Staying Ahead of the Curve: Modeling and Public Health Decision Making

January 19, 2016
Modeling to Support Outbreak Preparedness, Surveillance and Response

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What Are Models?

- Mathematical models use equations to represent disease transmission in the real world and can provide insights into outbreak emergence, spread and control.

- Using advanced methods for data analysis, optimization, and high performance computing, models can translate the basic science of infectious diseases into practical public health guidance.

- Models can predict where and when events will occur, allowing better outbreak preparedness and response.
The Questions

- Where are infectious diseases spreading today?

- Where will they be spreading tomorrow?

- How can we use limited resources to minimize death and illness during outbreaks?
Where Are Outbreaks Today?

- In initial stages of an outbreak, data are sparse and biased
- Novel modeling strategies glean useful information from diverse data sources

Characterization of Ebola transmission based on viral sequence data and Facebook case reports

Scarpino SV et al. Clinical Infectious Diseases. 2015 Jan
Where Are Outbreaks Today?

- Optimizing surveillance systems
  - Models learn from past outbreaks to improve data collection, situational awareness and outbreak prediction

Models used to determine where and when to collect influenza specimens to efficiently detect emerging viruses and select strains for inclusion in next season’s vaccine.

Scarpino SV, Dimitrov NB, Meyers LA. PLoS Computational Biology. 2012 Apr
http://www.aphl.org/aphlprograms/infectious/influenza/Pages/Influenza-Virologic-Right-Size-Sample-Size-Calculators.aspx
Where Are Outbreaks Today?

Biosurveillance Ecosystem Surveillance App

DTRA: Defense Threat Reduction Agency
BSVE: Biosurveillance Ecosystem
Where Will They Be Tomorrow?

CDC’s Predict the Influenza Season Contest

Flu activity

Week (2013-2014 season)

Early Season Flu Forecasted
Actual Flu Trajectory
Forecast to Support Decision Making

CDC’s Predict the Influenza Season Contest

Flu activity

Week (2013-2014 season)

Peak

Onset

End

Early Season Flu Forecasted

Actual Flu Trajectory
Focus Models on Key Quantities

CDC’s Predict the Influenza Season Contest

- Peak
- Onset
- End

Flu activity vs. Week (2013-2014 season)

- Early Season Flu Forecasted
- Actual Flu Trajectory
- Forecasted Point
- Actual Data
How Can We Use Models to Optimally Mitigate Outbreaks?

- Clearly articulate goals
- Deepen intuition
  - Transmission dynamics
  - Impacts of interventions
  - Biases of surveillance data
- Improve preparedness
  - Inform “quantitative” decisions
  - Optimize stockpiling and allocation of medical countermeasures

http://flu.tacc.utexas.edu
Singh B, Huang HC, Morton D, et al. Emerging Infectious Diseases. 2015 Feb
How Can We Optimally Mitigate Outbreaks?

**THE LANCET**

Ebola control: effect of asymptomatic infection and acquired immunity

Steve E Bellan, Juliet C Pulliam, Jonathan Dushoff, Lauren Ancel Meyers

Evidence suggests that many Ebola infections are asymptomatic, a factor overlooked by recent outbreaks.

**The Journal of Infectious Diseases**

Evaluating Large-scale Blood Transfusion Therapy for the Current Ebola Epidemic in Liberia

Alexander Gutfraind and Lauren Ancel Meyers

Gutfraind A, Meyers LA. J Infect Dis. 2015 Apr
Opportunities

- **Transformative moment for modeling**
  - Upsurge in government appreciation and investment
  - Widening collaborations between decision-makers and modelers
  - Increase in model-driven policies for outbreak prevention and control
Challenges

- **New opportunities bring “new” (and old) challenges**
  - Access to reliable historical data and real-time data
    - Model outputs only as good as their inputs
    - Legitimate concerns about privacy and safety
    - Urgent need for best practices and shared resources
  - Sustainability of modeling tools
    - Rapidly changing technological infrastructure and data resources
    - User training and support
What Do Policy Makers Expect from Modelers during a Response?

Martin I. Meltzer, PhD
Lead, Health Economics and Modeling Unit
Division of Preparedness and Emerging Infections
National Center for Emerging and Zoonotic Infectious Diseases
Initial Questions from Leadership That Modeling Helps Inform

- **Forecasting**: How many cases will there be at any point and in total (with frequent updates)?

- **What would be the impact of interventions?**

- **When will the epidemic end?**
  - With an intervention
  - Without an intervention
Key Questions During The 2009 H1N1 Influenza Pandemic

- **Spring**
  - How virulent and transmissible is 2009 H1N1?
  - School closures — when and where for best impact?

