

Supplemental material to “Sample size allocation to regions in multiregional dose-finding study using MCP-Mod”

1 Probability of consistency by true dose-response model

Figure A1 shows the probability of consistency by true dose-response model: local consistency, simultaneous consistency and consistency in maximum absolute difference.

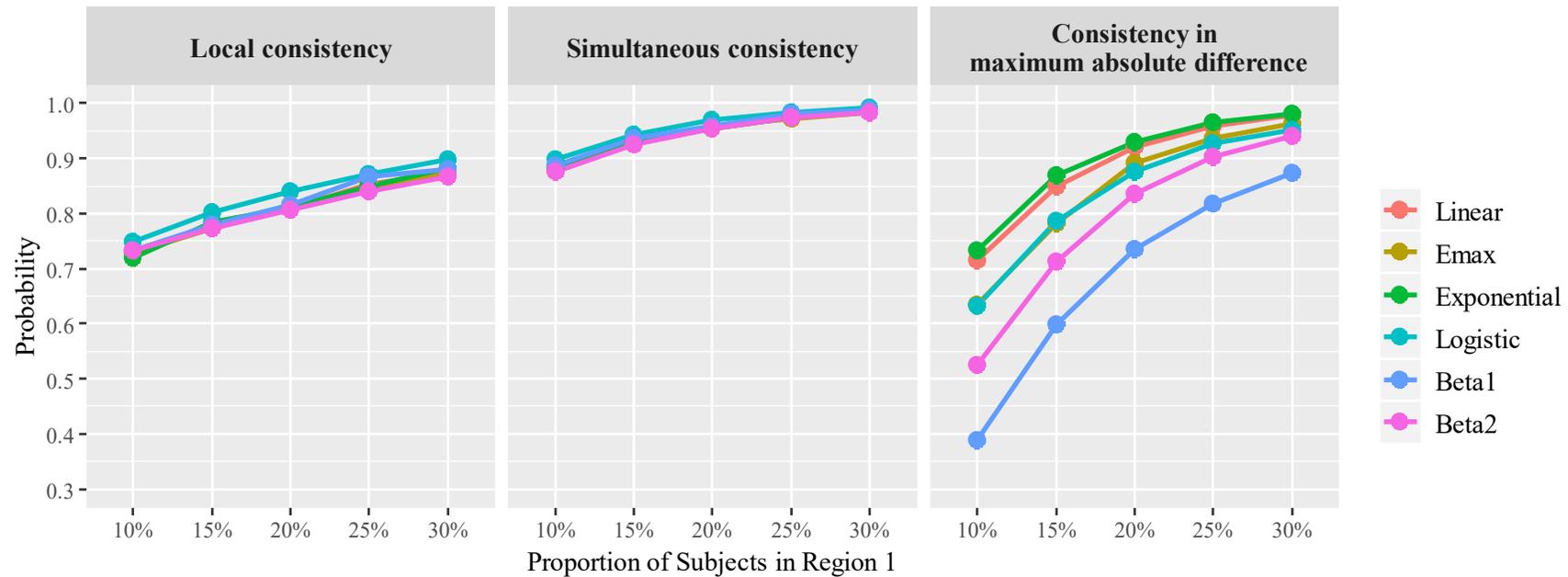


Figure A1. Probability of consistency with the mean summary function: Local consistency in contrast statistics with $\pi = 0.5$ (left panel), Simultaneous consistency in contrast statistics (central panel), and Consistency in maximum absolute difference for $\delta = 0.4$ (right panel).

2 Summary measures of dose-response curve by true dose-response model

Figure A2 shows heat maps of proportions of MED categories for the entire population and Region 1 by true dose-response models. Figure A3.1- A3.6 show the heat maps of proportions of MED cross-categories for the entire population and Region 1 by true dose-response models. Figure A4 shows the probability that the MED of Region 1 was the same, higher or lower as that for the entire population by true dose-response models.

