



INTEGRATED EPIDEMIOLOGICAL AND PHYLOGEOGRAPHICAL ANALYSIS OF A H3N1 LOW PATHOGENIC AVIAN INFLUENZA OUTBREAK WITH ATYPICAL PATHOGENICITY, BELGIUM, 2019.

S.Van Borm^{1*‡}, G.Boseret^{2*}, S.Dellicour^{3*}, M. Steensels¹, V. Roupie¹, F. Vandebussche¹, E. Mathijs¹, A. Vilain², M. Driesen², M. Dispas², M. Gilbert³, B. Lambrecht¹, T. van den Berg¹.

¹NRL Belgium, Animal Infectious Diseases, Sciensano, Brussels, Belgium

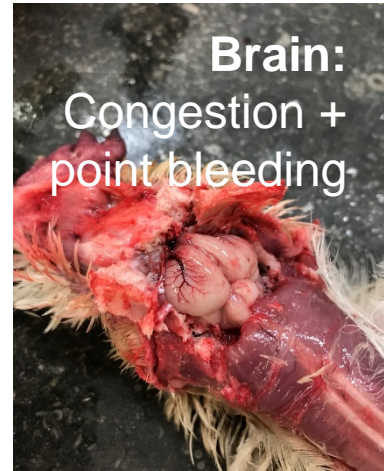
²Veterinary Epidemiology, Sciensano, Brussels, Belgium

³Spatial epidemiology Lab, Université Libre de Bruxelles, Brussels, Belgium

Steven.Vanborm@sciensano.be

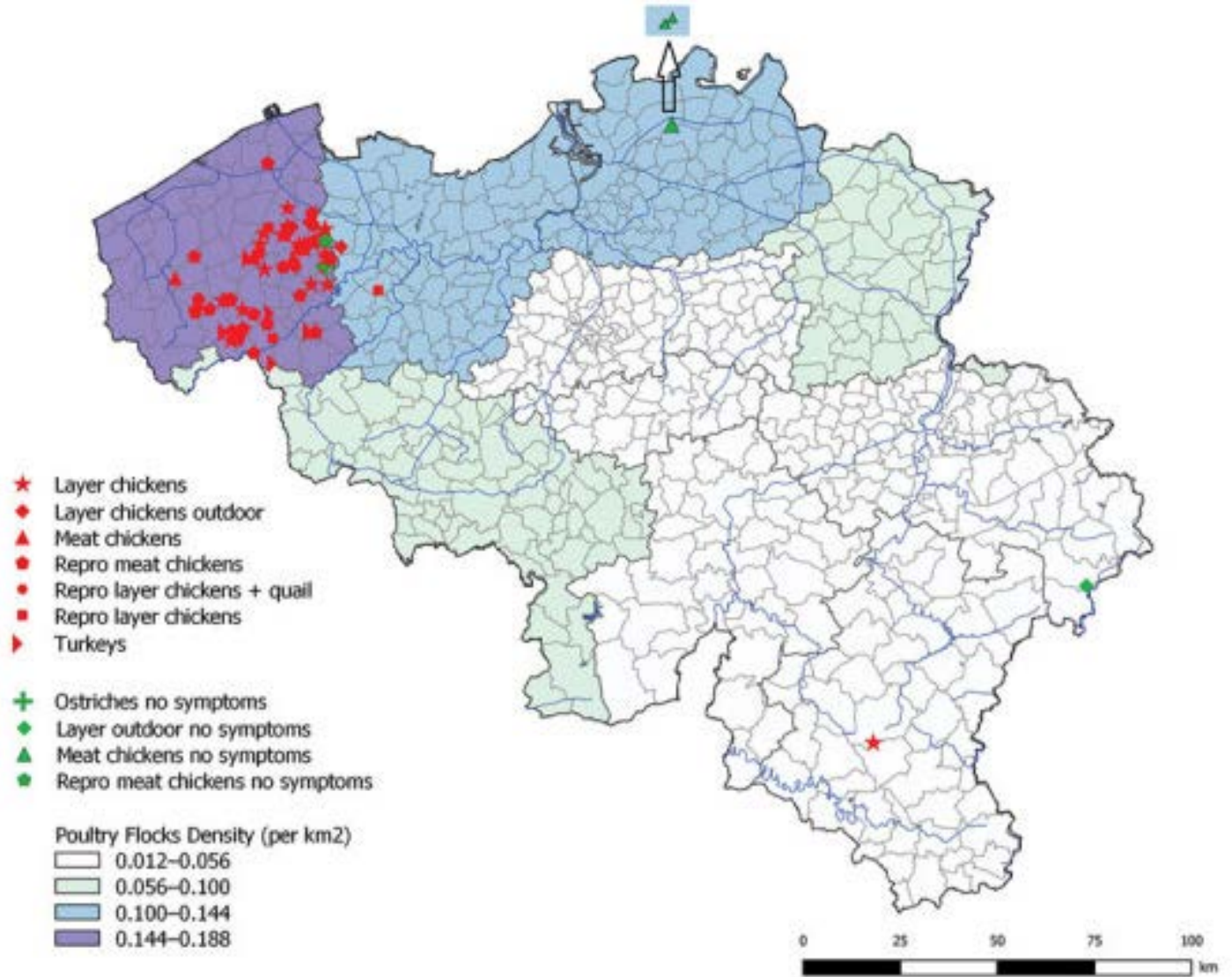
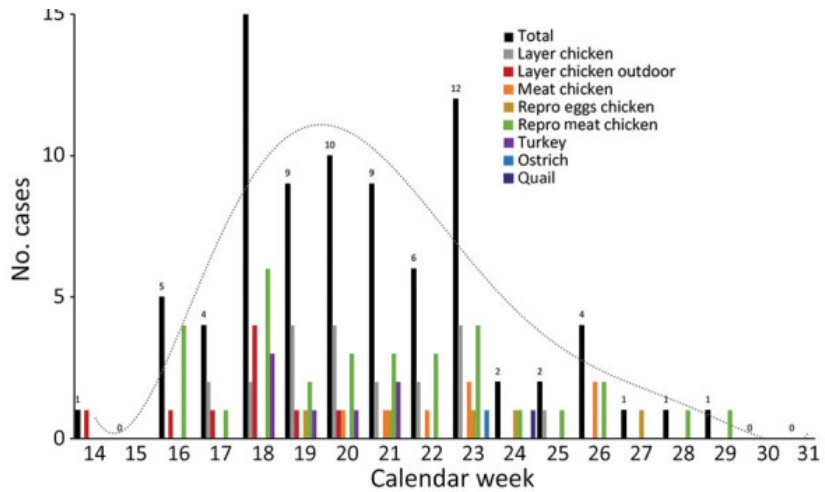
Introduction: the outbreak, the virus ...