- **Fall and Winter**
  - When would the fall wave begin?
  - When would the fall wave peak?
    - How much benefit will vaccination deliver?
  - Would age-specific attack rates change?
  - Would there be a winter (third) wave?
2009 H1N1 Influenza Burden: Near Real-time Estimates

Estimating the Burden of 2009 Pandemic Influenza A (H1N1) in the United States (April 2009–April 2010)

Sundar S. Shrestha,1 David L. Swerdlow,2 Rebekah H. Borse,3 Vimalanand S. Prabhu,4 Lyn Finelli,5 Charisma Y. Atkins,3 Kwame Owusu-Edusei,6 Beth Bell,2 Paul S. Mead,7 Matthew Biggerstaff,5 Lynnette Brammer,5 Heidi Davidson,5 Daniel Jernigan,5 Michael A. Jhung,5 Laurie A. Kamimoto,5 Toby L. Merlin,8 Mackenzie Nowell,2 Stephen C. Redd,8 Carrie Reed,5 Anne Schuchat,2 and Martin I. Meltzer3

1Division of Diabetes Translation, 2Office of the Director, National Center for Immunization and Respiratory Diseases, 3Office of the Associate Director for Science and Emerging Infections, 4Division of Global HIV/AIDS, 5Influenza Division, 6Division of Sexually Transmitted Disease Prevention, 7Division of HIV/AIDS Prevention, 8Division of Influenza, and 9Office of Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia.

To calculate the burden of 2009 pandemic influenza A (pH1N1) in the United States...

61 million cases
(range: 43 million to 89 million)

274,000 hospitalizations
(range: 195,000 to 403,000)

12,470 deaths
(range: 8,870 to 18,300)

Archive: Updates of CDC estimates at: http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm
### Yes, There Really Was a Pandemic: 2009 pH1N1 to Seasonal Influenza

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<th>Age (years)</th>
<th>Numbers per 100,000</th>
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<td>90.2</td>
<td>52.4</td>
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Emergency Preparedness and Response

WEST AFRICA
Ebola Outbreak

Ebola Virus Disease
Get the CDC's Latest Information

NATURAL DISASTERS
Wildfires, Floods, Hurricanes & more

RECENT INCIDENTS
Ebola, Chikungunya & more

Activations
- Ebola: 2014 West Africa Outbreak
- Polio Eradication

Photo by Spencer Lowell for TIME magazine
Liberia: August 2014 Estimates

Corrected for potential underreporting by multiplying reported cases by a factor of 2.5
MMWR Surveill Summ 2014;63 Suppl 3
Response Time Matters –
Cases Could Triple For Every Month of Inaction

Liberia Case Estimates, Based on August 2014 Data

Data are not corrected for potential underreporting
MMWR Surveill Summ 2014;63 Suppl 3
Estimates Compared to Actual Reported Cases with and without Correction for Underreporting

Liberia Estimates, Based on August 2014 Data

Reported cases, ~8,500 through mid-January, were within 23% of model estimates.

Blue vertical bar represents correction for underreporting, by factor of 2.5.
Regional Spread of Ebola Virus, West Africa, 2014

Gabriel Rainisch, Manjunath Shankar, Michael Wellman, Toby Merlin, Martin I. Meltzer
Modeling’s Major Contributions During Emergency Response

- Estimation of possible size of outbreak before large amounts of data are available
- Assessment of impact of interventions
- Identification of key data needs
  - Value of what is known
  - Value of what is not known
  - Prioritize data collection efforts
Modeling’s Major Contributions During Emergency Response

- **Simple modeling tools that can be widely disseminated**

  **SurvCost** – [http://www.cdc.gov/idsr/survcost.htm](http://www.cdc.gov/idsr/survcost.htm)
  to aid public health officials to estimate the cost of Integrated Disease Surveillance and Response (IDSR) systems

  to estimate the potential number of days lost from work due to an influenza pandemic

  **MedCon** – [http://emergency.cdc.gov/planning/medcon/](http://emergency.cdc.gov/planning/medcon/)
  to estimate the baseline medical care requirements of a displaced population following a disaster

  to estimate the number of Ebola cases in a community, and assess the potential impact of proposed interventions using a spreadsheet-based model
What Is Needed For Modeling To Be Of Use To Leadership In A Response

- **Accessible to leadership**
  - Best if modeling and modelers are on site iterations
  - Need for lots of “back and forth” to clarify data and the question
  - Publication NOT the main goal

- **Fast and frequent updates**
  - Available fast enough to help guide policy decisions
  - Can be rapidly and easily updated when situation changes or more data are available

- **Simple models**
  - Has to be able to be easily conveyed to decision and policy makers
  - Spreadsheets or equivalent — post or make widely available
Application of Modeling and Forecasting for Preventing Influenza

