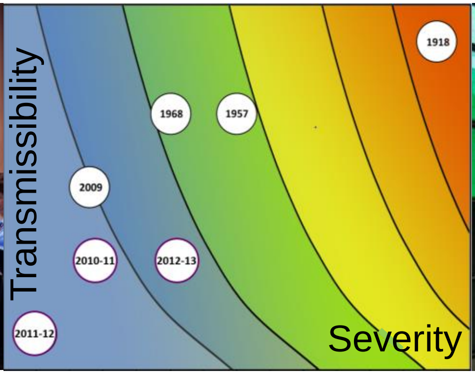
CDC PUBLIC HEALTH GRAND ROUNDS

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

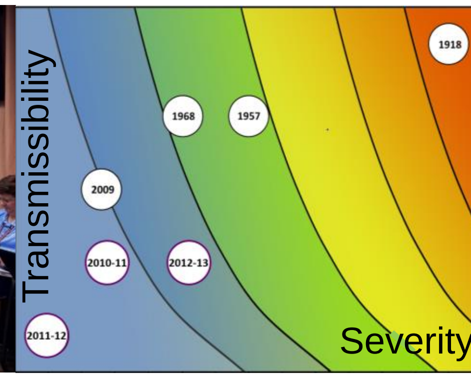


Accessible version: https://youtu.be/WPfehEIPdWQ

January 19, 2016

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Modeling to Support Outbreak Preparedness, Surveillance and Response



Lauren Ancel Meyers, PhD

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Department of Statistics and Data Sciences

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TEXAS
The University of Texas at Austin

U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

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**

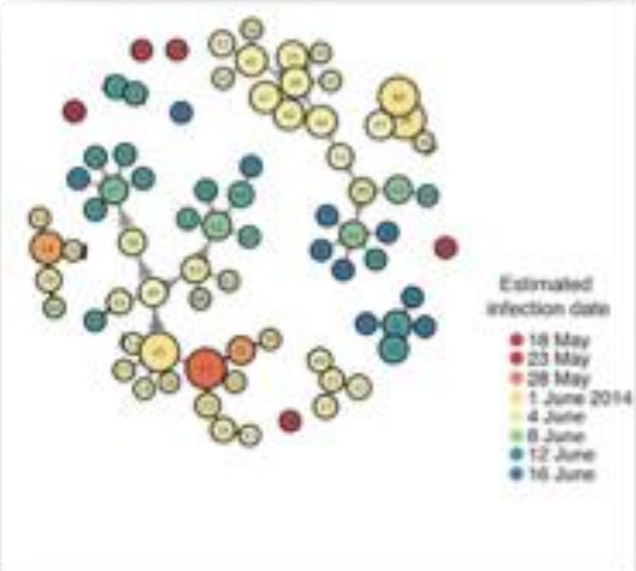
- **Using advanced methods for data analysis, optimization, and high performance computing, models can translate the basic science of infectious diseases into practical public health guidance**

- **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?

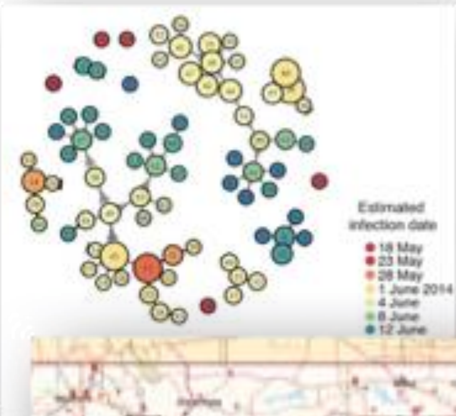


Characterization of Ebola transmission based on viral sequence data and Facebook case reports

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

Scarpino SV et al. Clinical Infectious Diseases. 2015 Jan

Where Are Outbreaks Today?



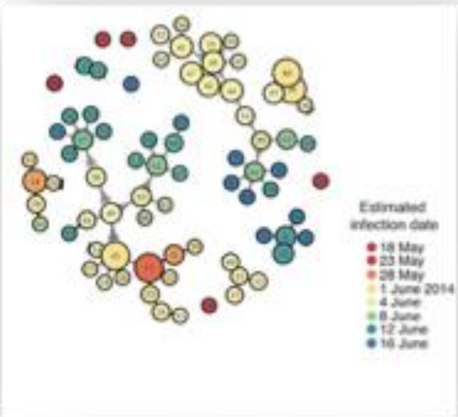
- **Optimizing surveillance systems**
  - Models learn from past outbreaks to improve data collection, situational awareness and outbreak prediction

