Table 1: Probabilities (×100) of reaching each possible conclusion for a study design with 1 vaccine arm with 1900 placebo recipients and 1100 vaccine recipients

Average VE(0-18)*	Average HR(0-18)	Potential-Harm VE(0-18)<0%	Non-Efficacy VE(0-18)<40%	Efficacy VE(0-18)>0%	High-Efficacy VE(0-36)>60%
–	3.0	94.0	6.0	0.0	0.0
–	2.5	79.9	20.1	0.0	0.0
–	2.0	52.5	47.5	0.0	0.0
–	1.5	18.1	81.9	0.0	0.0
0%	1.0	2.7	94.5	2.8	0.0
20%	0.8	0.8	71.4	27.8	0.0
30%	0.7	0.6	45.4	54.0	0.0
40%	0.6	0.4	18.9	80.7	0.0
50%	0.5	0.2	4.1	95.7	0.0
60%	0.4	0.1	0.7	98.8	0.4
70%	0.3	0.1	0.7	92.8	6.4
80%	0.2	0.0	8.1	46.4	45.5

*VE halved in the first 6 months

N=1900/1100 placebo/vaccine group

4% annual incidence in the placebo group

5% annual dropout

Cox & cumulative incidence-based non-efficacy monitoring

Cumulative hazard-based Wald test

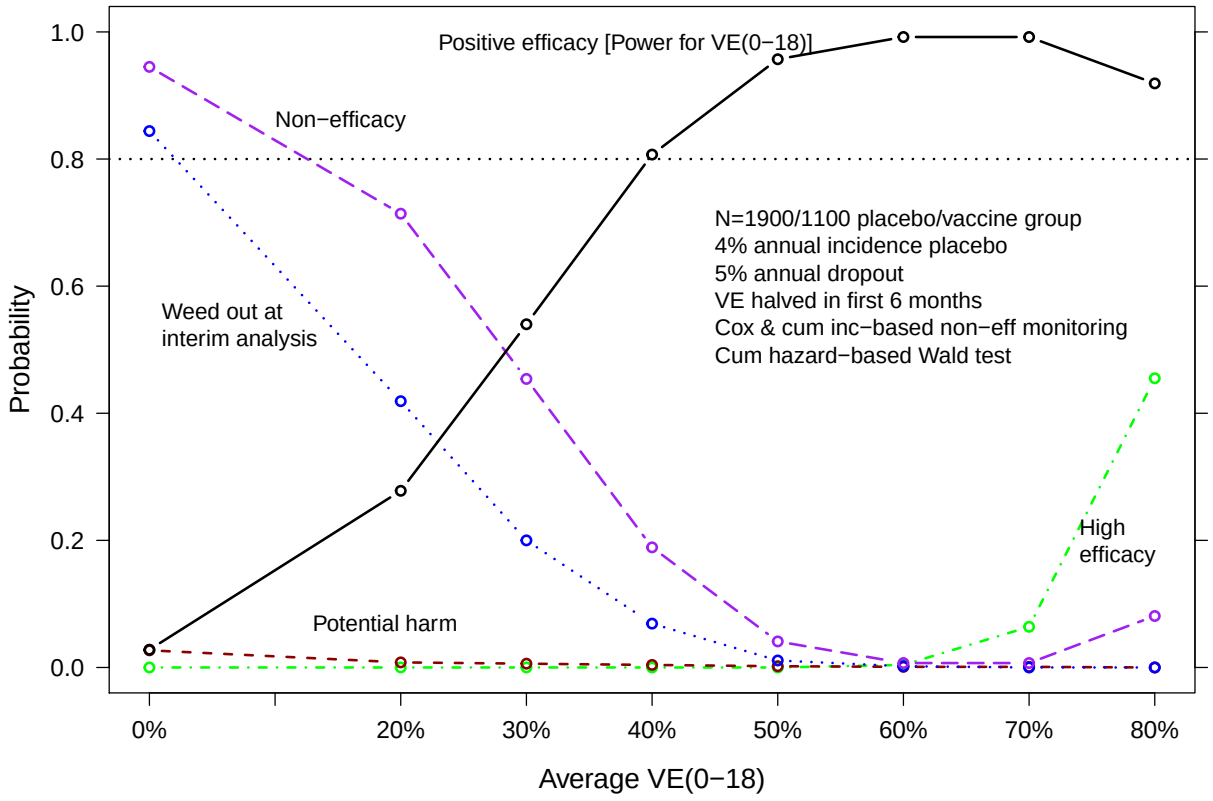

Figure 1: Probabilities of reaching each possible conclusion for a vaccine regimen