| Minimum Effective Dose (mg) | Linear | | | | | | Emax | | | | | | Exponential | | | | | |
|-----------------------------|----------|------|------|------|------|--------|-------|------|------|------|------|--------|-------------|------|------|------|------|--------|
| | 10% | 15% | 20% | 25% | 30% | Entire | 10% | 15% | 20% | 25% | 30% | Entire | 10% | 15% | 20% | 25% | 30% | Entire |
| <=10 | 8.8 | 8 | 7.1 | 7.4 | 6.9 | 3.7 | 33.2 | 33.4 | 34.2 | 34.3 | 34.3 | 31.5 | 3.5 | 3.5 | 3.3 | 3.2 | 3.3 | 1.4 |
| >10 to <=25 | 6 | 5.4 | 4.3 | 4.9 | 4.9 | 8.4 | 11.8 | 12.3 | 12.3 | 13.7 | 14.6 | 28.5 | 2.8 | 2.2 | 2.3 | 1.7 | 2 | 3.4 |
| >25 to <=50 | 22.1 | 21.2 | 19.8 | 19.4 | 18.7 | 14.1 | 15.1 | 16.1 | 16.9 | 16.4 | 16.5 | 18.2 | 19.7 | 16.5 | 15.7 | 14.1 | 13.4 | 6.9 |
| >50 to <=100 | 23.6 | 27.6 | 32.3 | 35.4 | 37.7 | 55.4 | 12.3 | 14 | 15.9 | 16.7 | 17.9 | 18.6 | 26.2 | 32.1 | 33.4 | 37.4 | 39.1 | 51.4 |
| >100 to <=150 | 18.2 | 19.2 | 21.1 | 20.8 | 21.5 | 18.3 | 5 | 5.3 | 5.4 | 5.2 | 5.7 | 2.6 | 25.5 | 29.1 | 30.2 | 31.9 | 33.1 | 36.8 |
| >150 | 21.3 | 18.6 | 15.4 | 12.1 | 10.4 | 0.1 | 22.2 | 18.6 | 15.2 | 13.6 | 11 | 0.6 | 22.4 | 16.6 | 15.1 | 11.6 | 9.1 | 0 |
| Minimum Effective Dose (mg) | Logistic | | | | | | Beta1 | | | | | | Beta2 | | | | | |
| | 10% | 15% | 20% | 25% | 30% | Entire | 10% | 15% | 20% | 25% | 30% | Entire | 10% | 15% | 20% | 25% | 30% | Entire |
| <=10 | 10.9 | 10.3 | 9.7 | 8.5 | 8 | 1.8 | 17 | 19.8 | 18.8 | 20.4 | 19.5 | 14.4 | 22.3 | 21.3 | 21.7 | 20.5 | 19.7 | 10.1 |
| >10 to <=25 | 8.1 | 8.6 | 8.4 | 8.7 | 9.1 | 9.1 | 1.9 | 1.4 | 1.1 | 1 | 1 | 0.1 | 10.3 | 11.5 | 12 | 13.2 | 14.4 | 22 |
| >25 to <=50 | 25.4 | 26.1 | 26.4 | 27.6 | 27.4 | 33.2 | 1.8 | 1.3 | 0.8 | 0.3 | 0.3 | 0 | 16.6 | 17.4 | 17.6 | 18.6 | 19.5 | 36.4 |
| >50 to <=100 | 23 | 27.5 | 30.8 | 33.5 | 36 | 52.8 | 1.6 | 1.1 | 0.9 | 0.5 | 0.2 | 0 | 14 | 17.4 | 19.3 | 20.3 | 21.2 | 27.3 |
| >100 to <=150 | 9 | 9.2 | 9.3 | 8.8 | 8.6 | 2.7 | 1.4 | 0.8 | 0.4 | 0.3 | 0.2 | 0 | 4.2 | 4.2 | 4.1 | 3.5 | 3.7 | 0.4 |
| >150 | 23.2 | 18.3 | 15.4 | 12.9 | 11 | 0.3 | 70.7 | 70.7 | 74.1 | 74.5 | 76.4 | 85.4 | 31.6 | 27.8 | 25 | 23.8 | 21.3 | 3.7 |

Figure A2. Proportion in MED categories (%) for entire population and Region 1, by true dose-response model.

