# Figures



**Figure 1. Model and expectations under different imprinting hypotheses. (A)** Reconstructed, birth year-specific probabilities of imprinting (representative example specific to USA for cases observed in 2015). **(B**) Expected imprinting protection against H1N1 or H3N2 under the three tested models. (**C**) Cartoon of age-specific risk curve. The shape of this curve is purely hypothetical, but each tested model fit a similar step function to data. (**D**-**F)** Fraction of each birth year unprotected by their childhood imprinting (from A) determines the shape of birth year-specific risk. (**G-I)** A linear combination of age-specific risk (C), and birth year-specific risk (D-F) give the expected age distribution of H1N1 or H3N2 cases under each model.

**Figure 2. Observed age distributions, Arizona**. Points show fraction of confirmed H1N1 or H3N2 cases observed in each single year of age. Lines show a smoothing spline fit to observed distributions. **(A)** All confirmed cases in the data (aggregate across seasons). (**B-G**) Age distributions from individual seasons in which both H1N1 and H3N2 circulated (≥ 50 confirmed cases of each).

**Figure 3**. **Model fits and model selection**. **(A)** Fitted effects of age and **(B)** imprinting from model AN, which provided the best fit to data**. (C-D)** Model fits to observed age distributions of H1N1 (**C)** and H3N2 **(D**) cases**.** Model name abbreviations indicate which factors were included: A = age-specific risk, N = NA subtype-level imprinting, S = HA subtype-level imprinting, G = HA group-level imprinting.

**Figure 4. Effect of antigenic advance on age distribution. (A)** Relationship between annual antigenic advance and the fraction of cases observed in children (0-10), or in adult age groups. Each data point represents a single influenza season in which at least 100 confirmed cases of a given subtype were observed. Blue label shows Pearson correlation between the fraction of H3N2 cases observed in each age group and annual antigenic advance. Blue dashes show linear trend fitted using lm() in R. **(B)** Season-specific age distributions of infection, colored by antigenic advance since the previous season.

# Tables

**Table 1. Confirmed cases in surveillance data from Arizona Department of Health Services.** Data representing the first and second waves of the 2009 H1N1 pandemic (2008-2009 and 2009-2010 seasons) were excluded.

|  |  |  |
| --- | --- | --- |
| **Season** | **Confirmed H1N1** | **Confirmed H3N2** |
| 1993-94 | 0 | 101 |
| 1994-95 | 12 | 38 |
| 2002-03 | 71 | 8 |
| 2003-04 | 0 | 71 |
| 2004-05 | 0 | 131 |
| 2005-06 | 1 | 321 |
| 2006-07 | 212 | 28 |
| 2007-08 | 196 | 244 |
| 2010-11 | 472 | 1204 |
| 2011-12 | 595 | 348 |
| 2012-13 | 80 | 1578 |
| 2013-14 | 1475 | 151 |
| 2014-15 | 5 | 2109 |
| **Total** | **3119** | **6332** |

**Table 2. Maximum likelihood parameter estimates and 95% profile confidence intervals from each model fit to ADHS data.** All estimated parameters represent the relative risk of confirmed infection, given the factors listed in the left-hand column. Model name abbreviations specific which factors were included. A = age-specific risk, N = NA subtype-level imprinting, S = HA subtype-level imprinting, G = HA group-level imprinting.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Model | AN | AS | AG | A |
| ΔAIC | 0.00 | 23.42 | 245.18 | 380.47 |
| H1N1 impr. protection | 0.34 (0.29-0.42) | 0.29 (0.24-0.35) | 0.67 (0.58-0.78) |  |
| H3N2 impr. protection | 0.71 (0.62-0.82) | 0.9 (0.78- >1) | 0.69 (0.6-0.8) |  |
| Ages 0-4 | Reference group: Value fixed to 1 | | | |
| Ages 5-10 | 0.68 (0.63-0.74) | 0.66 (0.61-0.72) | 0.66 (0.62-0.72) | 0.62 (0.57-0.68) |
| Ages 11-17 | 0.33 (0.3-0.36) | 0.31 (0.28-0.34) | 0.33 (0.3-0.37) | 0.3 (0.28-0.34) |
| Ages 18-24 | 0.38 (0.35-0.42) | 0.36 (0.32-0.4) | 0.39 (0.35-0.43) | 0.35 (0.32-0.39) |
| Ages 25-31 | 0.34 (0.32-0.38) | 0.33 (0.3-0.37) | 0.34 (0.31-0.38) | 0.31 (0.28-0.35) |
| Ages 32-38 | 0.28 (0.26-0.32) | 0.26 (0.24-0.3) | 0.28 (0.26-0.32) | 0.26 (0.24-0.29) |
| Ages 39-45 | 0.23 (0.2-0.27) | 0.21 (0.18-0.24) | 0.24 (0.22-0.28) | 0.21 (0.2-0.24) |
| Ages 46-52 | 0.24 (0.22-0.28) | 0.21 (0.19-0.24) | 0.24 (0.22-0.28) | 0.23 (0.2-0.26) |
| Ages 53-59 | 0.22 (0.2-0.26) | 0.2 (0.18-0.23) | 0.2 (0.18-0.24) | 0.2 (0.18-0.23) |
| Ages 60-66 | 0.21 (0.19-0.24) | 0.22 (0.2-0.26) | 0.19 (0.16-0.22) | 0.18 (0.16-0.21) |
| Ages 67-73 | 0.22 (0.2-0.26) | 0.25 (0.22-0.29) | 0.2 (0.18-0.23) | 0.19 (0.18-0.22) |
| Ages 74-80 | 0.23 (0.2-0.26) | 0.25 (0.22-0.3) | 0.2 (0.18-0.24) | 0.2 (0.18-0.23) |
| Ages 81+ | 0.15 (0.14-0.18) | 0.17 (0.15-0.2) | 0.13 (0.12-0.16) | 0.13 (0.12-0.15) |

# Supplementary Figures

**Figure S1.** **ADHS age distributions, all seasons**. Supplement to Fig. 2 showing observed age distributions from all influenza seasons. Observed case fractions (points) were only plotted if 10 or more cases of a given subtype were confirmed, to avoid extreme stretching of the y axis. Smoothing splines were only plotted if 50 or more cases of a given subtype were observed, as fits to fewer data points would not have been meaningful.

**Figure S2. Alternate smoothing parameters, AZDHS data.** Supplement to Fig. 2, with smoothing parameters chosen to fit splines that are less (**A-F**), or more (**G-L**) smooth than the splines shown in the main text. Differences between H1N1 and H3N2’s age-specific impacts remain evident, especially in the oldest cohorts.



**Figure S3. Comparison of rescaled antigenic distance estimates from the Bedford et al., and *Nextstrain* datasets.** Points represent average antigenic position of all isolates from a given calendar year.