Estimating transmission of avian influenza in wild birds from incomplete epizootic data: implications for surveillance and disease spread

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Summary

1. Estimating disease transmission in wildlife populations is critical to understand host–pathogen dynamics, predict disease risks and prioritize surveillance activities. However, obtaining reliable estimates for free-ranging populations is extremely challenging. In particular, disease surveillance programs may routinely miss the onset or end of epizootics and peak prevalence, limiting the ability to evaluate infectious processes.

2. We used profile likelihood to estimate the force of infection (FOI) in a low pathogenic avian influenza virus (LPAIv) epizootic model from censored time series of LPAIv prevalence in hatch-year waterfowl (order Anseriformes) at postbreeding and migration sites in North America.

3. We found a mean LPAIv FOI of 0.12 day⁻¹ [95% CI, 0.00–0.39], corresponding to an incidence rate of 0.11 day⁻¹, with geographic heterogeneity (min–max: 0.02–0.23 day⁻¹) among study sites. These high infection rates indicate that most hatch-year waterfowl are likely infected with LPAIv early in the fall migration.

4. Comparison of model-predicted and observed immunity confirmed our assumption of naïve hatch-year waterfowl and suggested long-term immunity (>6 months) for adults.

5. Using the mean LPAIv incidence rate, we predict a shorter and lower epizootic curve for highly pathogenic avian influenza virus (HPAIv; 5 weeks with peak prevalence of 28% and 30% mortality) than LPAIv (8 weeks with peak prevalence of 50%). These findings indicate it is harder to detect HPAIv than LPAIv with swabs from live birds, which are commonly used during disease surveillance.

6. Synthesis and applications. Our study highlights the potential of integrating incomplete surveillance data with epizootic models to quantify disease transmission and immunity. This modelling approach provides an important tool to understand spatial and temporal epizootic dynamics and inform disease surveillance. Our findings suggest focusing highly pathogenic avian influenza virus (HPAIv) surveillance on postbreeding areas where mortality of immunologically naïve hatch-year birds is most likely to occur, and collecting serology to enhance HPAIv detection. Our modelling approach can integrate various types of disease data facilitating its use with data from other surveillance programs (as illustrated by the estimation of infection rate during an HPAIv outbreak in mute swans Cygnus olor in Europe).

Key-words: epidemiological model, epizootic dynamics, force of infection, highly pathogenic avian influenza, incidence, low pathogenic avian influenza, maximum likelihood, prevalence

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Introduction

Infectious diseases of wildlife are of great concern for wildlife, domestic animal and human health and may cause significant economic loss (Daszak, Cunningham & Hyatt 2000; Dobson & Foufopoulos 2001; Jones et al. 2008). As much as 60% of emerging infectious diseases are zoonotic, with 72% originating from wildlife (Jones et al. 2008). Wildlife diseases represent a major threat to biodiversity and conservation of endangered wildlife (Daszak, Cunningham & Hyatt 2000). Avian malaria in Hawaiian forest birds (Samuel et al. 2011), facial tumour disease in Tasmanian devils Sarcophilus harrisii (McCallum et al. 2009) or upper respiratory tract disease in gopher tortoises Gopherus polyphemus (Ozgul et al. 2009) are examples of diseases causing major declines in wildlife populations. Understanding host–pathogen interactions, estimating the rate of disease transmission, and determining factors that drive epizootic dynamics in natural populations are central goals for researchers and managers to limit the impact of pathogens in wildlife populations, predict disease occurrence and reduce domestic animal and public health risks.

Transmission is a key process in host–pathogen interactions, and the rate of pathogen transmission to susceptible individuals is the primary driver of infectious disease dynamics (McCallum 2000). The force of infection (FOI) describes the incidence rate or instantaneous per capita rate a pathogen infects susceptible animals (McCallum 2000), whereby $f(t, \lambda) = 1 - \exp(-\lambda t)$, where $\lambda$ is the FOI and $t$ is the time period. The FOI determines the proportion of infected individuals in the population at a given time, defines the shape of the epizootic curve and predicts the number of susceptible individuals that will become infected. Such information is critical to predict epizootic dynamics, the number of infectious carriers and spread of pathogens across the landscape, and identify populations at risk. Although estimating FOI and identifying factors that drive transmission is informative for understanding disease dynamics, data are seldom available to estimate these parameters in wild animals where infection events are difficult to track and observe. As a result, little is typically known about epizootiological processes in wildlife, severely limiting our ability to predict pathogen spread or develop disease control strategies.