Daniel B. Jernigan, MD, MPH

Director, Influenza Division
National Center for Immunization and Respiratory Diseases
Organizing Framework for Use of Risk Assessment and Modeling Tools Before and After Emergence

Organizing Framework for Use of Risk Assessment and Modeling Tools Before and After Emergence

Influenza Risk Assessment Tool

Virus Fitness Forecasting

Burden and Impact Assessment

Disease Forecasting

Investigation | Recognition | Initiation | Acceleration | Deceleration | Preparation
Organizing Framework for Use of Risk Assessment and Modeling Tools Before and After Emergence

- Influenza Risk Assessment Tool
- Virus Fitness Forecasting
- Burden and Impact Assessment
- Disease Forecasting

Stages:
- Investigation
- Recognition
- Initiation
- Acceleration
- Deceleration
- Preparation
Estimated Hospitalizations
Influenza Surveillance 2011–2015

Unpublished CDC data for 2013-15
US Influenza Virologic Surveillance. www.cdc.gov/flu/weekly/overview.htm
Burden, Burden Averted and Modeling

- **Burden of influenza**
  - Hospitalization data and other inputs used to estimate
    - Total cases
    - Total office visits
    - Hospitalizations
    - Deaths

- **Burden averted through vaccines and antivirals**
  - Various inputs used to estimate number of cases, visits, hospitalizations and deaths averted through use of vaccine and antivirals
Estimation and Impact Modeling

- **Estimation of cases occurring due to novel influenza**
  - Determine total cases due to an emerging flu virus, e.g., H3N2v

- **Impact estimation of different mitigation strategies**
  - Monovalent vaccine production in emergency
  - Emergency use of antivirals at alternative care sites
Pandemic Severity Assessment Framework

- Available data evaluated for transmissibility and severity
- Scores are compared to past seasons and pandemics for historical grounding

Influenza Risk Assessment Tool

- Influenza Risk Assessment Tool
- Virus Fitness Forecasting
- Burden and Impact Assessment
- Disease Forecasting
Ten Elements Evaluated in Influenza Risk Assessment Tool (IRAT)

1. Genomic variation
2. Receptor binding
3. Transmission in laboratory animals
4. Antivirals and treatment options
5. Existing population immunity
6. Disease severity and pathogenesis
7. Antigenic relationship to vaccine candidates
8. Global geographic distribution
9. Infection in animals, human risk of infection
10. Human infections and transmission

Trock SC, Burke SA, Cox NJ. Avian Dis. 2012 Dec
CDC routinely conducts risk assessments on emerging novel influenza viruses

- Assess risk of emergence
- Assess impact, if emerges

Impact Risk

Emergence Risk

H5N1
H7N9
H3N2v
H5NX
North America
A/duck/New York/96

Trock S, Burke S. CDC Unpublished Data for H5NX Assessment
Trock S, Burke S, Cox N. Avian Dis. 2012 Dec
IRAT informs leadership regarding

- Readiness toolkit development (e.g., lab reagents)
- Vaccine and antiviral development, trials, and stockpiles
- Changes to diagnostics
- Changes to response posture
  - Medical countermeasures, deployment
Disease Forecasting

Influenza Risk Assessment Tool

Virus Fitness Forecasting

Burden and Impact Assessment

Disease Forecasting

Investigation | Recognition | Initiation | Acceleration | Deceleration | Preparation
Forecasts for the Onset and Peak of the 2015–2016 Influenza Season

- Ten academic partners receive standard weekly CDC data inputs and provide their best predictions for onset, peak, and other key estimates
- CDC serves as model broker to assure
  - Accurate and available data via web portal for participants
  - Collaboration and comparison of outputs
- Ensemble models may provide best estimates
Dynamic Modeling

- **Models of Infectious Disease Agent Study (MIDAS)**
  - Academic and government collaboration
  - Develop complex mathematical models to test impact of:
    - Different influenza emergence scenarios
    - Variations and timing of interventions
  - Models incorporate multiple inputs and assumptions

- **Other groups developing dynamic influenza models**
  - DHS, DoD, BARDA, LANL, ORNL, WHO
Virus Fitness Forecasting

- Influenza Risk Assessment Tool
- Virus Fitness Forecasting
- Burden and Impact Assessment
- Disease Forecasting
Possibilities for Real-Time Genomic and Antigenic Virus Fitness Forecasting?

- CDC, WHO, and collaborators work to develop models to combine:
  - Whole genome, next-generation, sequencing data
  - Antigenic data describing host responses to flu virus proteins
  - Geotemporal and epidemiologic data from surveillance

- Goal is to identify most likely viruses to predominate and improve selection of candidate vaccine viruses
Conclusions

- Practical use of historic and historical data can help estimate impact of emerging influenza severity.

