The seasonality of pandemic influenza emergence

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Pandemics emerge outside the typical influenza season
Pandemics emerge outside the typical influenza season

Average US Seasonal Epidemic 1997-2015

Influenza Incidence per 10,000 Individuals

Fox et al PLoS Comp, 2017
Short-term, generalized immunity could prevent emergence during seasonal epidemics

Influenza Incidence per 10,000 Individuals

Average US Seasonal Epidemic
1997-2015

Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep

1918 1957 1987 1968

Fox et al PLoS Comp, 2017
Short-term, generalized immunity could prevent emergence during seasonal epidemics

Influenza Incidence per 10,000 Individuals

Average US Seasonal Epidemic
1997-2015

Generalized Immunity


Fox et al PLoS Comp, 2017
Combination of refractory period and seasonality fit the historic pandemic emergence timing
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1. Two-strain model

Influenza Incidence per 10,000 Individuals

Fox et al PLoS Comp, 2017
Combination of refractory period and seasonality fit the historic pandemic emergence timing

1. Two-strain model
2. Fit to 2008-2009 data

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3. Test when pandemics emerge

Fox et al PLoS Comp, 2017
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3. Test when pandemics emerge
Pandemics that are successful emerge “slower” within the refractory period

Fox et al PLoS Comp, 2017
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Fox et al PLoS Comp, 2017
Conclusions
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• Reasonable

• Still need better understanding of short-term immunity, but it could explain pandemic emergence seasonality

![Influenza Incidence per 10,000 Individuals](image-url)
Conclusions

• Reasonable

• Still need better understanding of short-term immunity, but it could explain pandemic emergence seasonality

• Handwavy, but (maybe) cool implications

• Optimizing pandemic surveillance systems and response

• Seasonal flu vaccination
Pandemic wave dynamics

Incidence vs. Time (February to December)
Pandemic wave dynamics

2009 seasonal epidemic

pandemic 1st wave

pandemic 2nd wave
Pandemic wave dynamics

- 2009 seasonal epidemic
- Pandemic 1st wave
- Pandemic 2nd wave
Cities with larger seasonal flu epidemics had smaller initial pandemic waves.
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Many other factors to investigate, and needs some more intricate modeling
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1. Nonlinear effects
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1. Nonlinear effects
2. Spatial clustering
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1. Nonlinear effects
2. Spatial clustering
3. Climatic factors
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City flu data may hold clues.
Seasonal epidemics and short-term immunity create pandemic “refractory period”
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Fox et al PLoS Comp, 2017
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Fox et al | PLoS Comp, 2017
Influenza pandemics are defined by the two main antigens
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Viral proteins
- Influenza polymerase (PA, PB1, PB2)
- Nucleoprotein (NP)
- Viral RNA
- Hemagglutinin (HA)
- Neuraminidase (NA)
- Nuclear export protein (NEP)
- Membrane protein (M2)
How can there be strain replacement following pandemics
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Immunological dynamics underlying flu spread

- Increased Susceptibility
- Decreased Susceptibility
Immunological dynamics underlying flu spread

Increased Susceptibility  
Decreased Susceptibility

Homosubtypic Immunity

Immunological Duration (Years)
Immunological dynamics underlying flu spread

H1N1  H3N2

Homosubtypic Immunity

Increased Susceptibility
Decreased Susceptibility

Immunological Duration (Years)
Immunological dynamics underlying flu spread

H1N1 → H3N2

 Increased Susceptibility

 Decreased Susceptibility

Homosubtypic Immunity
Long-term HSI

Immunological Duration (Years)
Immunological dynamics underlying flu spread

- **H1N1**
- **H3N2**

- **Homosubtypic Immunity**
  - Long-term HSI
  - Short-term HSI

- Increased Susceptibility
- Decreased Susceptibility
Recent experiments show example of short-term HSI
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Recent experiments show example of short-term HSI.
Influenza pandemics consistently top the list of most worrisome infectious diseases