Grid search optimization results

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1 Grid search

The COBYLA algorithm, which we use for optimization of transition rate parameters $(\log(k_{0ij}), k_{1ij})$, is a local solver. This means that for any given set of initial values, the returned solution may only be locally optimal. In an effort to find the global optimum, we perform a grid search over different sets of initial values for $(\log(k_{0ij}), k_{1ij})$. The grid of values is comprised of pairwise combinations of equally spaced values $\log(k_{0ij}) = (-12, -10, -8, -6)$ and $k_{1ij} = (0.02, 0.04\overline{6}, 0.07\overline{3}, 0.10)$, for 16 possible sets of initial values. A given pair $(\log(k_0), k_1)$ is used as a set of initial values for all 12 transitions (24 parameters) in the optimization, i.e. the initial values for transitions $r_{12}, r_{16}, \ldots, r_{94}$ are all the same for some pair $(\log(k_0), k_1)$ from the grid.

Five pairs of initial values are *invalid*, meaning at least one of the constraints on the parameter space is violated at the initial values and the algorithm will not start. Additionally, for three sets of initial values that are *initially* valid, the algorithm ventures outside the constraint space within the first few iterations and does not return. We call these initial values invalid, and we ignore all invalid pairs of initial values. There are 8 valid pairs of initial values, which we let run to convergence.

We define convergence as a relative tolerance less than 0.005 for all parameters, where the relative tolerance between two values x and y is defined as

$$reltol(x, y) = |x - y| / \min(|x|, |y|). \tag{1}$$

For the algorithm to converge on iteration m, all 24 parameters k must have $reltol(k^{(m)}, k^{(m-1)}) < 0.005$.

2 Results

We ran each optimization to convergence. The minimum optimal value of the objective function was 0.335365, and the largest optimal value was 0.3571643. Each optimization converged within 12896 iterations.

2.1 Optimal parameters

The set of optimal parameters, corresponding to the optimization with the smallest optimal value of the objective function, is shown in Table 1.

Table 1: Optimal parameter values

	Lk0	k1
r12	-9.831	0.081
r16	-8.479	0.073
r18	-7.179	0.039
r23	-7.583	0.039
r29	-11.373	0.116
r34	-4.000	0.040
r63	-7.682	0.081
r67	-11.650	0.072
r74	-9.258	0.087
r87	-7.693	0.059
r89	-11.738	0.063
r94	-10.017	0.091

2.2 Transitions

The figures below show the transition probabilities for every transition $r_{ij}(a)$ for ages $a \in (50, \ldots, 95)$. Figure 1 has all y-axes fixed from 0 to 1, while Figure 1 has scales unique to each panel. The red line in each panel corresponds to transition probabilities for the optimal parameters in Table 1.

