R Notebook

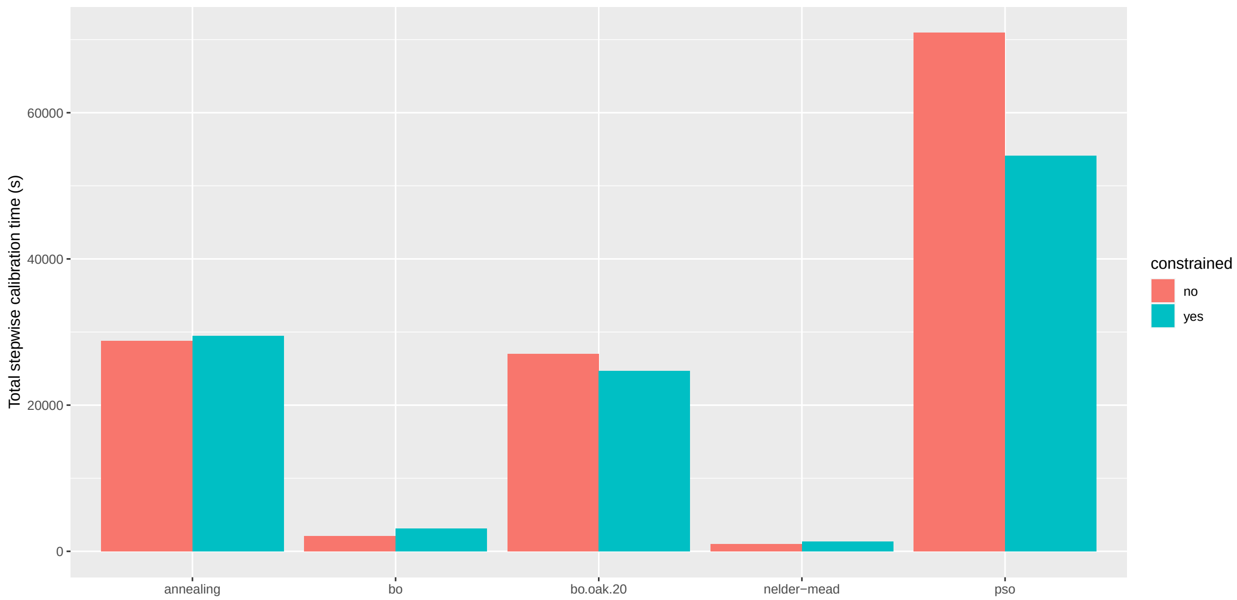
Stepwise calibration of lung cancer model with constraints

- 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
1	nelder-mead	1	86.21	839	0.1685787	0.100	yes
2	nelder-mead	2	79.72	775	0.1685787	0.100	yes
3	nelder-mead	3	81.66	793	0.1685787	0.100	yes
4	nelder-mead	4	101.61	985	0.2112280	0.100	yes
5	nelder-mead	5	128.52	1236	0.6645467	0.100	yes
6	nelder-mead	6	127.03	1233	1.9795078	0.100	yes
7	nelder-mead	7	231.11	2242	77.2779470	0.100	yes
8	nelder-mead	8	201.02	1948	81.3999553	0.100	yes
9	nelder-mead	9	288.74	2796	83.0570106	0.100	yes
10	bo	1	119.78	40	0.1237346	0.100	yes
11	bo	2	123.29	40	0.1284176	0.100	yes
12	bo	3	176.05	40	0.1537532	0.100	yes
13	bo	4	355.28	40	0.2191810	0.100	yes
14	bo	5	591.22	40	0.7689339	0.100	yes
15	bo	6	485.97	40	2.2675644	0.100	yes
16	bo	7	373.80	40	76.7939092	0.100	yes
17	bo	8	507.19	40	80.8674985	0.100	yes
18	bo	9	357.18	40	83.0535954	0.100	yes
19	annealing	1	2343.80	22637	0.1137244	0.100	yes
20	annealing	2	2376.90	22925	0.1137280	0.100	yes
21	annealing	3	2323.23	22361	0.1137493	0.100	yes
22	annealing	4	2586.64	24893	0.1562925	0.100	yes
23	annealing	5	3512.64	33701	0.6084468	0.100	yes
24	annealing	6	3763.44	36113	1.9237158	0.100	yes
25	annealing	7	3085.71	29561	77.1249233	0.100	yes
26	annealing	8	5591.71	53501	81.2325550	0.100	yes
27	annealing	9	3917.08	37421	82.8610077	0.100	yes
28	pso	1	1757.15	16980	0.1126824	0.100	yes
29	pso	2	964.73	9298	0.1126824	0.100	yes
30	pso	3	1039.33	10016	0.1126824	0.100	yes
31	pso	4	1121.64	10784	0.1552969	0.100	yes
32	pso	5	1642.14	15786	0.6158138	0.100	yes
33	pso	6	1735.28	16691	1.9305617	0.100	yes
34	pso	7	21155.12	202950	77.1683602	0.100	yes
35	pso	8	21197.11	202950	81.3903838	0.100	yes
36	pso	9	3465.25	33201	83.0449091	0.100	yes
37	nelder-mead	1	86.94	839	0.1685787	0.100	no
38	nelder-mead	2	80.58	775	0.1685787	0.100	no