- 2019 Jan -> reoccurrence April 2019 (same farm), higher mortality
- H3N1, LPAI (HA cl site sequencing, IVPI) (Steensels, M. et al. 2020. Emerg Infect Dis 26, 1899-1903).
- Full genome indicative of wild bird spillover (Steensels, M. et al. 2020. Emerg Infect Dis 26, 1899-1903).
- Fast spread in a DPPA, atypically pathogenic in layers and broiler breeders
 - Increased mortality, lay drop, respiratory issues, torticollis, petechia, red eyes: HP-like !
- Inoculation of adult layers: systemic replication & disease (Steensels, M. et al. 2020. Emerg Infect Dis 26, 1899-1903 ; De Wit, J.J. et al. 2020. Avian Pathol 49, 286-295).
- F.u. investigations (Schön, J. et al. 2021. PLoS Pathog 17, e109490.)
 - neuro- & epitheliotropism
 - Plasminogen recruitment allowing furin independent endoproteolytic HA activation



IMPACT

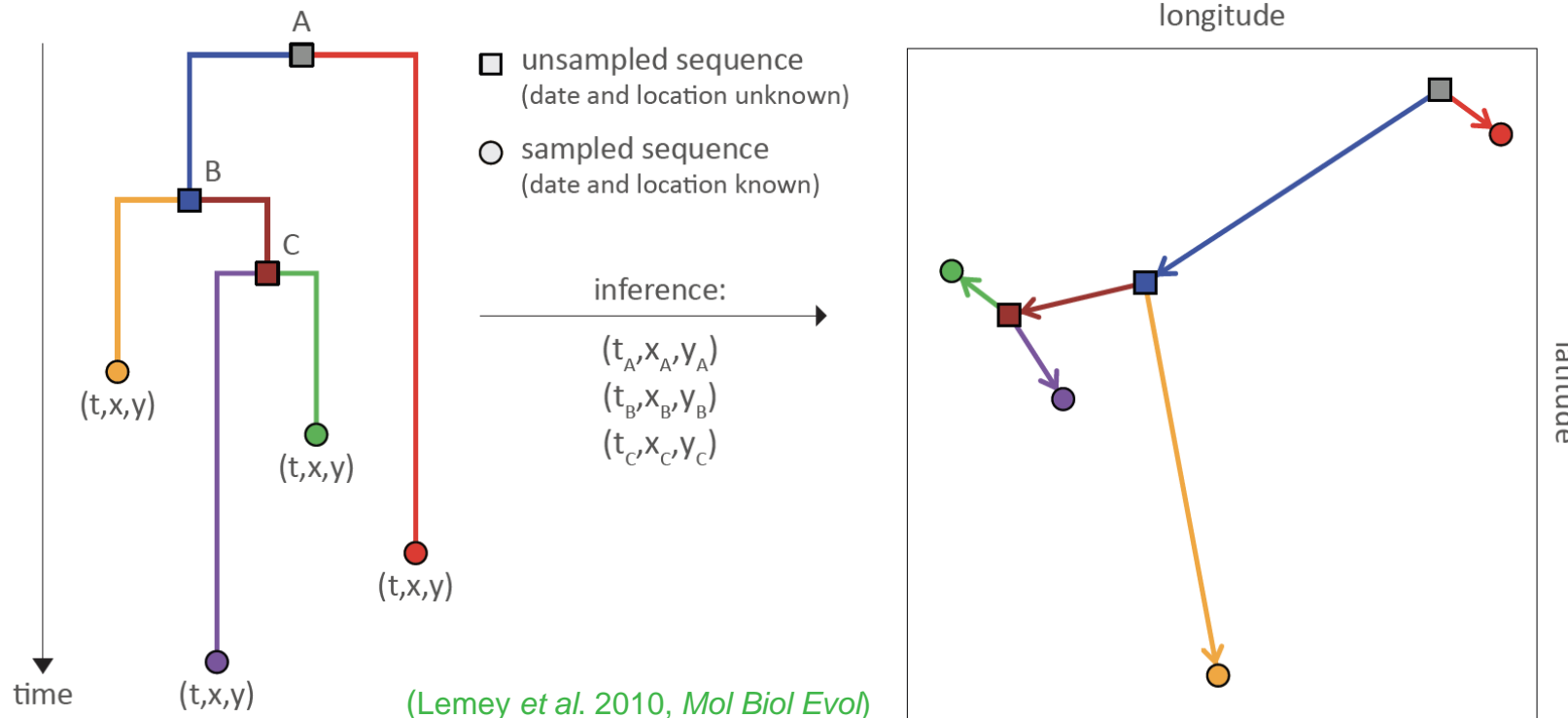
- 81 farms + 3 in France
- HPAI-like containment measures and impact
- ↔non notifiable



Outbreak dynamics & drivers of spread?

- Targeted IAV full **genome** sequences (n=104) + sample date
→ **time**-calibrated phylogenetic reconstruction
- Sample **geographical** coordinates

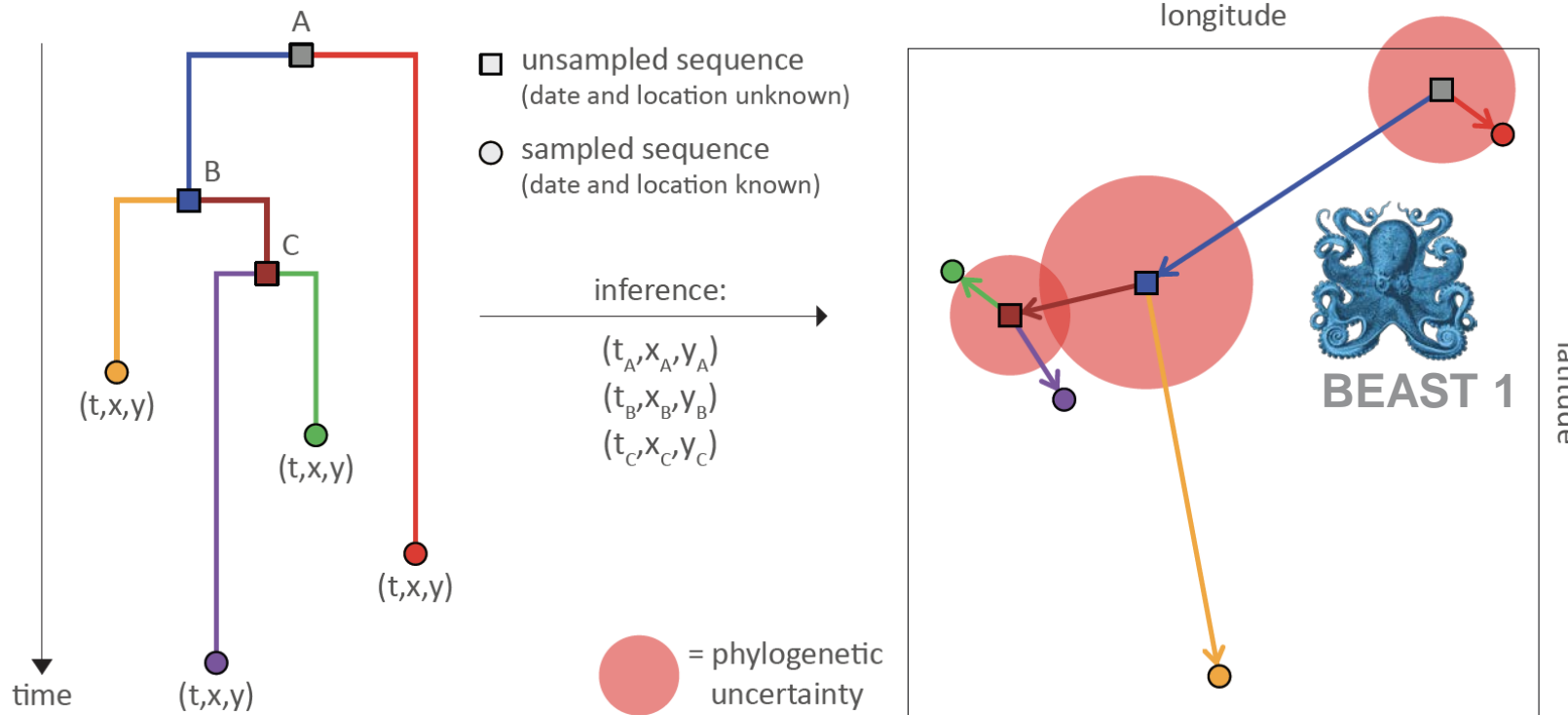
Spatially explicit outbreak reconstruction