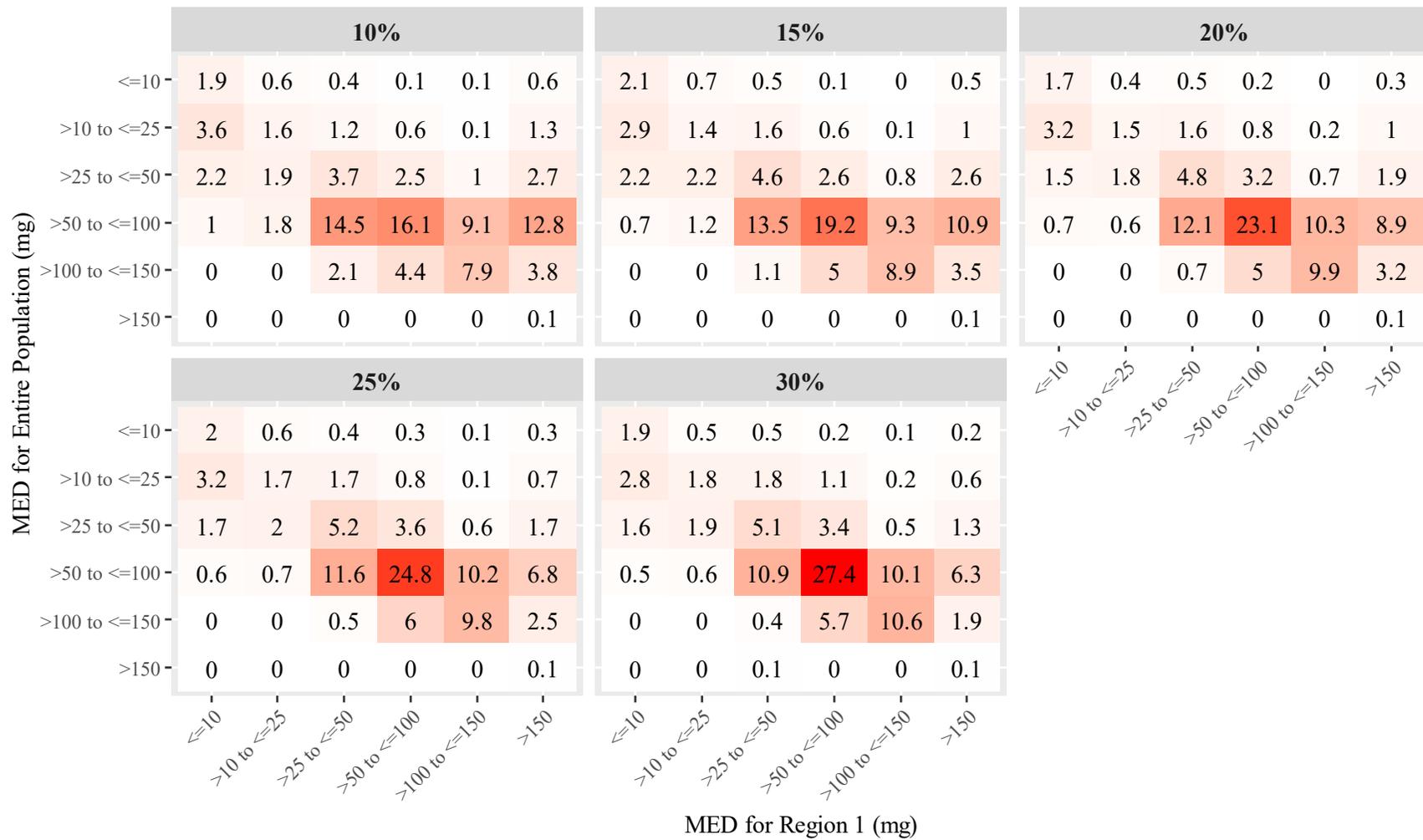


Figure A3.1. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Linear.

