Supplementary Information for the manuscript: Modelling the transmission dynamics of H9N2 avian influenza viruses in a live bird market

1 Supplementary Text

1.1 Supplementary Text S1: additional details on batch initialisation

Let us denote with $P^{(0)}_{g,b,X}$ the probability that a chicken of type b and from group g is in compartment $X \in \{S, E_1, E_2, I, R_+, R_-\}$ at recruitment. In the main text we assumed:

$$\begin{cases} P^{(0)}_{g,b,X} = 1 - \rho_{g,b} \text{ if } X = S \,, \\ P^{(0)}_{g,b,X} = \rho_{g,b} \cdot \bar{P}_X(\sigma_b, \mu, \eta, \lambda_b, \kappa_b) \text{ otherwise} \,, \end{cases} \tag{S1}$$

where $\rho_{g,b}$ is the probability of prior exposure and $\bar{P}_X$ is the probability of being in compartment $X \in \{E_1, E_2, I, R_+, R_-\}$ conditional on prior exposure, averaged over time since prior exposure.

We first consider the general case where an infected chicken goes through a sequence of n states with transition rates r_k, $k = 1, \ldots, n-1$ from state k to the $k+1$. In this case, the probability $P_k(\tau)$ that the chicken is in state k at time τ evolves according to:

$$\begin{cases} \dot{P}_1(t) = -r_1 P_1 \,, \\ \dot{P}_k(t) = r_{k-1} P_{k-1} - r_k P_k \text{ for } k = 2, \ldots, n-1 \,, \\ \dot{P}_n(t) = r_{n-1} P_{n-1} \,, \end{cases} \tag{S2}$$

with initial conditions $P_k(0) = \delta_{k,1}$, where $\delta_{i,j}$ is Kronecker delta. The dot notation is a shorthand for differentiation with respect to time. The general solution to Eq.SS2 is obtained by integrating equations recursively:

$$\begin{cases} P_1(\tau) = \exp(-r_1 \tau) \,, \\ P_k(\tau) = r_{k-1} \exp(-r_k \tau) \int_0^\tau P_{k-1}(x) \exp(r_k x) dx \text{ for } k = 2, \ldots, n-1 \,, \\ P_n(\tau) = r_{n-1} \int_0^\tau P_{n-1}(x) dx \,. \end{cases} \tag{S3}$$

The explicit solution to Eq.SS3 in the case of our SEEIRR model is:

$$\begin{cases} P_{E_1}(\tau) = \exp(-2\sigma\tau)\,, \\ P_{E_2}(\tau) = 2\sigma\tau\exp(-2\sigma\tau)\,, \\ P_I(\tau) = \left(\dfrac{2\sigma}{2\sigma-\mu}\right)^2 \left[\exp(-\mu\tau) - \exp(-2\sigma\tau)(1+(2\sigma-\mu)\tau)\right]\,, \\ P_{R_+}(\tau) = \mu\left(\dfrac{2\sigma}{2\sigma-\mu}\right)^2 \left[\exp(-\eta\tau)\dfrac{(2\sigma-\mu)^2}{(\mu-\eta)(2\sigma-\eta)^2} - \right. \\ \qquad\qquad \left. - \dfrac{exp(-\mu\tau)}{\mu-\eta} + \dfrac{\exp(-2\sigma\tau)}{2\sigma-\eta}\left[\dfrac{4\sigma-\mu-\eta}{2\sigma-\eta} + (2\sigma-\mu)\tau\right]\right]\,, \\ P_{R_-}(\tau) = 1 - P_{E_1}(\tau) - P_{E_2}(\tau) - P_I(\tau) - P_{R_+}(\tau)\,. \end{cases} \tag{S4}$$

We now average $P_X(\tau)$ over τ, under the assumption that the latter follows a gamma distribution $f(\tau|\lambda,\kappa)$ with inverse scale λ and shape κ. Mathematically, the average probability $\bar{P}_X$ for compartment X, is computed as $\bar{P}_X = \int_0^\infty P_X(\tau) f(\tau|\lambda,\kappa) d\tau$. In our SEEIRR model:

$$\begin{cases} \bar{P}_{E_1} = \left(\dfrac{\lambda}{\lambda+2\sigma}\right)^\kappa\,, \\ \bar{P}_{E_2} = \dfrac{2\sigma\kappa\lambda^\kappa}{(\lambda+2\sigma)^\kappa}\,, \\ \bar{P}_I = \dfrac{4\sigma^2\lambda^\kappa}{(2\sigma-\mu)^2}\left[\dfrac{1}{(\lambda+\mu)^\kappa} - \dfrac{\lambda-\kappa\mu+2(1+\kappa)\sigma}{(\lambda+2\sigma)^{\kappa+1}}\right]\,, \\ \bar{P}_{R_+} = \dfrac{4\mu\sigma^2\lambda^\kappa}{(2\sigma-\mu)^2}\left[\dfrac{(2\sigma-\mu)(2\sigma+\mu-2\eta)}{(\lambda+\eta)^\kappa(\mu-\eta)(2\sigma-\eta)^2} - \dfrac{1}{(\lambda+\mu)^\kappa(\mu-\eta)} + \right. \\ \qquad\qquad \left. + \dfrac{\lambda+2\sigma+\kappa(2\sigma-\mu)(2\sigma-\eta)+(2\sigma-\eta)(2\sigma+\lambda)}{(\lambda+2\sigma)^{\kappa+1}(2\sigma-\eta)^2}\right]\,, \\ \bar{P}_{R_-} = 1 - \bar{P}_{E_1} - \bar{P}_{E_2} - \bar{P}_I - \bar{P}_{R_+}\,. \end{cases} \tag{S5}$$