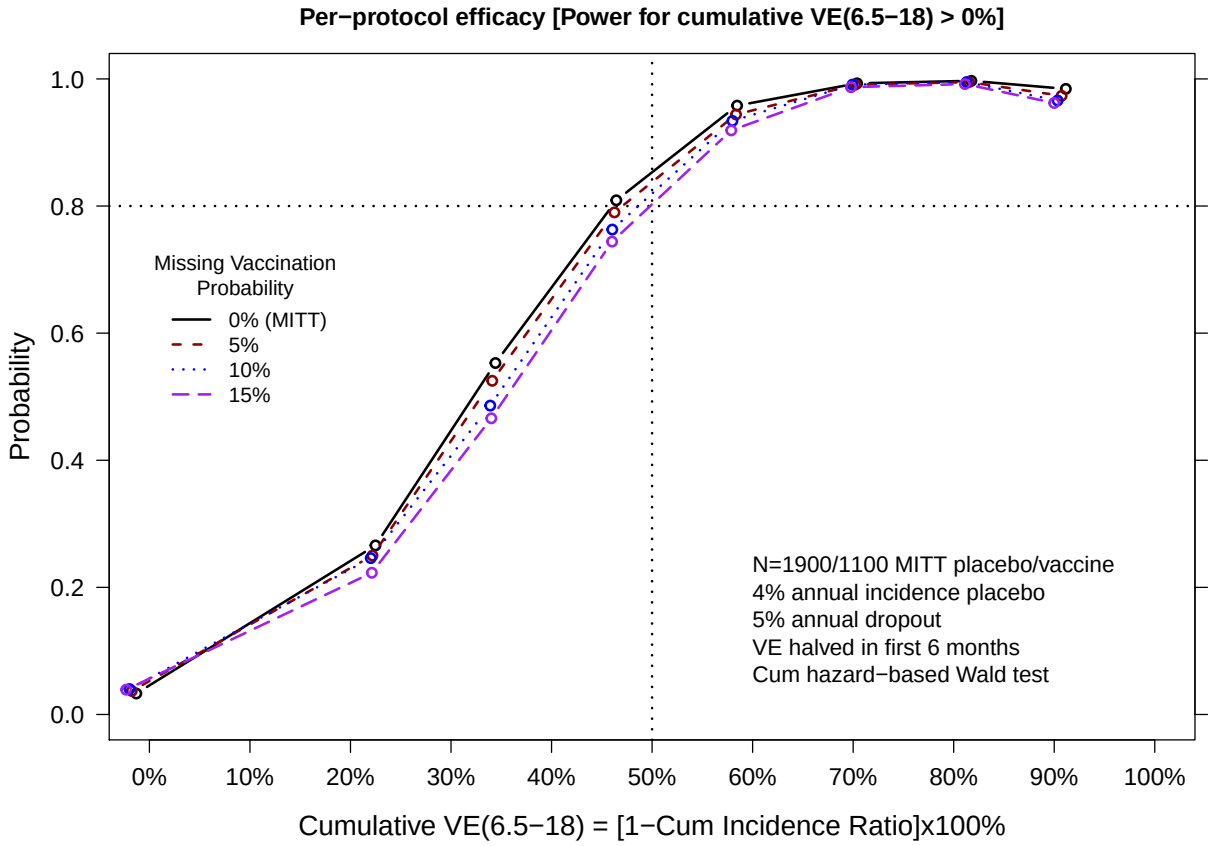

Figure 2: Power curves to detect VE(6.5–18)$>0\%$ in per-protocol cohorts with a varying probability of a missing vaccination

Table 2: Distribution of the number of Stage 1 infections pooled over the placebo group and the vaccine group with the maximum number of infections, ignoring sequential monitoring for potential-harm, non-efficacy, and high-efficacy (n=1900 in the placebo arm and n=1100 in each vaccine arm)