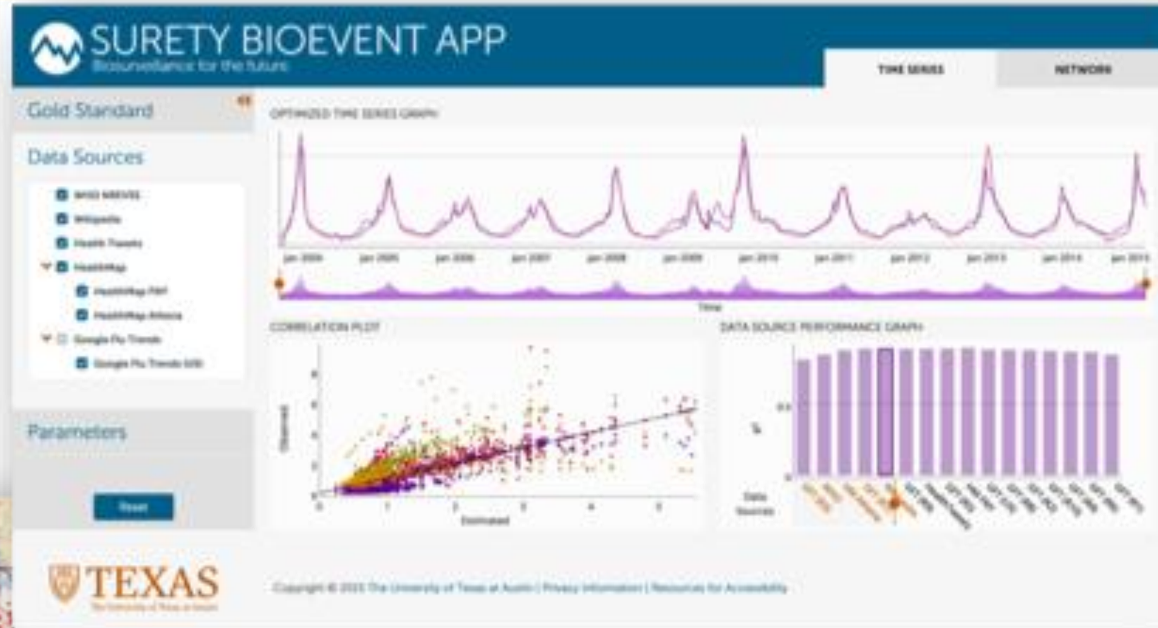
Models used to determine where and when to collect influenza specimens to efficiently detect emerging viruses and select strains for inclusion in next season's vaccine

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

MIDAS
Funded by the National Institutes of Health

Where Are Outbreaks Today?



