Month 2 culture and duration as predictors of TB relapse

RS Wallis, MD, FIDSA, FRCPE
Chief Science Officer, Aurum Institute, Johannesburg
rwallis@auruminstitute.org

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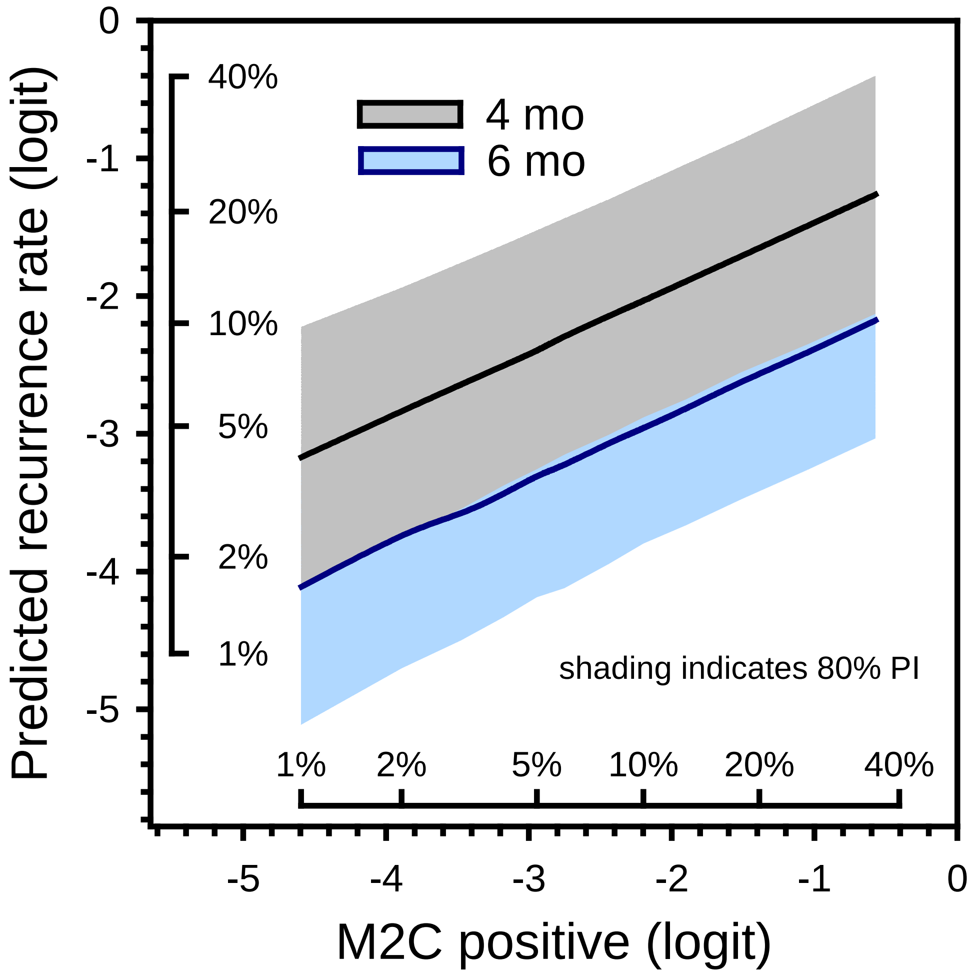
M2C and duration as predictors of relapse