Outbreak dynamics & drivers of spread?

- Targeted IAV full **genome** sequences (n=104) + sample date
→ **time**-calibrated phylogenetic reconstruction
- Sample **geographical** coordinates

Spatially explicit outbreak reconstruction



Outbreak dynamics & drivers of spread?

- Targeted IAV full **genome** sequences (n=104) + sample date
→ **time**-calibrated phylogenetic reconstruction
- Sample **geographical** coordinates

Spatially explicit outbreak reconstruction = independent dispersal model **1**

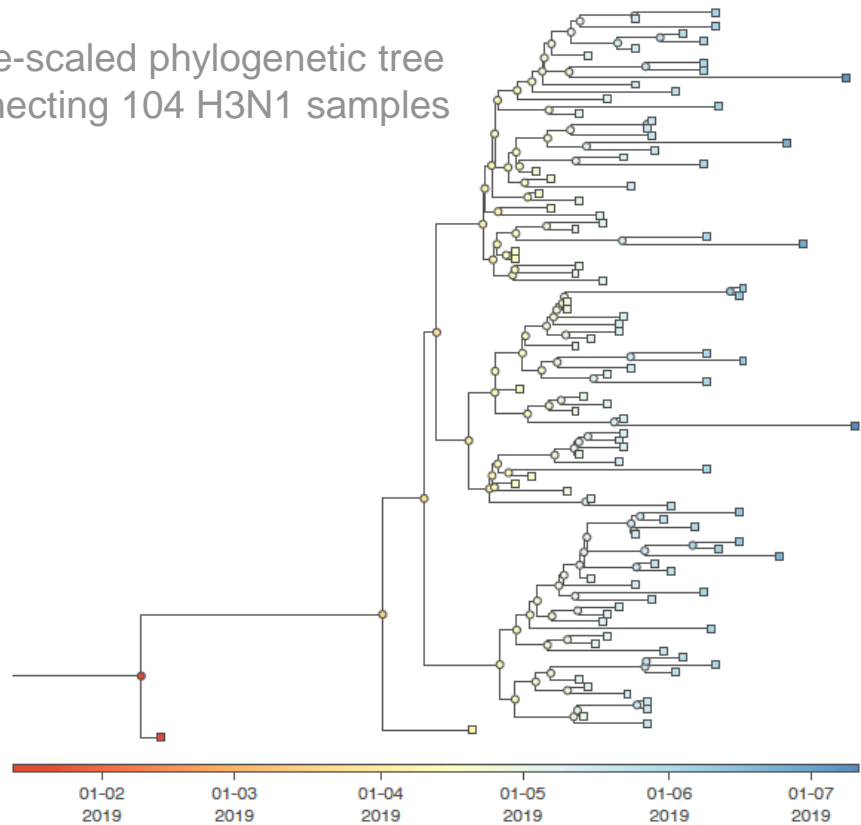
- Meteorological data
- Epidemiological data
 - Transport links (feed, animals, cadavres)
 - Social contacts (vets, family, collaborations, ...)