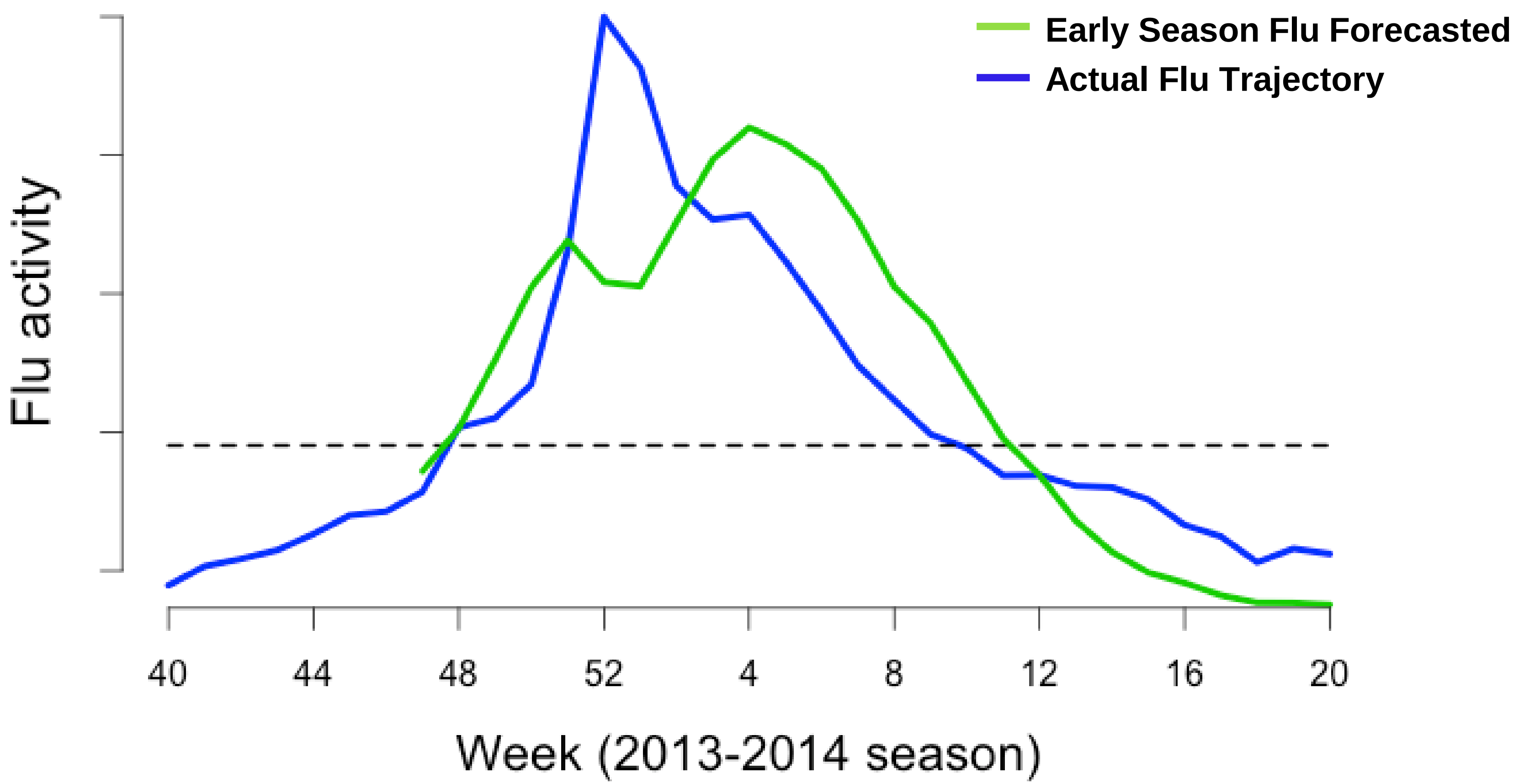


Biosurveillance Ecosystem Surveillance App

DTRA: Defense Threat Reduction Agency
