Modelling TB transmission in clusters of maximum size two

Shannon Gallagher and Dean Follmann

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Abstract. We examine the transmission of TB of clusters of individuals of maximum size two.
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1 Toss 'til failure (TTF)

The toss til failure (TTF) data generation process works by flipping a single coin until failure, for each agent in an order corresponding to their generation.

The Exogenous or Outside (O) flips a coin with probability of success $\alpha < 1$, where success denotes a transmission of the disease from the outside to a single individual. Person O tosses the coin until failure. We say that $n_{k,O}$ is the number of individuals infected by person O. Since there is an independent and equal probability of infecting each person (given a previous success), then $n_{k,O} \sim \text{Geometric}(\alpha)$.

If $n_{k,O} = 0$, then no one is infected, and we move on to generating the next cluster. Otherwise, we number the individuals as $1, 2, \dots, n_{k,0}$ and draw demographic characteristics $X_{k,i} \overset{iid}{\sim} F$ where F is some distribution of demographic characteristics such as smear status.

We then proceed in the following manner. We flip a coin for person $n_{k,1}$. We say that person 1 has probability $p_{k,1} = f(X_{k,i}) < 1$ of successfully infecting another individual. The number of infected individuals from person i is $n_{k,i}$ and similar to the last step, $n_{k,i} \sim \text{Geometric}(p_{k,1})$, as we toss 'til failure. If $n_{k,1} > 0$, we enumerate the individuals as $n_{k,0} + 1, \dots, n_{k,0} + n_{k,1}$ and draw demographic characteristics $X_{k,i} \overset{iid}{\sim} F$ for the newly infected individuals.

The general process is then we flip a coin for person $i > 0$ who has probability of $p_{k,i} = f(X_{k,i}) < 1$ of success of infecting another. The number of infected individuals from person i is $n_{k,i} \sim \text{Geometric}(p_{k,i})$ and we enumerate the newly infected individuals as $\sum_{j=0}^{i-1} n_{k,j} + 1, \dots, \sum_{j=0}^{i-1} n_{k,j} + n_{k,i}$. The process continues with flipping the coin for person $i + 1$ either until each infected individual flips a coin until failure and only a finite number of individuals are infected (e.g. the process dies off naturally) or until a maximum number of infections, say M, is reached in the cluster. We consider the latter situation as 'censoring.'

We repeat the above process until K clusters of generated. Note that in the above formulation, it is entirely possible for clusters of size 0 to be formed, which does not have a direct counterpart in actual disease transmission.

1.1 Likelihood of TTF

We only consider clusters of maximum size $M < \infty$.

The data D can be summarized in terms of each cluster where n_k is the size of the cluster and X_k is the matrix of covariates (order does not matter).

$$D = \{(n_k, X_k)\}_{1:K}$$

The likelihood is equal to the product of the likelihood of the independent clusters,

$$\begin{aligned}\mathcal{L}(\alpha, \beta_0, \beta_1; D) &= \prod_{k=1}^{K} \mathcal{L}_{n_k}(\alpha, \beta_0, \beta_1, D_k) \\ &= \sum_{\text{ordering}} \sum_{p} P(\text{path } p | \text{ordering}, n_k)\end{aligned}$$

For our purposes, we assume $p_{k,i} = \text{logit}(\beta_0 + \beta_1 X_{k,i,\text{smear}})$ where $X_{k,i,\text{smear}}$ is a binary variable taking either 0 (smear negative) or 1 (smear positive).

2 Enumerating all likelihoods for clusters up to size 5

Let α be the probability of infection from the outside and p_k be the probability of successful infection *from* individual k to another individual. We assume all transmissions are independent of one another.

The below show the unique trees up to isomorphism, meaning to get the full likelihood, we must sum over all permutations of the labels. Let $C \in \{0, 1\}$ be an indicator whether we censor or not once we have a chain of length K.