Finally, the statistics of time since past exposure differs between intervention and control chickens because of the delay in recruitment: if $f_c(\tau|\lambda,\kappa) = f(\tau|\lambda,\kappa)$ denotes the distribution of past exposure time for control chickens (i.e. since T_1), the corresponding distribution for intervention chickens is:

$$f_i(\tau|\lambda,\kappa,\delta t = T_1 - T_0) = f(\tau + T_1 - T_0|\lambda,\kappa) / \left[1 - F(T_1 - T_0|\lambda,\kappa)\right]\,, \tag{S6}$$

where $F(x|\lambda,\kappa) = \int_0^x f(u|\lambda,\kappa)du$. This follows from the assumption that intervention and control chickens share the same distribution, but the former can not be infected between T_0 and T_1, hence the condition $\tau > \delta t$; in addition, we must also shift τ by δt since we are now interested in time elapsed since exposure and T_0, not T_1.

Note that $f(\tau|\lambda,\kappa)$ denotes the probability density of time since past exposure without reference to which compartment a chicken ends up in at $t = 0$. Instead, the probability density $f(\tau|X,\lambda,\kappa)$ that a chicken was infected a time τ in the past, given it is in compartment X at $t = 0$, is given by Bayes' theorem:

$$f(\tau|X,\lambda,\kappa) = \frac{P_X(\tau)f(\tau|\lambda,\kappa)}{\bar{P}_X}\,. \tag{S7}$$

This equation suggests a sampling importance re-sampling scheme to sample τ, conditional on compartment X: first, draw a sample $\tau_k, k = 1,\ldots,n$ from the unconditional distribution $f(\tau|\lambda,\kappa)$ and compute a weight $w_k = P_X(\tau_k)/\bar{P}_X$; second, sample n values with replacement from the set $\{\tau_k\}$ using $w_k/\sum_k w_k$ as re-sampling probabilities. If one is interested in sampling from $f(\tau|X_1 \cup X_2,\lambda,\kappa)$, where X_1, X_2 are distinct compartments, it is possible to use the same procedure after noting that probabilities P_{X_1} and P_{X_2} add up to $P_{X_1\cup X_2}$.

1.2 Supplementary Text S2: additional details on inference procedure

This section contains further details on the choice of priors (listed in Table S1), and the likelihood function.

We considered a flat distribution for introduction probabilities $\rho_{g,b}$ and the positivity waning rate η and a $\chi^2(4)$ distribution for hyper-parameters λ_{BR}, λ_{BY}, κ_{BR} and κ_{BY} tuning the timing of past infections. Our experimental setup did not allow us to record time to recovery, hence we do not expect our data to be informative about the infectious period. In addition, experimental studies usually report the duration of shedding since the point of inoculation/infection. For these reasons, we decided to set a tight normal prior on the total time from exposure to recovery $T_{EI} = T_I + 0.5(T_{E,BR} + T_{E,BY})$. We did enforce $T_I > 0.5\,d$ and $T_R > 1\,d$. Finally, we penalized parameter configurations with a large $\beta/\mu l_\beta$ ratio, with $l_\beta > 0$ being an hyper-parameter: the smaller l_β, the stronger the penalty on β.

In order to define the model likelihood, we first denote with $p^+_{g,b}(j)$, $j = 0,1,2,3,4$ the probability that a chicken of type b and from recruitment group g is positive by T_j for the first time, where the time points T_j are defined in the Materials and Methods section in the main manuscript. Let us also denote the number of chickens of the same type and group becoming positive by T_j for the first time with $n^+_{g,b}(j)$. There are some differences between control and intervention groups in terms of how these counts are performed. First, $n^+_{i,b}(0)$ is the number of intervention chickens that are positive at T_0; note that, by design, $n^+_{c,b}(0) = 0$. Second, $n^+_{i,b}(1)$ is the number of intervention chickens that become positive between T_0 and T_1, while $n^+_{c,b}(1)$ is the number of control chickens that are already positive at T_1. $n^+_{g,b}(j)$, $j = 2,3,4$ represents the number of chickens that became positive in $[T_{j-1}, T_j]$. Finally, let us denote with $p^-_{g,b} = 1 - \sum_{j=0}^4 p^+_{g,b}(j)$ the probability to escape infection. Conditioned on these probabilities, the model likelihood $\mathcal{L}(D|\theta)$ is multinomial:

$$\mathcal{L}(D|\theta) \propto \prod_{b=BR,BY}\prod_{g=c,i}\left[p^-_{g,b}\right]^{n^-_{g,b}}\prod_{j=0}^{4}\left[p^+_{g,b}(j)\right]^{n^+_{g,b}(j)}\,, \tag{S8}$$

where $n^-_{g,b}$ is the number of chickens that remained negative for the whole experiment. Note that the likelihood above is based on the assumption that recruited chickens can be treated independently; as explained in the main text, this implicitly assumes that recruited chickens do not contribute to transmission, while remaining susceptible to infection due to other chickens at the market.

The likelihood function in Eq. SS8 also assumes that no chicken dies/is culled prematurely in the experiment. In order to include these chickens in our analysis, while also not modelling deaths/culling explicitly, we consider the corresponding data points as bingh right-censored. Hence, a negative chicken that drops out during the j-th time interval, contributes a factor $1 - \sum_{k=0}^{j-1} p^+_{g,b}(k)$ to $\mathcal{L}$. Chickens that die/are culled prematurely but turn positive at some point during the experiment, contribute the same to $\mathcal{L}$ as chickens that are not removed prematurely, and are already counted in $n^+_{g,b}(j)$.