Hypothesis testing: **2**
assess overall impact of variable on epidemic

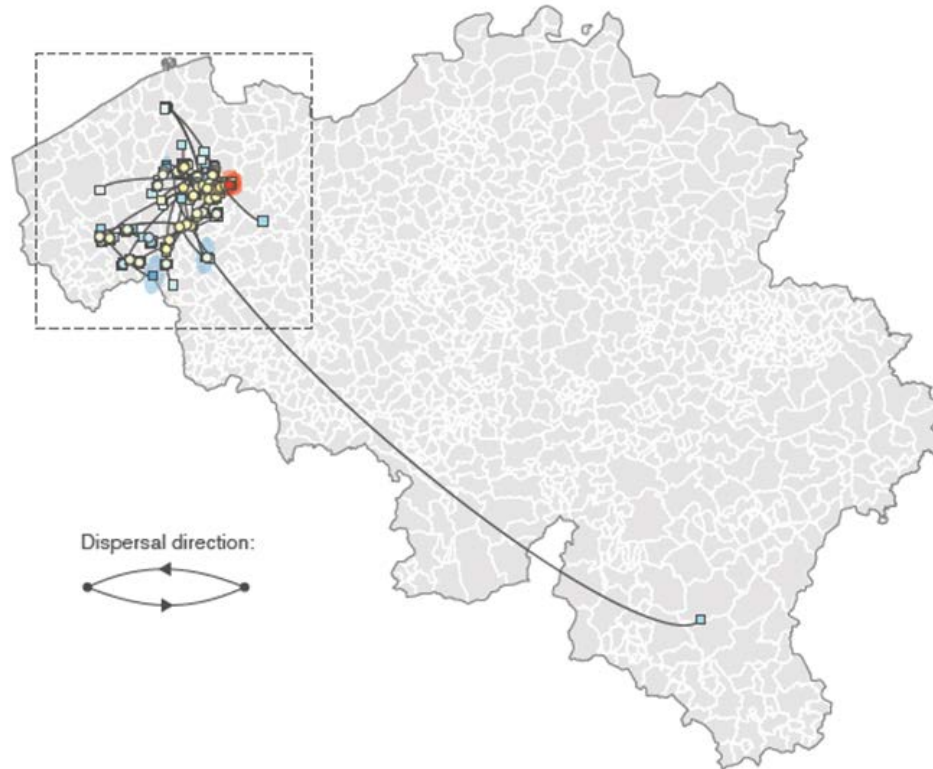
Local dynamics. Local correlation of epi drivers with spread as documented by spatially explicit phylo reconstruction **3**