Ave VE	Percentiles of the distribution of the number of Stage 1 infections														
(0-18)*	1%	2.5%	5%	10%	20%	30%	40%	50%	60%	70%	80%	90%	95%	97.5%	99%
0%	150	153	156	160	164	168	171	174	177	180	184	189	193	196	201
40%	123	126	130	134	138	141	145	148	150	153	156	161	166	169	174

*VE halved in the first 6 months

N=1900/1100 placebo/vaccine group

4% annual incidence in the placebo group

5% annual dropout

Cumulative hazard-based Wald test

Table 3: Distribution of the number of Stage 1 infections pooled over all 5 groups or over the placebo group and the vaccine group with the maximum number of infections, accounting for sequential monitoring for potential-harm, non-efficacy, and high-efficacy (n=1900 in the placebo arm and n=1100 in each vaccine arm)

Ave VE	Percentiles of the distribution of the number of Stage 1 infections														
(0-18)*	1%	2.5%	5%	10%	20%	30%	40%	50%	60%	70%	80%	90%	95%	97.5%	99%
Total Stage 1 infections pooled over all vaccine groups and the placebo group															
0%	115	143	159	181	217	249	275	301	321	335	348	361	369	375	385
40%	217	222	227	232	240	245	250	254	258	262	267	275	280	284	288
Stage 1 infections in the vaccine + placebo pair with the most infections															
0%	59	68	76	87	107	123	138	152	164	171	177	185	191	194	198
40%	123	126	130	134	138	141	145	147	150	153	156	161	165	169	173

*VE halved in the first 6 months

N=1900/1100 placebo/vaccine group

4% annual incidence in the placebo group

5% annual dropout

Cox & cumulative incidence-based non-efficacy monitoring

Cumulative hazard-based Wald test

Table 4: Distribution of the number of infections diagnosed between 6.5–18 months among vaccine recipients with immune response measured at Month 6.5 visit and hence used in the evaluation of an immunological correlate of risk, for vaccine regimens with average VE of 50%, halved in the initial 6 months ($n = 1900$ in the placebo arm, $n = 1100$ in each vaccine arm, and $p = 0.05$ the conditional probability of having missed a vaccination given HIV-negative and ongoing at the Month 6 [Week 26] visit).

Number of vaccine arms	Mean	Percentiles of the distribution of the number of month 6.5–18 infections						
		1%	5%	25%	50%	75%	95%	99%
	Month 6.5–18 infections in the MITT cohort							
1	16	8	10	13	15	18	23	26
2	32	20	23	29	32	36	42	46
3	49	33	38	44	49	54	62	67
4	66	46	52	61	66	72	80	85
	Month 6.5–18 infections in the per-protocol cohort							
1	15	7	9	12	15	17	21	25
2	31	19	22	27	31	35	40	44
3	47	31	35	42	47	51	59	64
4	63	43	49	58	63	68	75	81

N=1900/1100 MITT placebo/vaccine

p=0.05 probability of a missing vaccination

4% annual incidence in the placebo group

5% annual dropout

Average VE=50%, halved VE in the first 6 months

Table 5: Distribution of the number of infections diagnosed between 6.5–36 months among vaccine recipients with immune response measured at Month 6.5 visit and hence used in the evaluation of an immunological correlate of risk, for vaccine regimens with average VE of 50%, halved in the initial 6 months ($n = 1900$ in the placebo arm, $n = 1100$ in each vaccine arm, and $p = 0.05$ the conditional probability of having missed a vaccination given HIV-negative and ongoing at the Month 6 [Week 26] visit).