Disease surveillance provides an opportunity to detect and acquire information on pathogens circulating in wildlife (Mörner et al. 2002). An increasing number of studies rely on temporal and spatial prevalence data to assess the FOI (Caley & Hone 2002; Heisey, Joly & Messier 2006). The usual approach to estimating FOI is based on repeated monitoring of susceptible sentinel in a population to determine how quickly they become infected (McCallum 2000; McCallum, Barlow & Hone 2001). This method is especially applicable to chronic diseases, characterized by a prolonged course of infection, because newborn individuals can serve as uninfected tracers. In this context, a cross-sectional sample of the population gives age-specific apparent prevalence from which FOI can be estimated (Caley & Hone 2002; Heisey, Joly & Messier 2006). Analysis of longitudinal serology data for diseases with long-term antibody response to infection may also provide estimates for infection rate (Hazel et al. 2000). In some cases, cross-sectional and longitudinal data can be combined to estimate FOI (Atkinson & Samuel 2010). Accounting for heterogeneity in detection probabilities or mortality caused by disease is sometimes required to reduce bias (Jennelle et al. 2007; Atkinson & Samuel 2010).

Accurate FOI estimates are essential for evaluating the significance of short-term epizootics, determining the basic reproductive rate of the disease ($R_0$), informing disease management and guiding surveillance programs. However, cross-sectional and longitudinal analyses are seldom applicable to wildlife epizootics because of their transient nature. Most wildlife disease outbreaks are discovered after they have occurred, when most of the affected individuals are dead or have migrated (Wobeser 2007). This problem provides incomplete data, which makes the estimation of transmission parameters challenging. In contrast, disease surveillance programs usually provide discontinuous, short-term data, which results in censoring at the onset or end of epizootics or missing peak prevalence (Fig. 1). These incomplete data can mask the length and shape of epizootic curves and limit or prevent their evaluation and interpretation. However, combining surveillance data with epizootiological models may be an effective approach to deal with incomplete information from epizootics.

Wild aquatic birds (primarily Anseriform and Charadriiform) are considered to be the reservoir of most subtypes of low pathogenic avian influenza viruses (LPAIVs) (Olsen et al. 2006). The transmission of AI viruses among birds results primarily from faecal/oral transmission by direct contact or through the environment (Hinshaw, Webster & Turner 1980). When transmitted to domestic birds, H5 and H7 LPAIV may mutate to highly pathogenic (HP) AI viruses defined as an AI virus causing at least 75% mortality in 4- to 8-week-old chickens infected intravenously (Suarez 2008). HPAIV outbreaks can produce important domestic bird losses, are a potential source of zoontic infection (Stallknecht et al. 2007) and may spill-over into wild populations. Laboratory studies have demonstrated differences in the virulence of LP and HPAIV in waterfowl, which is essential to develop and inform epizootic models of LP and HPAIV infection in individual birds (Hénaux, Samuel & Bunck 2010). In parallel, the threat of migratory birds spreading HPAIVs (Feare & Yasué 2006) resulted in world-wide surveillance (Hoye et al. 2010) that has rarely detected HPAIVs (Chen et al. 2006; Gaidet et al. 2008) but provided extensive information on prevalence and subtypes of LPAIVs in wild birds.

In this paper, we use profile likelihood to estimate FOI for an LPAIV epizootic model (Hénaux, Samuel & Bunck 2010) using incomplete time series of LPAIV prevalence in hatch-year waterfowl at postbreeding and migration sites in North America (Fig. 2). We also investigate LPAIV
immunity in blue-winged teal Anas discors at one postbreeding site and verify predicted with observed seroprevalence. Because HPAIV outbreaks are rare, typically detected by sudden and significant mortality events at the end of epizootics, monitoring and estimating HPAIV dynamics in wild bird populations is more difficult. Using the FOI estimate for LPAIV as a proxy for HPAIV, we project potential HPAIV dynamics for wild birds in North America and evaluate the implications for surveillance and risk of spread. We also illustrate the application of our modelling framework to HPAIV mortality data in mute swan Cygnus olor during a 2006 outbreak in France (Appendix S1, Supporting Information).

