Sample size analysis with non informative prior

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Sample size calculation using non informative prior

The choice of non-informaitve prior for binomial distribution resulting in posterior distribution see http://www.stats.org.uk/priors/noninformative/YangBerger1998.pdf

- if we choose Beta(1,1), that is, the uniform distribution, then the posterior mean ADA+ rate would be (x + 1)/(n + 2) where x and n are the number of ADA+ incidence and the total number of subjects at cohort 1, respectively;
- if we choose Jefferys' prior, then the posterior mean ADA+ rate would be (x + 0.5)/(n + 1).

In the following section, we'll base sample size re-estimation on these two non-informative priors. Note that the initial sample size 102 (with 46 in the first cohort) is calculated based on the assumption that ADA+ rate is 1%.

The following is variable specifications for tables below:

- n_ADA: number of ADA observed in cohort 1
- n_cohort1: number of subjects enrolled in cohort 1
- obs_ADA_rate: n_ADA/n_cohort1
- posterior_ADA_rate: obtained using Bayes prior and data from cohort 1
- N_required_per_arm: sample size re-estimated using posterior_ADA_rate. This number has already accouted for 10% drop out.
- N_increased_per_arm: number of subjects needed per arm (N_required_per_arm - 51, and 51 is sample size per arm originally).

Please note that these sample sizes may change due to the type 1 error analysis, addressing comment 3 from FDA.

when initial ADA rate is 1%

In this part, the initial sample size 102 (with 46 in the first cohort) is calculated based on the assumption that ADA+ rate is 1%.

Uniform prior

n_ADA	n_cohort1	obs_ADA_rate	posterior_ADA_rate	N_required_per_arm	N_increase_per_arm
0	46	0.0000	0.0208	58	7
1	46	0.0217	0.0417	77	26
2	46	0.0435	0.0625	98	47
3	46	0.0652	0.0833	118	67
4	46	0.0870	0.1042	138	87
5	46	0.1087	0.1250	158	107
6	46	0.1304	0.1458	176	125
7	46	0.1522	0.1667	194	143

Jeffery's prior

n_ADA	n_cohort1	obs_ADA_rate	posterior_ADA_rate	N_required_per_arm	N_increase_per_arm
0	46	0.0000	0.0106	47	0
1	46	0.0217	0.0319	69	18
2	46	0.0435	0.0532	88	37
3	46	0.0652	0.0745	109	58
4	46	0.0870	0.0957	130	79
5	46	0.1087	0.1170	150	99
6	46	0.1304	0.1383	170	119
7	46	0.1522	0.1596	189	138

Reproducing Table 1 using our package

n_ADA	n_cohort1	obs_ADA_rate	posterior_ADA_rate	N_required_per_arm	N_increase_per_arm
0	46	0.0000	0.0068	41	0
1	46	0.0217	0.0136	50	0
2	46	0.0435	0.0204	57	6
3	46	0.0652	0.0272	63	12
4	46	0.0870	0.0340	70	19
5	46	0.1087	0.0408	77	26
6	46	0.1304	0.0476	84	33
7	46	0.1522	0.0544	91	40

when initial ADA rate is 3%

In this part, the initial sample size 132 (with 60 in the first cohort) is calculated based on the assumption that ADA+ rate is 3%.