Number of vaccine arms	Mean	Percentiles of the distribution of the number of month 6.5–36 infections						
		1%	5%	25%	50%	75%	95%	99%
	Month 6.5–36 infections in the MITT cohort							
1	42	28	32	38	43	47	53	59
2	86	60	70	80	86	93	102	106
3	132	90	110	124	133	141	153	163
4	176	132	149	166	176	186	201	207
	Month 6.5–36 infections in the per-protocol cohort							
1	40	26	30	36	40	44	51	56
2	82	58	66	76	82	88	97	102
3	126	84	104	118	126	134	146	154
4	167	128	141	157	168	177	191	197

N=1900/1100 MITT placebo/vaccine

p=0.05 probability of a missing vaccination

4% annual incidence in the placebo group

5% annual dropout

Average VE=50%, halved VE in the first 6 months

Table 6: Power to detect that relative VE(0–18) $> 0\%$ comparing head-to-head vaccine regimens 4 vs. 3 and VE(0–18) $> 0\%$ for vaccine regimen 4, and probability of correct ranking and selection of the winning most efficacious vaccine regimen

True average VE (%)[1] (Vx1, Vx2, Vx3, Vx4)	Power (×100) Vx4 vs. Vx3[2]	Probability (×100) select best vaccine[3]
(0, 0, 0, 40)	58.9	80.4
(0, 0, 30, 40)	10.0	71.0
(20, 20, 30, 40)	10.1	69.6
(0, 0, 0, 60)	95.7	99.5
(0, 0, 30, 60)	58.9	99.4
(0, 0, 45, 60)	21.1	95.0
(30, 30, 30, 60)	59.0	99.3
(30, 30, 45, 60)	21.1	94.9
(30, 45, 45, 60)	21.1	92.0

[1] VE halved in the first 6 months

[2] Cumulative hazard-based Wald tests of both Vx4/Vx3 and Vx4/Placebo VE(0–18) with 1-sided $\alpha = 0.025$

[3] Correct selection = Vx4 has highest estimated VE(0–36) and VE(0–18) significantly $> 0\%$

N=1900/1100 placebo/vaccine group

4% annual incidence in the placebo group

5% annual dropout

Cox & cumulative incidence-based non-efficacy monitoring

Table 7: Power to detect that relative VE(0–18) > 0% comparing head-to-head pooled vaccine regimens 3–4 vs. 1–2 and VE(0–18) > 0% for the pooled vaccine regimen 3–4, and probability of correct ranking and selection among the pooled pairs of the winning most efficacious regimen

True average VE (%)[1] (Vx1, Vx2, Vx3, Vx4)	Power (×100) Vx3-4 vs. Vx1-2[2]	Probability (×100) select best pooled Vx[3]
(0, 0, 0, 40)	21.5	34.9
(0, 0, 30, 40)	73.1	81.6
(20, 20, 30, 40)	27.5	79.5
(0, 0, 0, 60)	60.2	70.9
(0, 0, 30, 60)	95.2	96.8
(0, 0, 45, 60)	99.3	99.5
(30, 30, 30, 60)	32.8	96.2
(30, 30, 45, 60)	65.6	99.4
(30, 45, 45, 60)	36.2	97.5

[1] VE halved in the first 6 months

[2] Cumulative hazard-based Wald tests of both Vx3-4/Vx1-2 and Vx3-4/Placebo VE(0–18) with 1-sided $\alpha = 0.025$

[3] Correct selection = pooled Vx3-4 has highest estimated VE(0–36) and VE(0–18) significantly > 0%