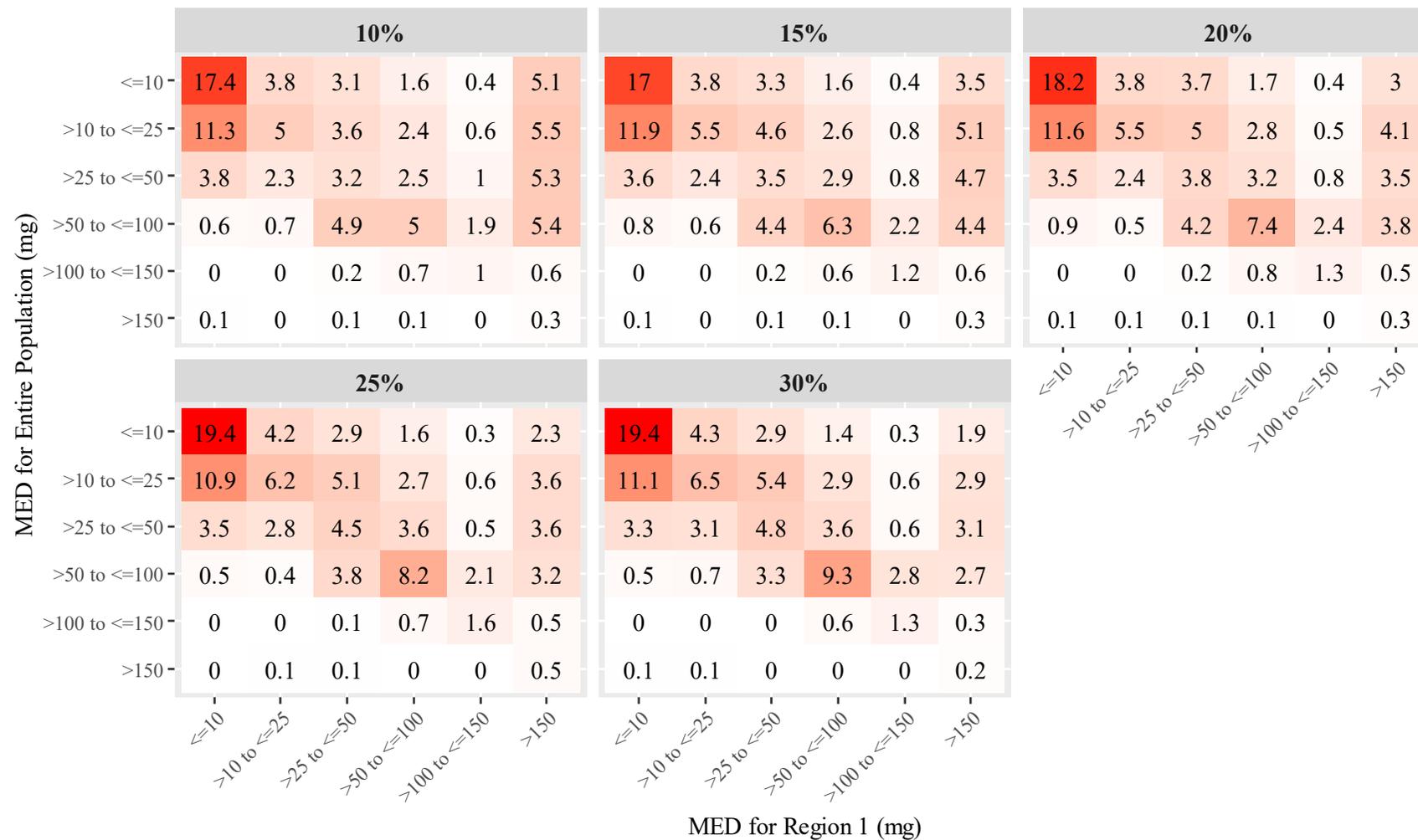


Figure A3.2. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Emax.

