria	AUT	WER	2011	15	5	288	162	0.22
Austria	AUT	WER	2012	14	13	234	158	0.22
Austria	AUT	WER	2013	11	5	238	131	0.22
Austria	AUT	WER	2014	11	7	238	118	0.22
Azerbaijan	AZE	FSU	2013	101	37	587	202	15
Bahrain	BHR	EMR	2011	8	1	23	9	0.22
Bahrain	BHR	EMR	2012	3	1	106	55	0.22
Bangladesh	BGD	SEA	2011	68	31	949	395	5.1
Belarus	BLR	FSU	2011	512	100	1075	269	17
Belarus	BLR	FSU	2012	1243	321	2600	747	17
Belarus	BLR	FSU	2013	1070	283	2481	761	17
Belarus	BLR	FSU	2014	1054	197	2370	433	17
Belgium	BEL	WER	2008	13	9	524	249	0.23
Belgium	BEL	WER	2010	15	4	547	275	0.23
Belgium	BEL	WER	2011	7	8	481	262	0.23
Belgium	BEL	WER	2012	10	10	484	251	0.23
Belgium	BEL	WER	2013	5	5	366	188	0.23
Belgium	BEL	WER	2014	7	2	360	174	0.23
Benin	BEN	AFR	2010	6	2	304	144	0.84
Botswana	BWA	AFR	2008	15	17	563	496	15
Bulgaria	BGR	WER	2010	42	14	698	270	0.56
Bulgaria	BGR	WER	2012	37	12	589	240	0.56
Canada	CAN	AMR	2005	9	6	611	447	0.07
Canada	CAN	AMR	2008	9	5	695	554	0.07
Canada	CAN	AMR	2010	10	5	593	469	0.07
Canada	CAN	AMR	2011	9	10	730	587	0.07
Canada	CAN	AMR	2012	1	8	823	543	0.07
Canada	CAN	AMR	2013	6	9	577	388	0.07
Canada	CAN	AMR	2014	6	5	545	383	0.07
Chile	CHL	AMR	2014	13	2	915	450	0.41
China	CHN	WPR	2007	262	139	2818	1111	4.9
China	CHN	WPR	2013	318	109	5257	2038	4.9
China, Hon	HKG	WPR	2005	29	12	3007	1344	0.8
China, Hon	HKG	WPR	2007	12	2	1999	929	0.8
China, Hon	HKG	WPR	2008	13	5	1877	876	0.8
China, Hon	HKG	WPR	2011	13	10	1411	788	0.8
China, Mac	MAC	WPR	2005	5	4	209	75	1.6
China, Mac	MAC	WPR	2007	2	3	220	82	1.6
China, Mac	MAC	WPR	2008	5	2	214	69	1.6

China, Mac	MAC	WPR	2010	5	1	23	9	1.6
China, Mac	MAC	WPR	2011	4	1	197	109	1.6
China, Mac	MAC	WPR	2012	3	5	220	103	1.6
China, Mac	MAC	WPR	2013	6	3	212	93	1.6
China, Mac	MAC	WPR	2014	4	4	77	193	1.6
Costa Rica	CRI	AMR	2006	4	1	200	84	0.13
Croatia	HRV	WER	2014	1	1	223	125	0
Cuba	CUB	AMR	2002	1	1	179	52	0.18
Cuba	CUB	AMR	2003	4	1	199	42	0.18
Cuba	CUB	AMR	2004	1	3	158	47	0.18
Cuba	CUB	AMR	2011	9	1	314	100	0.18
Cuba	CUB	AMR	2012	7	1	264	67	0.18
Czechia	CZE	WER	2008	7	4	350	170	0.16
Czechia	CZE	WER	2010	7	2	294	125	0.16
Czechia	CZE	WER	2012	3	1	267	130	0.16
Czechia	CZE	WER	2014	2	3	221	85	0.16
Denmark	DNK	WER	2011	2	1	171	100	0.03
Djibouti	DJI	EMR	2015	21	12	255	111	15
Egypt	EGY	EMR	2011	117	47	1044	370	2
Estonia	EST	FSU	2008	50	24	250	97	4.1
Estonia	EST	FSU	2010	47	17	196	67	4.1
Estonia	EST	FSU	2011	54	24	181	81	4.1
Estonia	EST	FSU	2012	44	17	173	66	4.1
Estonia	EST	FSU	2013	37	13	148	64	4.1
Estonia	EST	FSU	2014	41	7	137	46	4.1