Spatially explicit reconstruction of H3N1 outbreak

Time-scaled phylogenetic tree connecting 104 H3N1 samples

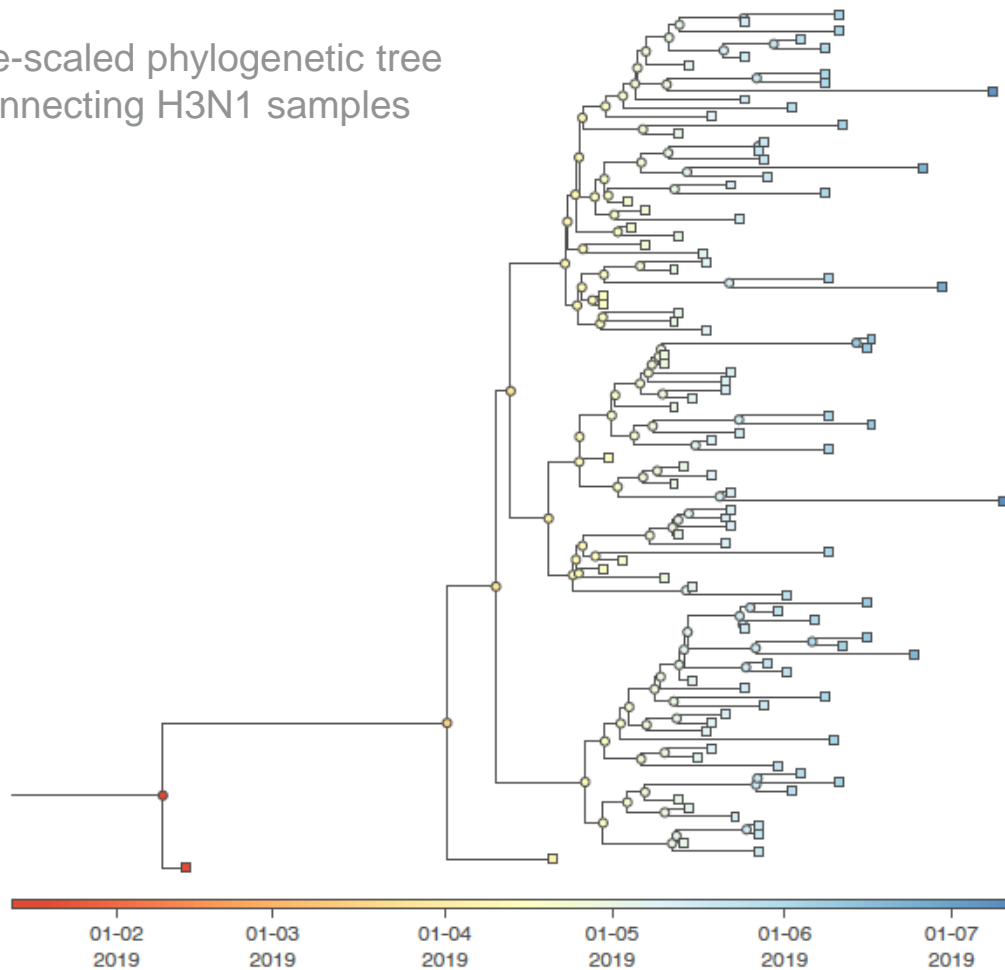


Spatially-explicit phylogeographic reconstruction

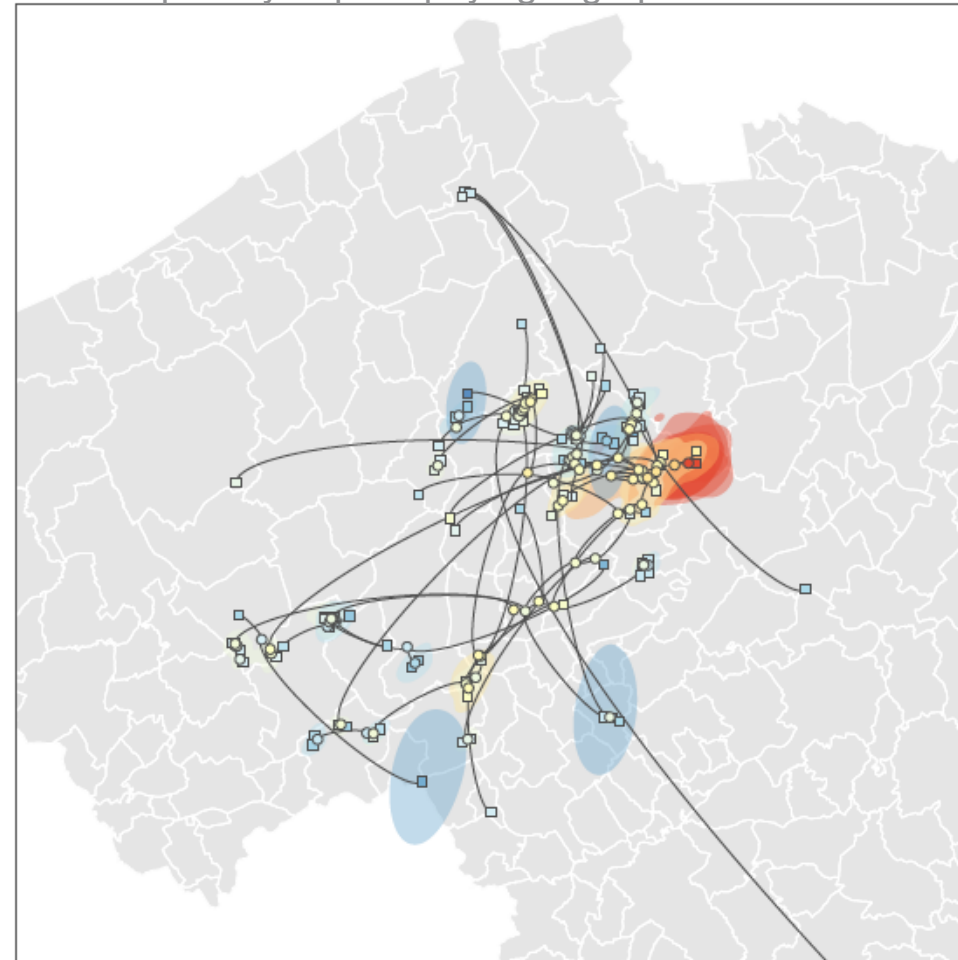