Unfortunately, most of the $p^+_{g,b}(j)$'s are unknown and can not be computed analytically. We hence estimate these probabilities by simulating $N_{rep} = 10^6$ recruited chickens for each combination of recruitment group g and type b. These N_{rep} chickens were split among $M = 10$ independent simulations.

We counted the mean number of chickens ($\hat{n}^+_{g,b}(j)$) that turn positive at different stages of the experiment, which we used to estimate $p^+_{g,b}(j)$:

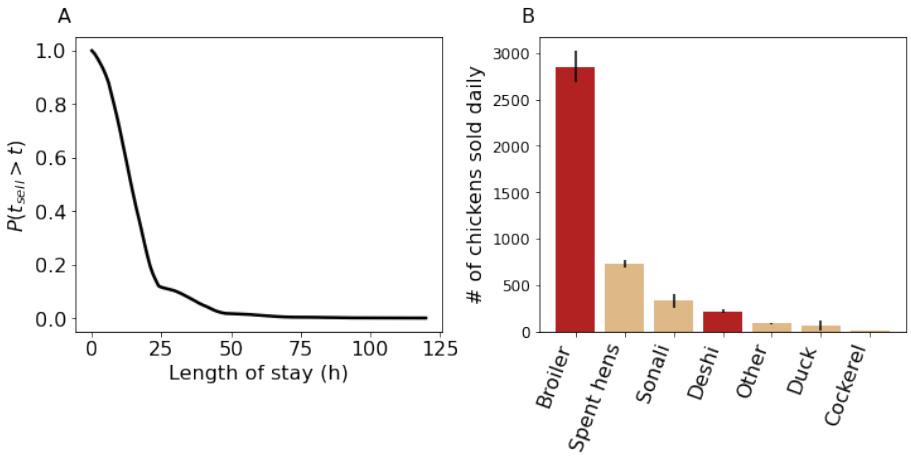
$$p^+_{g,b}(j) \approx \frac{\hat{n}^+_{g,b}(j)}{N_{rep}},\ j = 0, 1, 2, 3, 4\,. \tag{S9}$$

1.3 Supplementary Text S3: persistence of environmental contamination.

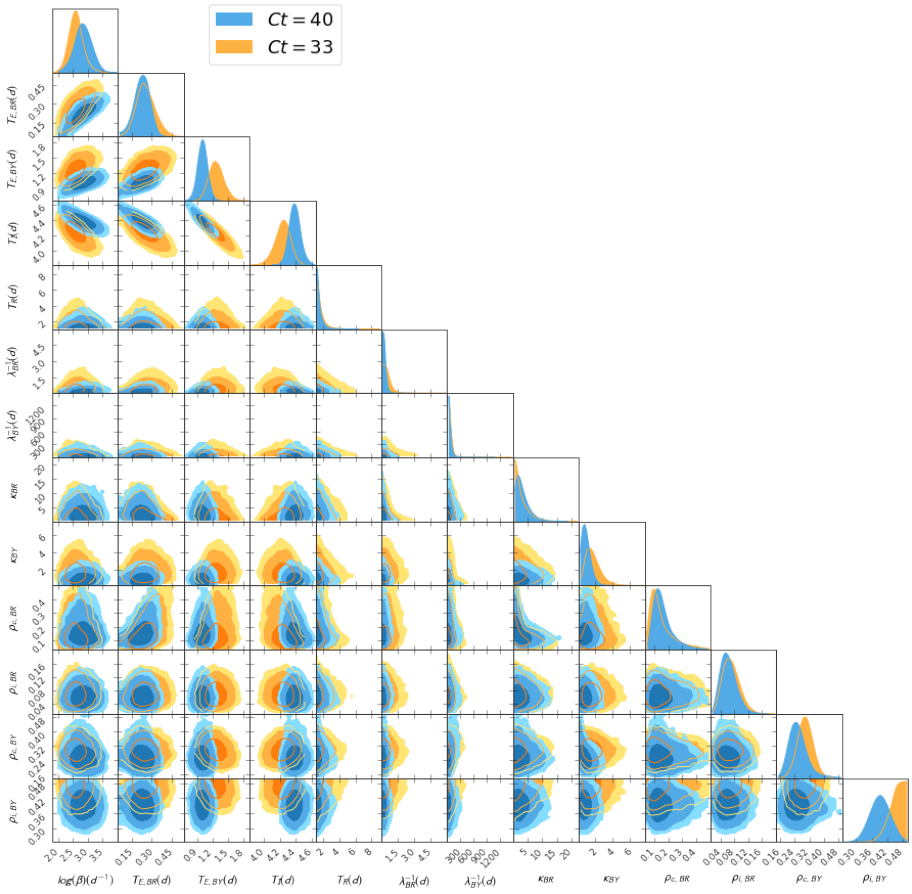
Contaminated faecal material shed by infectious chickens has been shown to retain its transmission potential for a significant amount of time. Nonetheless, available studies highlighted considerable variation in persistence depending on a number of environmental conditions, including temperature, humidity, wet or dry faeces, salinity and pH [1–5]. This suggests that properties of environmental contamination are likely to vary over months and across different types of chickens. In addition, it is possible that different influenza subtypes differ in their ability to persist in the environment, possibly as a consequence of evolutionary mechanisms [2].

Given this heterogeneity, we selected three values of decay rate Θ, namely $\Theta^{-1} = 10, 3, 1$ days, that are representative of a broad range of environmental conditions. In particular, these values roughly correspond to H9N2 AIV persistence in water at temperatures 15, 25 and 35 °C, respectively [2].

