The Transmissibility of Highly Pathogenic Avian Influenza in Commercial Poultry in Industrialized Countries

Tini Garske, Paul Clarke, Azra C. Ghani

Technical Appendix

1 The information matrix for discrete times

In the main paper, we assumed that distribution times followed a Weibull distribution which is a continuous distribution. However, our infection time data is discretized into whole days, and the likelihood must be discretized to reflect this.

To calculate the maximum likelihood (ML) estimate, substitute $W(t_j - t_i; \kappa, \eta)$ for $w(t_j - t_i; \kappa, \eta)$ in equation (6) of the main paper. The Weibull cumulative distribution function (CDF) is given by

$$W(T; \kappa, \eta) = 1 - \exp\left[-(\eta T)^\kappa\right], \tag{A.1}$$

and for every occurrence of $w(t_j - t_i; \kappa, \eta)$ we substituted

$$w_{ij} = W(T + 1/2; \kappa, \eta) - W(T - 1/2; \kappa, \eta) \tag{A.2}
= \exp[-(\eta(T - 1/2))^\kappa] - \exp[-(\eta(T + 1/2))^\kappa] \tag{A.3}
= E^- - E^+. \tag{A.4}$$

To calculate variance-covariance matrix in equation (8) of the main paper, we use the standard relationship

$$V(\theta) = J^{-1}(\theta) \tag{A.5}$$

where $J(\theta)$ is the observed information matrix given by

$$J(\hat{\theta}) = -\begin{pmatrix}
\frac{\partial^2 \ln L}{\partial \kappa^2} & \frac{\partial^2 \ln L}{\partial \kappa \partial \eta} \\
\frac{\partial^2 \ln L}{\partial \eta \partial \kappa} & \frac{\partial^2 \ln L}{\partial \eta^2}
\end{pmatrix} \tag{A.6}$$

with $\hat{\theta} = (\kappa, \eta)$ and $\ln L$ the log-likelihood with the cumulative density for the Weibull substituted.
To calculate $J$ it is first necessary to evaluate the first and second derivatives with respect to $\kappa$ and $\eta$, given by

$$\frac{\partial}{\partial \kappa} E^\pm = \beta_{\kappa \pm} E^\pm$$  \hspace{1cm} (A.7)

$$\frac{\partial}{\partial \eta} E^\pm = \beta_{\eta \pm} E^\pm$$  \hspace{1cm} (A.8)

$$\frac{\partial^2}{\partial \kappa^2} E^\pm = \beta_{\kappa \kappa \pm} E^\pm = \left( \beta_{\kappa \pm}^2 + \frac{\partial}{\partial \kappa} \beta_{\kappa \pm} \right) E^\pm$$  \hspace{1cm} (A.9)

$$\frac{\partial^2}{\partial \eta \partial \kappa} E^\pm = \beta_{\kappa \eta \pm} E^\pm = \left( \beta_{\kappa \pm} \beta_{\eta \pm} + \frac{\partial}{\partial \eta} \beta_{\kappa \pm} \right) E^\pm$$  \hspace{1cm} (A.10)

$$\frac{\partial^2}{\partial \eta^2} E^\pm = \beta_{\eta \eta \pm} E^\pm = \left( \beta_{\eta \pm}^2 + \frac{\partial}{\partial \eta} \beta_{\eta \pm} \right) E^\pm.$$  \hspace{1cm} (A.11)

With $T^\pm = T \pm 1/2$, we have

$$\beta_{\kappa \pm} = - \left( \eta T^\pm \right)^\kappa \ln \left( \eta T^\pm \right)$$  \hspace{1cm} (A.12)

$$\beta_{\eta \pm} = - \frac{\kappa}{\eta} \left( \eta T^\pm \right)^\kappa$$  \hspace{1cm} (A.13)

$$\beta_{\kappa \kappa \pm} = \beta_{\kappa \pm}^2 \left( \eta T^\pm \right)^\kappa \ln^2 \left( \eta T^\pm \right)$$  \hspace{1cm} (A.14)

$$\beta_{\kappa \eta \pm} = \beta_{\kappa \pm} \beta_{\eta \pm} \left( \frac{\eta T^\pm}{\eta} \right)^\kappa \ln \left( \eta T^\pm \right) (1 + \kappa \ln \left( \eta T^\pm \right))$$  \hspace{1cm} (A.15)

$$\beta_{\eta \eta \pm} = \beta_{\eta \pm}^2 \left( \frac{\kappa}{\eta^2} \right) \left( \eta T^\pm \right)^\kappa (\kappa - 1).$$  \hspace{1cm} (A.16)
Therefore the entries of the information matrix are