	method	group	time	iterations	error	delay	constrained
39	nelder-mead	3	73.84	708	0.1991849	0.100	no
40	nelder-mead	4	89.06	853	0.2418408	0.100	no
41	nelder-mead	5	163.21	1566	0.6940669	0.100	no
42	nelder-mead	6	135.69	1298	2.0092999	0.100	no
43	nelder-mead	7	74.80	716	76.1249879	0.100	no
44	nelder-mead	8	141.97	1356	80.0057314	0.100	no
45	nelder-mead	9	139.86	1336	81.2596918	0.100	no
46	annealing	1	2349.66	22661	0.1128548	0.100	no
47	annealing	2	2329.76	22433	0.1128691	0.100	no
48	annealing	3	2341.87	22541	0.1128693	0.100	no
49	annealing	4	2739.82	26357	0.1554071	0.100	no
50	annealing	5	3572.21	34373	0.6075151	0.100	no
51	annealing	6	3849.34	36965	1.9233890	0.100	no
52	annealing	7	2858.78	27329	76.0270601	0.100	no
53	annealing	8	4479.59	42893	79.7575312	0.100	no
54	annealing	9	4288.06	41141	81.0635058	0.100	no
55	bo	1	71.93	40	0.1237346	0.100	no
56	bo	2	69.49	40	0.1301805	0.100	no
57	bo	3	92.83	40	0.1840909	0.100	no
58	bo	4	190.90	40	0.2901077	0.100	no
59	bo	5	469.89	40	0.9046652	0.100	no
60	bo	6	388.85	40	2.4350920	0.100	no
61	bo	7	260.54	40	74.8822406	0.100	no
62	bo	8	320.04	40	80.7263702	0.100	no
63	bo	9	218.78	40	83.2432799	0.100	no
64	pso	1	1701.46	16418	0.1126843	0.100	no
65	pso	2	1096.36	10571	0.1126843	0.100	no
66	pso	3	1092.46	10499	0.1126843	0.100	no
67	pso	4	1040.99	10020	0.1552424	0.100	no
68	pso	5	1409.97	13557	0.6086457	0.100	no
69	pso	6	1111.77	10680	1.9245714	0.100	no
70	pso	7	21146.37	202950	76.0244206	0.100	no
71	pso	8	21096.04	202950	79.7500776	0.100	no
72	pso	9	21244.08	202950	81.0407388	0.100	no
91	bo.oak.20	1	3216.27	20	0.0011802	0.001	yes
92	bo.oak.20	2	1917.77	20	0.2723453	0.001	yes
93	bo.oak.20	3	7493.02	20	0.8998314	0.001	yes
94	bo.oak.20	4	1871.03	20	0.9581732	0.001	yes
95	bo.oak.20	5	1902.83	20	1.0931653	0.001	yes
96	bo.oak.20	6	1772.91	20	1.4200288	0.001	yes
97	bo.oak.20	7	717.54	20	49.4588533	0.001	yes
98	bo.oak.20	8	2122.02	20	49.4648184	0.001	yes
99	bo.oak.20	9	3658.97	20	50.4987649	0.001	yes
100	bo.oak.20	1	3572.00	20	0.0011802	0.001	no
101	bo.oak.20	2	2008.25	20	0.4008580	0.001	no
102	bo.oak.20	3	3724.99	20	0.8998314	0.001	no
103	bo.oak.20	4	2532.70	20	0.9286285	0.001	no
104	bo.oak.20	5	2060.39	20	0.9610243	0.001	no
105	bo.oak.20	6	4287.43	20	0.9882536	0.001	no
106	bo.oak.20	7	1902.83	20	42.9752158	0.001	no
107	bo.oak.20	8	3332.48	20	43.2180376	0.001	no
108	bo.oak.20	9	3570.89	20	43.9050200	0.001	no