Spatially explicit reconstruction of H3N1 outbreak

Time-scaled phylogenetic tree connecting H3N1 samples

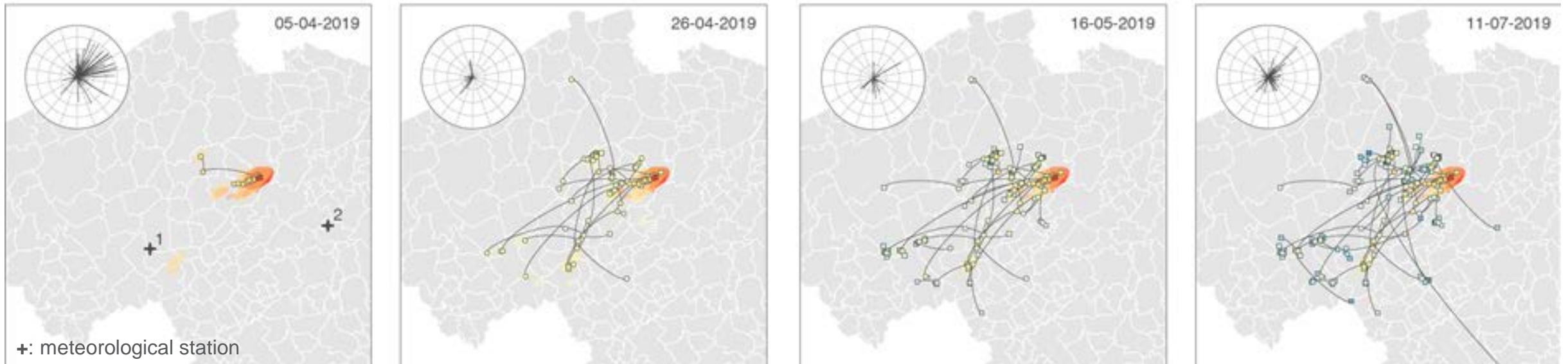


Spatially-explicit phylogeographic reconstruction



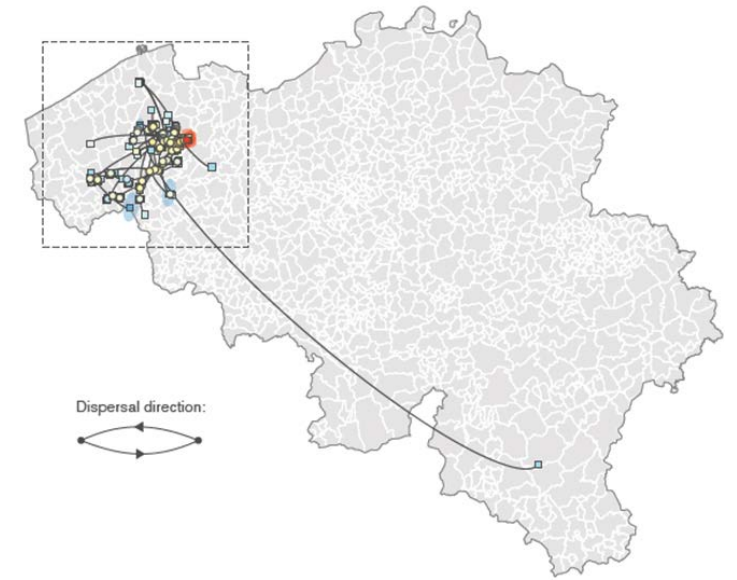
H° testing: wind?