- Modeling of epidemiologic and laboratory findings can be used to estimate likelihood of novel, animal-origin influenza emergence and severity.

- Influenza disease forecasting through ensemble modeling efforts may help disease control efforts.

- Use of epidemiologic, genomic, and antigenic modeling forecasts may help select best vaccine virus candidates.
Models as Decision Support Tools: Explanation, Foresight, Prediction

Richard J. Hatchett, MD
Chief Medical Officer and Deputy Director
Biomedical Advanced Research and Development Authority
Office of the Assistant Secretary for Preparedness and Response
“Prediction implies an ability to discern a particular turn of events. Foresight identifies variables and a range of alternatives that might better prepare for the future.”

– Richard Danzig

- Models provide an input to decision making by
  - Explaining phenomena
  - Providing foresight
  - Making predictions

Decision Makers Need to Recognize Limitations of Models

- Models are a tool to help frame decisions

- Models are highly stylized representations of the world and are typically fit to specific purpose
  - Whatever purpose decision makers defined

- Decision makers must be careful not to misuse them
  - Limit conclusions to domains that the model was designed to address
  - Models should not be used in isolation
Explanatory Models

- Models can provide a means for understanding observed outcomes.
- Modelers looked at the impact of the timing and use of NPIs (e.g., social distancing measures, including closing schools and banning large gatherings) on overall attack rates.
- Efficacy of such measures was substantially enhanced if they were introduced early in an epidemic.

NPIs: Nonpharmaceutical interventions
Importance of Timing and Nonpharmaceutical Interventions (NPIs) in 1918 Epidemic

1918 Death Rates: Philadelphia vs St Louis

- Timing of NPIs was the critical determinant of their efficacy
- Early implementation reduced epidemic peak intensity
- Relaxation of NPIs may explain the multiple waves in St. Louis

Hatchett RJ, Mecher CE, Lipsitch M. Proc Natl Acad Sci U S A. 2007 May
Bootsma MC, Ferguson NM. Proc Natl Acad Sci U S A. 2007 May
Importance of Timing and Nonpharmaceutical Interventions (NPIs) in 1918 Epidemic

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1918 Death Rates: Philadelphia vs St Louis

- Day 2 – St. Louis starts NPIs
- Day 16 – Philadelphia starts NPIs

Excess Weekly Deaths Rates per 100,000

Hatchett RJ, Mecher CE, Lipsitch M. Proc Natl Acad Sci U S A. 2007 May
Bootsma MC, Ferguson NM. Proc Natl Acad Sci U S A. 2007 May
Examples of Ways In Which Models Provide Foresight

- **Facilitate analysis and understanding of sparse datasets**
  - Early readouts during 2009 H1N1 response

- **Enhance intuition by allowing exploration of what-ifs**
  - Efficacy of isolation and quarantine in SARS, smallpox, and influenza

- **Establish risk boundaries**
  - Risk of sexual transmission of Ebola
Risk of Sexual Transmission of Ebola

- Ebola virus can persist in semen for months, producing a sustained risk of transmission
- Eggo, et al., combined recent data on viral RNA persistence with weekly disease incidence to estimate the current number of semen-positive men in affected West African countries
- The risk of sexual transmission has declined significantly but will persist into 2016

Ebola virus can persist in semen for months, producing a sustained risk of transmission.

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The risk of sexual transmission has declined significantly but will persist into 2016.

Repeated Comparison of Predict vs. Actual Outcomes Has Improved Accuracy of Models

NCEP Operational Forecast Skill
36 and 72 Hour Forecasts @ 500 MB over North America

Predictive Accuracy (%)

National Centers for Environmental Prediction at NOAA
Combining Multiple Predictive Models May Provide More Informative Forecasts

- There is usually no “best” predictive model

- For decision making, combining multiple models into a single risk forecast that captures model uncertainty may be preferable

Multiple pathways modeled for Hurricane Ike
Combining Multiple Predictive Models Shrinks Cone of Error

- As modeling techniques improve, the cone of error for aggregate models shrinks.
- As the time horizon is extended, the cone of error widens and uncertainty increases.
Looking to The Future of Epidemic Forecasting

Epidemic modelers are developing techniques that help emerging data to “speak for itself”

As data accumulate, the accuracy of the predictions improves

Figure based on a regression transmission model developed by Jason Asher, ASPR/BARDA (CTR)
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The Prosocial Function Of Modeling: Conduit for Communication

With thanks to Steve Bankes
Staying Ahead of the Curve: Modeling and Public Health Decision Making

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