

Risk of emergence of rifampin-resistance after loss to follow-up from tuberculosis treatment

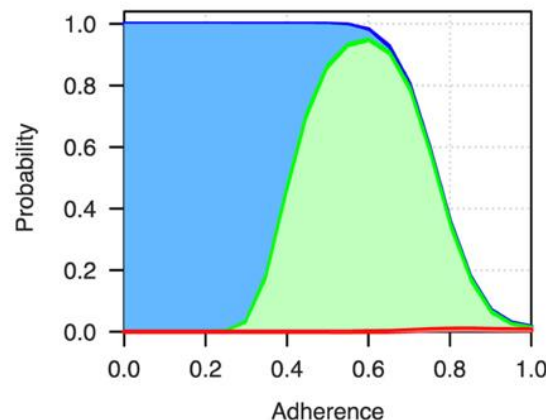
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Emergence of drug resistance following incomplete treatment



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- Ukraine is a high RR-TB burden country
- We know that inconsistent adherence to treatment can result in RR-TB
- How does stopping treatment early impact the risk of RR-TB?
- Specifically, how does treatment length impact the risk of RR-TB?



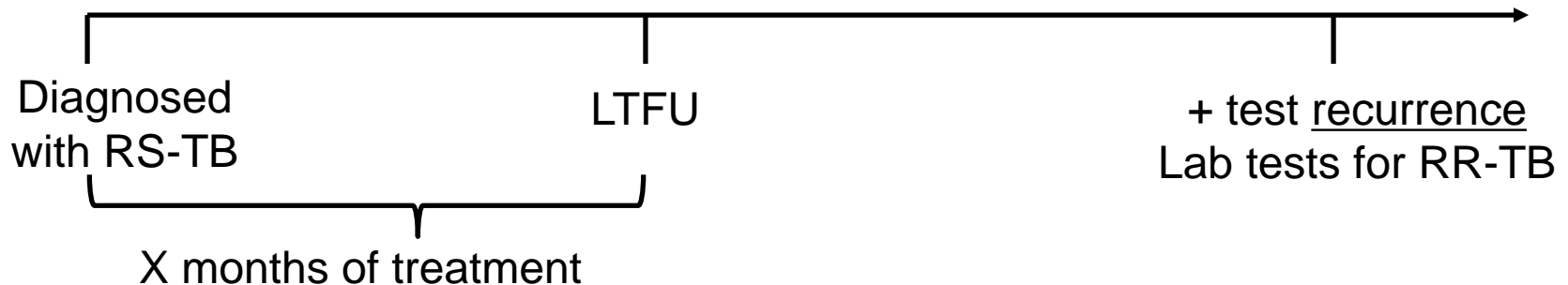
Green = Probability of emergence of drug resistance

Routinely collected TB data in Ukraine

- All TB diagnoses January 2015 – November 2018
- Wealth of demographic, laboratory, and outcomes data. No sequence data
- If people have TB more than once, this is recorded with a unique person identifier
- We can see what happened to people longitudinally – but also outcomes, e.g. if LTFU and then we have lab results if/when they re-engage in care

Risk of recurrence and rifampin resistance (RR) on TB recurrence

- Focused on people with confirmed rifampin-susceptible TB at baseline
- Aim: assess (1) risk of recurrence (within 18 mths) and, (2) if recurrence, RR-TB, dependent on how much treatment they initially received



- Included people with LTFU and <6 months of treatment for RR-TB analysis, and people with successful outcome and 6+ months of treatment as reference group for recurrence analysis
- Used log binomial regression to estimate risk ratios for both questions with length of treatment (months) as explanatory variable of interest
- Adjusted for many potential confounders (age, sex, cavitation, isoniazid resistance, housing status, employment etc)