BSVE: Biosurveillance Ecosystem

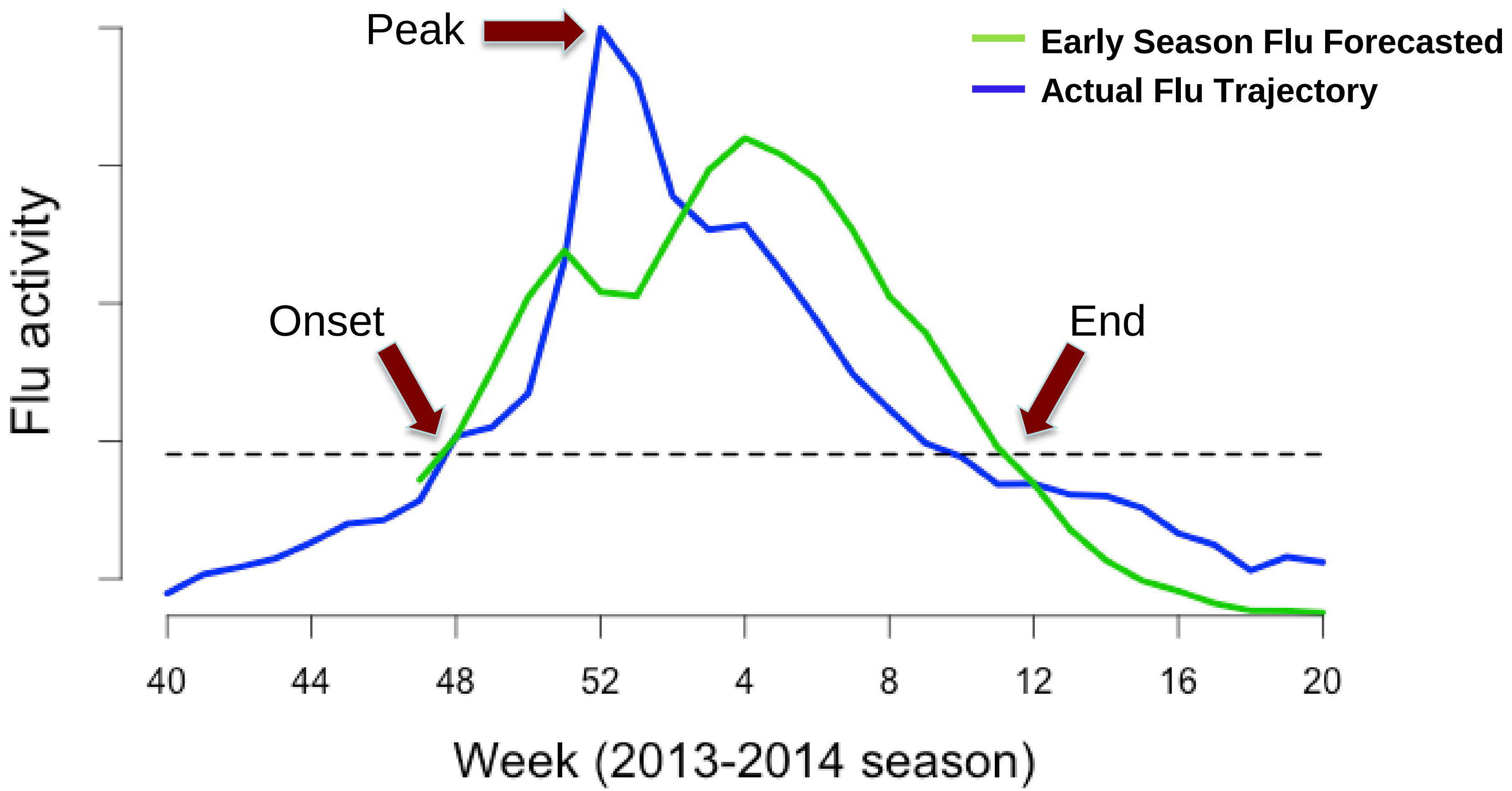
Where Will They Be Tomorrow?