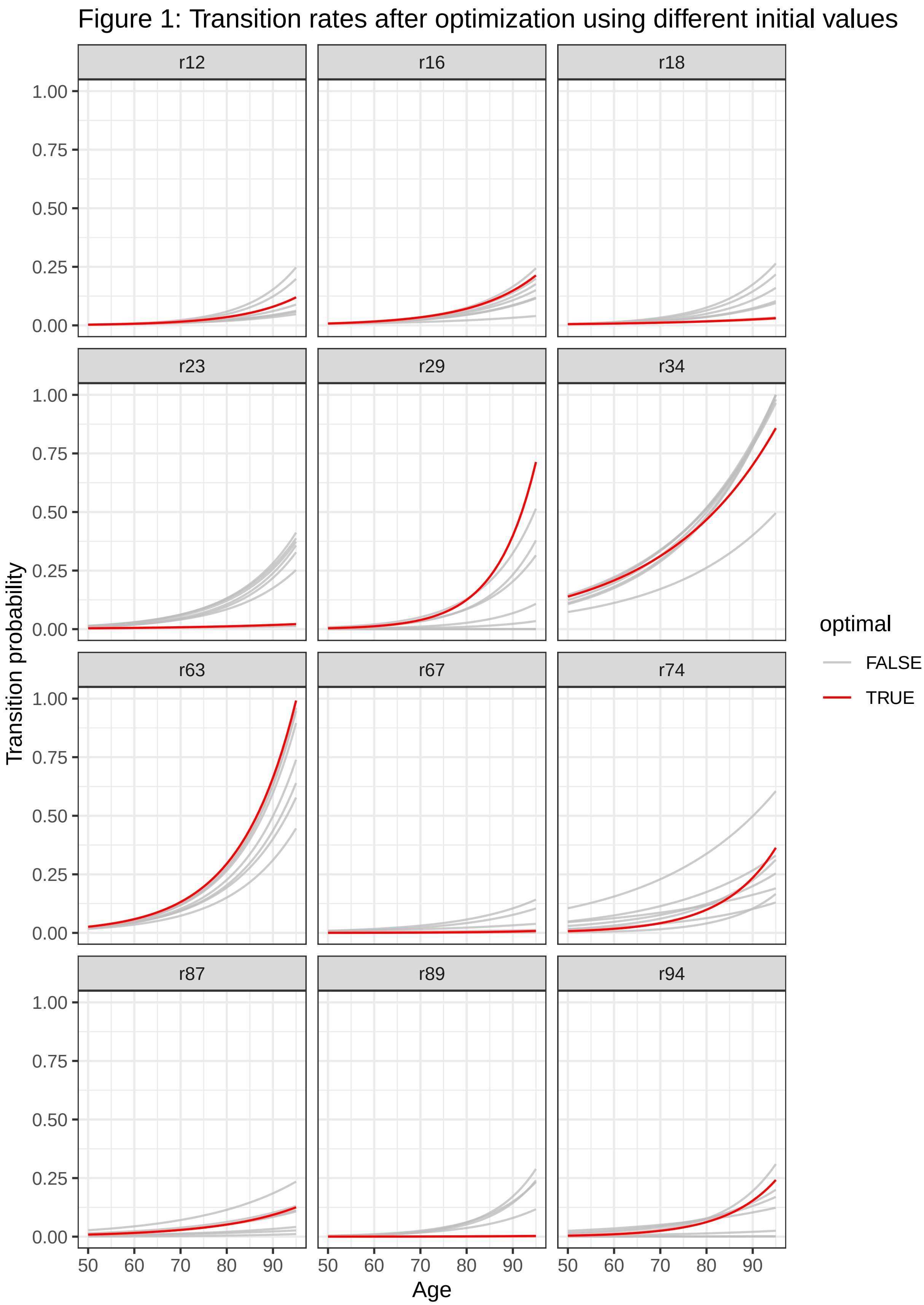
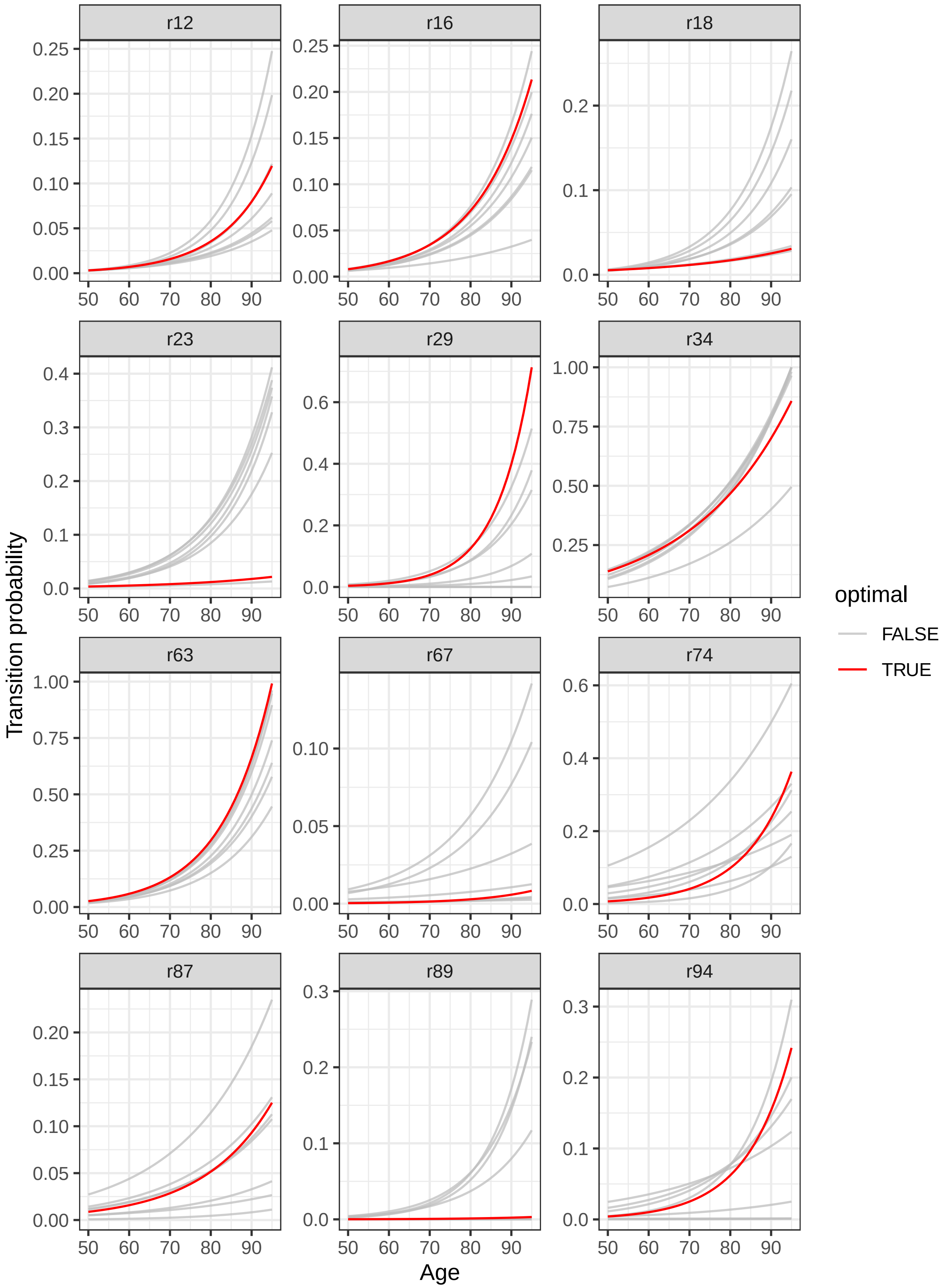