N=1900/1100 placebo/vaccine group

4% annual incidence in the placebo group

5% annual dropout

Cox & cumulative incidence-based non-efficacy monitoring

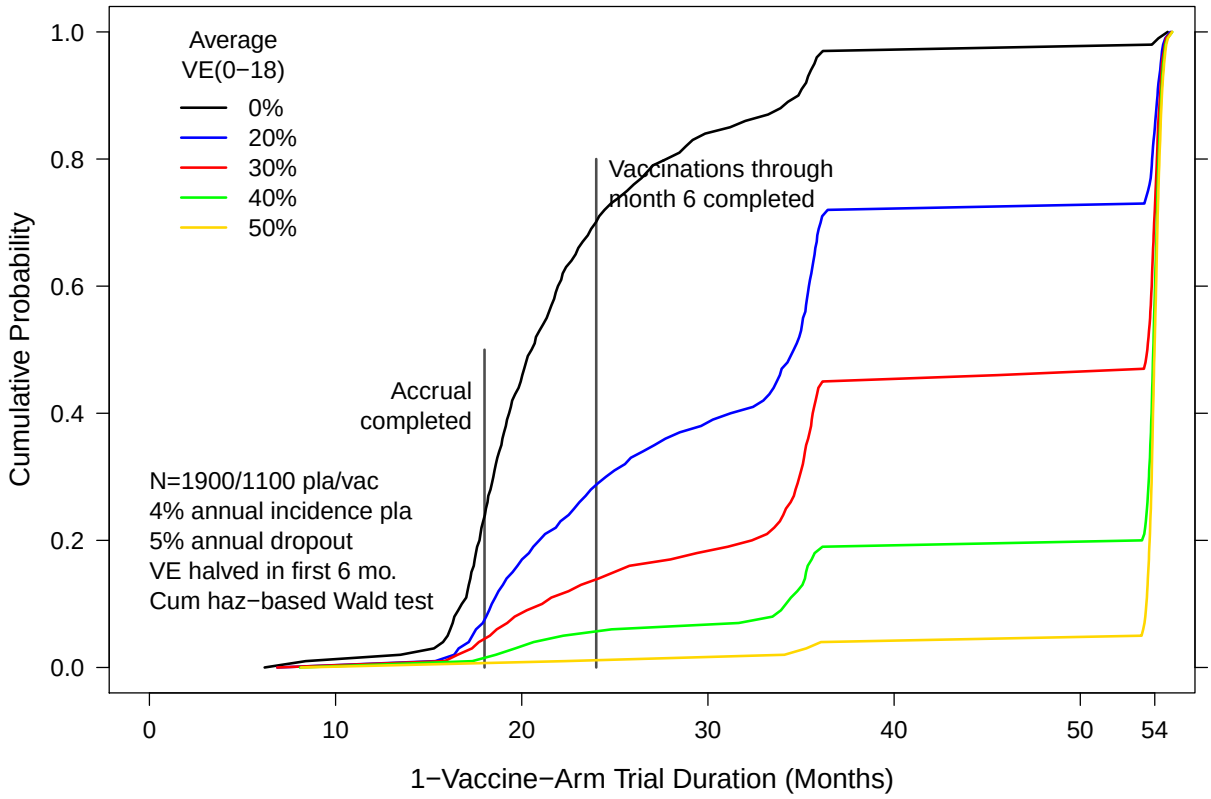

Figure 3: Duration of a vaccine regimen's evaluation (n =1900 in the placebo arm and n =1100 in the vaccine arm)