CDC's Predict the Influenza Season Contest



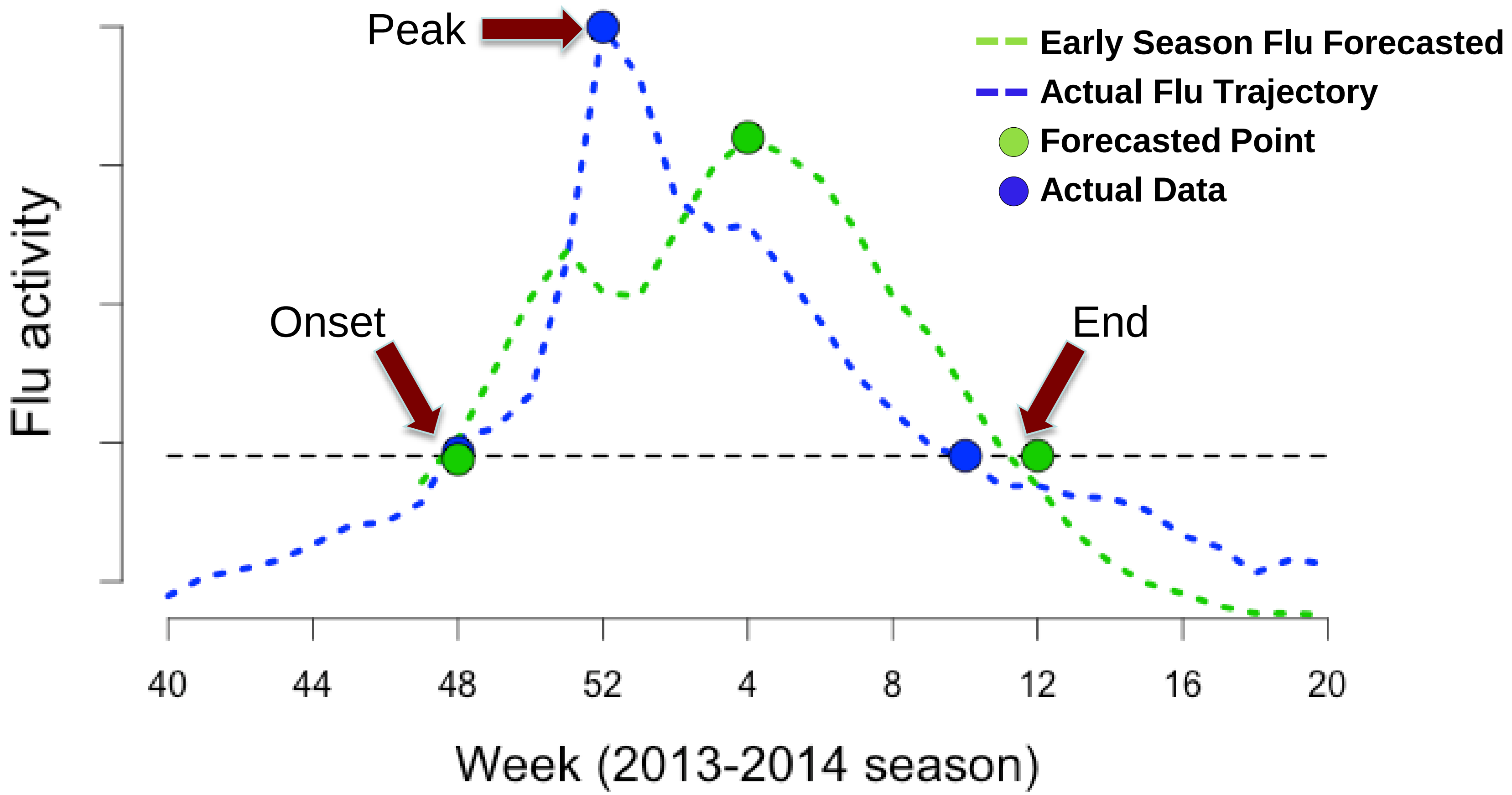
Forecast to Support Decision Making

CDC's Predict the Influenza Season Contest



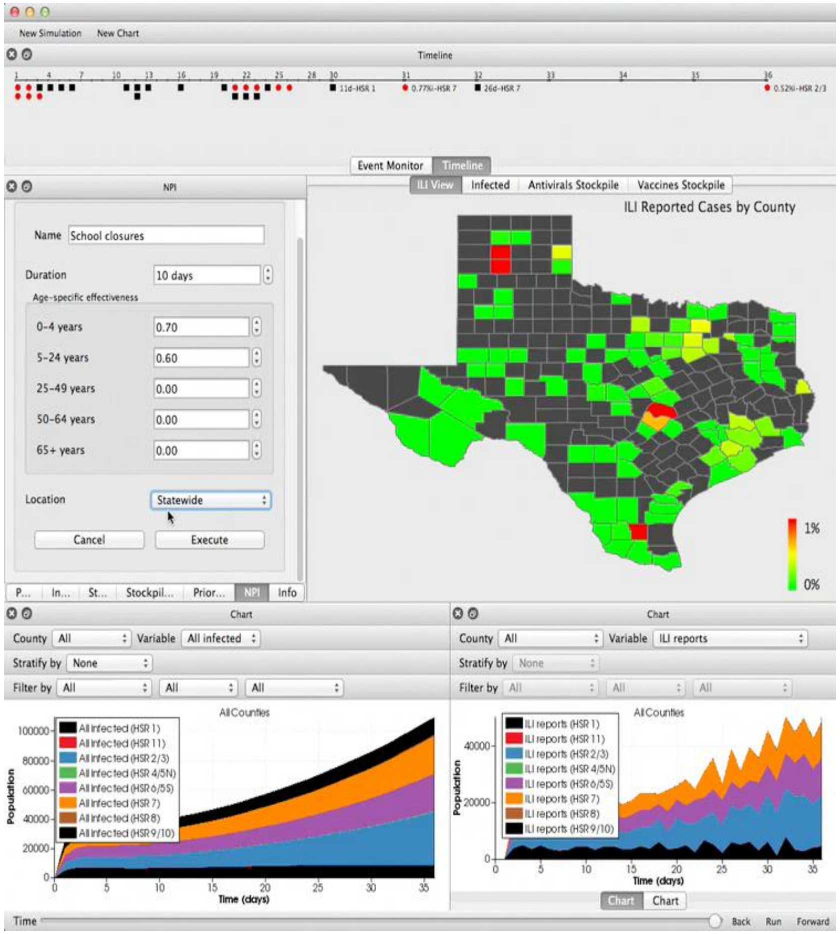
Focus Models on Key Quantities

CDC's Predict the Influenza Season Contest



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



How Can We Optimally Mitigate Outbreaks?

THE LANCET

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The Lancet, Early Online Publication, 16 October 2014
doi:10.1016/S0140-6736(14)61839-0 ? Cite or Link Using DOI

Ebola control: effect of asymptomatic infection and acquired immunity

Steve E Bellan [a], Juliet R C Pulliam [c d], Jonathan Dushoff [e], Lauren Ancel Meyers [b f]

Evidence suggests that many Ebola infections are asymptomatic,[1, 2] a factor overlooked by recent outbre

The Journal of Infectious Diseases

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Oxford Journals › Medicine & Health › The Journal of Infectious Diseases › Volume 211, Issue

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

Alexander Gutfraind[1,2] and Lauren Ancel Meyers[3,4]
+ Author Affiliations

Bellan SE, Pulliam JR, Dushoff J, Meyers LA. Lancet. 2014 Oct
Gutfraind A, Meyers LA. J Infect Dis. 2015 Apr