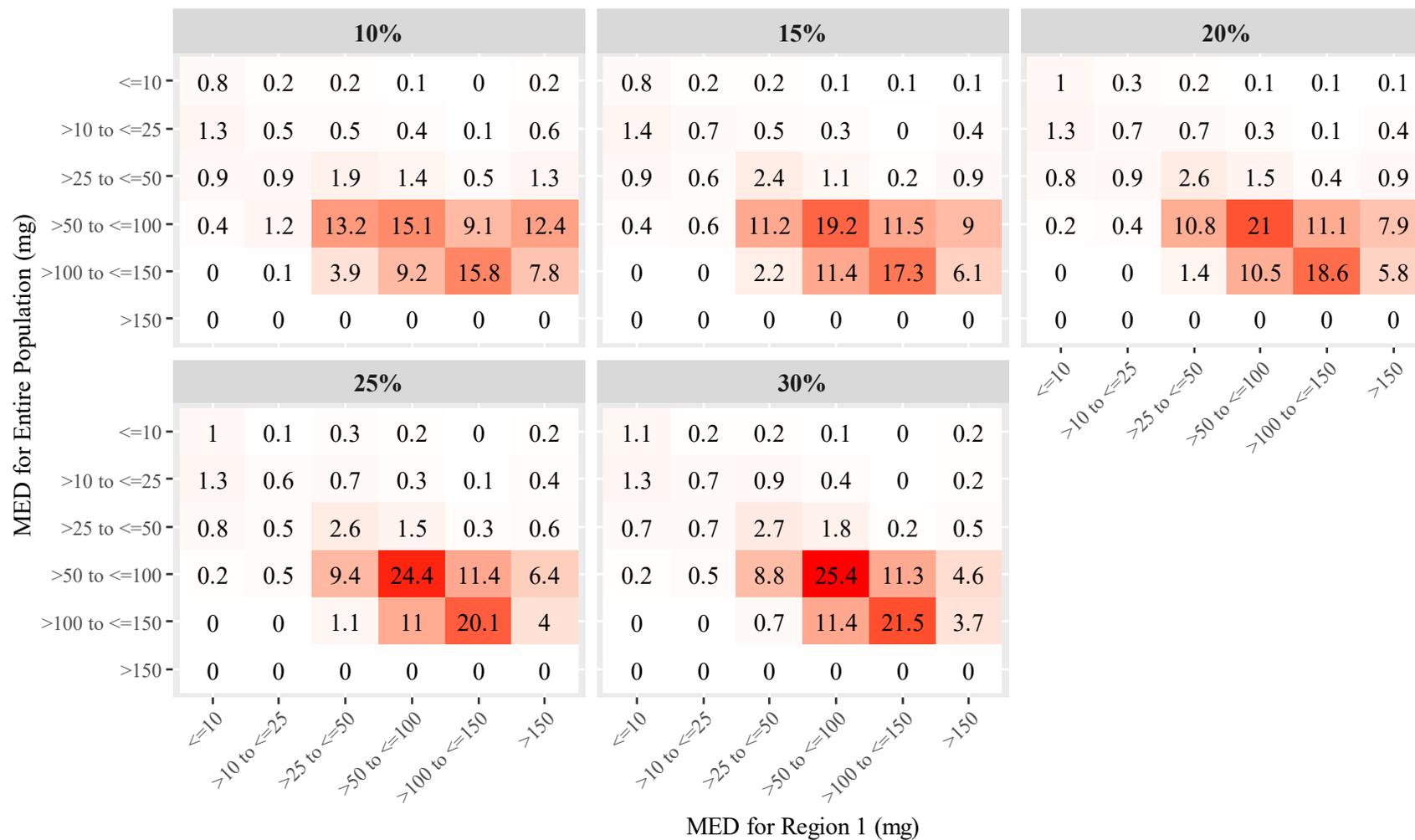


Figure A3.3. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Exponential.