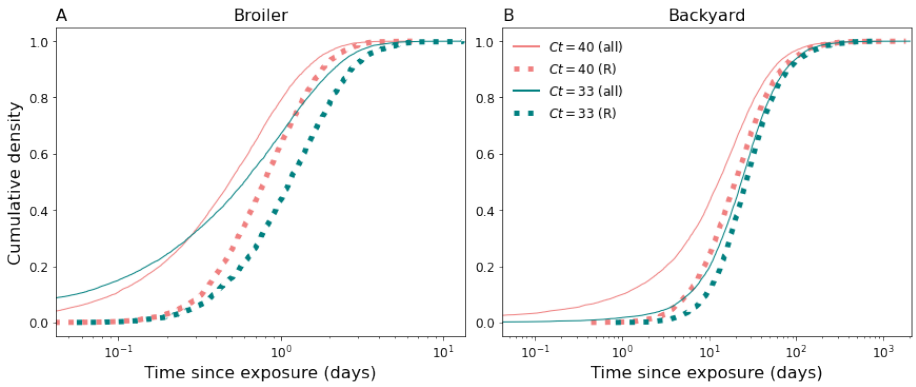
2 Supplementary Figures



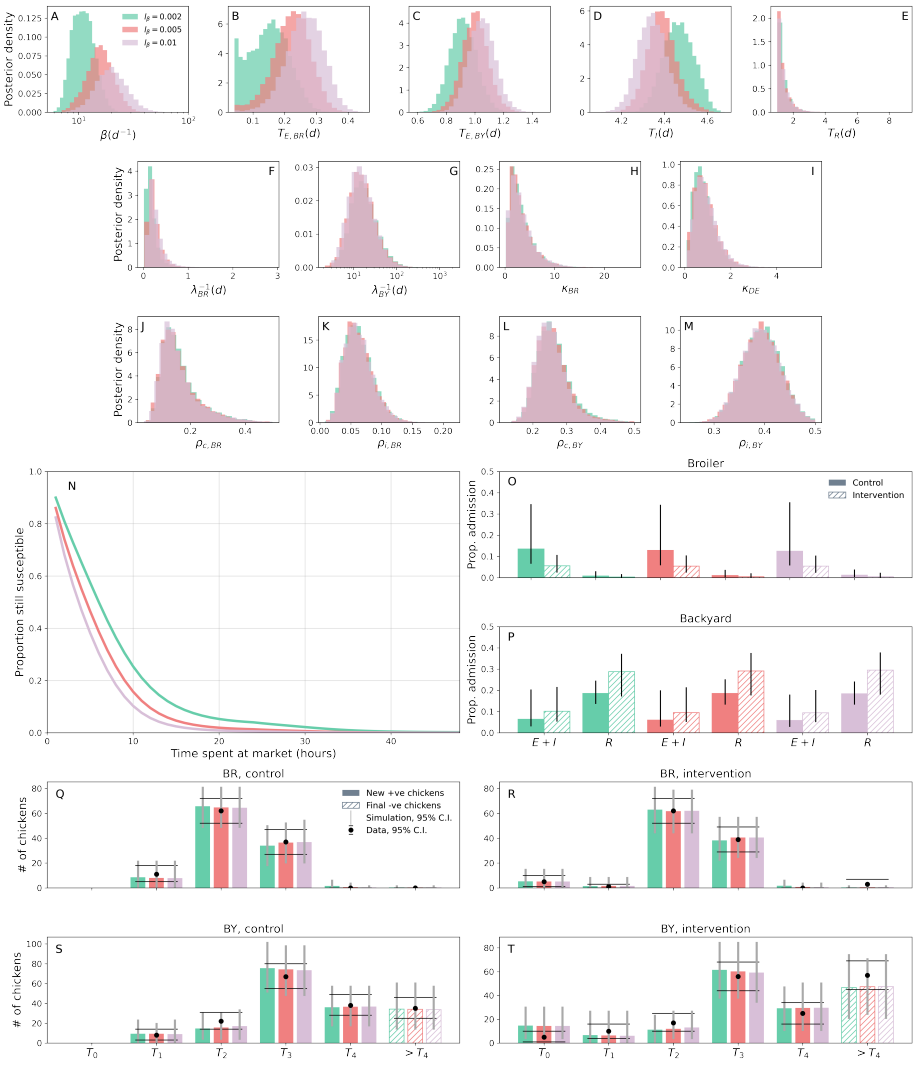
Supplementary Figure 1: **Length of stay distribution and chickens traded daily.** (A) Length of stay survival distribution used in the fit. (B) Number of chickens sold daily at the market. Black whiskers indicate corresponding ranges, as individual data are given as a range. Broiler and backyard chickens (Deshi) are highlighted in red. Data for both graphs were obtained from [6].