Materials and methods

ESTIMATION OF LPAIV INFECTION

Field data

We used data on prevalence of LPAIV infection in migratory waterfowl (order Anseriformes) collected during AV surveys at postbreeding areas in Canada during August–September 2005–2007 (Parmley, Lair & Leighton 2009; Pasick et al. 2010) and at United States migratory staging areas in the Pacific flyway during August–November 2006 (Dusek et al. 2009; Fig. 2). Matrix gene reverse real-time Polymerase Chain Reaction (rRT-PCR) was used to detect influenza A virus from cloacal swabs collected in Canada in 2005 and in the United States in 2006, and from pooled cloacal and oropharyngeal swabs in Canada in 2006–2007. Details on sampling protocol and laboratory analyses were provided previously (Dusek et al. 2009; Parmley, Lair & Leighton 2009; Pasick et al. 2010). Serum samples were collected from 44 adult and 149 hatch-year blue-winged teal during August 15–18, 2007, at the Saskatchewan (SK) site. Sera were frozen at −20°C until tested for influenza A specific nucleoprotein antibodies using a competitive ELISA as previously described (Zhou et al. 1998).

To estimate the FOI for LPAIV, we used infection rates from fledged hatch-year birds, which are unlikely to have been previously infected with LPAIV or have maternal antibodies against Alv (Swayne & Halvorson 2003, p. 149). We pooled LPAIV infection data for birds sampled within 7-day intervals and within a 100-km radius to reduce limitations from sparse data. We only used sample periods where at least 10 birds were tested; a sample sufficient to achieve >0.85 probability of detecting more than one Alv-infected individual given an expected prevalence >20% (Hoye et al. 2010). Surveillance was closely linked with bird-banding programs and was not specifically designed to track Alv epizootic patterns. Therefore, weekly patterns of LPAIV prevalence can provide an incomplete picture of the epizootic curve (Fig. 1) because sampling stopped before the epizootic ended (right censoring; Fig. 2, ON) or both right and left censoring (Fig. 2, QC) or infrequent sampling occurred (Fig. 2, ID). We only considered surveillance data where ≥3 weeks of prevalence depicted the typical increase or decrease in prevalence of an epizootic curve.

Epizootic model

We used an SEIR (susceptible, exposed, infectious and recovered) model for LPAIV epizootiology (Hénaux, Samuel & Bunck 2010). Following contact with LPAIV, a susceptible (S) host becomes exposed (E) and enters a latent period when the virus colonizes the digestive and respiratory tracts. Next, the host becomes infectious (I) and sheds virus for a period of time. Because LPAIV is not pathogenic in waterfowl (Stallknecht et al. 2007), all birds recover (R) from infection and no longer shed virus. This model was described by the following set of differential equations:

\[
\frac{dS}{dt} = -\lambda S \quad \text{eqn 1}
\]

\[
\frac{dE}{dt} = \lambda S - \sigma E \quad \text{eqn 2}
\]

\[
\frac{dI}{dt} = \sigma E - \gamma I \quad \text{eqn 3}
\]

\[
\frac{dR}{dt} = \gamma I \quad \text{eqn 4}
\]

where \( \lambda \) is the FOI, \( \sigma \) is the rate latent birds become infectious and \( \gamma \) is the recovery rate. This SEIR model assumes a geographically closed population (no immigration or emigration), no disease-induced mortality, a similar probability of detecting susceptible and
infected birds, and the initial population is completely susceptible. For our model, we assumed a single LPAIv such that recovered birds are assumed to be resistant to further AIv infection for the rest of the epizootic which is equivalent to complete cross-immunity among LPAIv subtypes. We did not include background mortality, given the short duration of LPAIv epizootics, nor birth because data were collected during the nonbreeding season. The model had a 1-day time step with LPAIv introduced on day 1. We used latent and recovery rates for young (<1.5-month-old) individuals from Hénaux, Samuel & Bunck (2010) (Table 1); because sampling was conducted in October–November at WA2, we ran the model with parameter values for adult birds (Table 1) at this site.