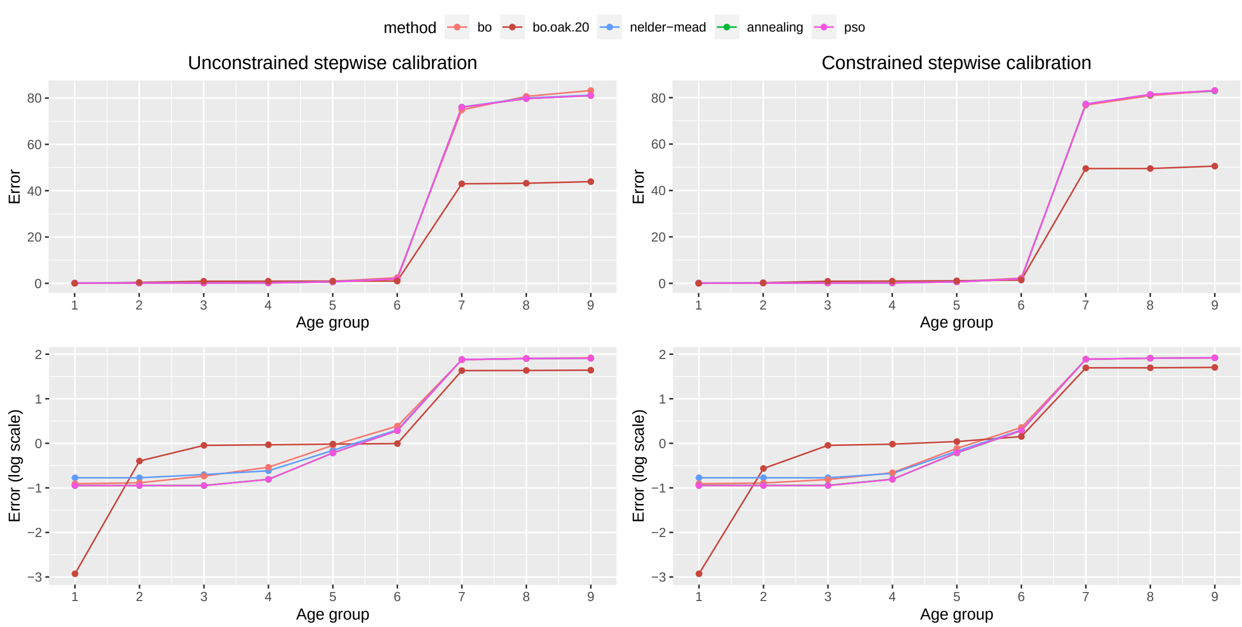
Overall results



With a delay of 100 ms (therefore $t_{sim} \approx 100$ms), 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

