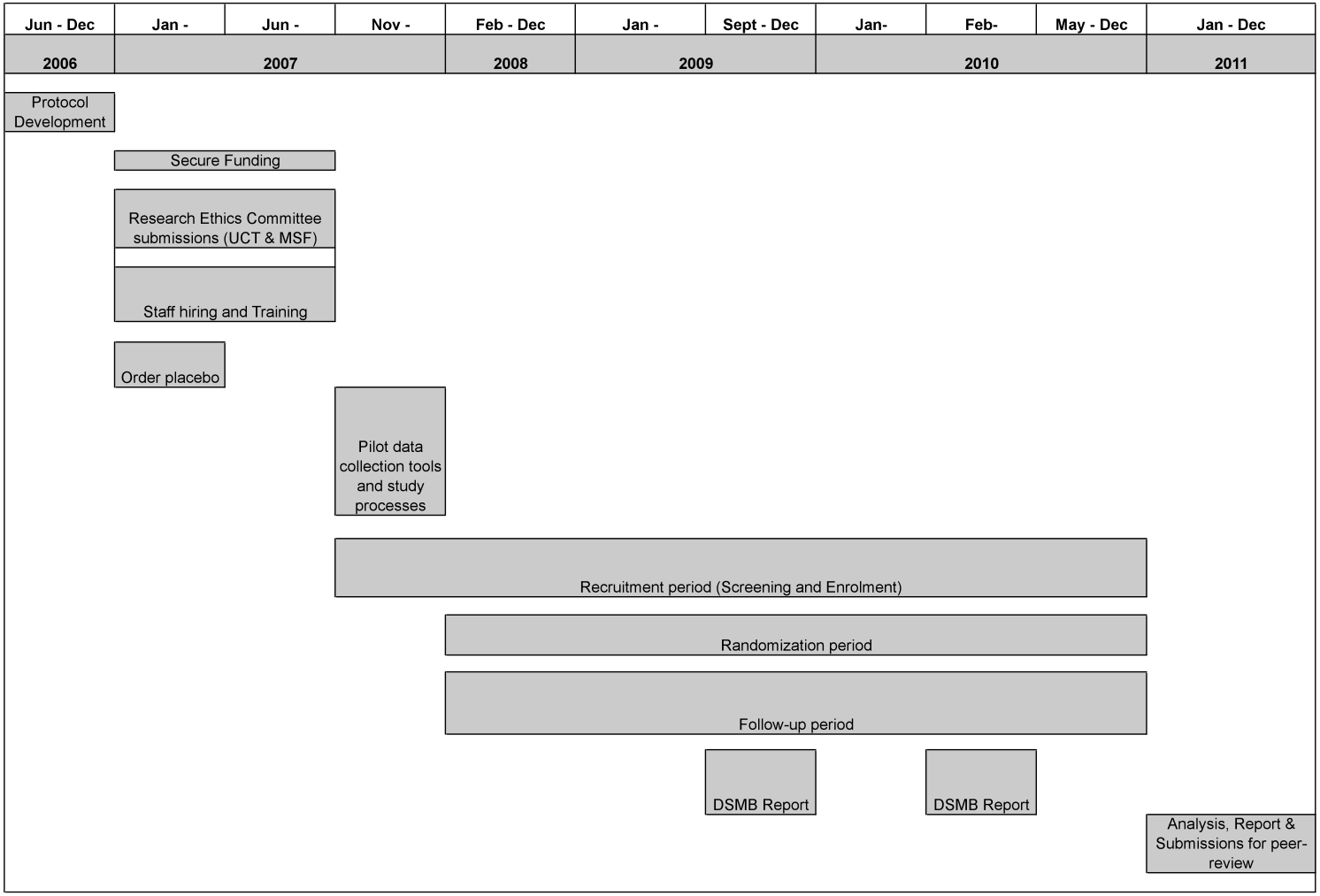