Profile likelihood approach

We used profile likelihood methods (Hobbs & Hilborn 2006) to calculate FOI ($\lambda_i$) for each sample location ($i$) using our SEIR model, parameter estimates ($\sigma$ and $\gamma$) and the weekly ($t$) observed prevalence of LPAIv infection ($\rho_{i,t}$). $\rho_{i,t}$ corresponds to the binomial probability that birds sampled at site $i$ and period $t$ were infected with LPAIv. We evaluated a model with constant FOI (exponentially distributed), which provided a mean FOI for each epizootic. We also considered Weibull (i.e. increasing or decreasing rate) and loglogistic models (i.e. rate increases initially and then decreases) to evaluate nonconstant FOI, which could result when infectious contact is density or frequency dependent.

Table 1. Transition rates between epidemiological states for low (LPAIv) and highly pathogenic avian influenza virus (HPAIv) in waterfowl (from Hénaux, Samuel & Bunck 2010)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HPAIv</th>
<th>LPAIv</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
<td>Young</td>
</tr>
<tr>
<td>$\sigma^*$ (Exponential)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate $\pm$ SD</td>
<td>2.47 ± 0.40</td>
<td>1.12 ± 0.15</td>
</tr>
<tr>
<td>$\gamma^*$ (Logistic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scale $\pm$ SD</td>
<td>4.62 ± 1.17</td>
<td>5.32 ± 1.07</td>
</tr>
<tr>
<td>Shape</td>
<td>2.46</td>
<td>2.46</td>
</tr>
<tr>
<td>$d^d$ (Loglogistic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scale $\pm$ SD</td>
<td>17.90 ± 1.29</td>
<td>5.16 ± 1.09</td>
</tr>
<tr>
<td>Shape</td>
<td>2.26</td>
<td>2.26</td>
</tr>
</tbody>
</table>

$^*\sigma$ = latent rate.
$^*\gamma$ = recovery rate.
$^d$d = disease-induced mortality rate; not applicable (n/a) for LPAIv.
or occurs through direct vs. environmental routes of transmission. Because surveillance at each location usually occurred before or after the onset of the epizootic, we estimated a lag parameter (t) to temporally align modelled LPAIV epizootics and field observations (Fig. 1). A lag of t days (or ≤4 days) indicated that the first day of sampling occurred t days after (or before) the predicted onset of the epizootic. We determined the maximum likelihood value for λc and t by maximizing \( \sum \ln(L(\lambda_c, t)) \) wi, Lc, η0, σ, γ), the sum of the binomial log-likelihood values of the model-predicted prevalence on the first day of week t given the number of LPAIV-positive birds (Lc) among all birds (ni, wi) sampled in week t at location i. We used Akaike information criterion (AIC) corrected for small sample size (Burnham & Anderson 2002) to determine which FOI model (exponential, Weibull or loglogistic) provided the best fit to epizootic data at each site.

We estimated the 95% confidence interval of λc, as the two λ values for which the marginal log-likelihood was 1.92 (half of the \( \chi^2_{0.999} \) critical value) less than the maximum value of log-likelihood (Bolker 2008, p. 188). We approximated standard error, SE(λc), by dividing the confidence interval of λc, which may be asymmetric, by 3.92 (2 × \( \text{z}_{0.975} \)). We estimated the average rate of infection \( \lambda \) and SE(\( \lambda \)) across all sites using multiple imputation to combine parameters (Rubin 1987, p. 85). Let m denote the number of epizootics, then \( \hat{\lambda} = \frac{1}{m} \sum_{i=1}^{m} \hat{\lambda}_i \), and SE(\( \lambda \)) = \( \sqrt{\text{SE}^2(\hat{\lambda}) + (1 + \frac{1}{m})B} \), with the within epizootic variance \( \text{SE}^2(\hat{\lambda}) = \frac{1}{m} \sum_{i=1}^{m} \text{SE}^2(\hat{\lambda}_i) \) and the between epizootic variance \( B = \frac{1}{m} \sum_{i=1}^{m} (\hat{\lambda}_i - \hat{\lambda})^2 \).