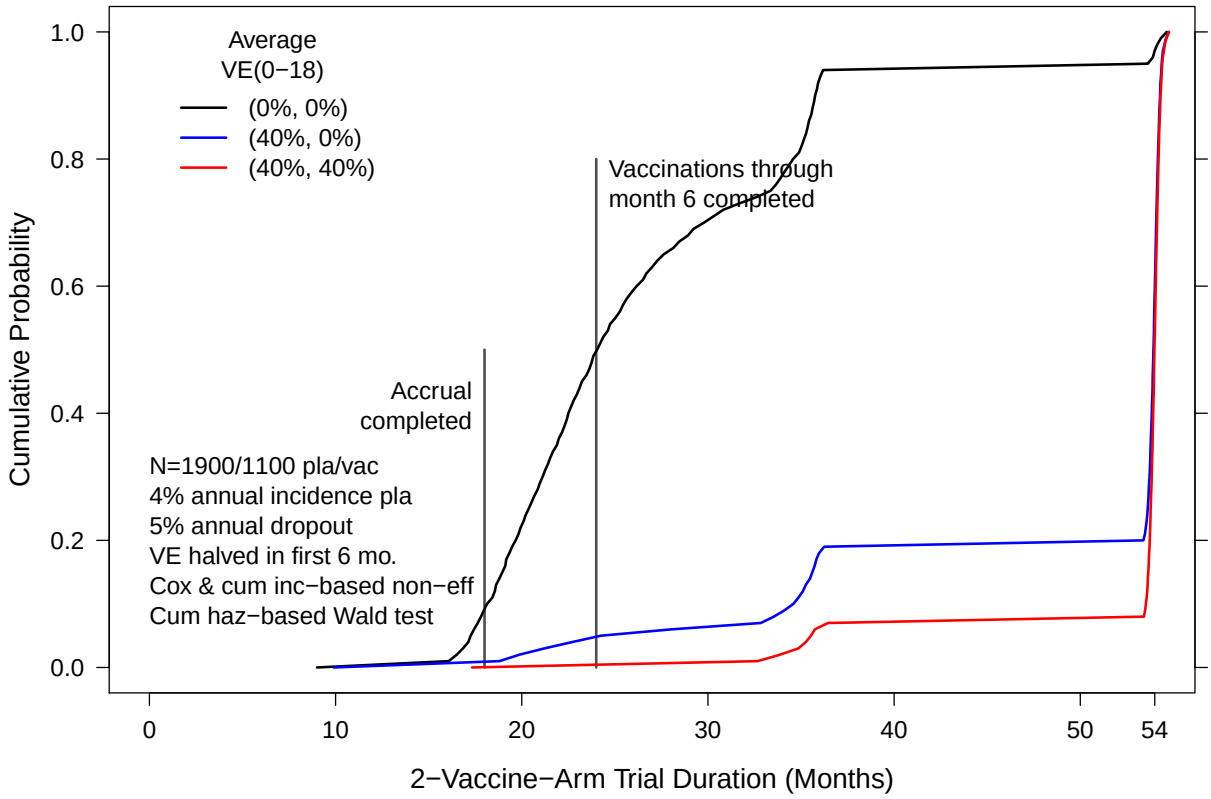

Figure 4: Total trial duration for the evaluation of 2 vaccine regimens ($n = 1100$ per arm) versus one placebo arm ($n = 1900$)

