R Notebook

Stepwise calibration of lung cancer model with constraints

- 9 age groups, 11 parameters per age group: total of 99 parameters to be calibrated.
- 9 of those parameters (one per age group) are probabilities of developing cancer, with the constraint of these probabilities increasing with age.

method	group	time	iterations	error	delay	constrained
nelder-mead	1	86.21	839	0.1685787	0.1	yes
nelder-mead	2	79.72	775	0.1685787	0.1	yes
nelder-mead	3	81.66	793	0.1685787	0.1	yes
nelder-mead	4	101.61	985	0.2112280	0.1	yes
nelder-mead	5	128.52	1236	0.6645467	0.1	yes
nelder-mead	6	127.03	1233	1.9795078	0.1	yes
nelder-mead	7	231.11	2242	77.2779470	0.1	yes
nelder-mead	8	201.02	1948	81.3999553	0.1	yes
nelder-mead	9	288.74	2796	83.0570106	0.1	yes
bo	1	119.78	40	0.1237346	0.1	yes
bo	2	123.29	40	0.1284176	0.1	yes
bo	3	176.05	40	0.1537532	0.1	yes
bo	4	355.28	40	0.2191810	0.1	yes
bo	5	591.22	40	0.7689339	0.1	yes
bo	6	485.97	40	2.2675644	0.1	yes
bo	7	373.80	40	76.7939092	0.1	yes
bo	8	507.19	40	80.8674985	0.1	yes
bo	9	357.18	40	83.0535954	0.1	yes
annealing	1	2343.80	22637	0.1137244	0.1	yes
annealing	2	2376.90	22925	0.1137280	0.1	yes
annealing	3	2323.23	22361	0.1137493	0.1	yes
annealing	4	2586.64	24893	0.1562925	0.1	yes
annealing	5	3512.64	33701	0.6084468	0.1	yes
annealing	6	3763.44	36113	1.9237158	0.1	yes
annealing	7	3085.71	29561	77.1249233	0.1	yes
annealing	8	5591.71	53501	81.2325550	0.1	yes
annealing	9	3917.08	37421	82.8610077	0.1	yes
pso	1	1757.15	16980	0.1126824	0.1	yes
pso	2	964.73	9298	0.1126824	0.1	yes
pso	3	1039.33	10016	0.1126824	0.1	yes
pso	4	1121.64	10784	0.1552969	0.1	yes
pso	5	1642.14	15786	0.6158138	0.1	yes
pso	6	1735.28	16691	1.9305617	0.1	yes
pso	7	21155.12	202950	77.1683602	0.1	yes
pso	8	21197.11	202950	81.3903838	0.1	yes
pso	9	3465.25	33201	83.0449091	0.1	yes
nelder-mead	1	86.94	839	0.1685787	0.1	no
nelder-mead	2	80.58	775	0.1685787	0.1	no

method	group	time	iterations	error	delay	constrained
nelder-mead	3	73.84	708	0.1991849	0.1	no
nelder-mead	4	89.06	853	0.2418408	0.1	no
nelder-mead	5	163.21	1566	0.6940669	0.1	no
nelder-mead	6	135.69	1298	2.0092999	0.1	no
nelder-mead	7	74.80	716	76.1249879	0.1	no
nelder-mead	8	141.97	1356	80.0057314	0.1	no
nelder-mead	9	139.86	1336	81.2596918	0.1	no
annealing	1	2349.66	22661	0.1128548	0.1	no
annealing	2	2329.76	22433	0.1128691	0.1	no
annealing	3	2341.87	22541	0.1128693	0.1	no
annealing	4	2739.82	26357	0.1554071	0.1	no
annealing	5	3572.21	34373	0.6075151	0.1	no
annealing	6	3849.34	36965	1.9233890	0.1	no
annealing	7	2858.78	27329	76.0270601	0.1	no
annealing	8	4479.59	42893	79.7575312	0.1	no
annealing	9	4288.06	41141	81.0635058	0.1	no
bo	1	71.93	40	0.1237346	0.1	no
bo	2	69.49	40	0.1301805	0.1	no
bo	3	92.83	40	0.1840909	0.1	no
bo	4	190.90	40	0.2901077	0.1	no
bo	5	469.89	40	0.9046652	0.1	no
bo	6	388.85	40	2.4350920	0.1	no
bo	7	260.54	40	74.8822406	0.1	no
bo	8	320.04	40	80.7263702	0.1	no
bo	9	218.78	40	83.2432799	0.1	no
pso	1	1701.46	16418	0.1126843	0.1	no
pso	2	1096.36	10571	0.1126843	0.1	no
pso	3	1092.46	10499	0.1126843	0.1	no
pso	4	1040.99	10020	0.1552424	0.1	no
pso	5	1409.97	13557	0.6086457	0.1	no
pso	6	1111.77	10680	1.9245714	0.1	no
pso	7	21146.37	202950	76.0244206	0.1	no
pso	8	21096.04	202950	79.7500776	0.1	no
pso	9	21244.08	202950	81.0407388	0.1	no