We used \( \hat{\lambda} \) to investigate and compare simulated LPAIV and HPAIV dynamics at postbreeding grounds using a waterfowl population of 10 000 susceptible birds, composed of 50% adult and 50% hatch-year birds (Bellrose 1980, p. 230). For the simulation of the HPAIV epizootic, we included an HPAIV-induced mortality rate (d) in the SEIR model so eqn 3 was \( \frac{dI}{dt} = aE - \gamma I - dI \). We used parameter values for latent (\( \gamma \)) and mortality (d) rates estimated for HPAIV-infected waterfowl (Table 1).

LPAIV IMMUNITY

We also illustrate the application of this modelling approach for estimating LPAIV immunity in adult waterfowl. We used LPAIV surveillance data of hatch-year (n = 4 weeks) and adult (n = 4 weeks) waterfowl at the SK site to estimate both FOI and the proportion of LPAIV immune birds; this was the only site where serology data were collected on large numbers of adult and hatch-year birds. We used profile likelihood to estimate the lag and FOI (constrained to be the same for adult and hatch-year birds) and estimate the proportion of immune adults (1 – proportion of susceptible adults) at the onset of the epizootic; we used latent and recovery rates from Hénaux, Samuel & Bunc (2010) (Table 1) and assumed all hatch-year birds were susceptible. We calculated an approximate confidence interval for the predicted seroprevalence of blue-winged teal using the lower and upper bound values of the 95% CI for FOI and compared this to observed data.

HPAIV INFECTION IN MUTE SWANS

Documented HPAIV outbreaks in wild waterfowl consist exclusively of the number of HPAIV-positive dead birds reported to the World Animal Health Organization (OIE). We used cumulative counts of HPAIV-positive mute swan carcasses found during the H5N1 epizootic in the Dombes region in France during February–April 2006 to estimate FOI. We describe in Appendix S1 (Supporting Information) how to apply our modelling framework to this epizootic.

Results

LPAIV INFECTION IN NORTH AMERICAN WATERFOWL

Weekly LPAIV prevalence data were obtained for hatch-year birds (primarily mallard Anas platyrhynchos, American black duck A. rubripes and blue-winged teal A. discors) in July–November 2005–2007 at multiple locations in North America (Table 2). The model considering a constant FOI at each study site provided the best (or similar) fit to the epizootic data compared to other FOI distributions (Table S1, Supporting Information). Our maximum likelihood estimates of FOI (\( \lambda \)) ranged from 0.02 to 0.26 day\(^{-1} \) among study sites (Table 2) with an average daily FOI (\( \hat{\lambda} \)) of 0.12 [left truncated 95% CI, 0.00–0.39], corresponding to an incidence rate of 0.11 day\(^{-1} \) [0.00–0.32]. We found lower incidence rates (0.04–0.09) in the Pacific flyway (BC, WA and ID), high rates in central Canada (0.23 at SK and 0.21 at MB) and variable, intermediate rates in eastern provinces (0.02–0.18 in ON, QC, NB and NS; Fig. 2).

Our model predicted that 32.6% [95% CI: 24.4–42.2] of hatch-year birds in SK were seropositive during the second week of sampling in 2007 and 23.5% [16.7–30.3] of sampled hatch-year blue-winged teal had AIv antibodies. We extended our model to assess adult immunity to circulating LPAIV at SK (2007); adult bird species were primary mallard (56%), northern pintail A. acuta (31%) and blue-winged teal (12%), with a mean number of 146 individuals sampled per week (min–max: 46–222). Based on weekly LPAIV prevalence in hatch-year and adult birds, our model predicted a FOI of 0.22 day\(^{-1} \) [0.17–0.29] and estimated that 51% [42–60] of the adult waterfowl population had immunity to circulating LPAIV before the start of the epizootics (Fig. 2) and 69.7% [65.1–75.0] by the second week. Field data indicated that 84.1% [73.3–94.9] of adult blue-winged teal were seropositive during that week.