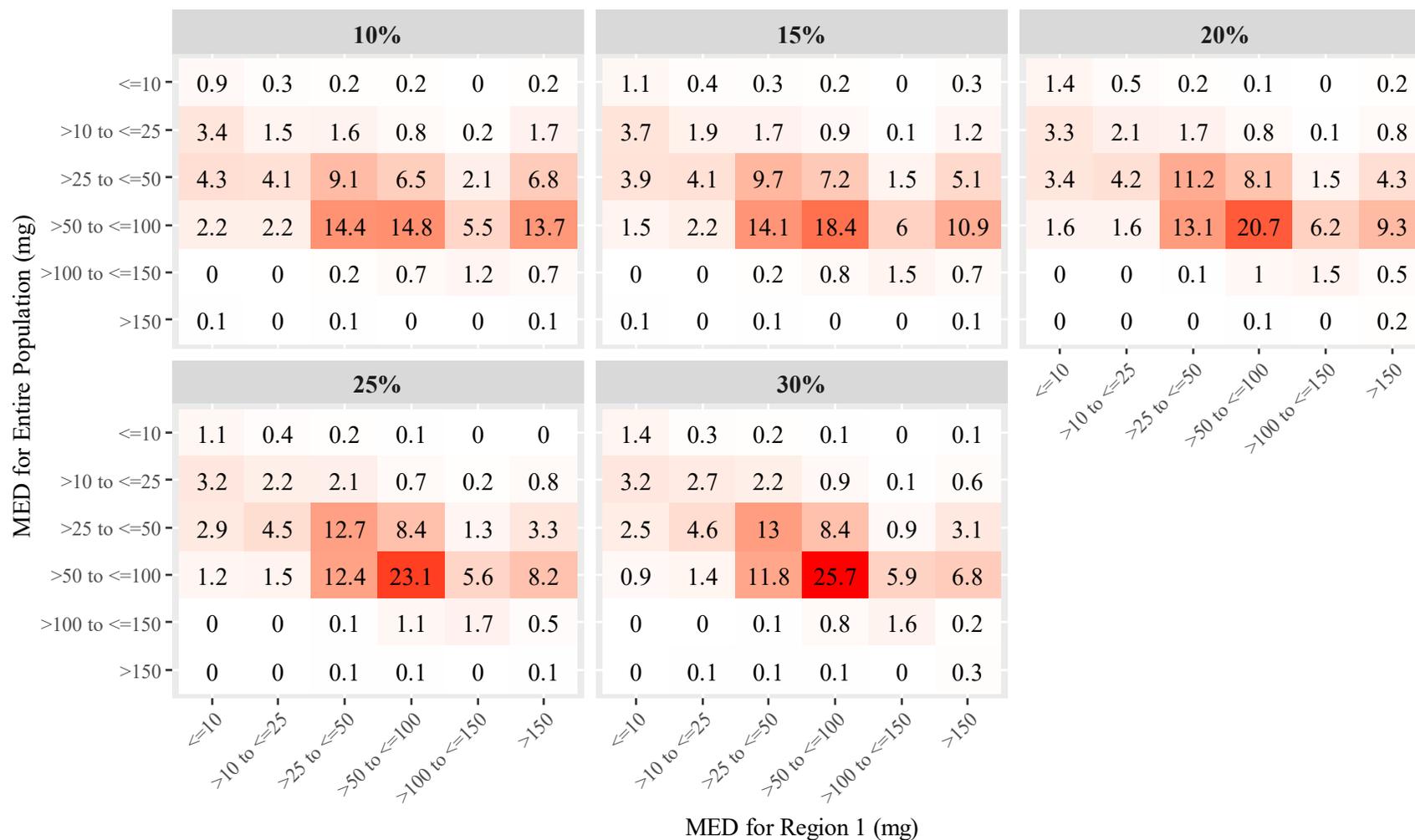


Figure A3.4. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Logistic.

| MED for Entire Population (mg) | 10% | | | | | | 15% | | | | | | 20% | | | | | | |
|--------------------------------|------|------------|------------|-------------|--------------|------|------|------------|------------|-------------|--------------|------|------|------------|------------|-------------|--------------|------|--|
| | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | |
| ≤10 | 3.6 | 0.5 | 0.4 | 0.3 | 0.3 | 8.1 | 5.1 | 0.4 | 0.3 | 0.3 | 0.2 | 7 | 5.6 | 0.3 | 0.3 | 0.3 | 0.2 | 6.5 | |
| >10 to ≤25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| >25 to ≤50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| >50 to ≤100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| >100 to ≤150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| >150 | 13.4 | 1.4 | 1.4 | 1.3 | 1.1 | 62.5 | 14.6 | 1 | 1 | 0.8 | 0.7 | 63.6 | 13.2 | 0.8 | 0.5 | 0.5 | 0.3 | 67.6 | |
| | | | | | | | | | | | | | | | | | | | |
| MED for Entire Population (mg) | 25% | | | | | | 30% | | | | | | | | | | | | |
| | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | ≤10 | >10 to ≤25 | >25 to ≤50 | >50 to ≤100 | >100 to ≤150 | >150 | |
| ≤10 | 6.8 | 0.3 | 0.1 | 0.2 | 0.1 | 6.1 | 6.3 | 0.4 | 0.1 | 0.1 | 0.1 | 7.2 | | | | | | | |
| >10 to ≤25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | | | | |
| >25 to ≤50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | | | | |
| >50 to ≤100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | | | | |
| >100 to ≤150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | | | | |
| >150 | 13.5 | 0.8 | 0.2 | 0.2 | 0.2 | 68.3 | 13.1 | 0.6 | 0.2 | 0.1 | 0.1 | 69.2 | | | | | | | |

Figure A3.5. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Beta1.