Risk of TB recurrence in Ukraine

Of 29,363 people included in the analysis, 1,165 (4.0%) had a recurrence

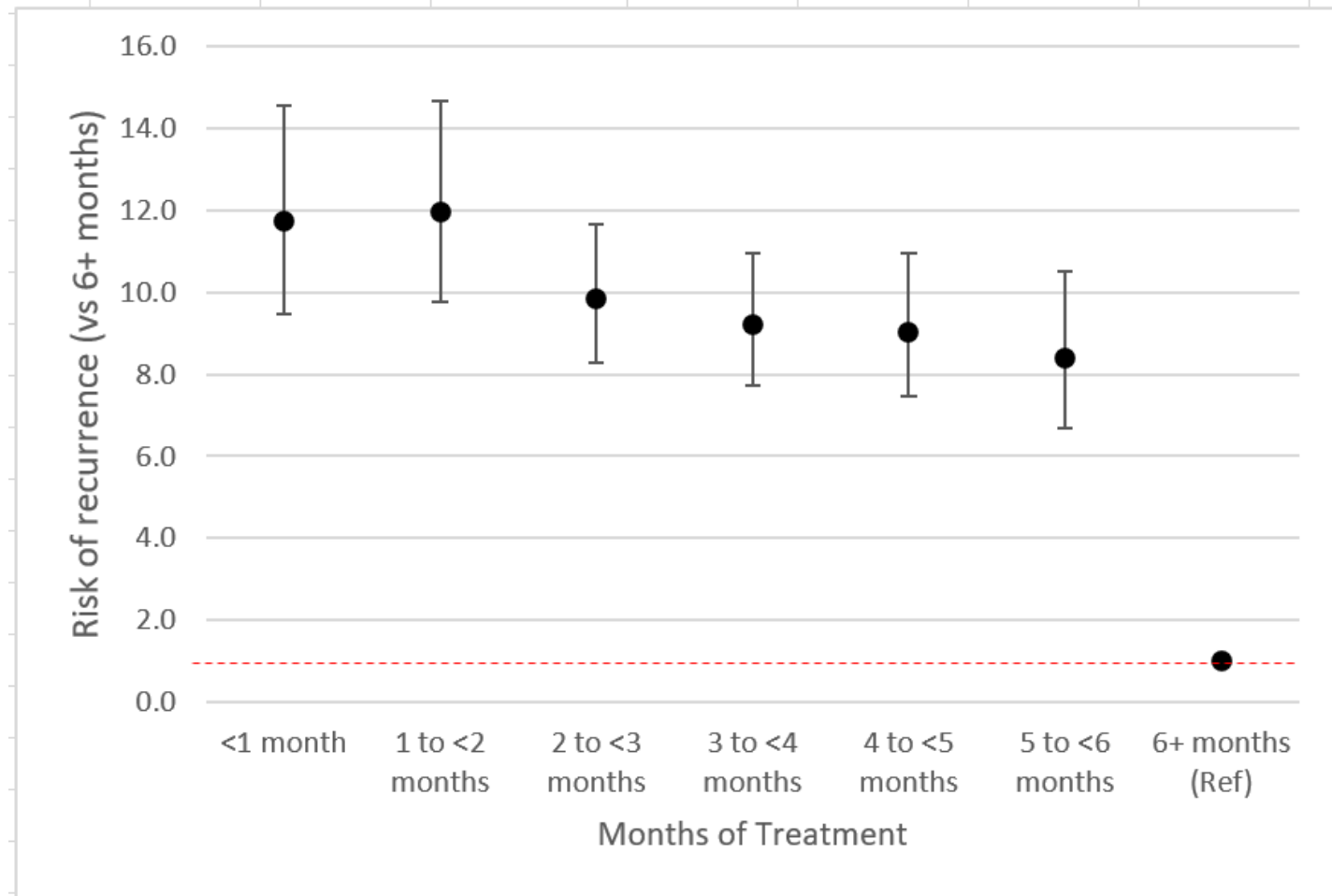
	Analysis of recurrence			N
Months of treatment	Risk Ratio	95% CI ¹		
<1 month	11.8	9.5, 14.6		81
1 to <2 months	12.0	9.8, 14.7		100
2 to <3 months	9.8	8.3, 11.7		144
3 to <4 months	9.2	7.7, 11.0		143
4 to <5 months	9.0	7.4, 11.0		119
5 to <6 months	8.4	6.7, 10.5		77
6+ months	Ref	Ref		664
¹ CI = Confidence Interval				