method	param	value	constrained	error	distance
initial	1	0.0310692	yes	0.0000000	0.0000000
initial	2	0.0310699	yes	0.0000000	0.0000000
initial	3	0.0319403	yes	0.0000000	0.0000000
initial	4	0.0319527	yes	0.0000000	0.0000000
initial	5	0.0346737	yes	0.0000000	0.0000000
initial	6	0.0373947	yes	0.0000000	0.0000000
initial	7	0.0401158	yes	0.0000000	0.0000000
initial	8	0.0408170	yes	0.0000000	0.0000000
initial	9	0.0415183	yes	0.0000000	0.0000000
nelder-mead	1	0.0155379	yes	-0.0155313	0.0155313
nelder-mead	2	0.0342692	yes	0.0031993	0.0031993
nelder-mead	3	0.0355458	yes	0.0036055	0.0036055
nelder-mead	4	0.0428892	yes	0.0109365	0.0109365
nelder-mead	5	0.0520106	yes	0.0173369	0.0173369
nelder-mead	6	0.0560921	yes	0.0186974	0.0186974

method	param	value	constrained	error	distance
nelder-mead	7	0.0560927	yes	0.0159770	0.0159770
nelder-mead	8	0.0612255	yes	0.0204085	0.0204085
nelder-mead	9	0.0622774	yes	0.0207591	0.0207591
bo	1	0.0218011	yes	-0.0092681	0.0092681
bo	2	0.0273477	yes	-0.0037222	0.0037222
bo	3	0.0288643	yes	-0.0030760	0.0030760
bo	4	0.0326866	yes	0.0007339	0.0007339
bo	5	0.0413211	yes	0.0066474	0.0066474
bo	6	0.0424886	yes	0.0050939	0.0050939
bo	7	0.0456570	yes	0.0055412	0.0055412
bo	8	0.0475564	yes	0.0067394	0.0067394
bo	9	0.0503978	yes	0.0088795	0.0088795
annealing	1	0.0155402	yes	-0.0155290	0.0155290
annealing	2	0.0443652	yes	0.0132953	0.0132953
annealing	3	0.0448168	yes	0.0128766	0.0128766
annealing	4	0.0456655	yes	0.0137128	0.0137128
annealing	5	0.0517008	yes	0.0170271	0.0170271
annealing	6	0.0530996	yes	0.0157049	0.0157049
annealing	7	0.0531124	yes	0.0129967	0.0129967
annealing	8	0.0531626	yes	0.0123455	0.0123455
annealing	9	0.0532066	yes	0.0116883	0.0116883
pso	1	0.0155346	yes	-0.0155346	0.0155346
pso	2	0.0277014	yes	-0.0033684	0.0033684
pso	3	0.0411837	yes	0.0092435	0.0092435
pso	4	0.0475172	yes	0.0155646	0.0155646
pso	5	0.0520106	yes	0.0173369	0.0173369
pso	6	0.0560921	yes	0.0186973	0.0186973
pso	7	0.0560927	yes	0.0159769	0.0159769
pso	8	0.0612247	yes	0.0204076	0.0204076
pso	9	0.0622774	yes	0.0207591	0.0207591
initial	1	0.0310692	no	0.0000000	0.0000000
initial	2	0.0310699	no	0.0000000	0.0000000
initial	3	0.0319403	no	0.0000000	0.0000000
initial	4	0.0319527	no	0.0000000	0.0000000
initial	5	0.0346737	no	0.0000000	0.0000000
initial	6	0.0373947	no	0.0000000	0.0000000
initial	7	0.0401158	no	0.0000000	0.0000000
initial	8	0.0408170	no	0.0000000	0.0000000
initial	9	0.0415183	no	0.0000000	0.0000000
nelder-mead	1	0.0155379	no	-0.0155313	0.0155313
nelder-mead	2	0.0342692	no	0.0031993	0.0031993
nelder-mead	3	0.0382314	no	0.0062912	0.0062912
nelder-mead	4	0.0374326	no	0.0054799	0.0054799
nelder-mead	5	0.0304106	no	-0.0042631	0.0042631
nelder-mead	6	0.0552330	no	0.0178383	0.0178383
nelder-mead	7	0.0200579	no	-0.0200579	0.0200579
nelder-mead	8	0.0205794	no	-0.0202376	0.0202376
nelder-mead	9	0.0207593	no	-0.0207590	0.0207590
annealing	1	0.0155368	no	-0.0155324	0.0155324
annealing	2	0.0159028	no	-0.0151671	0.0151671
annealing	3	0.0470258	no	0.0150856	0.0150856
annealing	4	0.0319416	no	-0.0000111	0.0000111