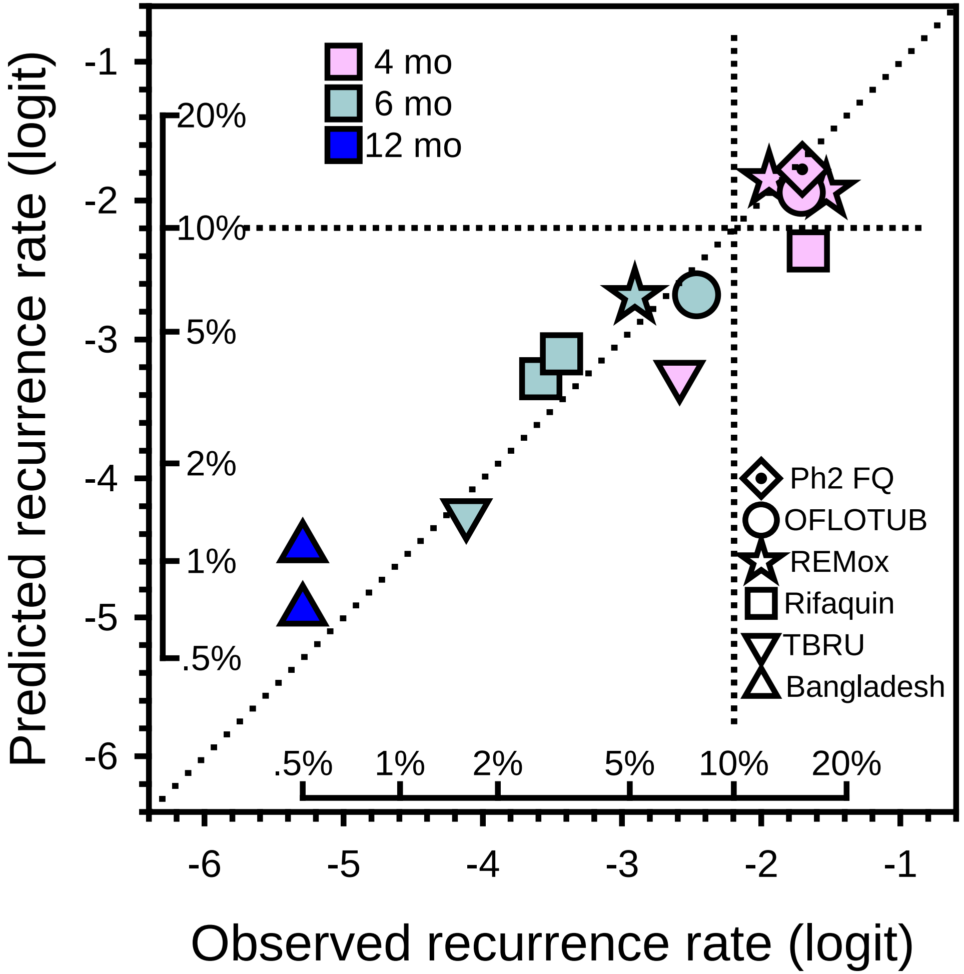
- A 2013 analysis of 24 trials published from 1973 to 1997 of 58 regimens studied in 7793 patients identified positive month 2 culture status using solid medium (M2C) and treatment duration as independent predictors of relapse.
- Predictions took the form: logit(relapse) = $a+bx+cy$, where x=logit(M2C) and y=log(duration)
- The model was subsequently validated using independent data from 6 studies of 12 regimens involving 3907 patients.



Wallis,
PLoS One
2013

M2C and duration as predictors of relapse

- **REMox, OFLOTUB and RIFAQUIN:** Results of the four-month arms were first predicted based on data from 5 phase 2 trials of FQ-containing regimens giving 443 patients [illegible]
- Relapse rates in all 8 arms of these 3 trials (3388 patients) were later predicted based on M2C and duration of each arm, at $R^2 = .86$ [illegible] that duration was a predictor of relapse, contrary to the study hypothesis.



Wallis, *PLoS One* 2015

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M2C and duration as predictors of relapse

Database characteristics

	Total	Duration			Location	
		3-5mo	*6mo*	*7-18mo*	*Africa*	*Asia/Pacific*
Regimens	70	11	48	11	28	50
Subjects	11790	2824	7435	1531	7296	7814

Model parameters

	Estimate	SE	P
Intercept	2.529	0.478	0.00002
Ln duration	-2.502	0.221	<.00001
Logit M2C+	0.440	0.010	0.00008

Online calculator at rswallis.com

M2C and duration as predictors of relapse

- The model is accurate (R^2 >.9) and generalizable (remaining accurate under previously untested conditions):
  - FQ results were predicted w/o FQ data
  - TBRU results were predicted w/o host data
  - MDR results were predicted w/o MDR or clofazimine data
- None of the studies in the training dataset and few in the validation dataset excluded recurrence due to reinfection
  - Presumably noise would be reduced and accuracy increased had they done so
- Data are insufficient to create a similar model using time to culture conversion in liquid medium, or one including baseline parameters
  - Collecting such data should be a research priority

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