Estimate of transition probability and 95% Confidence bounds

From the theory of absorbing Markov chains, we can calculate the total probability of arriving at an absorbing state from any of the four transient states. If we define Q as the 4 x 4 matrix of the transition probability of any transient state to another, R as the 4 x 2 matrix of transition probabilities from transient to absorbing states, and I as the 4 x 4 identity matrix, $N = (I - Q)^{-1}$ and we can produce a 4 x 2 matrix NR, the first column of which gives total probability of entering the absorbing state clear from any transient state (row), the second column gives complementary information on the probability of entering a cancer state from a starting transient state. The general form for Q and R respectively are

$$Q = \begin{pmatrix} p_{HPV \to HPV} & p_{HPV \to CIN\ 1} & p_{HPV \to CIN\ 2} & p_{HPV \to CIN\ 3} \\ p_{CIN\ 1 \to HPV} & p_{CIN\ 1 \to CIN\ 1} & p_{CIN\ 1 \to CIN\ 2} & p_{CIN\ 1 \to CIN\ 3} \\ p_{CIN\ 2 \to HPV} & p_{CIN\ 2 \to CIN\ 1} & p_{CIN\ 2 \to CIN\ 2} & p_{CIN\ 2 \to CIN\ 3} \\ p_{CIN\ 3 \to HPV} & p_{CIN\ 3 \to CIN\ 1} & p_{CIN\ 3 \to CIN\ 2} & p_{CIN\ 3 \to CIN\ 3} \end{pmatrix}$$

$$R = \begin{pmatrix} p_{HPV \to Clear} & p_{CIN\ 1 \to Clear} & p_{CIN\ 2 \to Clear} & p_{CIN\ 3 \to Clear} \\ p_{HPV \to Cancer} & p_{CIN\ 1 \to Cancer} & p_{CIN\ 2 \to Cancer} & p_{CIN\ 3 \to Cancer} \end{pmatrix}$$

where $p_{A \to B}$ denotes the transition probability from state A to state B, some of which will be zero valued depending on the model employed as outlined in the prior section. As the sum of probabilities of each state in a Markov chain model must always sum to unity[1], caution was required in estimating 95% confidence intervals. This was done in this work by bootstrapping methods, taking discrete steps of 0.01 along each parameters 95% confidence interval and finding all possible combinations of parameters that summed to unity. For these, the absorbing probabilities were calculated, and a large vector of allowed values produced. Resulting vectors were approximately normally distributed with several thousand values, with mean μ and standard deviation σ of the distribution found, with 95% confidence bounds at $\mu \pm 1.96\sigma$. Histograms for all three models are given in the technical appendix.

[1] Grinstead and Snell's Introduction to Probability, American Mathematical Society, 1997

Estimate of transition probability / 95% Confidence bound bootstrap histograms

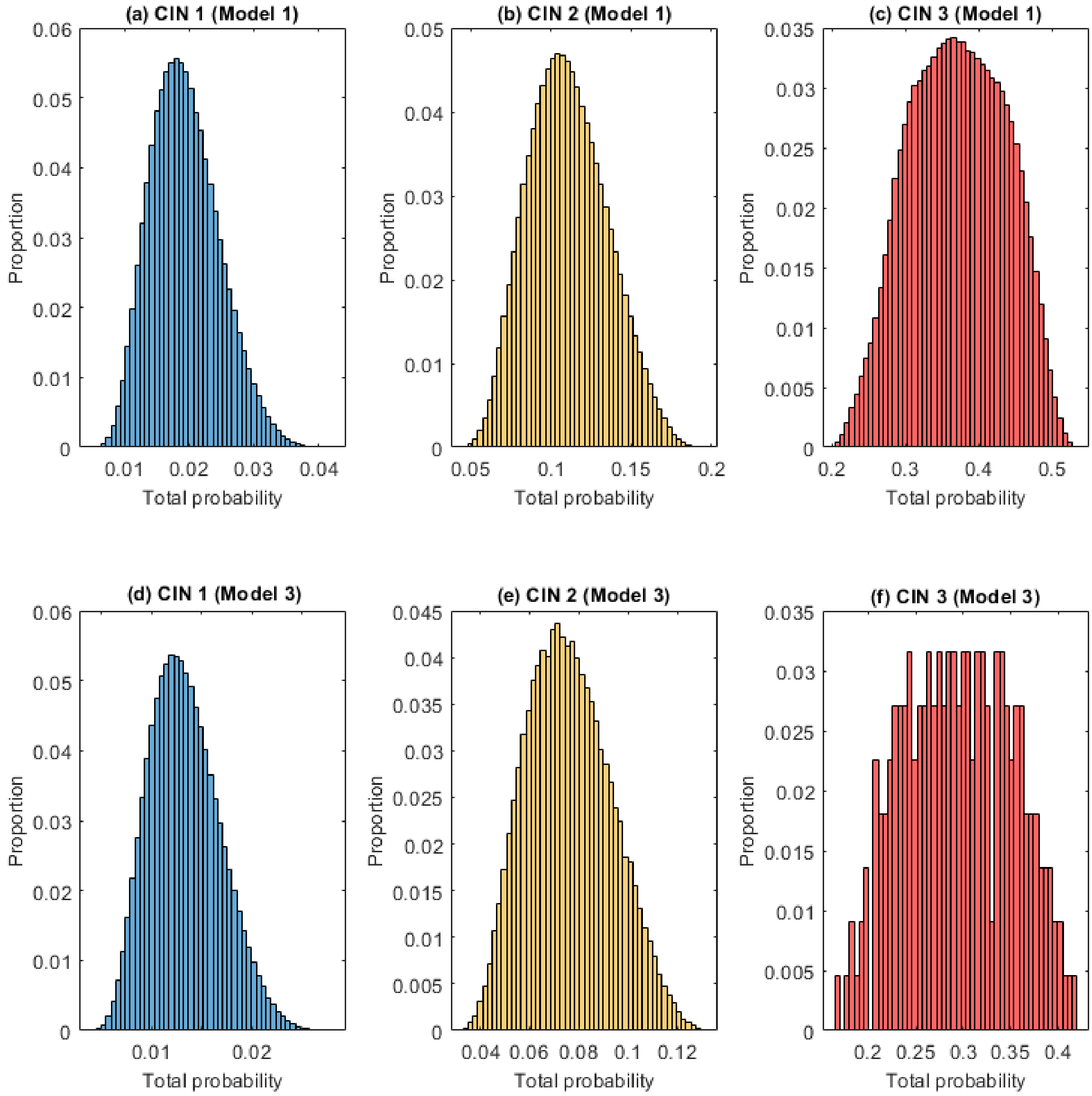

Figure 8 - Histograms of all 678,210 possible outcomes for all values in the 95% confidence intervals. Distributions are approximately symmetrical and were used to obtain 95% confidence intervals as outlined in the models section.