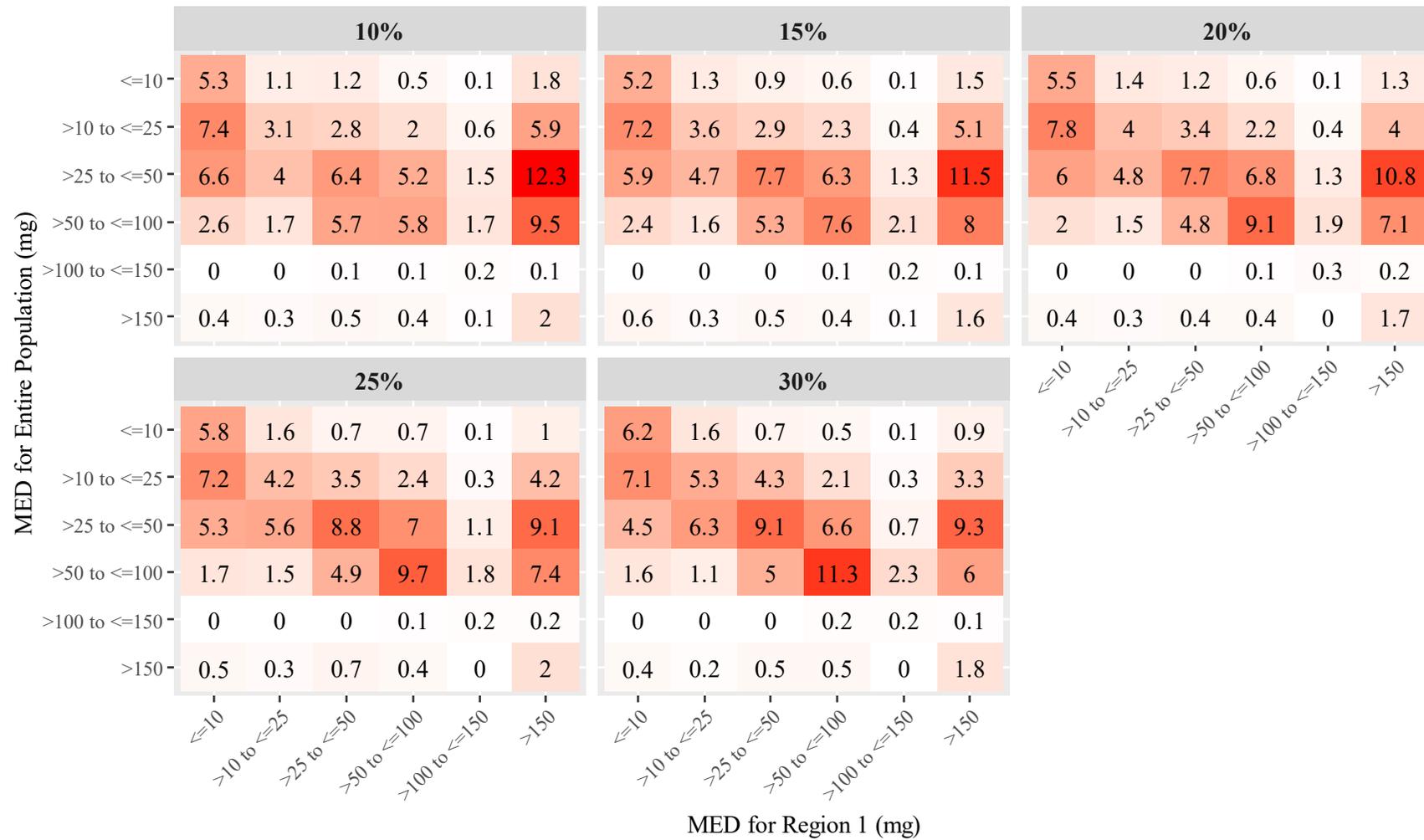


Figure A3.6. Proportion in MED cross-categories (%) for entire population and Region 1: true dose-response model = Beta2.

