Sensitivity analysis for optimization results

Contents

1 Grid search recap

We performed a grid search over initial values of transition rate parameters $\boldsymbol{k}$ in an effort to find the global optimum of the objective function

$$f(\boldsymbol{k}) = \frac{1}{n_1} \sum_{a=65}^{90} \Big(\log(\widehat{I}(\boldsymbol{k}, a)) - \log(I(a)) \Big)^2 + \frac{1}{n_2} \sum_{i \in I} \sum_{a=50}^{95} \Big(\log(\widehat{Pu}_i(\boldsymbol{k}, a)) - \log(Pu_i(a)) \Big)^2. \tag{1}$$

The initial values used to obtain the "optimal optimum" were (-12, 0.02) for $(\log(k_0), k1)$.

2 Sensitivity analysis

We now perform a sensitivity analysis where we use "low" and "high" values for prevalence and incidence targets $Pu_i(a)$ and $I(a)$. Low (high) prevalence targets are calculated by first calculating the probability C(a) of being preclinical (in states 1-8) for low (high) values of the transition $\widetilde{r}_{45}(a)$, the probability of transitioning from state 4 (AN) to state 5 (AN + MCI) in the AN model. Transitions $\widetilde{r}_{45}(a)$ are multiplied by 0.66 for a low transition rate and by 1.65 for a high transition rate. The probability of being preclinical will be larger (smaller) in the low (high) sensitivity analysis, as the probability of transitioning to MCI is smaller (larger).

We multiply incidence rates I(a) by 0.5 for the low sensitivity analysis and by 1.5 for the high sensitivity analysis.

We also assume the transition rates $r_{45}(a)$ (ATN to ATN + MCI) and $r_{5,10}$ (ATN + MCI to AD Dementia) are lower and higher for the low and high sensitivity analyses. For the low analysis we multiply r_{45} by 0.66 and say $r_{5,10} = 0.26$, and for the high analysis we multiply r_{45} by 1.65 and say $r_{5,10} = 0.34$.

3 Results

3.1 Lifetime risks

Lifetime risks for females. Values in parentheses are from the low and high sensitivity analyses, while the values outside parentheses are from the main analysis.

Table 1: Lifetime risks of AD dementia for females

Age	Normal	A	A+T
60	13.37 % (8.12 %, 28.68 %)	14.12 % (6.92 %, 30.98 %)	42.44 % (32.26 %, 75 %)
65	12.26 % (7.37 %, 26.76 %)	13.21 % (6.38 %, 30.12 %)	39.85 % (30.07 %, 71.9 %)
70	10.77 % (6.4 %, 24.1 %)	11.89 % (5.65 %, 28.55 %)	36.19 % (27.05 %, 67.27 %)
75	8.91 % (5.21 %, 20.63 %)	10.12 % (4.72 %, 26.01 %)	31.3 % (23.09 %, 60.62 %)
80	6.77 % (3.89 %, 16.3 %)	7.95 % (3.64 %, 22.18 %)	25.05 % (18.18 %, 51.26 %)
85	4.68 % (2.66 %, 11.61 %)	5.67 % (2.56 %, 17.12 %)	17.86 % (12.75 %, 38.88 %)
90	3.25 % (1.83 %, 8.05 %)	3.93 % (1.78 %, 12.24 %)	11.38 % (8.11 %, 25.15 %)

Table 2: Lifetime risks of AD dementia for females

Age	A+T+N	A+T+N + MCI	T
60	45.91 % (35.56 %, 80.35 %)	94.75 % (94.75 %, 96.26 %)	32.39 % (23.75 %, 59.11 %)
65	43.86 % (33.88 %, 78.25 %)	92.29 % (92.29 %, 94.5 %)	30.3 % (22.01 %, 56.42 %)
70	40.77 % (31.37 %, 74.82 %)	88.2 % (88.2 %, 91.44 %)	27.31 % (19.6 %, 52.34 %)
75	36.4 % (27.87 %, 69.58 %)	82.09 % (82.09 %, 86.71 %)	23.33 % (16.48 %, 46.48 %)
80	30.46 % (23.17 %, 61.59 %)	72.75 % (72.75 %, 78.94 %)	18.32 % (12.7 %, 38.37 %)
85	23.1 % (17.48 %, 50.18 %)	59.74 % (59.74 %, 67.24 %)	12.78 % (8.72 %, 28.08 %)
90	15.58 % (11.83 %, 35.47 %)	42.83 % (42.83 %, 50.27 %)	8.26 % (5.66 %, 17.87 %)