Lost to follow-up



Successful outcome

Risk of TB recurrence in Ukraine

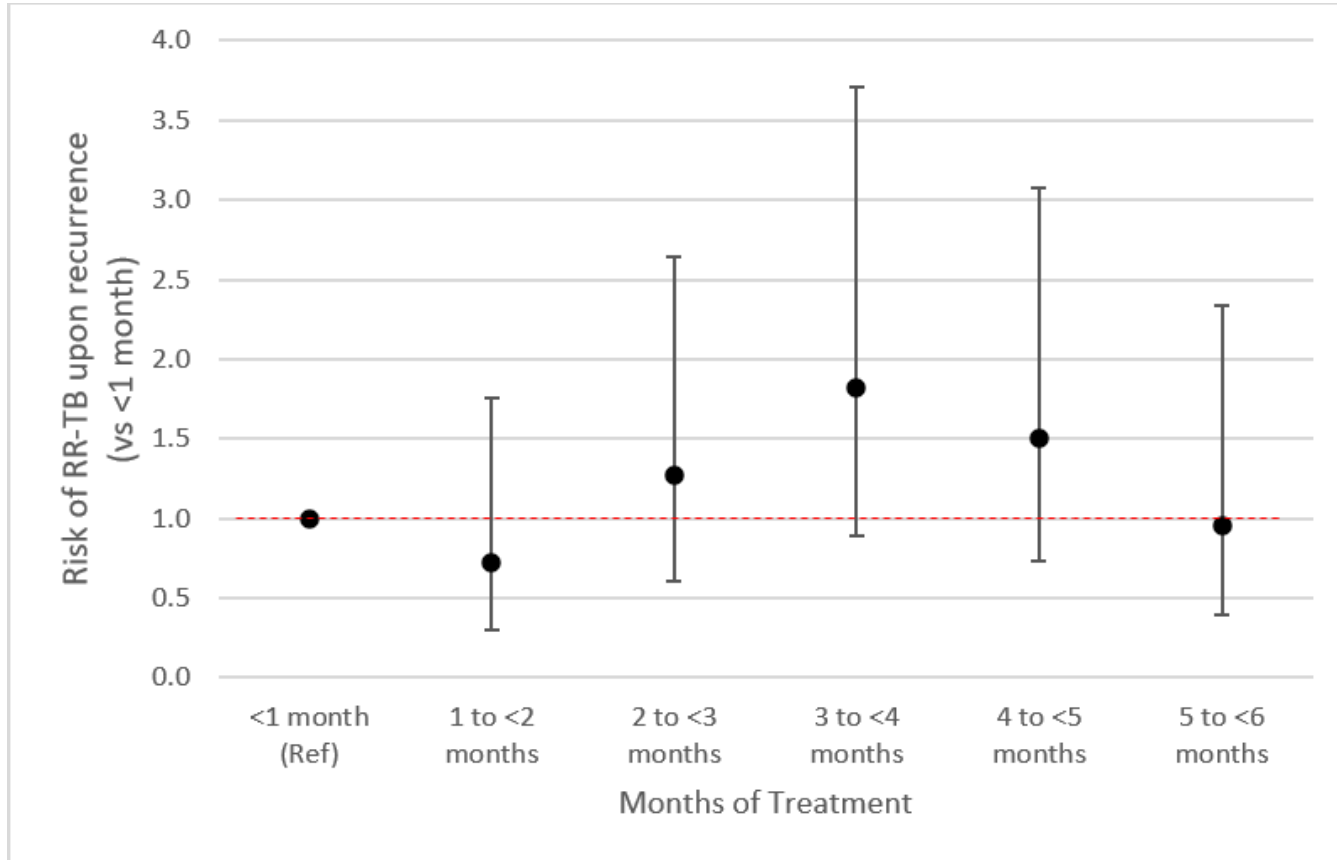


Risk of RR-TB on recurrence in Ukraine

- 227/1025 (21.3%) people had RR-TB on recurrence
- 227/29,363 - 0.8% of all people with DS-TB
- Analysis incl. 580 people (with LTFU < 6 months and DST on recurrence)
- 87/580 (15%) had RR-TB on recurrence (after LTFU < 6 months)