Eswatini	SWZ	AFR	2009	46	76	309	324	25
Eritrea	ERI	AFR	2018	11	4	276	287	1.7
Finland	FIN	WER	2010	5	1	152	98	0.23
Finland	FIN	WER	2011	1	4	136	110	0.23
Finland	FIN	WER	2012	2	1	131	91	0.23
Finland	FIN	WER	2013	1	1	117	54	0.23
Finland	FIN	WER	2014	3	2	81	76	0.23
Georgia	GEO	FSU	2006	181	38	1169	251	15
Georgia	GEO	FSU	2010	301	58	2023	522	15
Georgia	GEO	FSU	2011	381	72	2291	581	15
Georgia	GEO	FSU	2012	267	79	1898	574	15
Georgia	GEO	FSU	2013	303	81	1627	529	15
Georgia	GEO	FSU	2014	303	66	1495	490	15
Germany	DEU	WER	2008	28	17	1763	1085	0.23
Germany	DEU	WER	2010	23	28	1720	1142	0.23
Germany	DEU	WER	2011	31	23	1712	1150	0.23
Germany	DEU	WER	2012	38	23	1765	1050	0.23
Germany	DEU	WER	2013	55	29	1525	836	0.23
Germany	DEU	WER	2014	59	24	1509	787	0.23
Greece	GRC	WER	2010	1	1	72	23	0.1
Guatemala	GTM	AMR	2002	31	29	628	490	0.75
Honduras	HND	AMR	2004	11	6	338	192	0.88
Hungary	HUN	WER	2010	15	4	396	174	0.27
Iran (Islami	IRN	EMR	2014	13	9	647	507	0.24
Iraq	IRQ	EMR	2013	21	17	563	464	3.4
Ireland	IRL	WER	2011	2	1	154	95	0.07
Ireland	IRL	WER	2012	3	2	158	107	0.07
Ireland	IRL	WER	2013	2	2	128	71	0.07
Israel	ISR	WER	2008	6	3	139	86	0.25
Israel	ISR	WER	2010	11	1	166	81	0.25
Israel	ISR	WER	2011	6	5	203	81	0.25

Israel	ISR	WER	2012	10	7	203	121	0.25
Israel	ISR	WER	2013	3	4	113	44	0.25
Israel	ISR	WER	2014	11	4	135	67	0.25
Italy	ITA	WER	2010	31	56	987	1588	0.3
Italy	ITA	WER	2012	44	30	1495	926	0.3
Japan	JPN	WPR	2002	42	18	2211	911	0.45
Jordan	JOR	EMR	2004	16	2	93	40	0.49
Kazakhstar	KAZ	FSU	2011	3028	1547	7834	4289	21
Kazakhstar	KAZ	FSU	2012	5221	2387	5517	2864	21
Kazakhstar	KAZ	FSU	2013	4138	1894	7719	6854	21
Kenya	KEN	AFR	2014	12	3	1226	649	5
Kuwait	KWT	EMR	2010	4	1	233	204	0.57
Kuwait	KWT	EMR	2013	1	2	215	225	0.57
Kuwait	KWT	EMR	2014	5	2	191	129	0.57
Latvia	LVA	FSU	2008	96	33	607	221	3.6
Latvia	LVA	FSU	2010	64	24	499	217	3.6
Latvia	LVA	FSU	2011	75	20	443	201	3.6
Latvia	LVA	FSU	2012	84	22	536	230	3.6
Latvia	LVA	FSU	2013	57	18	469	181	3.6
Latvia	LVA	FSU	2014	55	15	415	158	3.6
Lao People	LAO	WPR	2018	9	4	647	299	2.3
Lebanon	LBN	EMR	2003	9	3	119	87	0.25
Lesotho	LSO	AFR	2014	46	24	156	715	41
Lithuania	LTU	FSU	2008	223	53	1214	402	11
Lithuania	LTU	FSU	2010	240	70	1010	353	11
Lithuania	LTU	FSU	2011	243	53	1031	372	11
Lithuania	LTU	FSU	2012	214	57	1014	354	11
Lithuania	LTU	FSU	2013	214	39	1008	307	11
Lithuania	LTU	FSU	2014	218	50	885	340	11
Luxembour	LUX	WER	2011	1	1	12	7	0.23
Madagasca	MDG	AFR	2007	2	1	344	221	1.7
Malawi	MWI	AFR	2011	17	16	1009	768	1.8
Malaysia	MYS	WPR	2014	79	17	8761	4192	1.5