method	param	value	constrained	error	distance
annealing	5	0.0455787	no	0.0109050	0.0109050
annealing	6	0.0344746	no	-0.0029202	0.0029202
annealing	7	0.0201162	no	-0.0199996	0.0199996
annealing	8	0.0204420	no	-0.0203751	0.0203751
annealing	9	0.0207756	no	-0.0207427	0.0207427
bo	1	0.0218011	no	-0.0092681	0.0092681
bo	2	0.0410437	no	0.0099738	0.0099738
bo	3	0.0456724	no	0.0137322	0.0137322
bo	4	0.0267801	no	-0.0051726	0.0051726
bo	5	0.0173369	no	-0.0173369	0.0173369
bo	6	0.0285527	no	-0.0088421	0.0088421
bo	7	0.0200579	no	-0.0200579	0.0200579
bo	8	0.0204085	no	-0.0204085	0.0204085
bo	9	0.0348354	no	-0.0066829	0.0066829
pso	1	0.0155346	no	-0.0155346	0.0155346
pso	2	0.0257011	no	-0.0053688	0.0053688
pso	3	0.0265071	no	-0.0054331	0.0054331
pso	4	0.0349283	no	0.0029757	0.0029757
pso	5	0.0378479	no	0.0031742	0.0031742
pso	6	0.0237726	no	-0.0136221	0.0136221
pso	7	0.0200579	no	-0.0200579	0.0200579
pso	8	0.0204085	no	-0.0204085	0.0204085
pso	9	0.0207591	no	-0.0207592	0.0207592