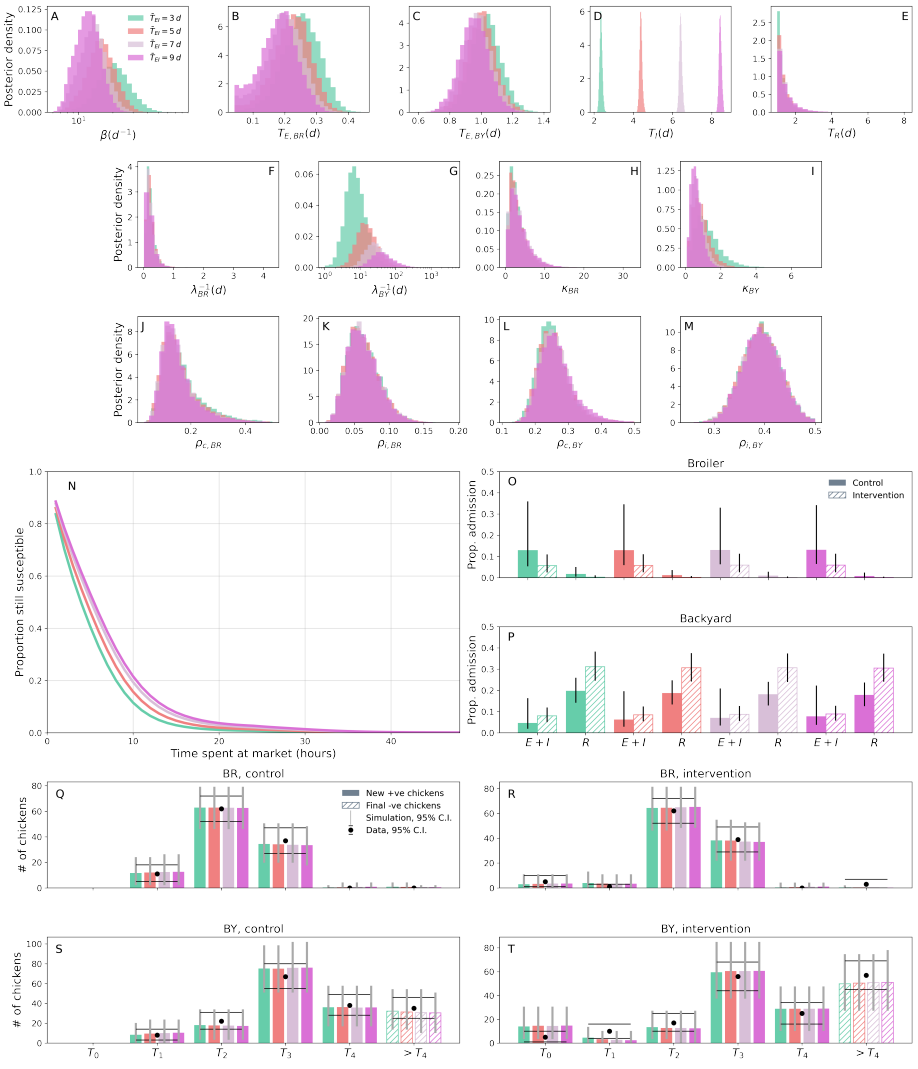
Supplementary Figure 2: **Marginal posterior distributions and pair correlations for fitted parameters.** Diagonal panels show posterior marginal distribution for fits to $Ct = 40$ (blue) and $Ct = 33$ (orange) data. Off-diagonal panels show kernel-smoothed pairwise projections, with 68%, 95% and 99% contour levels. For both fits we set $l_\beta = 0.005$ and $\bar{T}_{EI} = 5$ days. This plot was realised using *pygtc* module, version 0.4.0 [7].



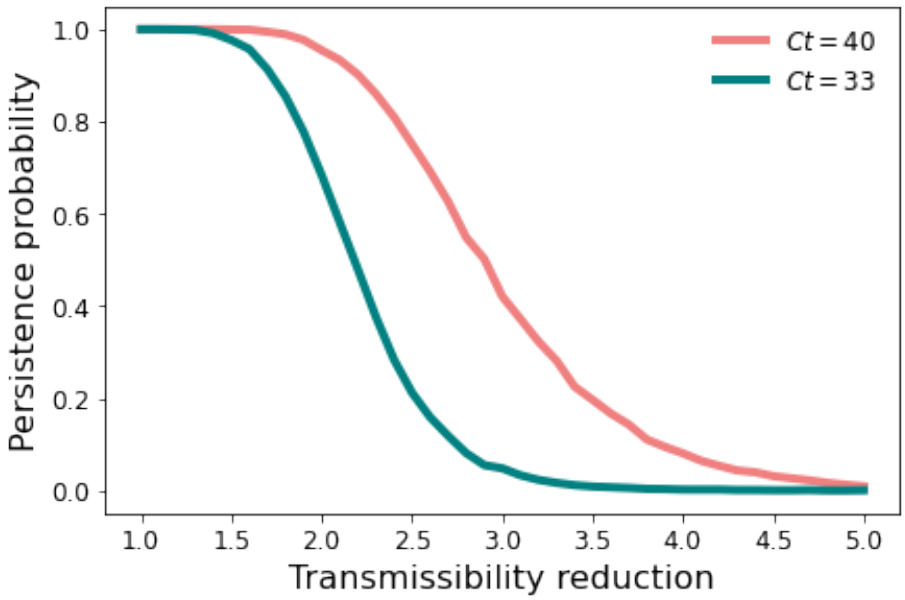
Supplementary Figure 3: **Time since prior exposure.** Panels show cumulative distributions of time since prior exposure for BR (A) and BY (B) chickens, respectively. Red and teal lines correspond to distributions obtained from fits to $Ct = 40$ and $Ct = 33$ data, respectively. Solid lines account for any possible state a chicken might be in when it is introduced in the LBM, provided it had been exposed to AIV previously, whereas dashed lines are restricted to recovered (R_+ and R_-) chickens only. In the former case, we sample once from $f(\tau) \sim \Gamma(\lambda_b, \kappa_b)$, $b = BR, BY$ for each available sample from the posterior distribution. In the latter case, we used sampling importance re-sampling to sample from $f(\tau|R_+ \cup R_-)$ (see Eq. SS7). For both fits we set $l_\beta = 0.005$ and $\bar{T}_{EI} = 5$ days.