Opportunities

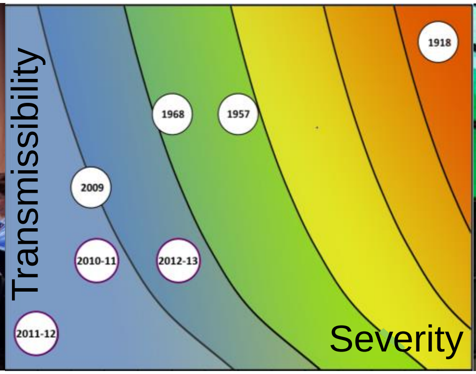
- **Transformative moment for modeling**
  - Upsurge in government appreciation and investment
  - Widening collaborations between decision-makers and modelers
  - Increase in model-driven policies for outbreak prevention and control

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

SUPPLEMENT ARTICLE

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,[5] Stephen C. Redd,[8] Carrie Reed,[5] Anne Schuchat,[2] and Martin I. Meltzer[3]

[1]Division of Diabetes Translation, [2]Office of the Director, National Center for Immunization and Respiratory Disease
Emerging Infections, [4]Division of Global HIV/AIDs, [5]Influenza Division, [6]Division of Sexually Transmitted Disease Preve
Infectious Diseases, and [8]Office of Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georg

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

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

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

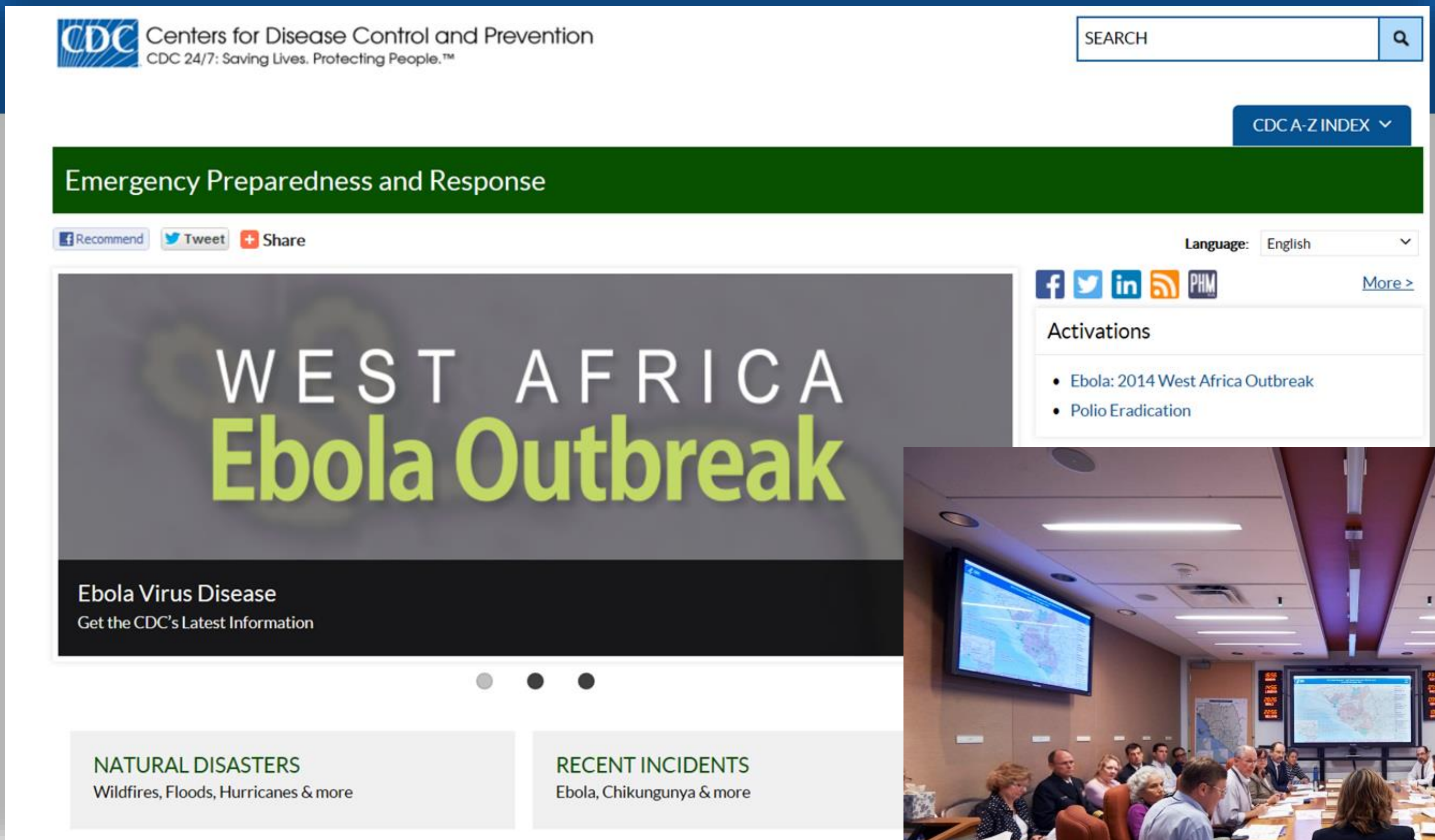
12,470 deaths
(range: 8,870 to 18,300)