Marshall Isl	MHL	WPR	2012	1	2	37	36	0
Mauritius	MUS	AFR	2010	1	1	82	30	0.22
Mexico	MEX	AMR	2009	30	15	1455	666	0.72
Mongolia	MNG	WPR	2007	44	20	551	299	27
Mongolia	MNG	WPR	2016	67	43	849	574	27
Montenegr	MNE	WER	2014	1	1	40	28	0.01
Morocco	MAR	EMR	2006	21	7	863	375	1.5
Morocco	MAR	EMR	2014	17	11	974	307	1.5
Mozambiqu	MOZ	AFR	2007	86	42	696	431	29
Myanmar	MMR	SEA	2008	54	21	938	432	25
Namibia	NAM	AFR	2008	47	52	813	622	27
Namibia	NAM	AFR	2015	69	75	1914	1268	27
Nepal	NPL	SEA	2007	27	14	683	246	5.2
Nepal	NPL	SEA	2011	30	12	584	222	5.2
Netherland	NLD	WER	2008	4	9	423	305	0.1
Netherland	NLD	WER	2010	6	5	451	333	0.1
Netherland	NLD	WER	2011	7	9	425	301	0.1
Netherland	NLD	WER	2012	5	6	386	270	0.1
Netherland	NLD	WER	2013	5	9	241	130	0.1
New Zealar	NZL	WPR	2004	2	1	145	142	0.23
New Zealar	NZL	WPR	2005	1	3	135	126	0.23
New Zealar	NZL	WPR	2007	1	1	109	119	0.23
New Zealar	NZL	WPR	2009	4	3	123	121	0.23

New Zealai	NZL	WPR	2011	1	1	116	118	0.23
New Zealai	NZL	WPR	2012	2	2	130	103	0.23
Nicaragua	NIC	AMR	2006	7	5	220	148	0.67
Nigeria	NGA	AFR	2010	46	22	935	500	12
Norway	NOR	WER	2008	2	2	123	104	0.2
Norway	NOR	WER	2010	3	5	154	121	0.2
Norway	NOR	WER	2011	1	3	138	120	0.2
Norway	NOR	WER	2012	3	3	158	123	0.2
Norway	NOR	WER	2013	2	3	123	87	0.2
Norway	NOR	WER	2014	6	2	142	101	0.2
Oman	OMN	EMR	2002	3	3	105	69	0
Oman	OMN	EMR	2003	3	4	92	70	0
Oman	OMN	EMR	2004	3	2	109	53	0
Oman	OMN	EMR	2007	1	4	87	73	0
Oman	OMN	EMR	2011	1	3	122	100	0
Oman	OMN	EMR	2012	2	4	136	120	0
Oman	OMN	EMR	2014	4	2	151	87	0
Pakistan	PAK	EMR	2013	44	52	884	708	13
Paraguay	PRY	AMR	2008	6	2	266	100	0.99
Peru	PER	AMR	2014	922	374	13380	6465	9.4
Philippines	PHL	WPR	2012	68	25	1978	692	26
Poland	POL	WER	2008	43	9	3116	1249	0.24
Poland	POL	WER	2011	32	9	3448	1545	0.24
Poland	POL	WER	2012	25	6	3314	1345	0.24
Poland	POL	WER	2013	33	7	3152	1172	0.24
Poland	POL	WER	2014	28	7	3036	1264	0.24
Portugal	PRT	WER	2008	21	7	1122	519	0.26
Portugal	PRT	WER	2010	18	11	1140	479	0.26
Portugal	PRT	WER	2011	19	12	1042	427	0.26
Portugal	PRT	WER	2012	9	8	908	413	0.26
Puerto Ricc	PRI	AMR	2007	2	1	58	29	0
Puerto Ricc	PRI	AMR	2011	2	1	34	14	0
Qatar	QAT	EMR	2014	1	1	127	23	0.57
Republic of	MDA	FSU	2006	1016	189	2337	542	35
Republic of	MDA	FSU	2011	813	188	1909	476	35
Republic of	MDA	FSU	2012	713	181	1732	484	35
Romania	ROU	WER	2015	75	15	1517	458	3.7
Rwanda	RWA	AFR	2015	18	5	767	350	1.1
Saudi Arab	SAU	EMR	2010	49	26	1195	702	0.36
Senegal	SEN	AFR	2006	6	3	194	83	1.5
Senegal	SEN	AFR	2014	14	7	647	268	1.5
Serbia	SRB	WER	2008	12	4	651	407	0.27