Overall results
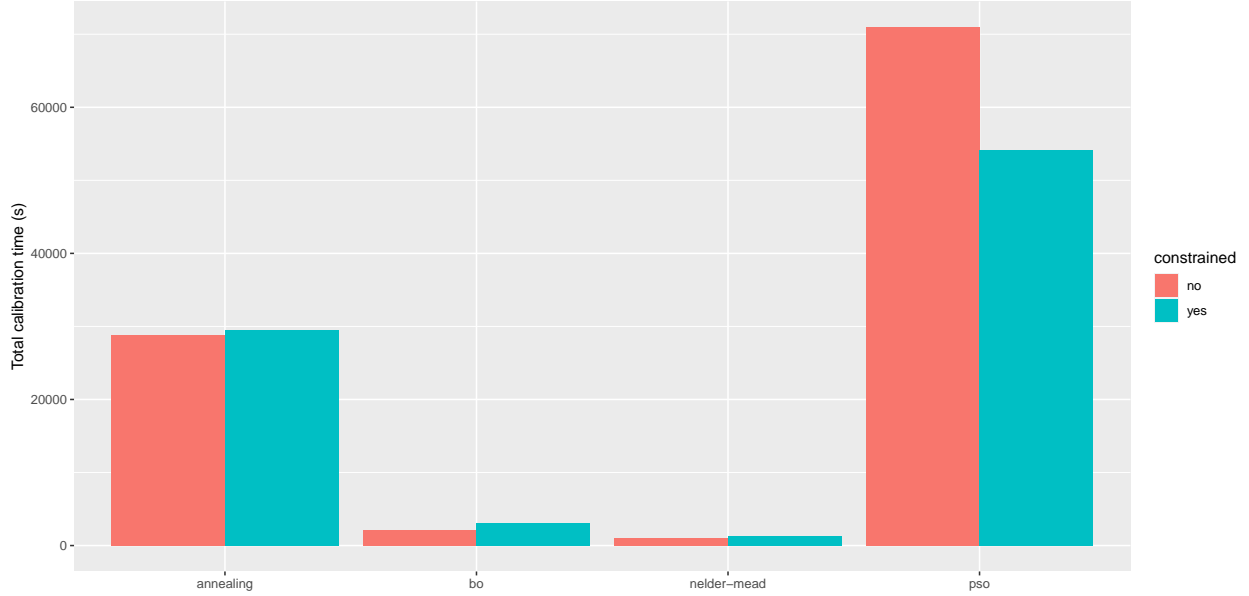

With a delay of 100 ms (therefore $t_{sim} \approx 100ms$), both PSO and SA need a lot of time due to its large number of iterations. NM and BO use a comparable amount of time for similar results, even if for this simulation time NM is faster. Constrained calibration takes more time for all methods except PSO, but seems to be reasonable for these dimensionalities.

In absolute terms, calibration with BO using the stepwise method takes around **50 minutes**. Even the

unconstrained version of the regular calibration proved to be unfeasible, requiring many days of computation while finding low-quality solutions. Adding constraints to the regular calibration would increase even further the computational cost of an already unfeasible problem.

Calibration errors by age group
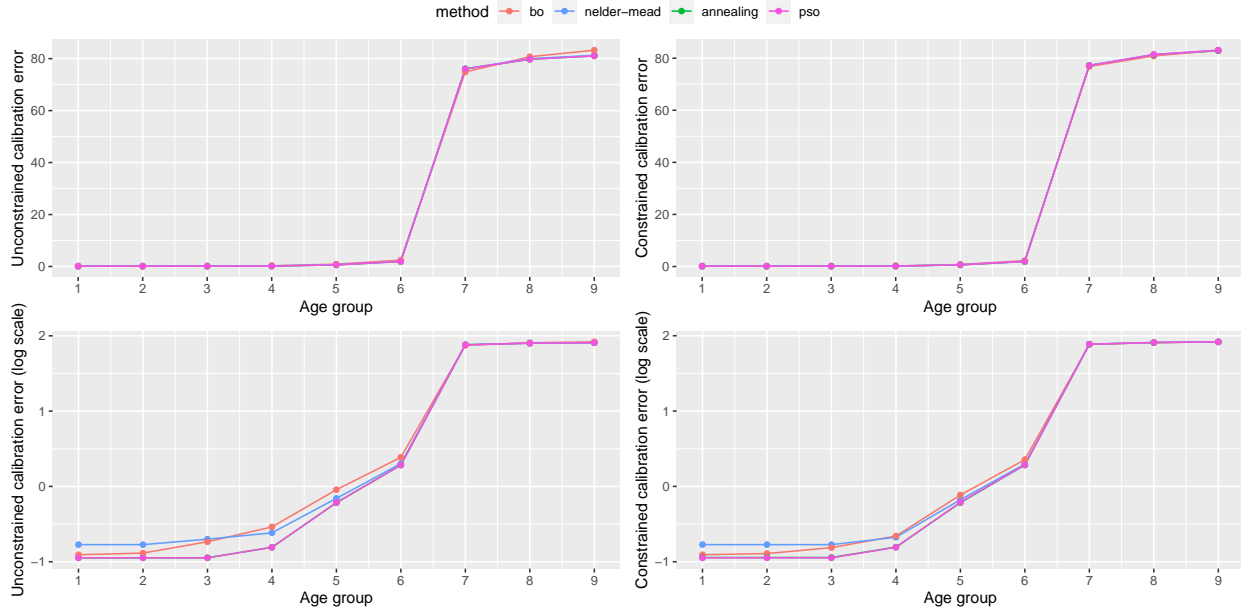
Solutions reached by the different methods have very similar errors (unconstrained calibration on the left, constrained calibration on the right), so the final results are comparable among methods. The slight increase in BO error at the final age group might not be too important due to how these models work (it is very small and the outputs at the end of the simulation have less impact).