	Analysis of RR-TB on recurrence		N
Months of treatment	Risk Ratio	95% CI ¹	
<1 month	Ref	Ref	9
1-2 months	0.72	0.30, 1.76	8
2-3 months	1.27	0.61, 2.65	17
3-4 months	1.82	0.89, 3.70	24
4-5 months	1.50	0.73, 3.08	21
5-6 months	0.96	0.39, 2.33	8
¹ CI = Confidence Interval			

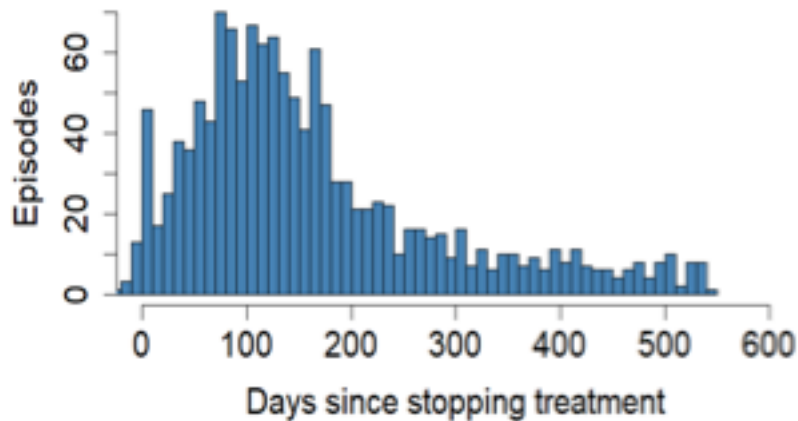
Risk of RR-TB on TB recurrence in Ukraine



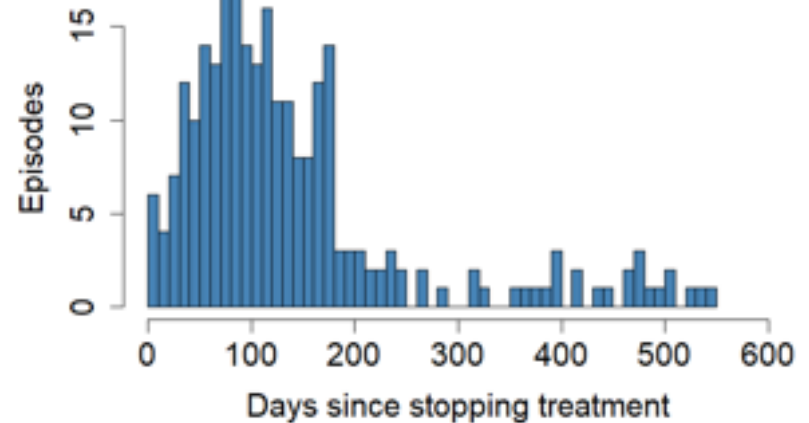
Timing of recurrence

- Lack of sequence data means we cannot distinguish recurrence/RR-TB related to previous treatment episode versus new infection
- However, timing is strong indicator that the majority are linked

Recurrence



RR-TB



Conclusions

- “Real world” evidence of relationship between treatment length and risk of RR-TB development
- Risk of recurrence analysis supports shortened regimens for some people
- However, risk of RR-TB analysis shows potential risk of shortened regimens
- We need to support people in completing treatment to reduce emergence of resistance
- Increased awareness (and drug resistance testing!) of the RR-TB risk for people returning after LTFU
- Importance of follow-up and monitoring throughout treatment and post-treatment

In the context of the Russian war

- Reports from colleagues are that although there is wide availability of testing and treatment, many people are not coming for TB care
- Potentially higher risks of incomplete treatment and return to care
- Potential increased risk for people who have fled the country – maybe limited TB services and awareness elsewhere

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