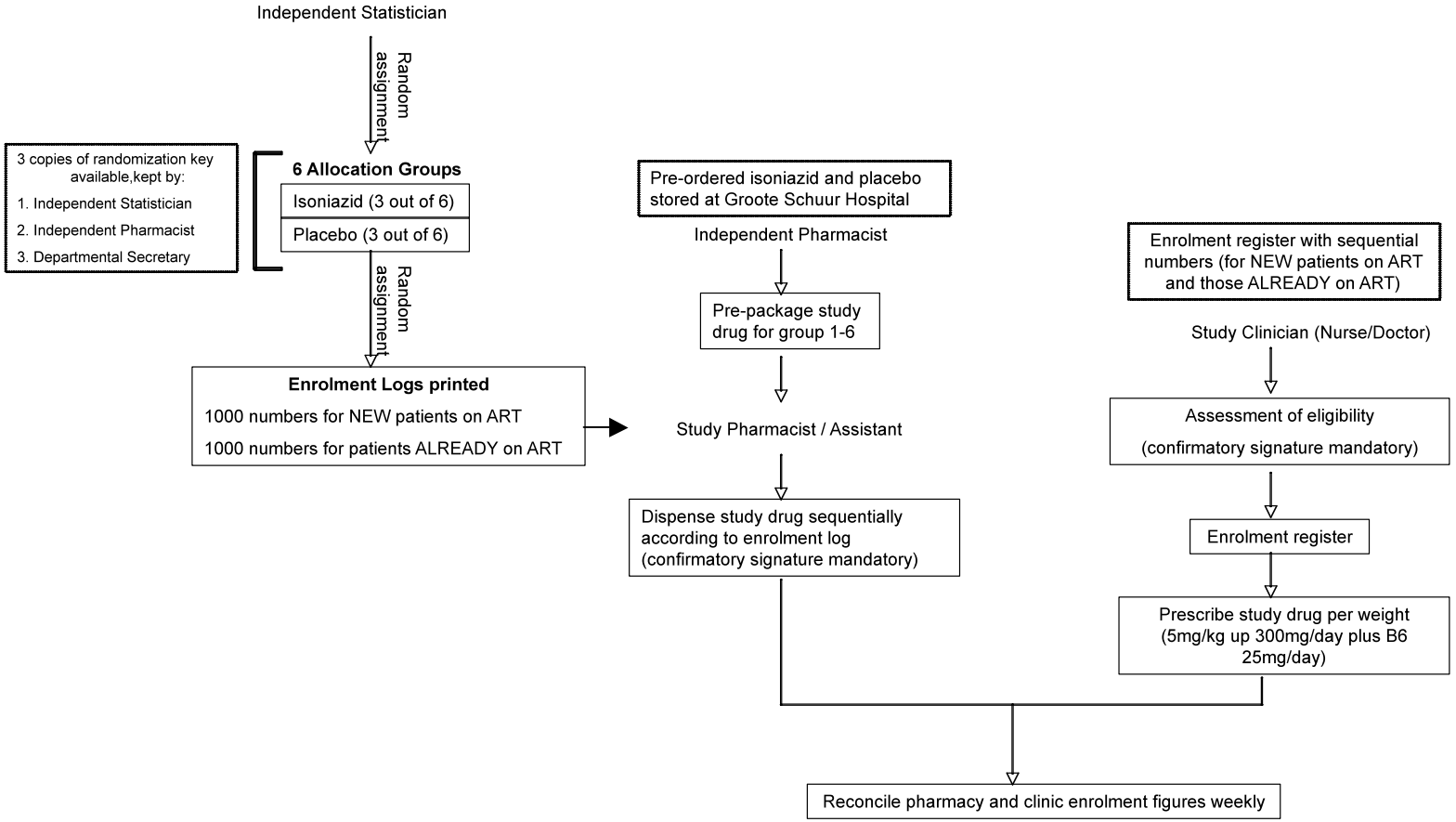
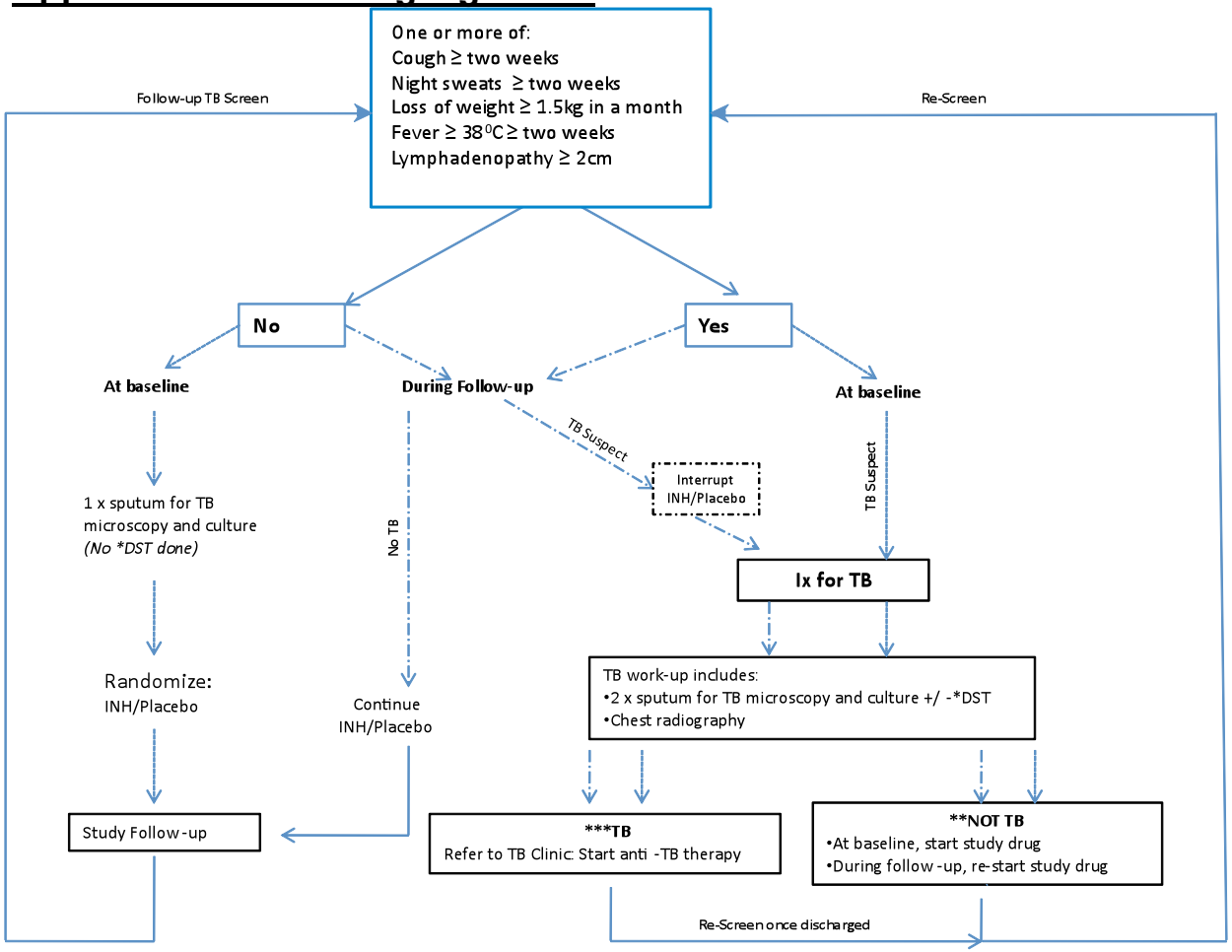
Appendix A: ART IPT Study Project Plan