Serbia	SRB	WER	2010	11	1	568	360	0.27
Serbia	SRB	WER	2011	7	2	592	374	0.27
Serbia	SRB	WER	2012	7	2	501	299	0.27
Serbia	SRB	WER	2013	8	2	509	283	0.27
Singapore	SGP	WPR	2002	3	1	688	232	0.78
Singapore	SGP	WPR	2003	3	2	723	261	0.78
Singapore	SGP	WPR	2004	1	1	712	243	0.78
Singapore	SGP	WPR	2005	2	1	739	261	0.78
Singapore	SGP	WPR	2006	4	2	711	251	0.78
Singapore	SGP	WPR	2010	2	1	718	284	0.78
Singapore	SGP	WPR	2011	4	2	775	281	0.78
Singapore	SGP	WPR	2012	11	11	911	360	0.78
Singapore	SGP	WPR	2013	6	6	787	346	0.78
Singapore	SGP	WPR	2014	6	6	765	323	0.78

Slovenia	SVN	WER	2008	1	1	124	71	0
Somalia	SOM	EMR	2011	62	25	600	250	28
Sudan	SDN	EMR	2017	35	18	937	348	2.8
Sweden	SWE	WER	2008	5	7	214	209	0.2
Sweden	SWE	WER	2010	13	5	299	223	0.2
Sweden	SWE	WER	2011	10	7	282	193	0.2
Sweden	SWE	WER	2012	9	5	290	213	0.2
Sweden	SWE	WER	2013	4	3	175	146	0.2
Sweden	SWE	WER	2014	10	1	186	135	0.2
Switzerlanc	CHE	WER	2008	3	2	216	190	0.42
Switzerlanc	CHE	WER	2010	1	8	238	216	0.42
Switzerlanc	CHE	WER	2011	6	2	270	184	0.42
Switzerlanc	CHE	WER	2012	3	5	206	167	0.42
Switzerlanc	CHE	WER	2013	5	7	170	134	0.42
Switzerlanc	CHE	WER	2014	9	2	101	191	0.42
Syrian Arak	SYR	EMR	2003	35	11	261	131	1.7
Tajikistan	TJK	FSU	2014	238	133	1514	851	18
Thailand	THA	SEA	2006	11	2	565	229	5.7
The Forme	MKD	WER	2010	4	3	6	5	0
The Forme	MKD	WER	2012	2	2	111	70	0
The Forme	MKD	WER	2014	1	1	107	56	0
Togo	TGO	AFR	2018	15	6	641	257	0.82
Turkey	TUR	WER	2012	206	85	3744	1639	0.7
Turkey	TUR	WER	2013	172	56	3856	1674	0.7
Turkmenist	TKM	FSU	2013	100	42	374	187	8.3
Uganda	UGA	AFR	2011	21	10	881	444	4.8
Ukraine	UKR	FSU	2014	360	120	1160	390	30
United King	GBR	WER	2007	28	28	2703	1999	0.16
United King	GBR	WER	2011	42	42	3126	2186	0.16
United King	GBR	WER	2012	55	26	3083	2067	0.16
United King	GBR	WER	2013	29	17	1755	1116	0.16
United King	GBR	WER	2014	18	19	1702	1028	0.16
United Rep	TZA	AFR	2018	13	4	839	348	2.9
United Stat	USA	AMR	2005	70	51	6648	3815	0.09
United Stat	USA	AMR	2008	64	61	6371	3823	0.09
United Stat	USA	AMR	2010	40	47	4150	2574	0.09
United Stat	USA	AMR	2011	68	49	4455	2767	0.09
United Stat	USA	AMR	2012	38	43	4472	2716	0.09
United Stat	USA	AMR	2013	51	31	3825	2111	0.09
United Stat	USA	AMR	2014	42	41	3807	1997	0.09
Uruguay	URY	AMR	2005	1	1	250	116	0.19
Uzbekistan	UZB	FSU	2011	213	159	585	452	21
Viet Nam	VNM	WPR	2012	71	20	1002	308	7
Yemen	YEM	EMR	2011	22	10	716	521	1.3

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1.9	23	52191	931365	1036116				
1.9	23	52191	931365	1036116				