Archive: Updates of CDC estimates at: http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm
Shrestha SS, Swerdlow DL, Borse RH, et al. Clin Infect Dis. 2011 Jan

Yes, There Really Was a Pandemic: 2009 pH1N1 to Seasonal Influenza

Age (years)	Numbers per 100,000			
	Deaths		Hospitalizations	
	Median	Average	Median	Average
	pH1N1	1990 to 1999	pH1N1	1979 to 2001
0–17	1.7	0.2	117.4	15.8
18–64	5.0	0.4	83.8	20.8
≥65	4.2	22.1	70.1	282.0
All	4.1	3.1	90.2	52.4

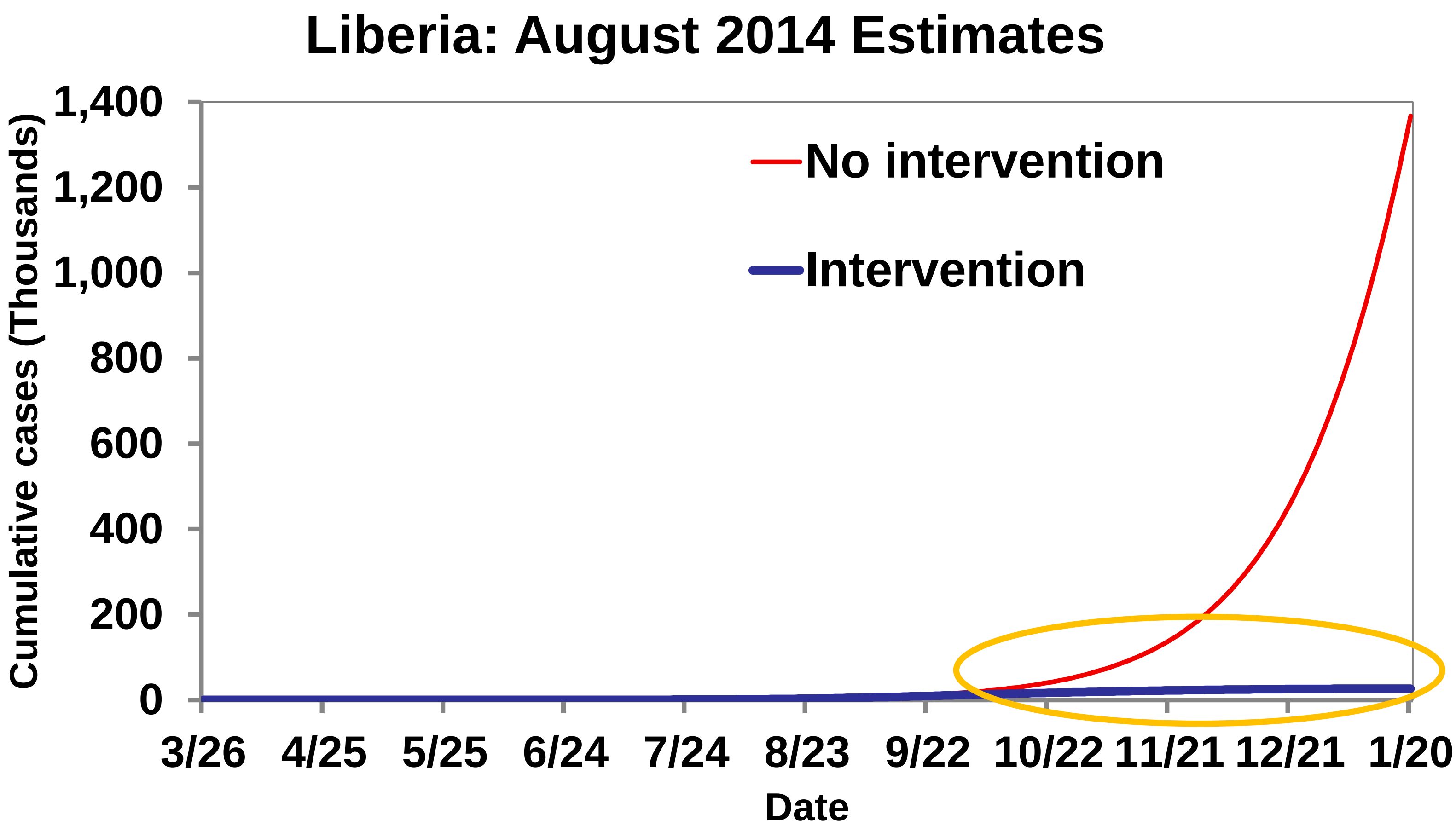
Shrestha SS, Swerdlow DL, Borse RH, et al. Clin Infect Dis. 2011 Jan