Table 3: Lifetime risks of AD dementia for females

Age	T+N	N	A+N
60	31.68 % (17.88 %, 67.79 %)	12.69 % (5.41 %, 36.82 %)	19.87 % (11.2 %, 47.55 %)
65	29.19 % (16.23 %, 64.57 %)	11.17 % (4.59 %, 33.95 %)	18.39 % (10.17 %, 45.81 %)
70	25.89 % (14.13 %, 59.91 %)	9.35 % (3.68 %, 30.12 %)	16.38 % (8.86 %, 43.03 %)
75	21.75 % (11.61 %, 53.43 %)	7.31 % (2.75 %, 25.29 %)	13.83 % (7.28 %, 38.93 %)
80	16.82 % (8.77 %, 44.59 %)	5.22 % (1.87 %, 19.48 %)	10.79 % (5.52 %, 33.06 %)
85	11.65 % (5.98 %, 33.35 %)	3.38 % (1.16 %, 13.34 %)	7.62 % (3.79 %, 25.39 %)
90	7.49 % (3.87 %, 21.6 %)	2.18 % (0.72 %, 8.55 %)	5.09 % (2.5 %, 17.39 %)

Lifetime risks for males.

Table 4: Lifetime risks of AD dementia for males

Age	Normal	A	A+T
60	8.75 % (5.16 %, 20.32 %)	9.47 % (4.41 %, 22.13 %)	33.97 % (25.15 %, 66.02 %)
65	7.99 % (4.66 %, 18.88 %)	8.84 % (4.06 %, 21.62 %)	31.75 % (23.33 %, 62.94 %)
70	6.92 % (3.97 %, 16.8 %)	7.89 % (3.55 %, 20.47 %)	28.47 % (20.71 %, 58.1 %)
75	5.59 % (3.15 %, 14.09 %)	6.6 % (2.91 %, 18.51 %)	24.14 % (17.33 %, 51.31 %)
80	4.08 % (2.25 %, 10.77 %)	5.02 % (2.16 %, 15.5 %)	18.73 % (13.21 %, 42.01 %)
85	2.64 % (1.43 %, 7.26 %)	3.39 % (1.44 %, 11.57 %)	12.79 % (8.84 %, 30.59 %)
90	1.71 % (0.92 %, 4.69 %)	2.19 % (0.94 %, 7.79 %)	7.56 % (5.2 %, 18.52 %)

Table 5: Lifetime risks of AD dementia for males

Age	A+T+N	A+T+N + MCI	T
60	37.66 % (28.51 %, 72.72 %)	91.66 % (91.66 %, 93.88 %)	24.23 % (17.26 %, 48.27 %)
65	35.94 % (27.15 %, 70.69 %)	88.63 % (88.63 %, 91.65 %)	22.59 % (15.92 %, 45.93 %)
70	33.14 % (24.95 %, 67 %)	83.63 % (83.63 %, 87.78 %)	20.12 % (14 %, 42.11 %)
75	29.18 % (21.87 %, 61.43 %)	76.46 % (76.46 %, 81.96 %)	16.85 % (11.52 %, 36.68 %)
80	23.85 % (17.77 %, 53.08 %)	66.13 % (66.13 %, 73.01 %)	12.81 % (8.56 %, 29.35 %)
85	17.51 % (12.97 %, 41.84 %)	52.56 % (52.56 %, 60.21 %)	8.51 % (5.57 %, 20.59 %)
90	11.19 % (8.3 %, 28.36 %)	36.49 % (36.49 %, 43.56 %)	5.07 % (3.32 %, 12.12 %)