## Calibrated parameters by age group
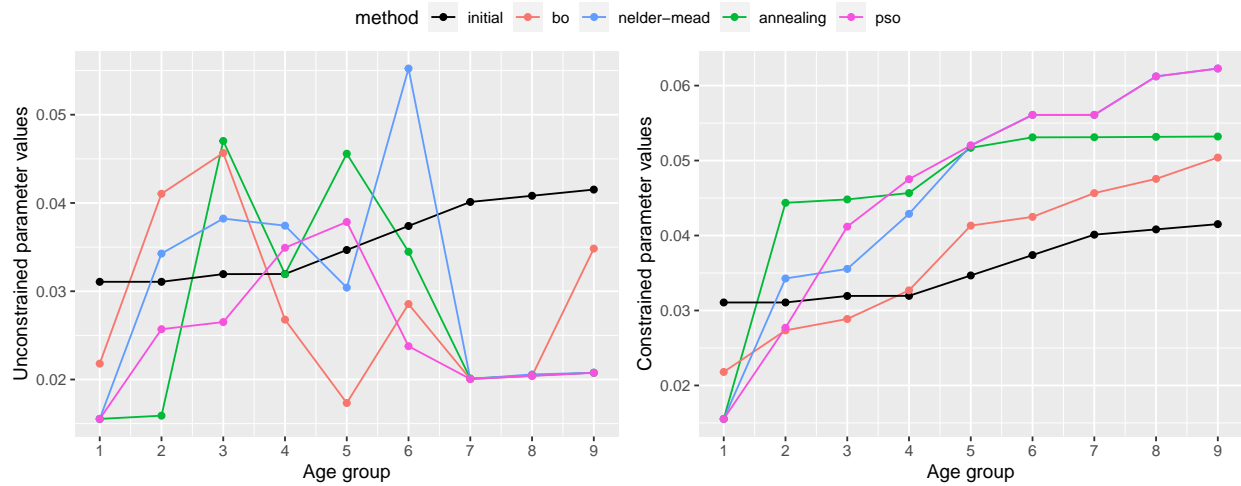
BO finds the solution that resembles the initial parameters the most. For some reason, Nelder-Mead and PSO find very similar constrained solutions for group ages 5+ and they can't be distinguished in the right figure.

Number of iterations per age group
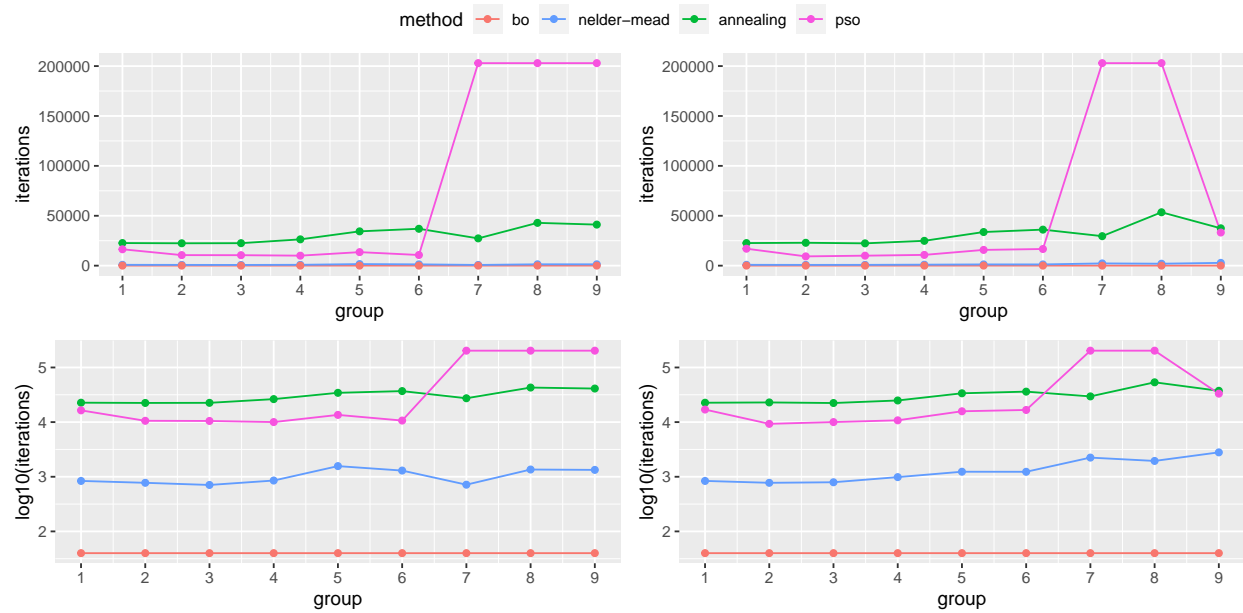
BO was run with a fixed budget of 40 iterations, including 10 random initial observations. Even though SA has a lower error we can see that it requires a very large number of iterations for a very modest improvement on the solution. PSO gets stuck in the last age groups and stops at the established maximum iterations.