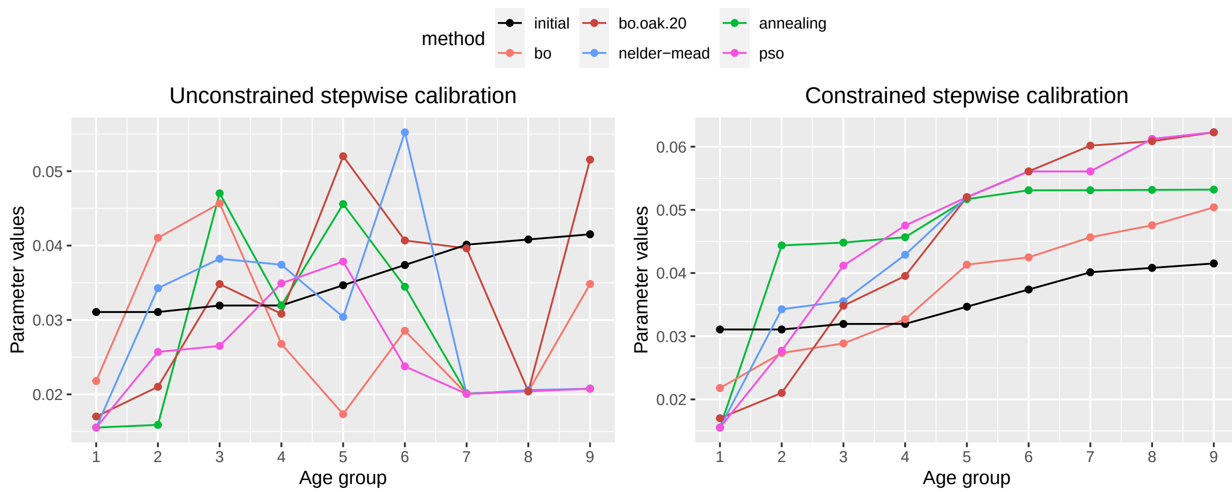


Solutions reached by the different methods have very similar errors (unconstrained calibration on the left, constrained calibration on the right), so the final results are comparable among methods. The slight increase in BO error at the final age group might not be too important due to how these models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

Calibrated parameters by age group

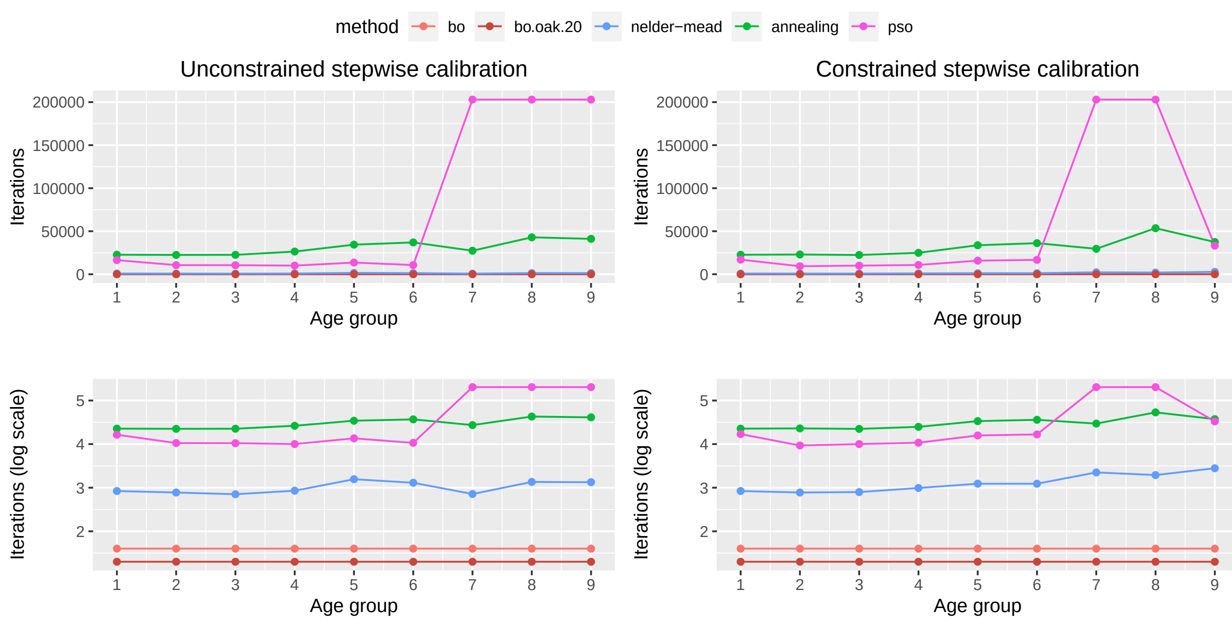
	method	param	value	constrained	error	distance
1	initial	1	0.03107	yes	0.00000	0.00000
2	initial	2	0.03107	yes	0.00000	0.00000
3	initial	3	0.03194	yes	0.00000	0.00000
4	initial	4	0.03195	yes	0.00000	0.00000
5	initial	5	0.03467	yes	0.00000	0.00000
6	initial	6	0.03739	yes	0.00000	0.00000
7	initial	7	0.04012	yes	0.00000	0.00000
8	initial	8	0.04082	yes	0.00000	0.00000
9	initial	9	0.04152	yes	0.00000	0.00000
10	nelder-mead	1	0.01554	yes	-0.01553	0.01553
11	nelder-mead	2	0.03427	yes	0.00320	0.00320
12	nelder-mead	3	0.03555	yes	0.00361	0.00361
13	nelder-mead	4	0.04289	yes	0.01094	0.01094
14	nelder-mead	5	0.05201	yes	0.01734	0.01734
15	nelder-mead	6	0.05609	yes	0.01870	0.01870
16	nelder-mead	7	0.05609	yes	0.01597	0.01597