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1.9	23	52191	931365	1036116				
1.9	23	52191	931365	1036116				
1.9	23	52191	931365	1036116				
1.9	23	52191	931365	1036116				
1.9	23	52191	931365	1036116				
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2.3	18	51936	63034	78322	583	364	12	12
2.3	18	51936	63034	78322	583	364	12	12
2.3	18	51936	63034	78322	583	364	12	12
2.3	18	51936	63034	78322	583	364	12	12
2.3	18	51936	63034	78322	583	364	12	12
12	28	18036						
1.3	21	50103						
1.3	21	50103						
1.6	29	4561						
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38	67	20008						
38	67	20008						
38	67	20008						
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1.2	19	23154						
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0.82	6.3	49775	1352339	1549093				
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0.82	6.3	49775	1352339	1549093				
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2.5	0	122490						
2.5	0	122490						

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2.2	4.2							
2.2	4.2							
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21	52	33842						
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1	11	8936						
3.7	20	1275						
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5	12	11613						
5	12	11613						
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2.2	15	2842						
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1.7	6.3	56436	201321	252283	867	625	10	10
1.7	6.3	56436	201321	252283	867	625	10	10
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537	300	survey
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632	351	survey
7271	3839	survey
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16853	2882	survey
26168	15432	surveillance
204	71	surveillance
119	110	surveillance
23520	2000	survey
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77	59	surveillance
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132025	43548	survey
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8575		survey
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104904	43829	survey
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16627	6446	survey
21054	928	survey
520	423	surveillance
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555		surveillance
2845	791	survey
6279	3084	surveillance
82008	24470	survey
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219	155	surveillance
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12046	5916	surveillance