SIMULATED LP VS. HPAIV EPIZOOTIC DYNAMICS

Using \( \hat{\lambda} = 0.12 \), our model predicted an LPAIV epizootic of 8 weeks with peak prevalence (50%) during the second week (Fig. 3) at postbreeding grounds in North America. In contrast, this transmission rate in the HPAIV epizootic model produced an epizootic curve lasting 5 weeks with a peak prevalence of 28% during the first week and cumulative HPAIV-induced mortality reached 30% of the population (Fig. 3).
**Table 2.** Data description, estimated lag (t) and site-specific force of infection (λ) for low pathogenic avian influenza virus in hatch-year birds in North America in 2005–2007

<table>
<thead>
<tr>
<th>Site*</th>
<th>Sampling period</th>
<th>Species†</th>
<th>T‡</th>
<th>Mean weekly sample size (min–max)</th>
<th>λ [95% CI]§</th>
<th>t [95% CI]¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB</td>
<td>08/2005</td>
<td>MALL (45%), REDH (37%), BWTE (13%)</td>
<td>4 44 (16–77)</td>
<td>0.24 [0.11–1.00]</td>
<td>10 [5–15]</td>
<td></td>
</tr>
<tr>
<td>NS</td>
<td>08/2005</td>
<td>MALL (47%), ABDU (31%), AMWI (11%)</td>
<td>4 30 (10–53)</td>
<td>0.11 [0.06–1.00]</td>
<td>10 [2–17]</td>
<td></td>
</tr>
<tr>
<td>BC</td>
<td>08/2006</td>
<td>MALL (94%)</td>
<td>5 126 (12–229)</td>
<td>0.07 [0.06–0.09]</td>
<td>4 [3–7]</td>
<td></td>
</tr>
<tr>
<td>ID</td>
<td>08–10/2006</td>
<td>MALL (50%), AMWI (18%), AGWT (20%)</td>
<td>4 22 (10–38)</td>
<td>0.07 [0.05–0.11]</td>
<td>9 [5–14]</td>
<td></td>
</tr>
<tr>
<td>WA1</td>
<td>07–08/2006</td>
<td>MALL (100%)</td>
<td>5 25 (12–35)</td>
<td>0.07 [0.03–0.17]</td>
<td>8 [3–24]</td>
<td></td>
</tr>
<tr>
<td>WA2**</td>
<td>10–11/2006</td>
<td>NSHO (61%), CACG (39%)</td>
<td>5 22 (11–33)</td>
<td>0.09 [0.05–0.17]</td>
<td>7 [3–15]</td>
<td></td>
</tr>
<tr>
<td>SK</td>
<td>08/2007</td>
<td>BWTE (58%), NOPI (22%), MALL (19%)</td>
<td>4 75 (49–153)</td>
<td>0.26 [0.15–0.58]</td>
<td>6 [4–8]</td>
<td></td>
</tr>
<tr>
<td>QC</td>
<td>08/2007</td>
<td>MALL (93%), ABDU (5%)</td>
<td>3 147 (95–278)</td>
<td>0.11 [0.09–0.15]</td>
<td>5 [4–6]</td>
<td></td>
</tr>
<tr>
<td>NS/NB2</td>
<td>08/2007</td>
<td>ABDU (45%), MALL (33%), AMWI (10%)</td>
<td>5 106 (32–237)</td>
<td>0.02 [0.02–0.03]</td>
<td>4 [3–8]</td>
<td></td>
</tr>
<tr>
<td>NB1</td>
<td>09/2007</td>
<td>ABDU (71%), AGWT (23%), MALL (6%)</td>
<td>3 70 (21–139)</td>
<td>0.20 [0.15–0.26]</td>
<td>2 [1–3]</td>
<td></td>
</tr>
<tr>
<td>BC</td>
<td>08–09/2007</td>
<td>MALL (91%)</td>
<td>4 86 (12–162)</td>
<td>0.04 [0.03–0.07]</td>
<td>17 [4–21]</td>
<td></td>
</tr>
<tr>
<td>ON</td>
<td>08–09/2007</td>
<td>MALL (100%)</td>
<td>4 45 (10–71)</td>
<td>0.14 [0.06–1.00]</td>
<td>22 [15–28]</td>
<td></td>
</tr>
</tbody>
</table>

*Study sites were in the Canadian provinces of British Columbia (BC), Manitoba (MB), New Brunswick (NB), Nova Scotia (NS), Ontario (ON), Quebec (QC), and Saskatoon (SK), Canada, and US states of Idaho (ID) and Washington (WA).