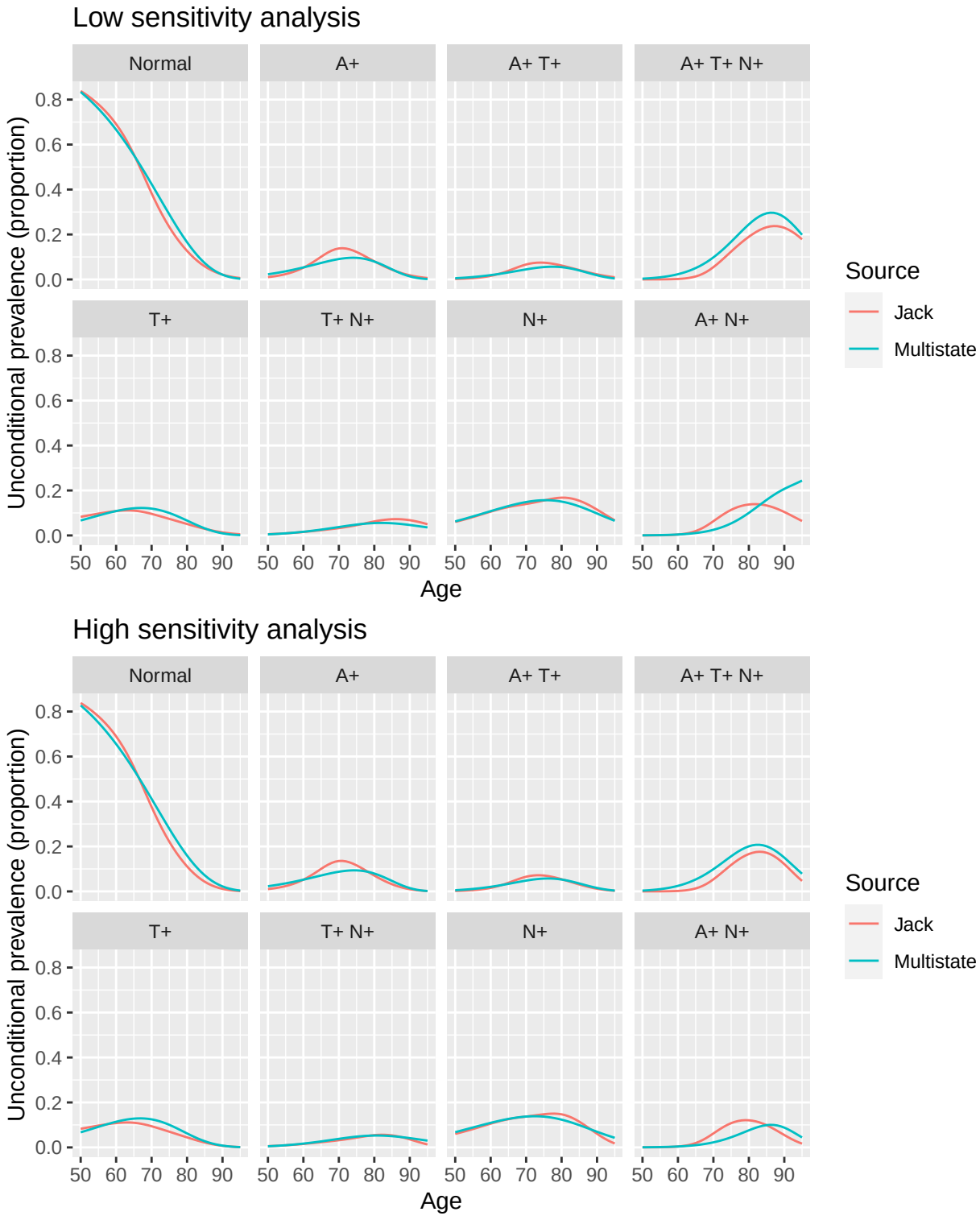
Table 6: Lifetime risks of AD dementia for males

Age	T+N	N	A+N
60	23.95 % (12.8 %, 57.89 %)	8.46 % (3.41 %, 27.79 %)	14.21 % (7.75 %, 37.67 %)
65	21.95 % (11.56 %, 54.86 %)	7.38 % (2.86 %, 25.46 %)	13.12 % (7.01 %, 36.33 %)
70	19.21 % (9.93 %, 50.25 %)	6.06 % (2.24 %, 22.26 %)	11.56 % (6.03 %, 33.93 %)
75	15.81 % (7.99 %, 43.94 %)	4.6 % (1.62 %, 18.25 %)	9.6 % (4.86 %, 30.32 %)
80	11.84 % (5.83 %, 35.56 %)	3.13 % (1.04 %, 13.57 %)	7.27 % (3.56 %, 25.17 %)
85	7.82 % (3.77 %, 25.57 %)	1.89 % (0.6 %, 8.8 %)	4.89 % (2.33 %, 18.71 %)
90	4.65 % (2.26 %, 15.48 %)	1.13 % (0.35 %, 5.19 %)	3.04 % (1.42 %, 12.04 %)

There are some strange values in here. The low sensitivity analysis gives lifetime risks for state 2 (A) that are lower than state 1 (normal). The same goes for state 8 (N) and state 1. Values from the high sensitivity analysis look reasonable.