$$\frac{\partial^2 \ln L}{\partial \kappa^2} = \sum_{j=k}^N \frac{\sum_{i \in S_j} \left( \beta_{\kappa E^-} - \beta_{\kappa E^+} \right)}{\sum_{i \in S_j} (E^- - E^+)} \left[ \frac{\left( \sum_{i \in S_j} \left( \beta_{\kappa E^-} - \beta_{\kappa E^+} \right) \right)^2}{\left( \sum_{i \in S_j} (E^- - E^+) \right)^2} \right]$$  \hspace{1cm} (A.17)

$$\frac{\partial^2 \ln L}{\partial \kappa \eta} = \sum_{j=k}^N \frac{\sum_{i \in S_j} \left( \beta_{\kappa \eta E^-} - \beta_{\kappa \eta E^+} \right)}{\sum_{i \in S_j} (E^- - E^+)} \left[ \frac{\left( \sum_{i \in S_j} \left( \beta_{\kappa \eta E^-} - \beta_{\kappa \eta E^+} \right) \right) \left( \sum_{i \in S_j} \left( \beta_{\eta E^-} - \beta_{\eta E^+} \right) \right)}{\left( \sum_{i \in S_j} (E^- - E^+) \right)^2} \right]$$  \hspace{1cm} (A.18)

$$\frac{\partial^2 \ln L}{\partial \eta^2} = \sum_{j=k}^N \frac{\sum_{i \in S_j} \left( \beta_{\eta E^-} - \beta_{\eta E^+} \right)}{\sum_{i \in S_j} (E^- - E^+)} \left[ \frac{\left( \sum_{i \in S_j} \left( \beta_{\eta E^-} - \beta_{\eta E^+} \right) \right)^2}{\left( \sum_{i \in S_j} (E^- - E^+) \right)^2} \right]$$  \hspace{1cm} (A.19)

Once this is done standard formulae for a) the inverse of a two-by-two matrix and b) the conditional normal distribution, can be used to calculate \( V = J^{-1} \) and generate draws from the bivariate normal distribution. For completeness, we give each of these results below.

### 2 Inversion of the information matrix

The variance-covariance matrix is obtained by inverting the information matrix. The general inversion formula for a \( 2 \times 2 \) matrix

$$M = \begin{pmatrix} A & B \\ C & D \end{pmatrix}$$  \hspace{1cm} (A.20)

is given by

$$M^{-1} = \left( \begin{array}{cc} D & -B \\ -C & A \end{array} \right) \frac{1}{\det}$$  \hspace{1cm} with \( \det = AD - BC \).  \hspace{1cm} (A.21)

### 3 Marginal and conditional distributions

The distribution function of a bivariate normal distribution is given by

$$P(x_1, x_2) = \frac{1}{2\pi\sigma_1\sigma_2\sqrt{1-\rho^2}} \exp \left[ -\frac{z}{2(1-\rho^2)} \right]$$  \hspace{1cm} (A.22)
with
\[ z = \frac{(x_1 - \mu_1)^2}{\sigma_1^2} - \frac{2\rho(x_1 - \mu_1)(x_2 - \mu_2)}{\sigma_1\sigma_2} + \frac{(x_2 - \mu_2)^2}{\sigma_2^2}. \] (A.23)

The variance-covariance matrix \( V \) determines the variances and correlations via
\[
V = \begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{pmatrix} = \begin{pmatrix} \sigma_1^2 & \rho\sigma_1\sigma_2 \\ \rho\sigma_1\sigma_2 & \sigma_2^2 \end{pmatrix}. \] (A.24)

The marginal probability for any \( x_i \) is given by the univariate normal distribution
\[
P(x_i) = \frac{1}{\sigma_i\sqrt{2\pi}} \exp \left[-\frac{(x_i - \mu_i)^2}{2\sigma_i^2}\right]. \] (A.25)

The conditional probability of \( x_2 \) given that \( x_1 = a \) is also a normal distribution, but with mean \( \bar{\mu}_2 \) and variance \( \bar{\sigma}_2^2 \), which are given as
\[
\bar{\mu}_2 = \mu_2 + \frac{\Sigma_{21}}{\Sigma_{11}}(a - \mu_1) \] (A.26)
\[
\bar{\sigma}_2^2 = \Sigma_{22} - \frac{\Sigma_{21}\Sigma_{12}}{\Sigma_{11}} \] (A.27)