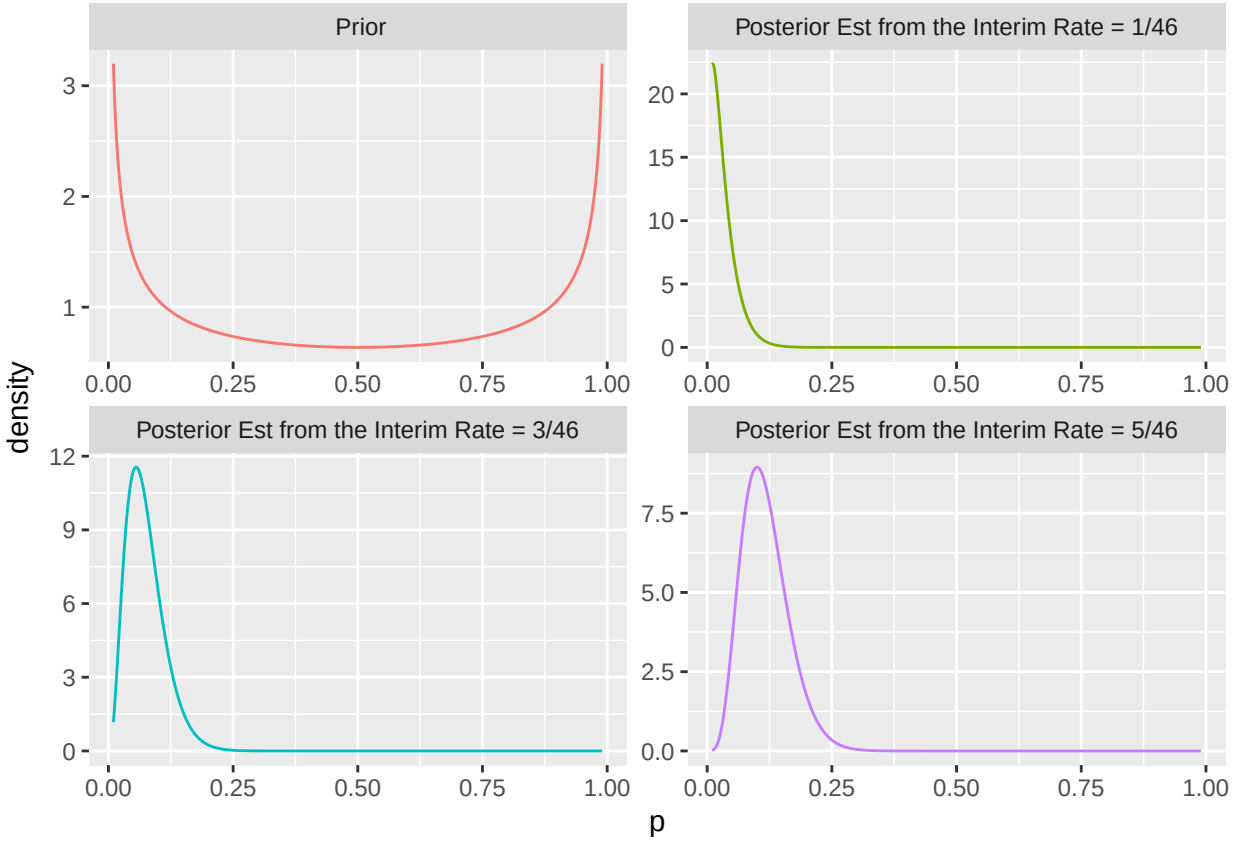
Uniform prior

n_ADA	n_cohort1	obs_ADA_rate	posterior_ADA_rate	N_required_per_arm	N_increase_per_arm
0	60	0.0000	0.0161	52	0
1	60	0.0167	0.0323	69	3
2	60	0.0333	0.0484	84	18
3	60	0.0500	0.0645	101	35
4	60	0.0667	0.0806	116	50
5	60	0.0833	0.0968	131	65
6	60	0.1000	0.1129	147	81
7	60	0.1167	0.1290	161	95

Jeffery's prior

n_ADA	n_cohort1	obs_ADA_rate	posterior_ADA_rate	N_required_per_arm	N_increase_per_arm
0	60	0.0000	0.0082	43	0
1	60	0.0167	0.0246	61	0
2	60	0.0333	0.0410	77	11
3	60	0.0500	0.0574	93	27
4	60	0.0667	0.0738	109	43
5	60	0.0833	0.0902	125	59
6	60	0.1000	0.1066	140	74
7	60	0.1167	0.1230	156	90

Posterior distribution based on Jeffreys prior and 1% initial ADA rate



The top left is the Jeffreys prior. The top right shows the posterior distribution Beta(1.5, 45.5); The lower left Beta(3.5, 43.5) and the lower right Beta(5.5, 41.5).