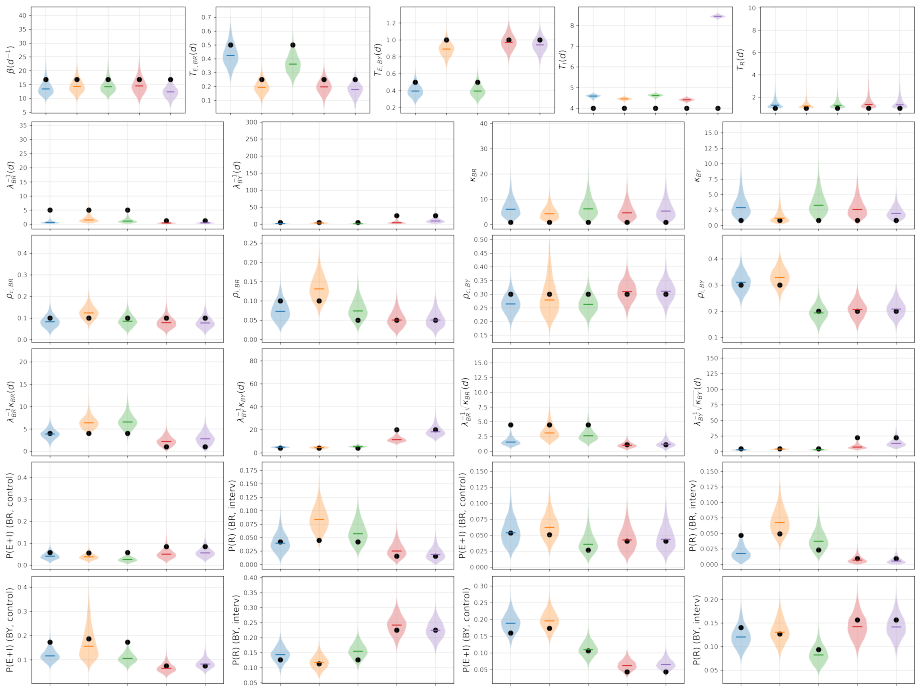
Supplementary Figure 4: **Sensitivity to prior assumptions on β.** Here we repeated the fit to $Ct = 40$ data whilst varying l_β. (A-M) Posterior marginal distributions of fitted parameters. (N) Probability of a chicken remaining susceptible after a given amount of time spent at the market. Probability of broiler (O) and backyard chickens (P) being already in E or I compartments (filled) or recovered (hatched) at market entrance. (Q-T) Posterior mean (bars) and 95% C.I. (grey error bars) for the numbers of chickens becoming positive (filled) at different stages of the experiment or remaining susceptible (hatched). Black dots and error bars denote data and 95% C.I. computed under a binomial distribution assumption. We ran 30000 simulations with 5 control and 5 intervention chickens from 3000 independent posterior samples to estimate the probability of turning positive at different times. Expected counts were obtained by multiplying these probabilities by the number of recruited chickens in each category. We set $\bar{T}_{EI} = 5\,d$ for all fits.



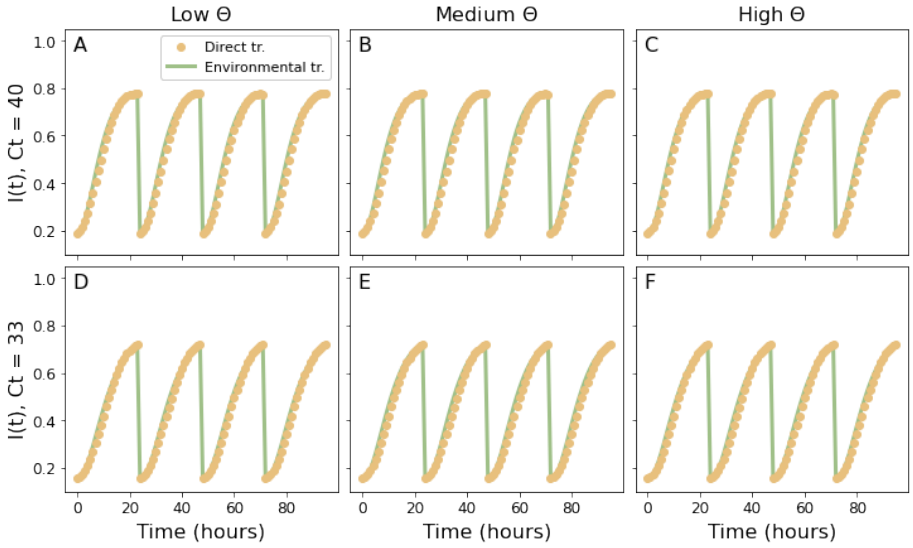
Supplementary Figure 5: **Sensitivity to prior assumptions on $\bar{T}_{EI}$.** Here we repeat the fit to $Ct = 40$ data whilst varying the hyper-parameter $\bar{T}_{EI}$. Figure structure is the same as Fig. S4. We set $l_\beta = 0.005$ for all fits.