12046	5916	surveillance
2232	1085	survey
47170	16915	survey
31584	19937	survey
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5567	3408	surveillance
5567	3408	surveillance
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9091	6540	surveillance
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9091	6540	surveillance
9091	6540	surveillance
9091	6540	surveillance
933	515	survey
19329	13855	survey
105733	41595	survey
9693	607	survey

APPENDIX

Table S1: *Countries and territories with sex-disaggregated MDR/RR-TB DST notification results, identifying years with available results, the male to female risk ratio and the p-value for rejecting the null hypothesis that the risk ratio is 1.*

Country	Years	MF risk ratio (95% confidence interval in brackets)	P-value for H0: MF risk ratio=1	Men with a DST result (positive in [])	Women with a DST result (positive in [])
Albania	2011	1.43 (0.16-12.52)	0.759	151 [4]	54 [1]
Argentina	2005	1.00 (0.52-1.92)	0.996	507 [22]	322 [14]
Armenia	2007	1.08 (0.76-1.54)	0.685	758 [171]	134 [28]
Australia	2002-2005, 2007-2008, 2010-2014	0.78 (0.59-1.03)	0.076	3996 [92]	3303 [98]
Austria	2008, 2010-2014	0.95 (0.66-1.39)	0.819	1599 [69]	929 [42]
Azerbaijan	2013	0.94 (0.67-1.32)	0.732	587 [101]	202 [37]
Bahrain	2011-2012	2.73 (0.62-1.95)	0.184	129 [11]	64 [2]
Bangladesh	2011	0.91 (0.61-1.37)	0.675	949 [68]	395 [31]
Belarus	2011-2014	1.12 (1.06-1.18)	<0.001	8526 [3879]	2210 [901]
Belgium	2008, 2010-2014	0.76 (0.51-1.14)	0.185	2762 [57]	1399 [38]
Benin	2010	1.42 (0.29-6.95)	0.678	304 [6]	144 [2]
Botswana	2008	0.78 (0.39-1.54)	0.480	563 [15]	496 [17]
Bulgaria	2010, 2012	1.20 (0.78-1.85)	0.406	1287 [79]	510 [26]
Canada	2005, 2008, 2010-2014	0.77 (0.52-1.14)	0.189	4574 [50]	3371 [48]
Chile	2014	3.20 (0.72-4.11)	0.125	915 [13]	450 [2]
China	2007, 2013	0.91 (0.79-1.05)	0.208	8075 [580]	3149 [248]
Hong Kong	2005, 2007-2008, 2011	1.10 (0.71-1.69)	0.690	8294 [67]	3937 [29]
Macao	2005, 2007-2008, 2010-2014	0.79 (0.47-1.33)	0.382	1372 [34]	733 [23]
Costa Rica	2006	1.68 (0.19-4.81)	0.653	200 [4]	84 [1]
Croatia	2014	0.56 (0.04-8.88)	0.695	223 [1]	125 [1]
Cuba	2002-2004, 2011-2012	0.87 (0.37-2.02)	0.756	1114 [22]	308 [7]
Czechia	2008, 2010, 2012, 2014	0.86 (0.40-1.83)	0.701	1132 [19]	510 [10]
Denmark	2011	1.17 (0.11-2.74)	0.906	171 [2]	100 [1]

Djibouti	2015	0.76 (0.39-1.49)	0.437	255 [21]	111 [12]
Egypt	2011	0.88 (0.64-1.21)	0.447	1044 [117]	370 [47]
Eritrea	2018	2.86 (0.92-8.87)	0.069	265 [11]	283 [4]