†For each site, the three most represented species (whose proportion ≥5%) included American black duck *Anas rubripes* (ABDU), American wigeon *A. americana* (AMWI), blue-winged teal *A. discors* (BWTE), American green-winged teal *A. crecca* (AGWT), mallard *A. platyrhynchos* (MALL), northern pintail *A. acuta* (NOPI), northern shoveler *A. clypeata* (NSHO), cackling goose *Branta hutchinsii* (CACG), lesser scaup *Aythya affinis* (LESC), redhead *A. americana* (REDH).

‡T is the number of weeks with LPAIv infection prevalence.

§Most likely site-specific force of infection and 95% confidence interval.

¶Most likely site-specific lag and 95% confidence interval; the lag parameter allows the most likely temporal scaling of model-predicted prevalence to field observations at the site. A lag of t days indicated that the first sampling occurred t days after the predicted onset of the epizootic.

**Because sampling was conducted in October–November, we ran the model with parameter values for adult birds (≥1.5-month-old).

Fig. 3. Simulated epizootic curve for low and highly pathogenic avian influenza at postbreeding grounds. Simulations are based on a daily force of infection of 0.12 day−1 in populations composed of 50% adult and 50% hatch-year birds. The grey line represents the change in prevalence of infection over time for low pathogenic avian influenza virus (LPAIv). The solid and dashed black lines represent the epizootic curve for highly pathogenic (HPAIv) and the cumulative proportion of dead birds over time, respectively.

**Discussion**

Transmission of infectious diseases, such as AIv, in wild populations is complex, nonlinear and difficult to extrapolate from laboratory experiments. Mathematical models can help unravel these processes and constitute an accepted tool to help control infectious diseases or develop efficient surveillance programs (Diekmann & Heesterbeek 2000). Simple analytical models may clarify essential components of the epidemiological process, simulate outbreaks and predict the rate and spread of infection in populations. The quantitative knowledge of AIv transmission is critical in epizootic dynamics because it determines the prevalence of infection over time and therefore the probability of detection during surveillance. This parameter may also be implemented in simulation models to evaluate alternative disease control scenarios. Such models have been previously applied to AIv in poultry populations (review in Stegeman, Bouma & de Jong 2010). Our paper highlights the value of using simple analytical models to integrate scientific knowledge from field and laboratory studies to overcome limitations from incomplete observational data (McCallum, Barlow & Hone 2001) and facilitate understanding rapid, short-lived epizootics in wildlife populations. We used multi-year surveillance data in North American waterfowl to investigate AIv infection rates, simulate epizootics dynamics, inform surveillance practices and identify important areas for further research. To our knowledge, these are the first estimates of LPAIv infection rates for wild waterfowl in North America.

Our analysis showed more support for a model with constant FOI for LPAIv epizootics; however, the short time series of prevalence data likely limited our ability to evaluate alternative FOI models. Site-specific FOI ranged...
from 0.02 to 0.26 day$^{-1}$ at postbreeding and northern migration sites in North America. The average FOI was 0.12 day$^{-1}$, corresponding to a daily incidence rate of 11% for susceptible birds. This average LPAIV incidence rate produced an 8-week epizootic with peak prevalence reaching 50%. This pattern implies that a high proportion of hatch-year birds are exposed to Alv during early fall migration and subsequently develop immunity (Journain et al. 2010) that reduces the susceptible pool during late fall and winter (e.g. Stallknecht et al. 1990; Olsen et al. 2006; Munster et al. 2007; Wallensten et al. 2007). In contrast, our model predicted shorter HPAIV epizootics, lower peak prevalence and 30% mortality. These features suggest a lower risk of spreading HPAIV than LPAIV because more infected birds will die or have a short infectious period (Hénaux, Samuel & Bunck 2010), and clinical disease (Brown et al. 2006; Middleton et al. 2007) may reduce the ability of birds to migrate. Our model predicts epizootic duration and provides site-specific rates of Alv infection over time; this knowledge is basic for disease control and assessing risk of disease spread by migration (Lebarbenchon et al. 2009; Guidet et al. 2011).