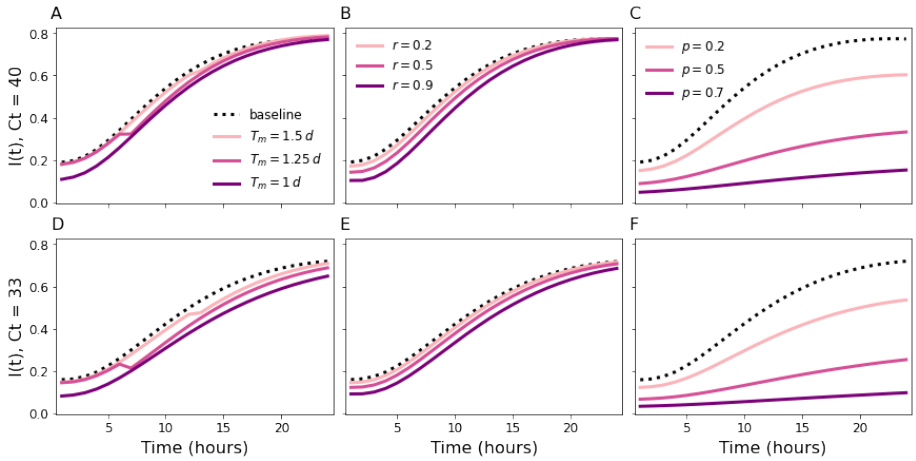
Supplementary Figure 6: **Probability of AIV persistence.** We measure the proportion of 2000 simulations where at least one latent or infectious chicken is observed at $t = 50$ days, assuming that all chickens entering the market after $t = 20$ days are susceptible. In other words, we compute the probability that AIV persists within the LBM for 30 days without any external supply of infected chickens. Each simulation corresponds to a different sample from the posterior distribution. Red and teal lines correspond to $Ct = 40$ and $Ct = 33$ posterior distributions, respectively. Lines show how the probability of persistence decays when β is reduced by a constant factor indicated on the x axis.



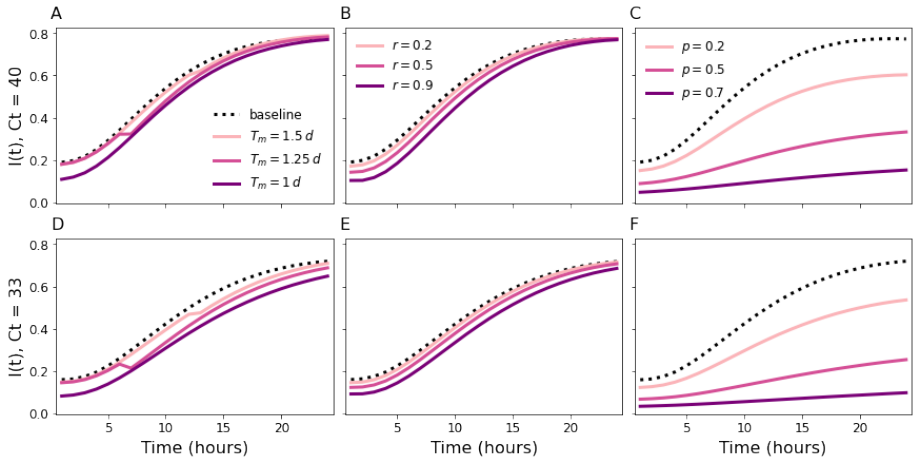
Supplementary Figure 7: **Model fit to simulated data.** We used our model to generate synthetic data under 5 different parameter sets. The model was then fitted to these data and its ability to recover true parameters was assessed. In the baseline scenario, the leftmost in each panel, model parameters are the same for broiler and backyard chickens (true parameter values are indicated with black markers). Scenarios 2 and 3 introduce differences in latent periods and $\rho_{g,b}$ across chicken types, respectively, while scenario 4 accommodates both variations simultaneously. Scenario 5 is identical to 4, but the prior distribution on total shedding time is strongly misspecified ($\bar{T}_{EI} = 9$ days instead of 5 days in previous fits). For each parameter set, we simulated 100 independent datasets of the same size as the empirical one; then, we selected the sample that deviated the least from the average trajectory $\bar{n}^{+/-}_{g,b}(t)$, based on the L_2 distance. Panels show posterior marginal distributions (violin plots) for fitted parameters, mean and standard deviation of type-specific time since past infection-given by $\lambda_b^{-1}\kappa_b$ and $\lambda_b^{-1}\sqrt{\kappa_b}$, respectively, and probabilities of chickens entering the market as latent or infectious, $P(E+I)$, and recovered, $P(R)$. For each fit, we obtained 3080 samples (using the same thinning and burn-in as in the main analysis). In all fits, we set $l_\beta = 0.005$.



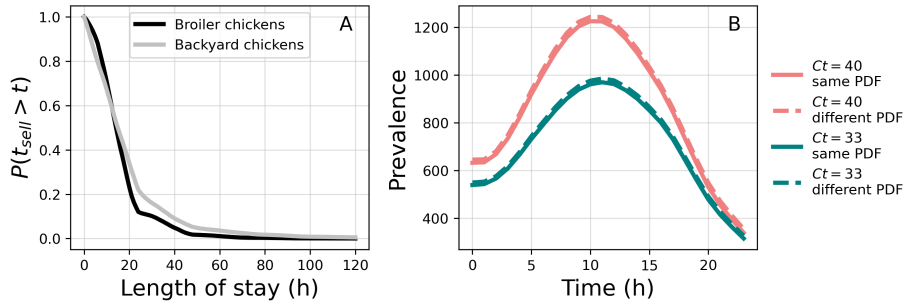
Supplementary Figure 8: **Comparison of direct vs environmental transmission.** Each panel shows average AIV prevalence in chickens under direct (dots) and environmental transmission (line) for three different values of decay rate Θ corresponding to different columns. First and second rows correspond to posterior samples from fits to $Ct = 40$ and $Ct = 33$ data, respectively. In both cases, we ran 5000 simulations from 500 posterior samples. In the case of environmental transmission, we mapped β to $\beta_{env} = \beta \cdot (1 - e^{-\Theta})$ for each posterior sample.