Estonia	2008, 2010-2014	1.04 (0.85-1.27)	0.721	1085 [273]	421 [102]
Eswatini	2009	0.63 (0.46-0.88)	0.007	309 [46]	324 [76]
Finland	2010-2014	0.93 (0.39-2.18)	0.872	617 [12]	429 [9]
Georgia	2006, 2010-2014	1.24 (1.12-1.37)	<0.001	10503 [1736]	2947 [394]
Germany	2008, 2010-2014	0.98 (0.80-1.21)	0.885	9994 [234]	6050 [144]
Greece	2010	0.32 (0.02-4.91)	0.421	72 [1]	23 [1]
Guatemala	2002	0.83 (0.51-1.36)	0.480	628 [31]	490 [29]
Honduras	2004	1.04 (0.39-2.77)	0.941	338 [11]	192 [6]
Hungary	2010	1.65 (0.55-4.89)	0.375	396 [15]	174 [4]
I.R. Iran	2014	1.13 (0.49-2.63)	0.786	647 [13]	507 [9]
Iraq	2013	1.02 (0.54-1.91)	0.959	563 [21]	464 [17]
Ireland	2011-2013	0.87 (0.28-2.71)	0.820	440 [7]	273 [5]
Israel	2008, 2010-2014	0.98 (0.61-1.58)	0.940	959 [47]	480 [24]
Italy	2010, 2012	0.88 (0.65-1.20)	0.433	2482 [75]	2514 [86]
Japan	2002	0.96 (0.56-1.66)	0.896	2211 [42]	911 [18]
Jordan	2004	3.44 (0.83-4.27)	0.088	93 [16]	40 [2]
Kazakhstan	2011-2013	1.41 (1.38-1.45)	<0.001	21070 [12387]	14007 [5828]
Kenya	2014	2.12 (0.60-7.48)	0.246	1226 [12]	649 [3]
Kuwait	2010, 2013-2014	1.75 (0.60-5.08)	0.310	639 [10]	558 [5]
Lao PDR	2018	1.04 (0.32-3.35)	0.953	638 [9]	295 [4]
Latvia	2008, 2010-2014	1.33 (1.11-1.60)	0.002	2969 [431]	1208 [132]
Lebanon	2003	2.19 (0.61-7.87)	0.230	119 [9]	87 [3]
Lesotho	2014	8.78 (5.53-3.95)	<0.001	156 [46]	715 [24]
Lithuania	2008, 2010-2014	1.45 (1.30-1.62)	<0.001	6162 [1352]	2128 [322]
Luxembourg	2011	0.58 (0.04-7.94)	0.699	12 [1]	7 [1]
Madagascar	2007	1.28 (0.12-4.09)	0.848	344 [2]	221 [1]
Malawi	2011	0.81 (0.41-1.59)	0.550	1009 [17]	768 [16]

Malaysia	2014	2.22 (1.32-3.75)	0.003	8761 [79]	4192 [17]
Marshall I.	2012	0.49 (0.05-5.13)	0.560	37 [1]	36 [2]
Mauritius	2010	0.37 (0.02-5.67)	0.481	82 [1]	30 [1]
Mexico	2009	0.92 (0.50-1.69)	0.790	1455 [30]	666 [15]
Mongolia	2007, 2016	1.09 (0.81-1.47)	0.584	1333 [111]	830 [63]
Montenegro	2014	0.70 (0.05-0.73)	0.810	40 [1]	28 [1]
Morocco	2006, 2014	0.78 (0.45-1.36)	0.396	1837 [38]	682 [18]
Mozambique	2007	1.27 (0.89-1.80)	0.183	696 [86]	431 [42]
Myanmar	2008	1.18 (0.72-1.94)	0.510	938 [54]	432 [21]
Namibia	2008, 2015	0.63 (0.50-0.81)	<0.001	2727 [116]	1890 [127]
Nepal	2007, 2011	0.81 (0.52-1.27)	0.366	1267 [57]	468 [26]
Netherlands	2008, 2010-2013	0.49 (0.30-0.81)	0.005	1926 [27]	1339 [38]
New Zealand	2004-2005, 2007, 2009, 2011-2012	0.96 (0.42-2.20)	0.933	758 [11]	729 [11]
Nicaragua	2006	0.94 (0.30-2.91)	0.924	220 [7]	148 [5]
Nigeria	2010	1.12 (0.68-1.84)	0.672	935 [46]	500 [22]