17	nelder-mead	8	0.06123	yes	0.02041	0.02041
18	nelder-mead	9	0.06228	yes	0.02076	0.02076
19	bo	1	0.02180	yes	-0.00927	0.00927
20	bo	2	0.02735	yes	-0.00372	0.00372
21	bo	3	0.02886	yes	-0.00308	0.00308
22	bo	4	0.03269	yes	0.00074	0.00074
23	bo	5	0.04132	yes	0.00665	0.00665
24	bo	6	0.04249	yes	0.00510	0.00510
25	bo	7	0.04566	yes	0.00554	0.00554
26	bo	8	0.04756	yes	0.00674	0.00674
27	bo	9	0.05040	yes	0.00888	0.00888
28	annealing	1	0.01554	yes	-0.01553	0.01553
29	annealing	2	0.04437	yes	0.01330	0.01330
30	annealing	3	0.04482	yes	0.01288	0.01288
31	annealing	4	0.04567	yes	0.01372	0.01372
32	annealing	5	0.05170	yes	0.01703	0.01703
33	annealing	6	0.05310	yes	0.01571	0.01571
34	annealing	7	0.05311	yes	0.01299	0.01299
35	annealing	8	0.05316	yes	0.01234	0.01234
36	annealing	9	0.05321	yes	0.01169	0.01169
37	pso	1	0.01553	yes	-0.01554	0.01554
38	pso	2	0.02770	yes	-0.00337	0.00337
39	pso	3	0.04118	yes	0.00924	0.00924
40	pso	4	0.04752	yes	0.01557	0.01557
41	pso	5	0.05201	yes	0.01734	0.01734
42	pso	6	0.05609	yes	0.01870	0.01870
43	pso	7	0.05609	yes	0.01597	0.01597
44	pso	8	0.06122	yes	0.02040	0.02040
45	pso	9	0.06228	yes	0.02076	0.02076
109	bo.oak.20	1	0.01702	yes	-0.01405	0.01405