Appendix B: ART IPT Randomization Process

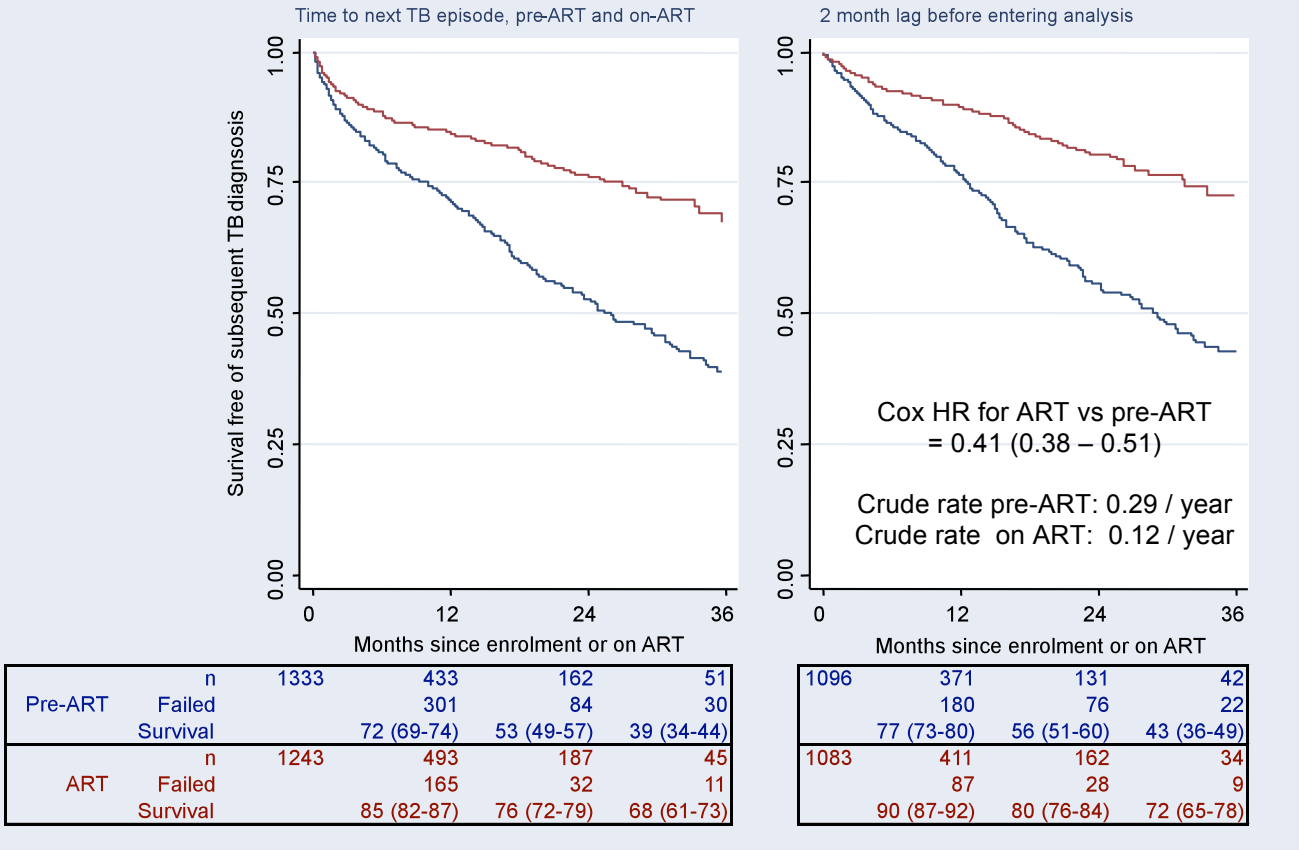


Appendix C: Screening algorithm



Note:
**DST= Drug sensitivity and testing for rifampicin and isoniazid resistance. Only requested on follow-up specimens of patients that are being worked up for TB; ** Only start/re-start the study drug if a 3-month 'grace' period has not lapsed. Otherwise, re-screen if still at baseline or permanently discontinue the study drug if the study drug was interrupted during follow-up. ***Pre-determined case definitions for prevalent and incident are available; described in main protocol. Study drug will be permanently discontinued once a diagnosis of active TB is made.*

Appendix D: Survival curves showing time to the next TB diagnosis, pre ART and post ART.



Pre-ART	n	1333	433	162	51	1096	371	131	42
	Failed		301	84	30		180	76	22
	Survival		72 (69-74)	53 (49-57)	39 (34-44)		77 (73-80)	56 (51-60)	43 (36-49)
ART	n	1243	493	187	45	1083	411	162	34
	Failed		165	32	11		87	28	9
	Survival		85 (82-87)	76 (72-79)	68 (61-73)		90 (87-92)	80 (76-84)	72 (65-78)

Kaplan-Meir survival curves showing time to the next TB episode in pre and on ART cohorts. There is a higher probability of being diagnosed with TB due to patients being referred or seeking care when ill, and similarly, a higher probability of 'unmasking' TB with or without IRIS phenomenon soon after starting ART (panel 1). The assessment of risk reported was limited to beyond 60 days on ART to limit confounding. Entry into the analysis was lagged by two months to remove that bias: patients entered the pre-ART analysis 2 months after first registering at the clinics, and entered the on-ART analysis two months after starting ART (panel 2). Courtesy of Andrew Boulle.

Appendix E: Exploration of power within subgroups

Subgroup size (Total N)	**50**	**150**	**180**	**200**	**500**	**1000**	**1050**	**1068**
Desired effect size (HR)	**0.647**	**0.647**	**0.647**	**0.647**	**0.647**	**0.647**	**0.647**	**0.647**
Actual power to detect effect size	0.08	0.18	0.22	0.26	0.46	0.76	0.78	0.80

This table explores what the actual power would be given a certain subgroup size, a fixed hazard ratio of 0.647 (0.055/0.085) and a 5% significance level. Methods used also considered a 1-year accrual period, 2 years of follow-up and 10% lost to follow-up proportions in the two arms of the study. 80% power would not be maintained for subgroups of <1000 in total size. STATA 10 MP was used for estimating the power. Methods are based on Lachin and Foulkes (Biometrics, 42, 507-519,1986).