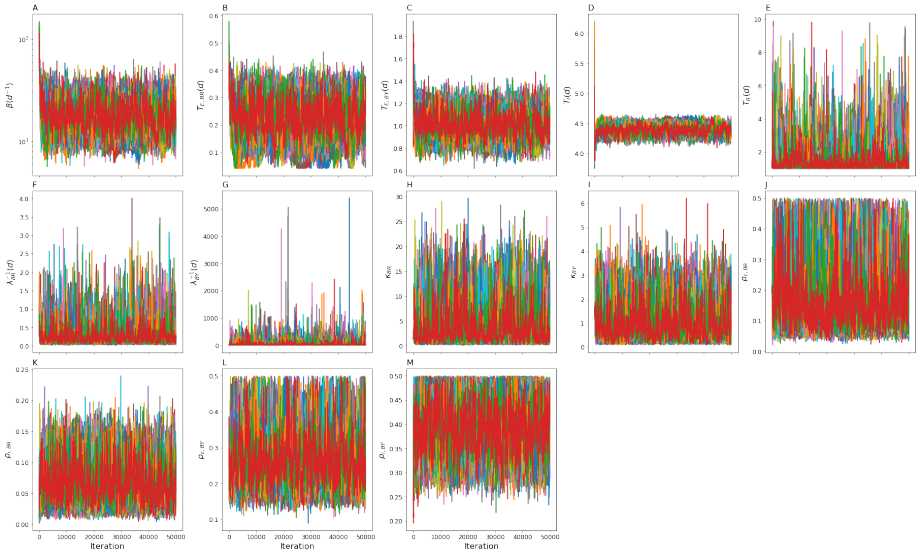
Supplementary Figure 9: **Prevalence dynamics under intervention measures and direct transmission.** Results for early chicken removal/culling (A,D), reduction in probability of prior exposure (B,E) and preemptive immunisation through vaccination (C,F). Each panel shows the time series of AIV prevalence over a single day, under varying levels of strength of intervention. Top and bottom rows correspond to posterior samples from fits to $Ct = 40$ and $Ct = 33$ data, respectively. In both cases, we ran 5000 simulations from 500 posterior samples.



Supplementary Figure 10: **Prevalence dynamics under intervention measures and environmental transmission.** Results for early chicken removal/culling (A,D), reduction in probability of prior exposure (B,E) and preemptive immunisation through vaccination (C,F). Each panel shows the time series of AIV prevalence over a single day, under varying levels of strength of intervention. Top and bottom rows correspond to posterior samples from fits to $Ct = 40$ and $Ct = 33$ data, respectively. In both cases, we ran 5000 simulations from 500 posterior samples. We mapped β to $\beta_{env} = \beta \cdot (1 - e^{-\Theta})$ for each posterior sample. We used the same value of Θ as in the main text.



Supplementary Figure 11: **Epidemic dynamics with different length of stay distributions.** (A) Length of stay survival distributions for broiler (black) and backyard (grey) chickens. (B) Average hourly number of infectious chickens when using a shared (solid) or a type-specific (dashed) length of stay distribution. Red and teal lines correspond to fits to $Ct = 40$ and $Ct = 33$ data, respectively. In both cases, we ran 5000 simulations from 500 posterior samples obtained under a shared length of stay distribution (as in the main analysis).



Supplementary Figure 12: **Trace plot for fitted parameters.** Each panel shows the dynamics of individual Markov chains obtained from the fit to $Ct = 40$ data, up to iteration 50000. For this fit we set $l_\beta = 0.005$ and $\bar{T}_{EI} = 5$ days.

3 Supplementary Tables

Supplementary Table 1: **Fitted parameters and priors.** We set a tight normal prior on $T_{EI} = \mu^{-1} + (\sigma_{BR}^{-1} + \sigma_{BY}^{-1})/2$, with mean $\bar{T}_{EI}$. The prior on β assigns a penalty to values that are too large compared to $N\mu l_\beta$, where N is the total number of chickens introduced on a given day and l_β is an hyper-parameter. Baseline values for hyper-parameters are indicated in bold.

Name	**Prior**	**Range**	**Notes**
β	$\propto \mu^{-1} e^{-\beta/N\mu l_\beta}$	$(0, \infty)$	$l_\beta = 0.002, \mathbf{0.005}, 0.1$
σ_{BR}	$T_{EI} \sim \mathcal{N}(\bar{T}_{EI}, 6.6 \cdot 10^{-3}\ d)$	$(0.05, 24)\ d^{-1}$	$\bar{T}_{EI} = 3, \mathbf{5}, 7, 9\ d$
σ_{BY}	$T_{EI} \sim \mathcal{N}(\bar{T}_{EI}, 6.6 \cdot 10^{-3}\ d)$	$(0.05, 24)\ d^{-1}$	See above
μ	$T_{EI} \sim \mathcal{N}(\bar{T}_{EI}, 6.6 \cdot 10^{-3}\ d)$	$(0.067, 0.5)\ d^{-1}$	See above
η	Flat	$(0.1, 1)\ d^{-1}$	-
λ_{BR}	$\chi^2(4)$	$(0, \infty)\ d^{-1}$	-
λ_{BY}	$\chi^2(4)$	$(0, \infty)\ d^{-1}$	-
κ_{BR}	$\chi^2(4)$	$(0, \infty)$	-
κ_{BY}	$\chi^2(4)$	$(0, \infty)$	-
$\rho_{c,BR}$	Flat	$(0, 0.5]$	-
$\rho_{i,BY}$	Flat	$(0, 0.5]$	-
$\rho_{c,BR}$	Flat	$(0, 0.5]$	-
$\rho_{i,BY}$	Flat	$(0, 0.5]$	-

References

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