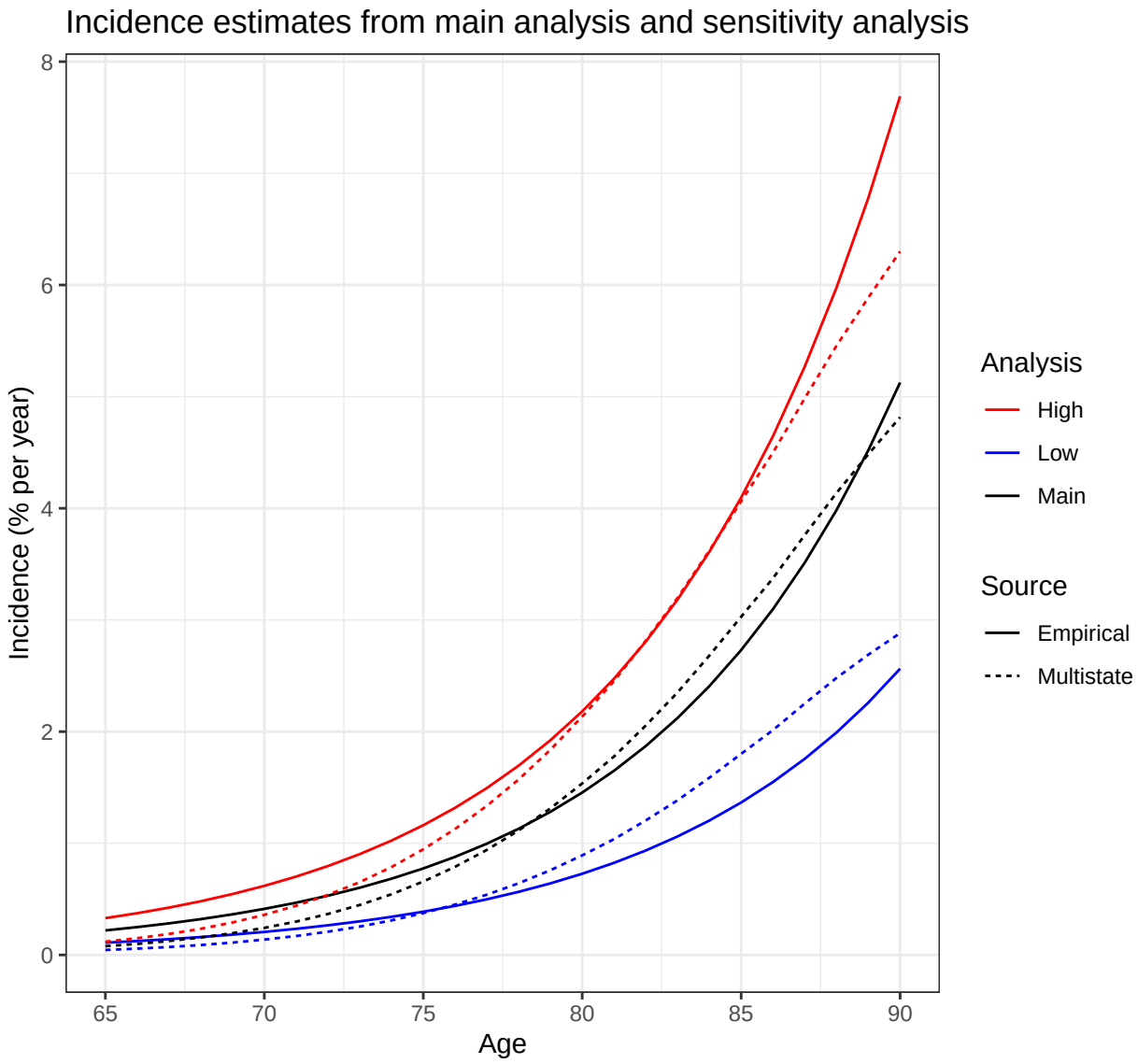
3.2 Prevalence

Multistate model estimates of low and high prevalence targets.