Figure 1: Transition rates after optimization using different initial values
r12
r16
r18
r23
r29
r34
r63
r67
r74
r87
r89
r94
1.00
0.75
0.50
0.25
0.00
Transition probability
50
60
70
80
90
Age
optimal
FALSE
TRUE

Figure 2: Transition rates after optimization using different initial values



2.3 Fit to Incidence and Prevalence data

Figures 3 and 4 below show the fit of optimized rates to the incidence data and prevalence data. In each plot, the dashed line represents the data from either the systematic review (for incidence) or Jack's 2017 paper (for prevalence), and the solid lines represent optimized estimates. The red line represents the most optimal solution.

Figure 3: Optimized and Empirical Incidence Rates

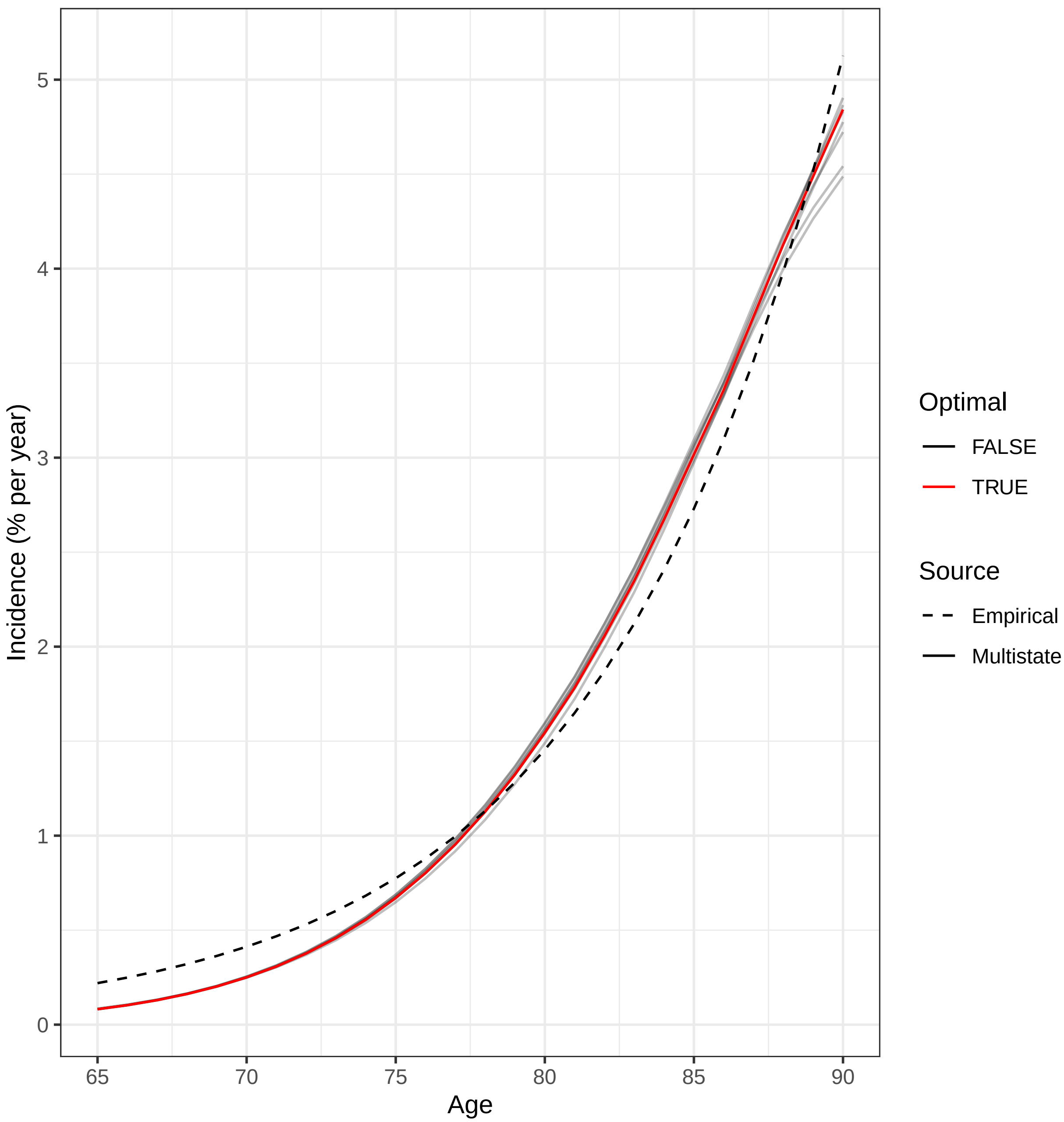
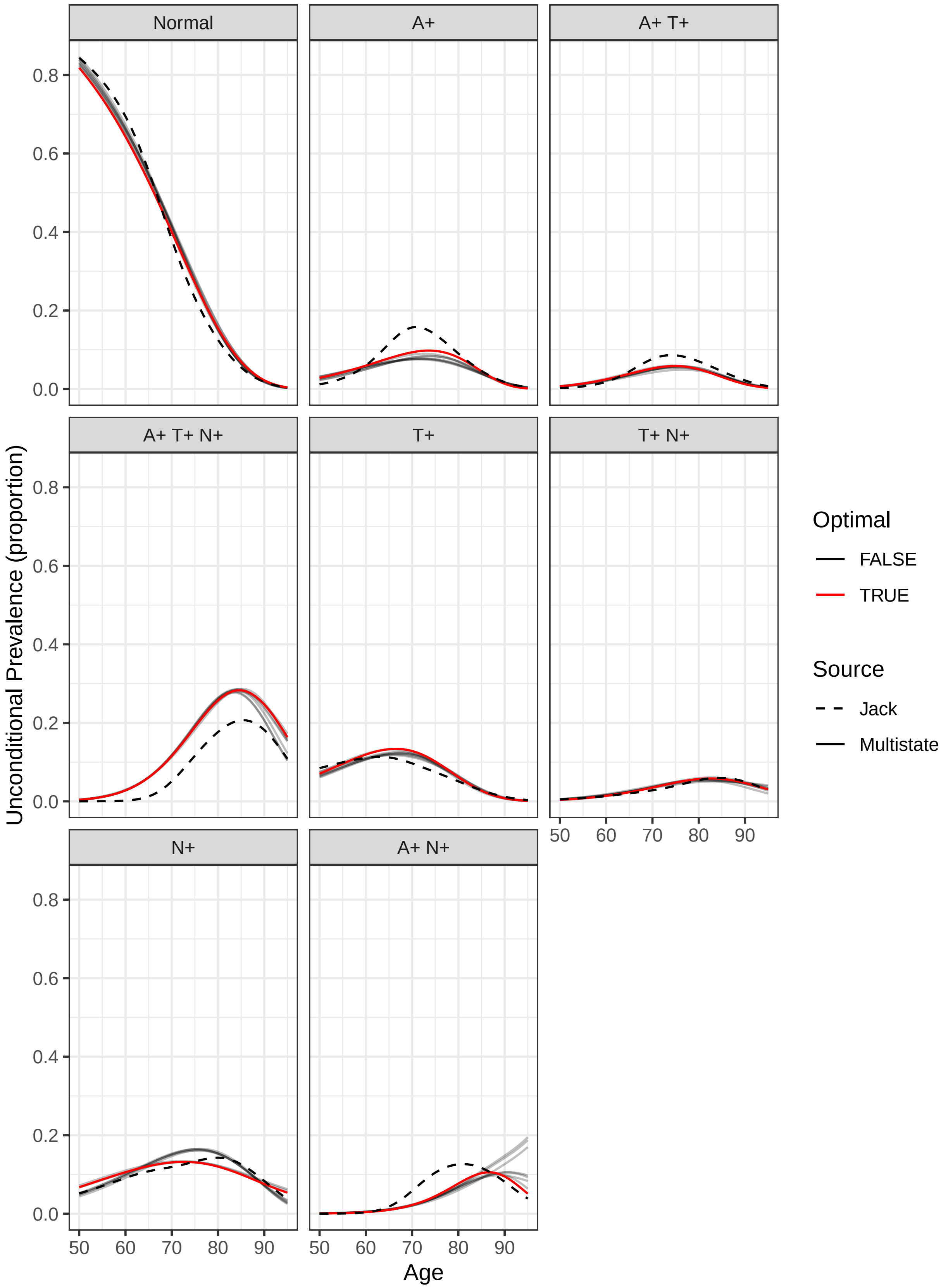