The likelihood of cluster k is then equal to the likelihood of observing a cluster of size n_k given the smear status of the individuals in the cluster,

$$\mathcal{L}_{n_k}(\alpha, \beta_0, \beta_1, D_k) = P(\text{Cluster size} = n_k | D_k).$$

When $n_k = 0$, there is only one possible way this happened, namely, a failure on the first coin toss,

$$L_0(\alpha, \beta_0, \beta_1, D_k) = (1 - \alpha).$$

When $n_k = 1$ (and $M > 1$), then there is exactly one sucess from the outside person followed by a failure, and a failure from person 1,

$$L_1(\alpha, \beta_0, \beta_1, D_k) = \alpha(1 - \alpha)(1 - p_1).$$

However, when $n_k = 2$, the likelihood becomes more complicated as we need to enumerate both all possible transmission paths that result in a cluster of two and the ordering of the individuals as p_i is dependent on the covariates. Thus,

$$L_2(\alpha, \beta_0, \beta_1, D_k) = \alpha(1-\alpha)(1-p_A)(1-p_B)\frac{1}{2}[(\alpha + p_A) + (\alpha + p_B)],$$

where the first term in the sum assumes that the ordering of the individuals was (A, B) and the second term assumes it to be (B, A). The factorered term $\alpha(1-\alpha)(1-p_A)(1-p_B)$ is in every single path because 1) we must begin with an outside success and 2) all three must fail if $M > 2$ as then n_k would no longer be 2. The paths are as follows

1. $O \to A, O \to B$
2. $O \to A, A \to B$
3. $O \to B, O \to A$
4. $O \to B, B \to A$.

Note that paths (1) and (3) are different in our model set up because in (1) A is enumerated as individual 1 and as indiivdual (2) in path (3). The above likelihood assumes that the ordering of the individuals have the same probability (e.g. 1/2).

In general, the likelihood can be written as

$$L_{n_k} \propto \sum_{\text{ordering}} \sum_{p} P(\text{path } p | \text{ordering}, n_k),$$

where the first sum is over all possible permutations of the orderings (e.g. (A,B) or (B,A) when $n_k = 2$) and the second is over the possible paths (up to isomorphism). The second sum is tricky, and we have not yet found a way to enumerate the possible paths in general. We have enumerated all possible paths and their corresponding likelihood for clusters up to size 5, which can be found in Section 3.

2.1 Properties of the likelihood

Although we cannot say everything we would like about the likelhood for L_{n_k} for any n_k, we do know some properties that will hold, as long as $n_k > 0$ and $M > \max n_k$

- Each sum in the likelihood will contain $\alpha(1-\alpha)\prod_{i=1}^{n_k}(1-p_{ki})$
- One path will be all infections from the outside $\alpha^{n_k}(1-\alpha)\prod_{i=1}^{n_k}(1-p_{ki})$
- (Conjecture) MLE at $(\alpha, \beta_0 + \beta_1 = -\infty)$ or equivalently $(\alpha, p_i = 0)$

3 Enumerating the paths

3.1 $K = 0$

Path via adjacency matrix

Adjacency Matrix

1. $()$

Likelihood

1. $1-\alpha$

3.2 $K = 1$

Path via adjacency matrix

Adjacency Matrix

1. $\begin{pmatrix} 1 \end{pmatrix}$

Likelihood

1. $\alpha(1-\alpha)$

3.3 $K = 2$

Adjacency Matrix

1. $\begin{pmatrix} 1 & 1 \\ 0 & 0 \end{pmatrix}$
2. $\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$

Likelihood

1. $\alpha^2 \left[(1-\alpha)(1-p_1)(1-p_2)\right]^C$
2. $\alpha(1-\alpha)p_1 \left[(1-p_1)(1-p_2)\right]^C$

3.4 $K = 3$

Adjacency Matrix

1. $\begin{pmatrix} 1 & 1 & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$
2. $\begin{pmatrix} 1 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 0 \end{pmatrix}$
3. $\begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 1 \\ 0 & 0 & 0 \end{pmatrix}$
4. $\begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$

Likelihood

1. $\alpha^3 \left[(1-\alpha)(1-p_1)(1-p_2)(1-p_3)\right]^C$
2. $\alpha^2(1-\alpha)p_1 \left[(1-p_1)(1-p_2)(1-p_3)\right]^C$
3. $\alpha(1-\alpha)^2p_1^2(1-p_1)p_2 \left[(1-p_2)(1-p_3)\right]^C$
4. $\alpha(1-\alpha)^2p_1(1-p_1)p_2 \left[(1-p_2)(1-p_3)\right]^C$