Norway	2008, 2010-2014	0.74 (0.38-1.42)	0.372	838 [17]	656 [18]
Oman	2002-2004, 2007, 2011-2012, 2014	0.55 (0.30-1.03)	0.061	802 [17]	572 [17]
Pakistan	2013	0.68 (0.46-1.00)	0.050	884 [44]	708 [52]
Paraguay	2008	1.13 (0.23-5.50)	0.891	266 [6]	100 [2]
Peru	2014	1.19 (1.06-1.34)	0.003	13380 [922]	6465 [374]
Philippines	2012	0.95 (0.61-1.49)	0.840	1978 [68]	692 [25]
Poland	2008, 2011-2014	1.73 (1.22-2.47)	0.002	16066 [161]	6575 [38]
Portugal	2008, 2010-2012	0.77 (0.52-1.14)	0.194	4212 [67]	1838 [38]
Puerto Rico	2007, 2011	0.93 (0.18-4.91)	0.942	92 [4]	43 [2]
Qatar	2014	0.18 (0.01-2.79)	0.223	127 [1]	23 [1]
R. Moldova	2006, 2011-2012	1.14 (1.07-1.23)	<0.001	5978 [2542]	1502 [558]
Romania	2015	1.51 (0.88-2.60)	0.138	1517 [75]	458 [15]
Rwanda	2015	1.64 (0.61-4.39)	0.327	767 [18]	350 [5]
Saudi Arabia	2010	1.11 (0.69-1.76)	0.682	1195 [49]	702 [26]
Senegal	2006, 2014	0.83 (0.39-1.77)	0.649	841 [20]	351 [10]

Serbia	2008, 2010-2013	2.50 (1.30-4.82)	0.006	2821 [45]	1723 [11]
Singapore	2002-2006, 2010-2014	0.48 (0.31-0.76)	0.002	7529 [42]	2842 [33]
Slovenia	2008	0.57 (0.04-9.01)	0.705	124 [1]	71 [1]
Somalia	2011	1.03 (0.67-1.60)	0.893	600 [62]	250 [25]
Sudan	2017	0.72 (0.41-1.26)	0.253	937 [35]	348 [18]
Sweden	2008, 2010-2014	1.41 (0.89-2.22)	0.139	1446 [51]	1119 [28]
Switzerland	2008, 2010-2014	0.94 (0.55-1.59)	0.818	1201 [27]	1082 [26]
Syrian A.R.	2003	1.60 (0.84-3.04)	0.155	261 [35]	131 [11]
Tajikistan	2014	1.01 (0.83-1.22)	0.958	1514 [238]	851 [133]
Thailand	2006	2.23 (0.50-9.98)	0.299	565 [11]	229 [2]
F.Y.R.M.	2010, 2012, 2014	0.68 (0.23-1.99)	0.493	224 [7]	131 [6]
Togo	2018	1.00 (0.39-2.55)	0.996	626 [15]	251 [6]
Turkey	2012-2013	1.17 (0.97-1.41)	0.106	7600 [378]	3313 [141]
Turkmenistan	2013	1.19 (0.87-1.63)	0.281	374 [100]	187 [42]
Uganda	2011	1.06 (0.50-2.23)	0.890	881 [21]	444 [10]
Ukraine	2014	1.01 (0.85-1.20)	0.928	1160 [360]	390 [120]
UK	2007, 2011-2014	0.88 (0.71-1.11)	0.289	12369 [172]	8396 [132]
UR Tanzania	2018	1.35 (0.44-4.11)	0.612	826 [13]	344 [4]
USA	2005, 2008, 2010-2014	0.68 (0.58-0.79)	<0.001	33728 [373]	19803 [323]
Uruguay	2005	0.46 (0.03-7.35)	0.598	250 [1]	116 [1]
Uzbekistan	2011	1.04 (0.88-1.22)	0.695	585 [213]	452 [159]
Viet Nam	2012	1.09 (0.68-1.76)	0.734	1002 [71]	308 [20]
Yemen	2011	1.60 (0.76-3.35)	0.214	716 [22]	521 [10]

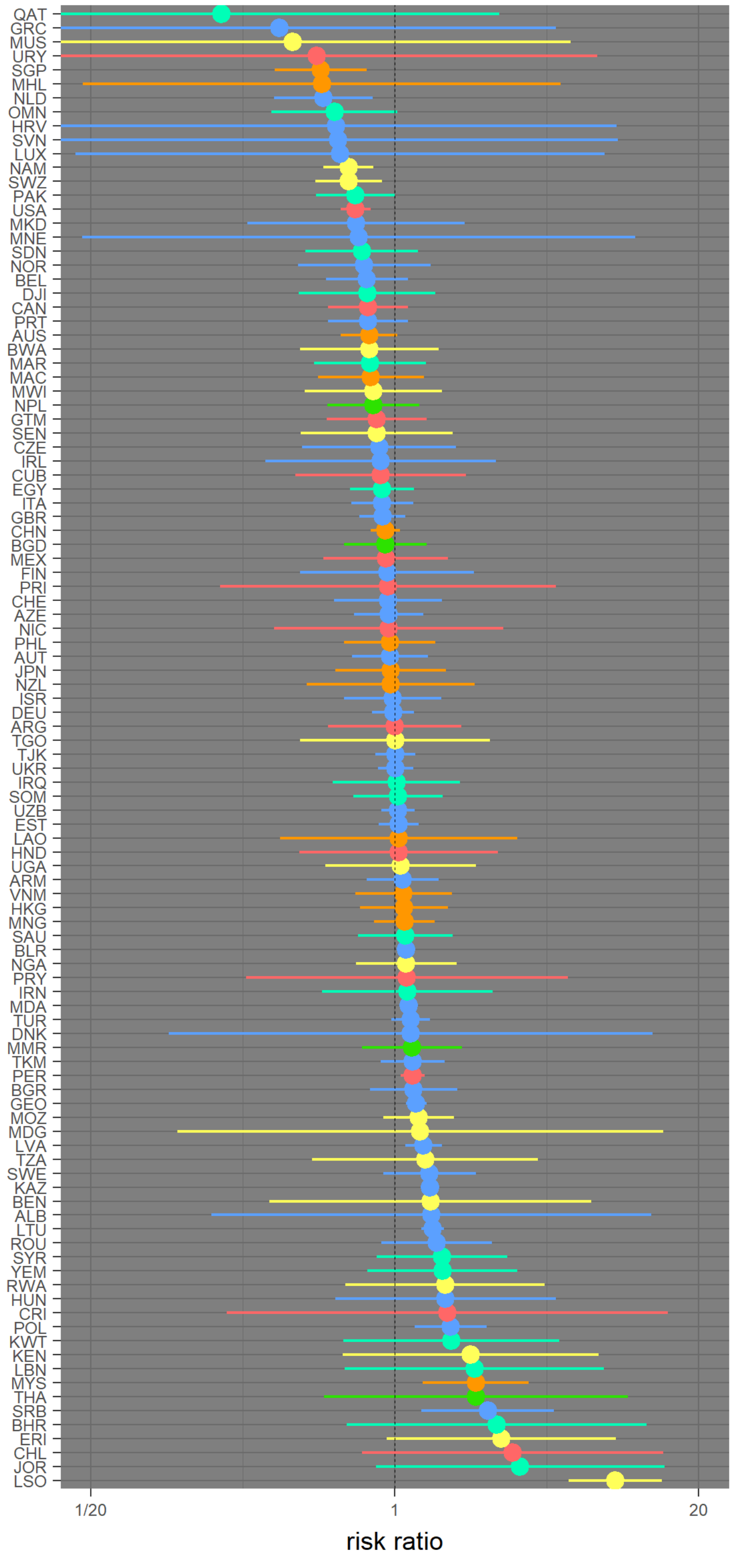

Figure S1: *Forest plot showing risk ratio and 95% confidence interval for MDR/RR-TB in men compared to women by country (iso3 code). Data among all (new and retreated) cases are presented.*