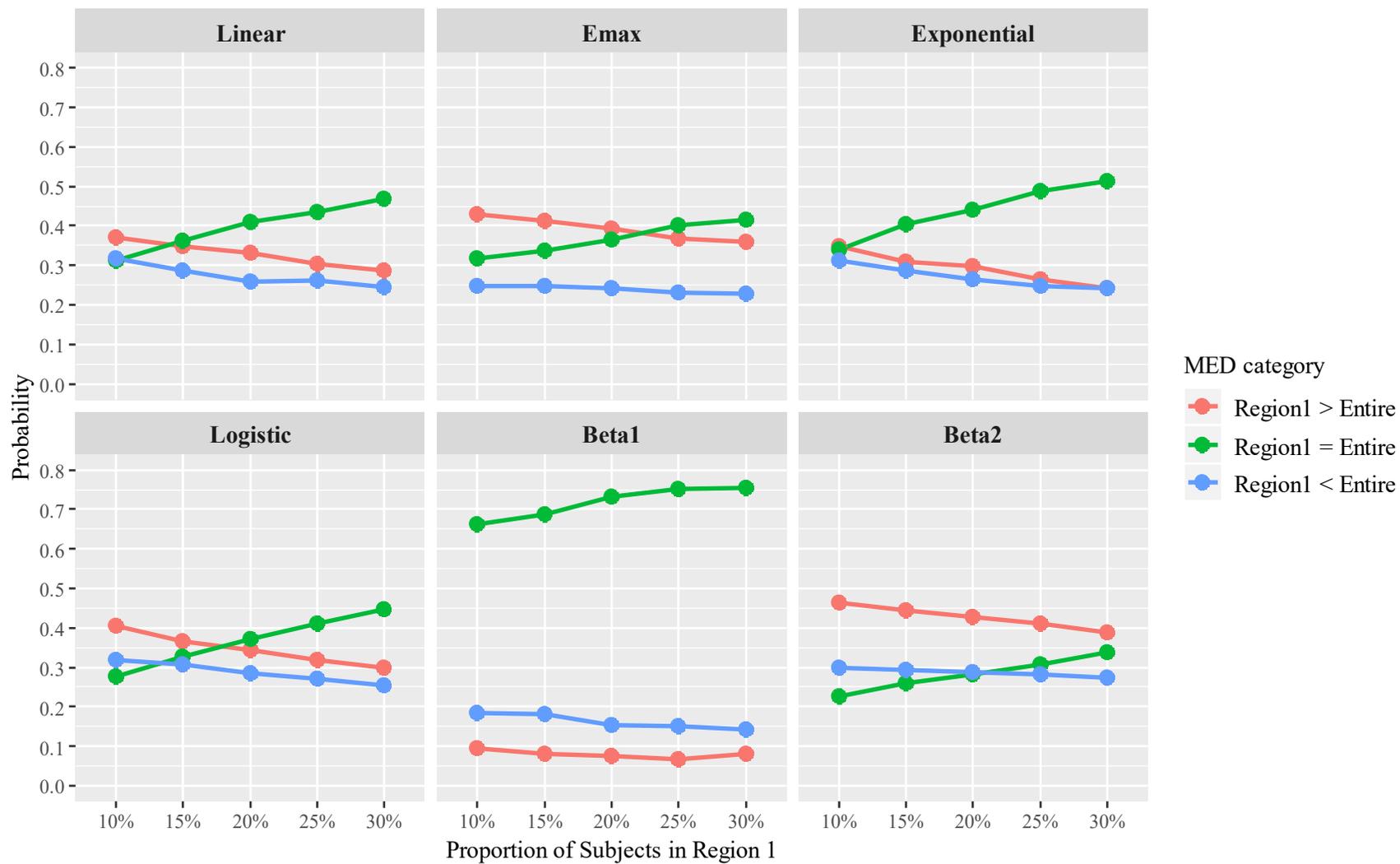


Figure A4. Probability that the MED of Region 1 was the same, higher or lower as that for the entire population, by true dose-response model.