Critical simulation time for constrained stepwise calibration
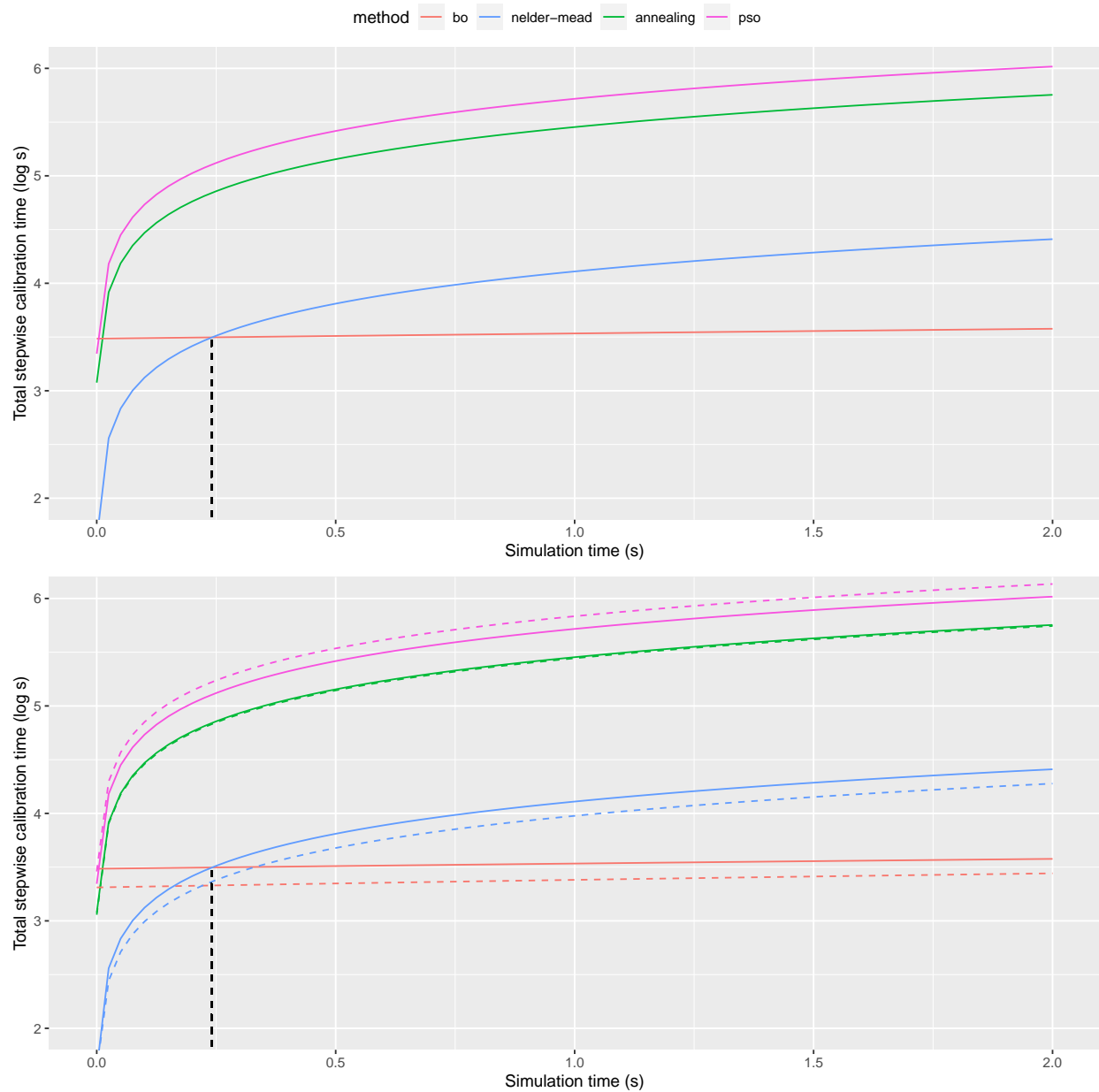
The critical simulation time for the whole model with all 9 age groups (that **we projected at 300 seconds using conventional calibration**) is reduced to ~**0.24 seconds using constrained stepwise calibration**. This proves that this method dramatically improves the efficiency of Bayesian Optimization by exploiting a major flaw of BO (high dimensionality), reducing the effective dimension of the problem from one 99-parameter problem to nine 11-parameter problems.

The critical simulation time doesn't change significantly when considering an unconstrained calibration.