We found that hatch-year blue-winged teal at SK had no or limited immunity to LPAIV at the onset of fall epizootics, suggesting LPAIV outbreaks are uncommon during the breeding and brood-rearing periods. This finding supports our modelling assumptions that hatch-year birds are generally naïve to LPAIV infection at this time. This seems unlikely later in fall and winter because our results predict many hatch-year birds become infected early during fall migration and subsequently develop immunity (Journain et al. 2010). In contrast, the majority of adult blue-winged teal had immunity before epizootics, indicating that many adult waterfowl were likely to be infected prior to the breeding period and immunity persisted for at least several months (Hoye et al. 2011). This finding suggests surveillance to detect Alv infection may be inefficient and underestimate rates of disease transmission if immune birds are considered in the susceptible population. However, it is also possible that some seropositive birds were not immune to all currently circulating Alv subtypes (Pasick et al. 2010). The markedly longer persistence of Alv antibodies compared to infection suggests that serology could provide enhanced knowledge about Alv circulation and detection of potential HPAIV subtypes. The difference between model predicted and observed immunity for adult ducks suggests our model may underestimate the initial proportion of immune adults, indicating more extensive data on adult immunity is needed. Because of the limited knowledge on immunity from homo- or heterosubtypic infection in waterfowl, we considered all subtypes as a single pathogen and that infected waterfowl developed immunity for the duration of the epizootic. These assumptions seem reasonable where infection with one LPAIV subtype provides protection against re-infections with the same or other common Alv strains (e.g. Journain et al. 2010), but we may have overestimated FOI at sites where LPAIV infection did not provide immunity to other circulating strains. Therefore, our study underlines the importance of further research to investigate cross-immunity and the length of antibody protection.

Little is known about the factors that influence Alv transmission in wild bird populations. Incidence rates tended to be low in the Pacific flyway (0.04–0.09), high in prairie Canada (0.21–0.23) and variable in eastern Canada (0.02–0.18). Differences underlying regional transmission patterns are unclear and deserve further investigation. Variations in waterfowl community composition (Brown et al. 2006) and age (Costa et al. 2010), as well as climate (e.g. cold weather; Reperant et al. 2010), and habitat characteristics may influence LPAIV transmission across the landscape. The size and composition of the host populations may also affect disease transmission rates. Hunting could impact local population size and affect FOI estimates if Alv-infected individuals are more prone to harvest (e.g. lead-poisoned waterfowl; Bellrose 1959). In addition, emigration and/or immigration could affect FOI estimation, especially if Alv delays migration of infected birds (e.g. Van Gils et al. 2007). We also expect the FOI may change over the course of an epizootic depending on whether infectious contact is density or frequency dependent or the importance of environmental reservoirs as a source of infection (e.g. Roche et al. 2009). Several factors including seasonal and inter-annual variation in habitat quality, water levels, turnover of migrants and bird abundance within wetlands (Zimpfer et al. 2011) could alter environmental transmission. Our evaluation estimates incidence rates during LPAIV epizootics, but does not explicitly consider the underlying mechanisms driving transmission because data on the density of hosts, environmental concentrations of Alv and other information were not available to evaluate these effects. Therefore, our findings emphasize the need for hypothesis-driven research (Hoye et al. 2010) to understand factors that drive transmission and spread of Alv across the landscape, especially H5 and H7 LPAIV which present a risk for poultry (Stallkncht et al. 2007).

We believe our data-driven modelling approach provides new insights on the epidemiology of the Alv disease system in wild waterfowl given the current level of data and scientific knowledge. Seroprevalence data from wild birds support key assumptions in our model, which provides an important and useful framework for further scientific investigation of ecological drivers and for development of more complex models as appropriate data and scientific information become available. In addition, our analytical tool may incorporate data on infection prevalence or cumulative mortality (e.g. HPAIV H5N1 in Appendix S1, Supporting Information) and also be extended to serology data. Our findings indicate a lower probability of detecting HPAIV- than LPAIV-infected birds during surveillance programs on live birds (DeLiberto et al. 2009; Dusek et al. 2009). Therefore, dead-bird
surveillance would probably enhance detection of HPAIV (Parmley, Lair & Leighton 2009), especially on postbreeding areas where mortality of immunologically naive hatch-year birds is most likely. Furthermore, the addition of Alv serology for live-bird surveillance would enhance detection of HPAIVs and improve our understanding of Alv epidemiology. We encourage further evaluations of Alv infection along migration flyways (e.g. Hoyo et al. 2011) and where year-round resident bird populations may affect Alv transmission (Héniaux et al. 2012). Such investigations are critical for identifying risks to domestic and wild bird populations and optimizing surveillance programs.

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References