	method	param	value	constrained	error	distance
110	bo.oak.20	2	0.02102	yes	-0.01005	0.01005
111	bo.oak.20	3	0.03483	yes	0.00289	0.00289
112	bo.oak.20	4	0.03954	yes	0.00759	0.00759
113	bo.oak.20	5	0.05201	yes	0.01734	0.01734
114	bo.oak.20	6	0.05609	yes	0.01870	0.01870
115	bo.oak.20	7	0.06017	yes	0.02005	0.02005
116	bo.oak.20	8	0.06087	yes	0.02005	0.02005
117	bo.oak.20	9	0.06228	yes	0.02076	0.02076



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.

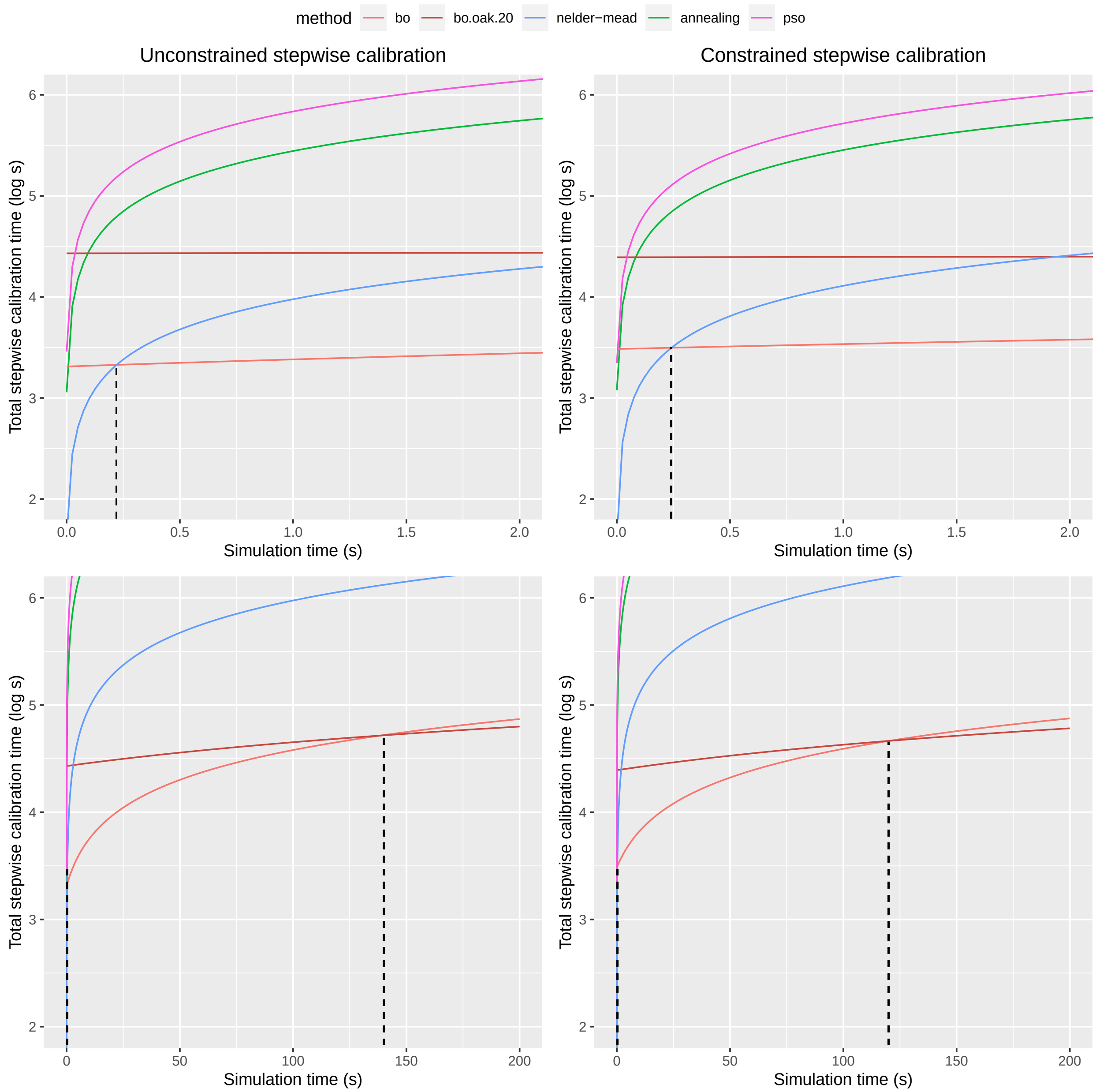
Number of iterations per age group



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

```
## [1] "annealing"
##
## Call:
## lm(formula = (total.time) ~ sim.time, data = df.model)
##
## Coefficients:
## (Intercept)     sim.time
##        1190       283113
##
## [1] "bo"
##
## Call:
## lm(formula = (total.time) ~ sim.time, data = df.model)
##
## Coefficients:
## (Intercept)     sim.time
##        3054          360
##
## [1] "bo.oak.20"
##
## Call:
## lm(formula = (total.time) ~ sim.time, data = df.model)
##
## Coefficients:
## (Intercept)     sim.time
##       24672          180
##
## [1] "nelder-mead"
##
## Call:
## lm(formula = (total.time) ~ sim.time, data = df.model)
##
## Coefficients:
## (Intercept)     sim.time
##       40.92     12847.00
##
## [1] "pso"
##
## Call:
## lm(formula = (total.time) ~ sim.time, data = df.model)
##
## Coefficients:
## (Intercept)     sim.time
##        2212       518656
```



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 with BO and a SE kernel (BO-SE)**.

Also, using a (non-optimized) implementation of **BO with orthogonal additive kernel (BO-OAK) we can improve BO-SE once the simulation time exceeds ~120 seconds**. The BO-OAK code has a lot of room for improvement, with a more efficient implementation this second critical time can be potentially improved. These results give us a criterion to choose the fastest optimization method while using stepwise calibration:

- $t_{sim} < 0.24$s: **Nelder-Mead**
- 0.24s $< t_{sim} < 120$s: **BO-SE**
- $t_{sim} > 120$s: **BO-OAK**

This proves that this method dramatically improves the efficiency of Bayesian Optimization, avoiding its major flaw (high dimensionality problems) by reducing the effective dimension of the calibration from one 99-parameter problem to nine 11-parameter problems.

The critical simulation time doesn't change significantly when considering an unconstrained calibration using BO-SE, but there are differences between constrained and unconstrained calibration times using BO-OAK. In any case the critical time for BO-OAK at this time is higher than the current models that we are working on, so BO-SE remains the best option for our most time-consuming models.