Figure 4: Optimized vs Jack unconditional prevalence rates



2.4 Lifetime risks

Tables 2 and 3 show the lifetime risks for ages $a \in (60, 65, \ldots, 90)$ for males and females using the transition parameters in Table 1.

Table 2: Lifetime risks for females

Age	Normal	A	A+T	A+T+N	A+T+N + MCI	T	T+N	N	A+N
60	18.18 %	16.98 %	54.41 %	58.4 %	95.63 %	42.34 %	32.15 %	13.34 %	24.81 %
65	16.85 %	15.95 %	51.54 %	56.21 %	93.57 %	39.92 %	30.71 %	12.15 %	23.75 %
70	15.01 %	14.58 %	47.4 %	52.82 %	90.06 %	36.38 %	28.47 %	10.63 %	22.08 %
75	12.62 %	12.78 %	41.69 %	47.89 %	84.71 %	31.54 %	25.27 %	8.77 %	19.64 %
80	9.76 %	10.51 %	34.1 %	40.91 %	76.19 %	25.22 %	20.91 %	6.68 %	16.3 %
85	6.84 %	7.96 %	24.88 %	31.79 %	63.81 %	17.89 %	15.64 %	4.65 %	12.29 %
90	4.77 %	5.92 %	15.94 %	21.73 %	46.77 %	11.51 %	10.79 %	3.2 %	8.65 %

Table 3: Lifetime risks for males

Age	Normal	A	A+T	A+T+N	A+T+N + MCI	T	T+N	N	A+N
60	12.25 %	11.39 %	44.94 %	49.4 %	92.93 %	32.67 %	23.89 %	8.71 %	17.87 %
65	11.3 %	10.67 %	42.37 %	47.5 %	90.37 %	30.69 %	22.85 %	7.91 %	17.15 %
70	9.94 %	9.66 %	38.49 %	44.28 %	85.99 %	27.65 %	21.07 %	6.83 %	15.87 %
75	8.17 %	8.34 %	33.2 %	39.61 %	79.54 %	23.51 %	18.47 %	5.52 %	13.96 %
80	6.08 %	6.67 %	26.33 %	33.05 %	69.91 %	18.22 %	14.93 %	4.05 %	11.33 %
85	4 %	4.84 %	18.43 %	24.88 %	56.66 %	12.33 %	10.76 %	2.67 %	8.22 %
90	2.6 %	3.39 %	10.98 %	16.17 %	40.19 %	7.32 %	6.95 %	1.71 %	5.42 %