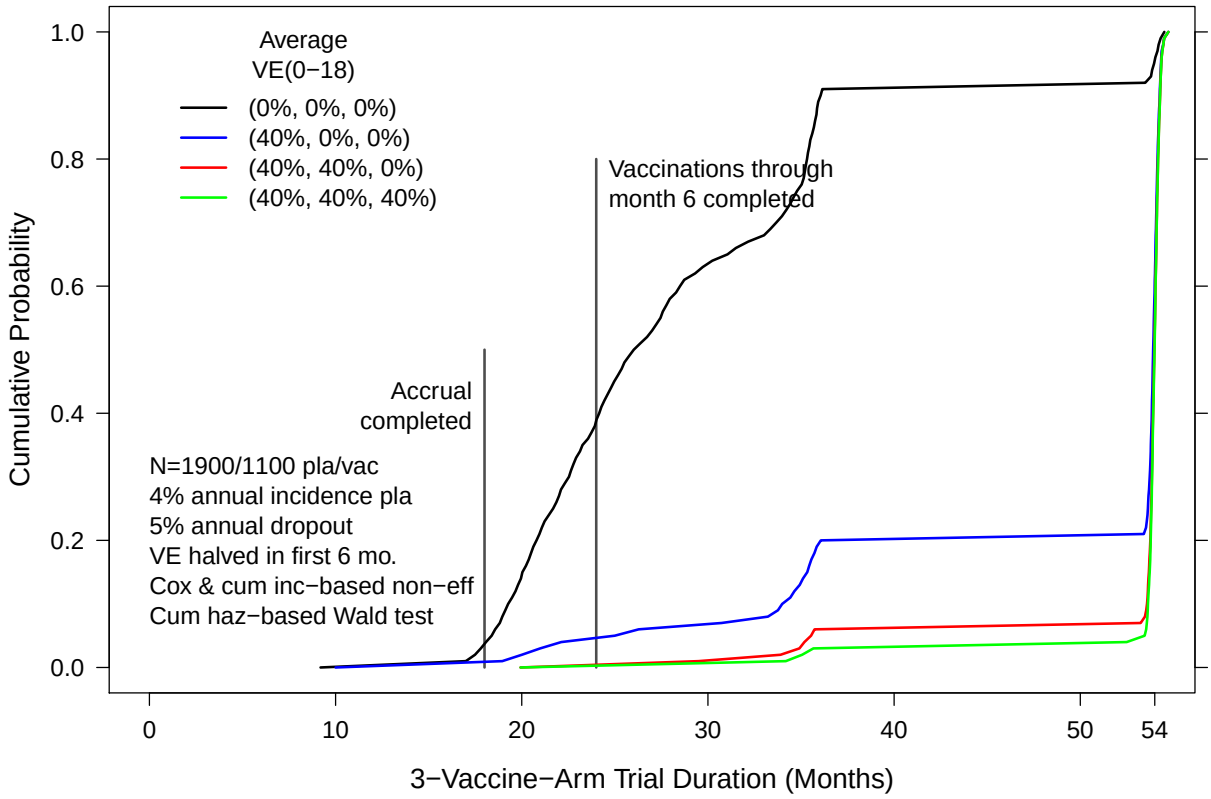

Figure 5: Total trial duration for the evaluation of 3 vaccine regimens ($n = 1100$ per arm) versus one placebo arm ($n = 1900$)

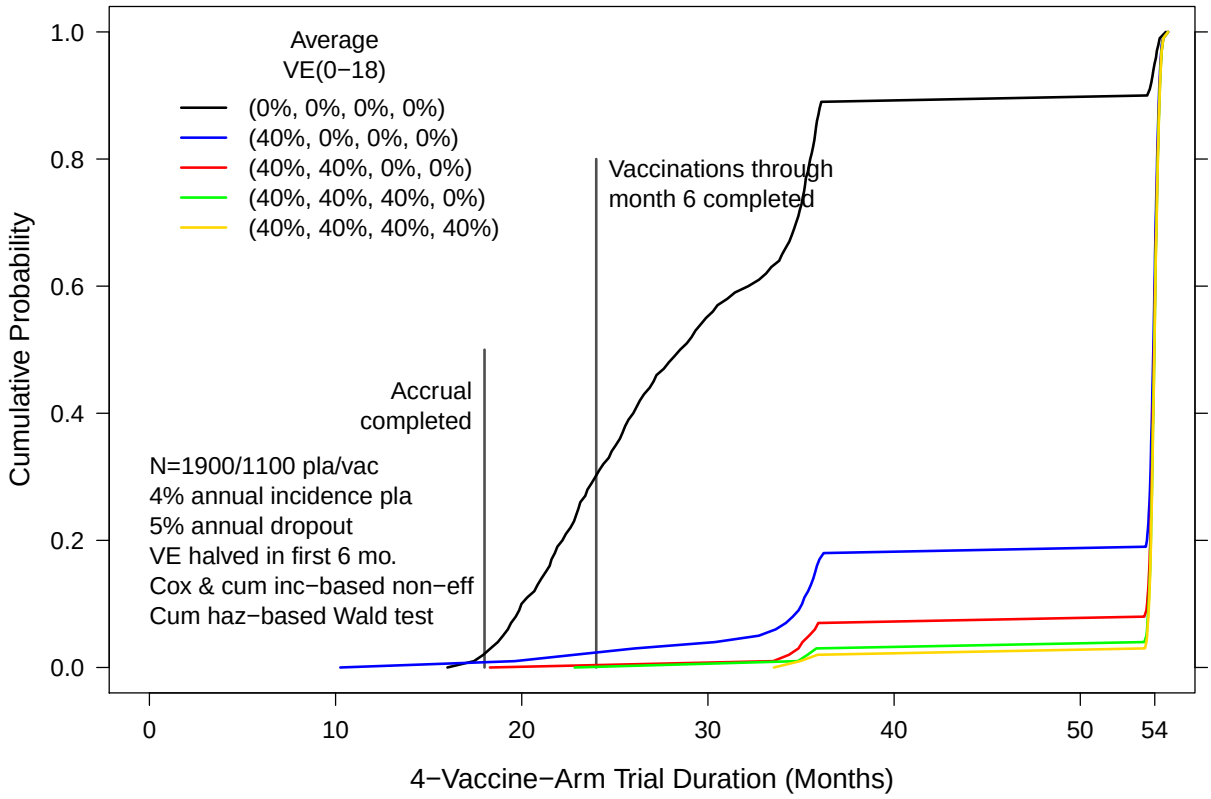

Figure 6: Total trial duration for the evaluation of 4 vaccine regimens ($n = 1100$ per arm) versus one placebo arm ($n = 1900$)