3.5 $K = 4$

Adjacency Matrix

1. $\begin{pmatrix} 1 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

Likelihood

1. $\alpha^4 \left[(1-\alpha)(1-p_1)(1-p_2)(1-p_3)(1-p_4)\right]^C$
2. $\alpha^3(1-\alpha)p_1 \left[(1-p_1)\right]^C$
3. $\alpha^2(1-\alpha)^2p_1(1-p_1)(1-p_2)p_3 \left[(1-p_3)(1-p_4)\right]^C$
4. $\alpha^2(1-\alpha)^2p_1^2 \left[(1-p_1)(1-p_2)(1-p_3)(1-p_4)\right]^C$

2. $\begin{pmatrix} 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

3. $\begin{pmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$

4. $\begin{pmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

5. $\begin{pmatrix} 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

6. $\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

7. $\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

8. $\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

9. $\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$

5. $\alpha^2(1-\alpha)^2 p_1(1-p_1)p_2\left[(1-p_2)(1-p_3)(1-p_4)\right]^C$
6. $\alpha(1-\alpha)^3 p_1^3\left[(1-p_1)(1-p_2)(1-p_3)(1-p_4)\right]^C$
7. $\alpha(1-\alpha)^3 p_1^2(1-p_1)p_2\left[(1-p_2)(1-p_3)(1-p_4)\right]^C$
8. $\alpha(1-\alpha)^3 p_1(1-p_1)^2 p_2(1-p_2)p_3\left[(1-p_3)(1-p_4)\right]^C$

3.6 $K = 3$

Adjacency Matrix

1. $\begin{pmatrix} 1 & 1 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

Likelihood

1. $\alpha^5[(1-\alpha)(1-p_1)(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$
2. $\alpha^4(1-\alpha)p_1[(1-p_1)(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$
3. $\alpha^3(1-\alpha)^2 p_1^2[(1-p_1)(1-p_2)(1-p_3)(1-$

2. $\begin{pmatrix} 1 & 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

3. $\begin{pmatrix} 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

4. $\begin{pmatrix} 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

5. $\begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

6. $\begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

7. $\begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

8. $\begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$

9. $\begin{pmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}$

$p_4)(1-p_5)]^C$

4. $\alpha^3(1-\alpha)^2 p_1(1-p_1)p_2[(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

5. $\alpha^2(1-\alpha)^3 p_1^3[(1-p_1)(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

6. $\alpha^2(1-\alpha)^3 p_1^2(1-p_1)(1-p_2)p_3[(1-p_3)(1-p_4)(1-p_5)]^C$

7. $\alpha^2(1-\alpha)^3 p_1^2(1-p_1)p_2[(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

8. $\alpha^2(1-\alpha)^3 p_1(1-p_1)^2 p_2(1-p_2)p_3[(1-p_3)(1-p_4)(1-p_5)]^C$

9. $\alpha^2(1-\alpha)^3 p_1(1-p_1)^2(1-p_2)^2 p_3(1-p_3)p_4[(1-p_4)(1-p_5)]^C$

10. $\alpha(1-\alpha)^4 p_1(1-p_1)^3 p_2(1-p_2)^2 p_3(1-p_3)p_4[(1-p_4)(1-p_5)]^C$

11. $\alpha(1-\alpha)^4 p_1^2(1-p_1)^2 p_2(1-p_2)^2(1-p_3)p_4[(1-p_4)(1-p_5)]^C$

12. $\alpha(1-\alpha)^4 p_1^2(1-p_1)^2 p_2^2[(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

13. $\alpha(1-\alpha)^4 p_1^3(1-p_1)p_2[(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

14. $\alpha(1-\alpha)^4 p_1^4[(1-p_1)(1-p_2)(1-p_3)(1-p_4)(1-p_5)]^C$

15. $\alpha(1-\alpha)^4 p_1(1-p_1)^3 p_2(1-p_2)^2 p_3^2[(1-p_3)(1-p_4)(1-p_5)]^C$

16. $\alpha(1-\alpha)^4 p_1(1-p_1)^3 p_2^2(1-p_2)p_3[(1-\alpha)((1-p_3)(1-p_4)(1-p_5)]^C$

10. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

11. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

12. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

13. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

14. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

15. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

16. $$\begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$