Time slices corresponding to main outbreak management decisions



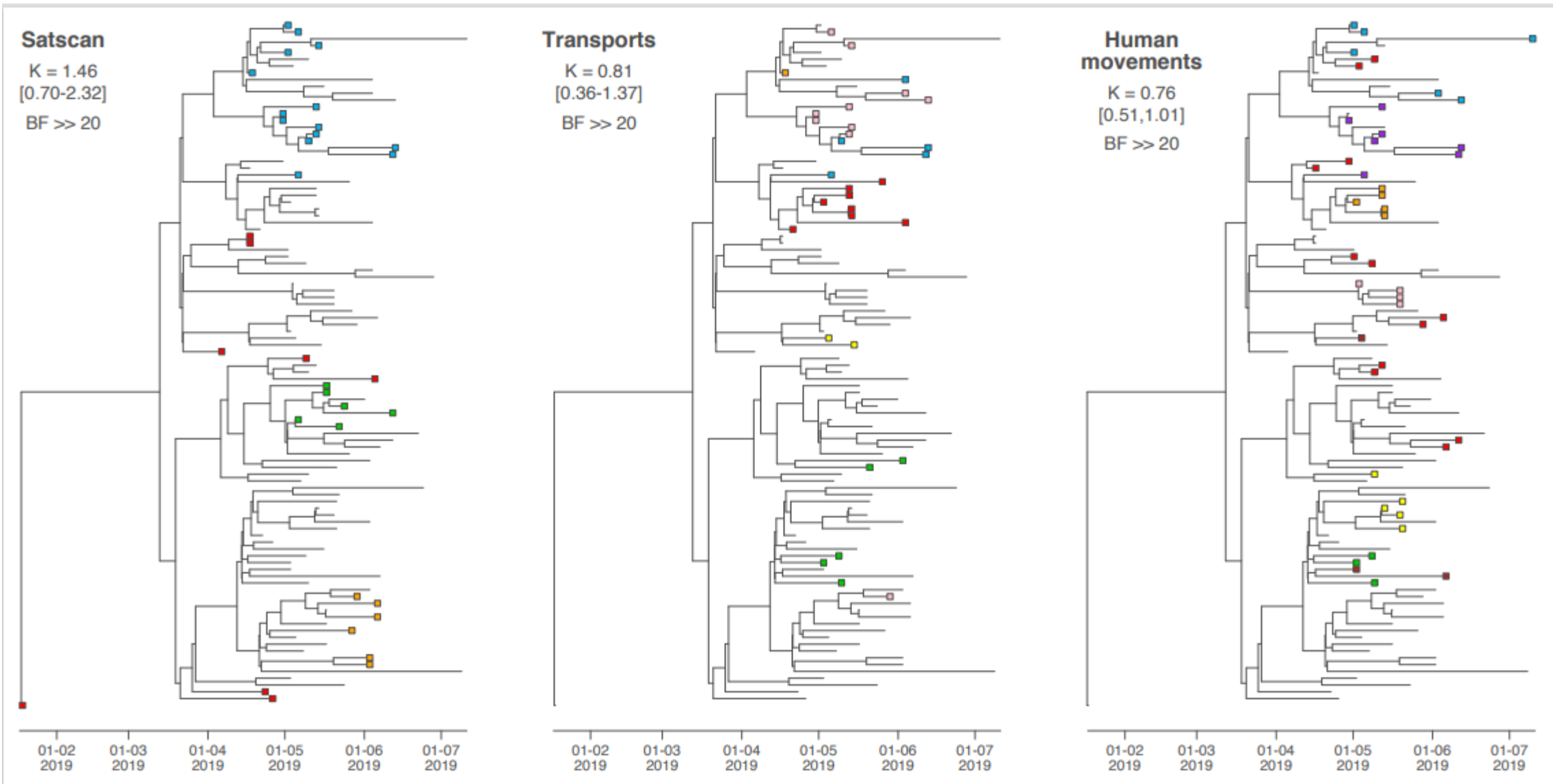
- positive yet not strong support ($3 < \text{Bayes factor} < 20$) when only considering H3N1 lineage dispersal events of $>1000\text{m}$
- when dividing by time periods: only a positive yet not strong support for a correlation during the second time period (06/04 - 26/04/2019)
- moderate impact of the wind on the dispersal of H3N1 during a specific phase of the epidemic.

H° testing: epidemiological variables: (geographical proximity, transport links, vet visits, family links, ...)



- Univariate tests:
 - Geographical distance
 - Visits same vet
- Multivariate regression analysis (to take co-dependency of variables into account)
→ geographical distance = main predictor of epidemiological connection

local correlation of epi drivers with spread



Conclusions:

- Full AIV genome: sufficient resolution for spatially explicit outbreak reconstruction
- Hypothesis testing (effect for whole epidemic)
 - Geographical proximity
 - Limited effect of wind during a specific phase of the outbreak
- Case specific/local opportunities for spread (social, geographical, transport) are exploited by the virus
- Highlights the complex multifactorial nature of (HP-like) AIV outbreaks

Acknowledgements

- Lab diagnostics & virus characterization: Mieke Steensels, Bénédicte Lambrecht, and team (NRL Belgium)
- AIV whole genome sequencing: Frank Vandebussche, Elisabeth Mathijs
- Epidemiological data collection and analysis: Géraldine Boseret and team (Veterinary Epidemiology team, Sciensano)
- Spatially explicit modelling and hypothesis testing, data visualization: Simon Dellicour and team (ULB spatial epidemiology laboratory)
- Meteorological data: Andy Delcloo (Royal Meteorological Institute)
- Funding: Federal Agency for the Safety of the Food Chain