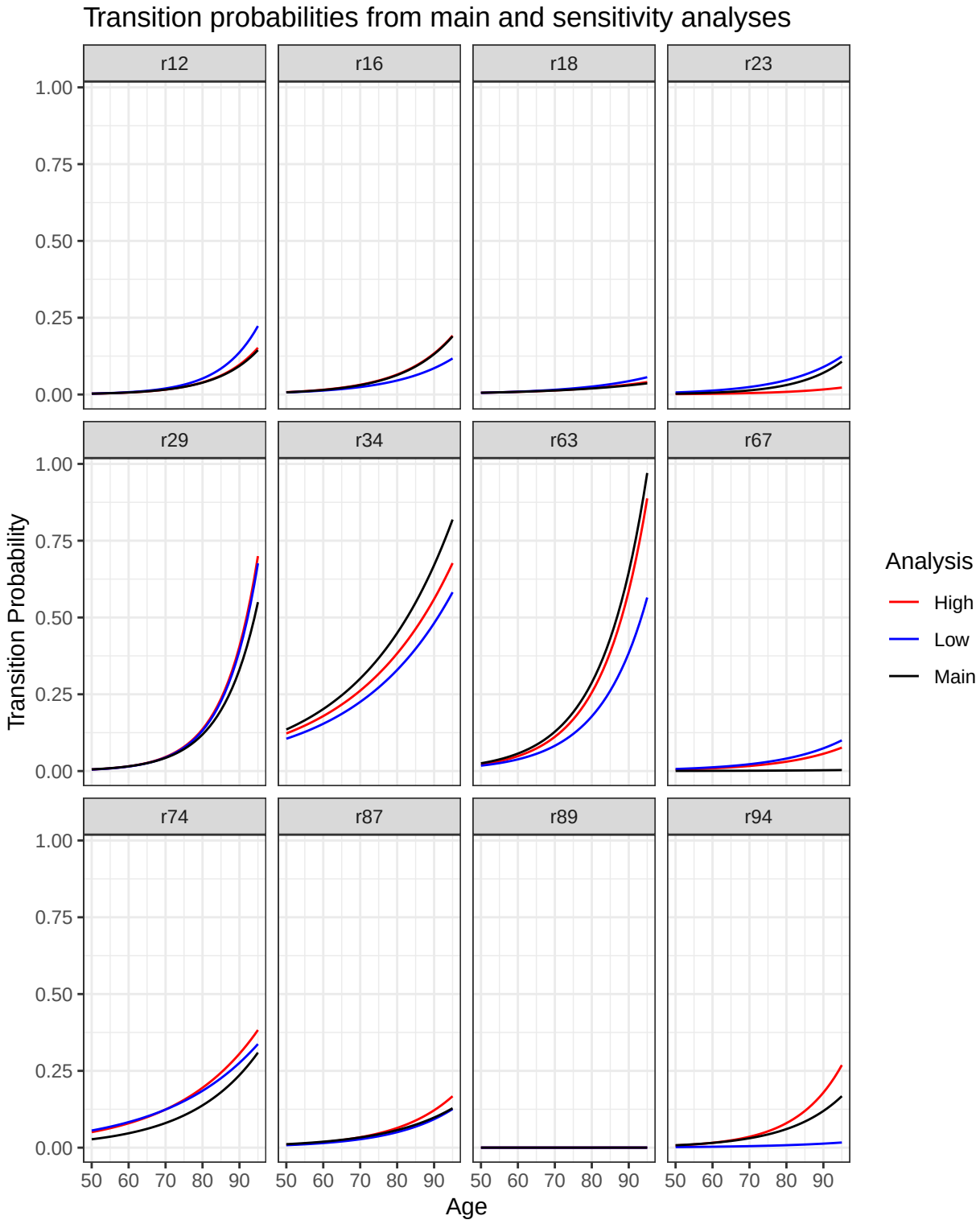
3.3 Incidence

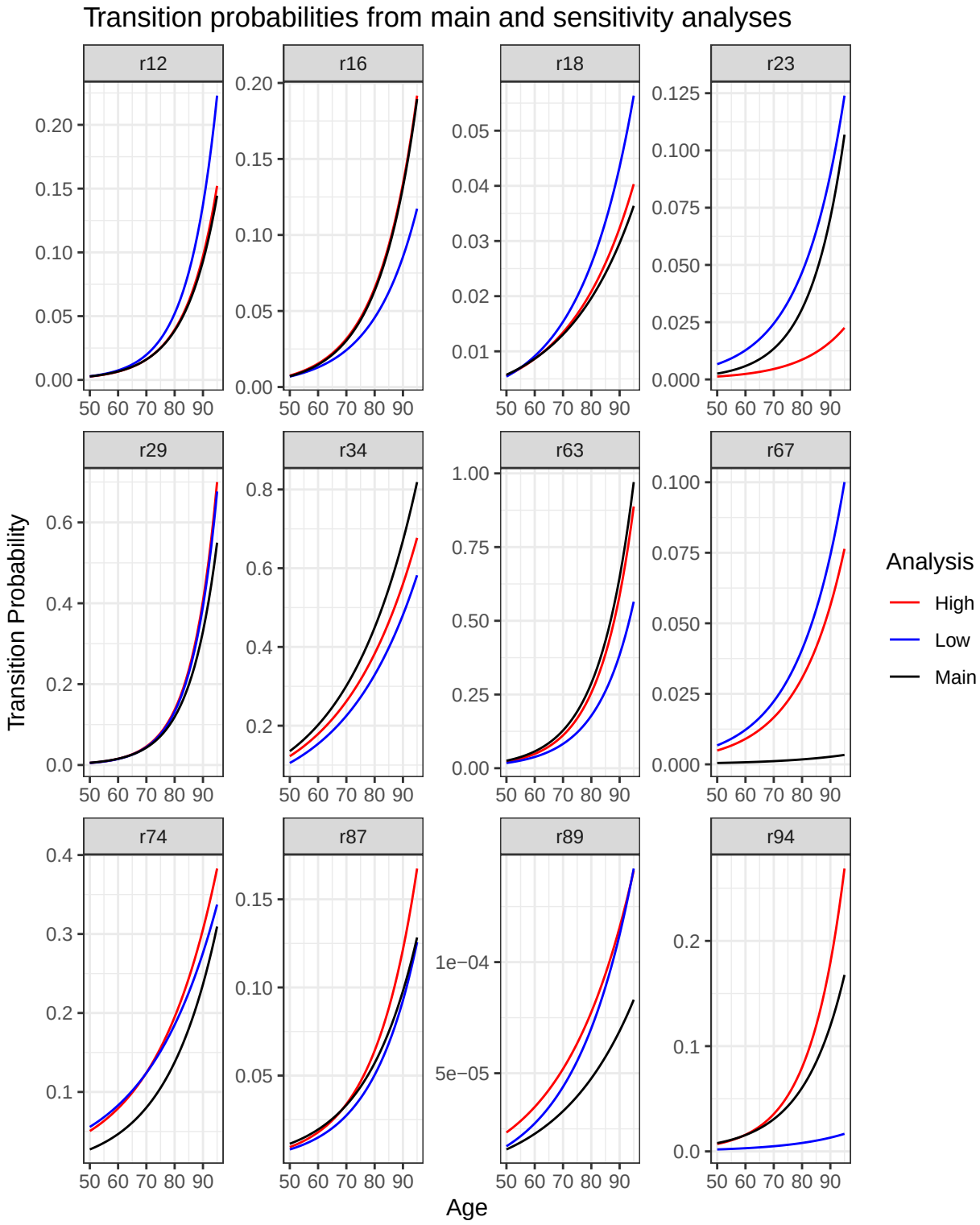
Multistate estimates of low and high incidence targets.



3.4 Transitions

Preclinical transition probabilities from each analysis. Second plot has free y-axes instead of all being fixed on (0, 1). It's interesting that the low and high sensitivity analyses don't consistently yield lower or higher transition probabilities.


Transition probabilities from main and sensitivity analyses
r12
r16
r18
r23
r29
r34
r63
r67
r74
r87
r89
r94
Transition Probability
1.00
0.75
0.50
0.25
0.00
50
60
70
80
90
Age
Analysis
High
Low
Main


Transition probabilities from main and sensitivity analyses
r12
r16
r18
r23
r29
r34
r63
r67
r74
r87
r89
r94
Transition Probability
Age
Analysis
High
Low
Main