CDC Emergency Operations Center

Photo by Spencer Lowell for TIME magazine

Modeling Projections of Cases With and Without Interventions

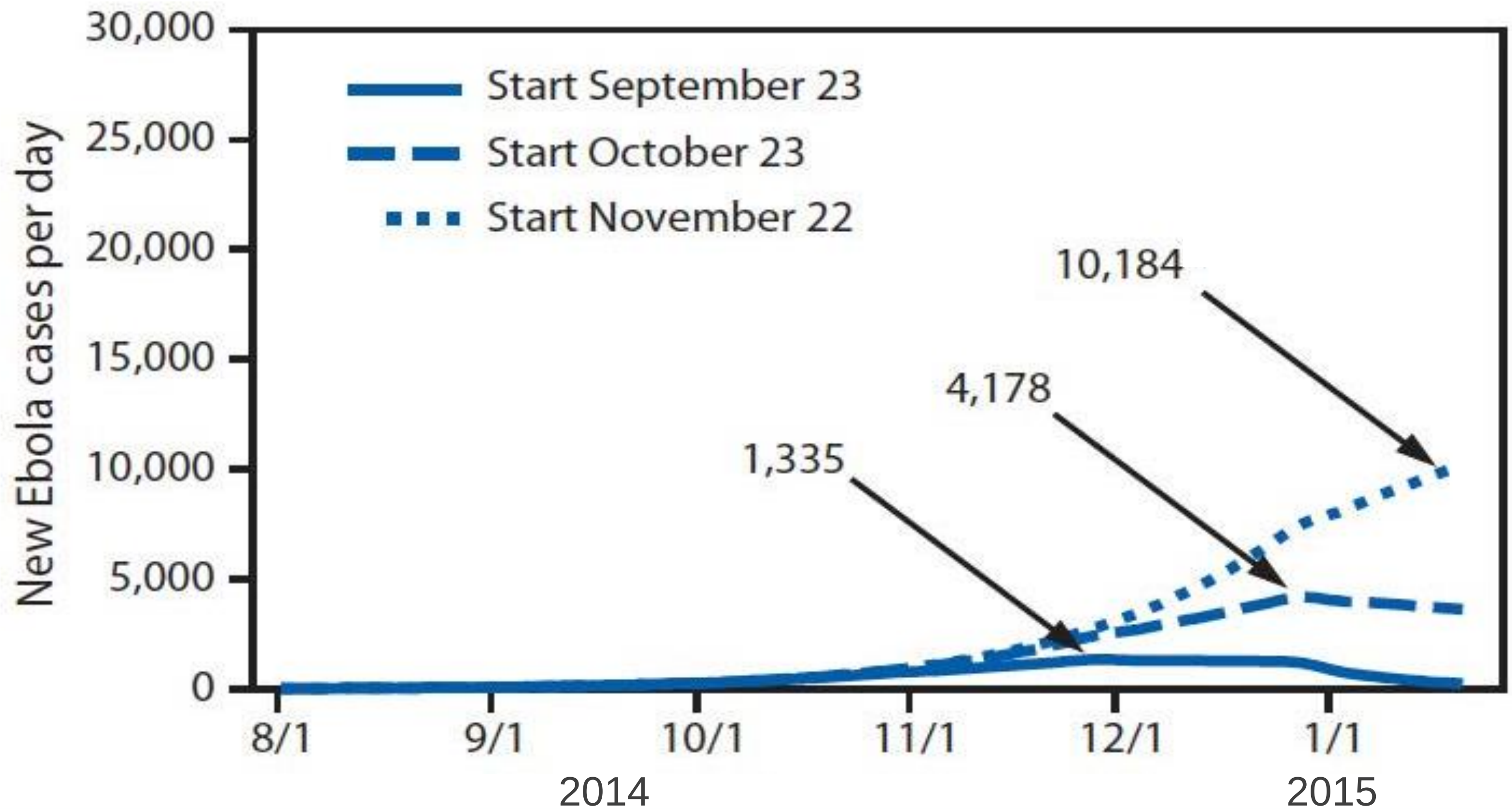


Corrected for potential underreporting by multiplying reported cases by a factor of 2.5

MMWR Surveill Summ 2014;63 Suppl 3

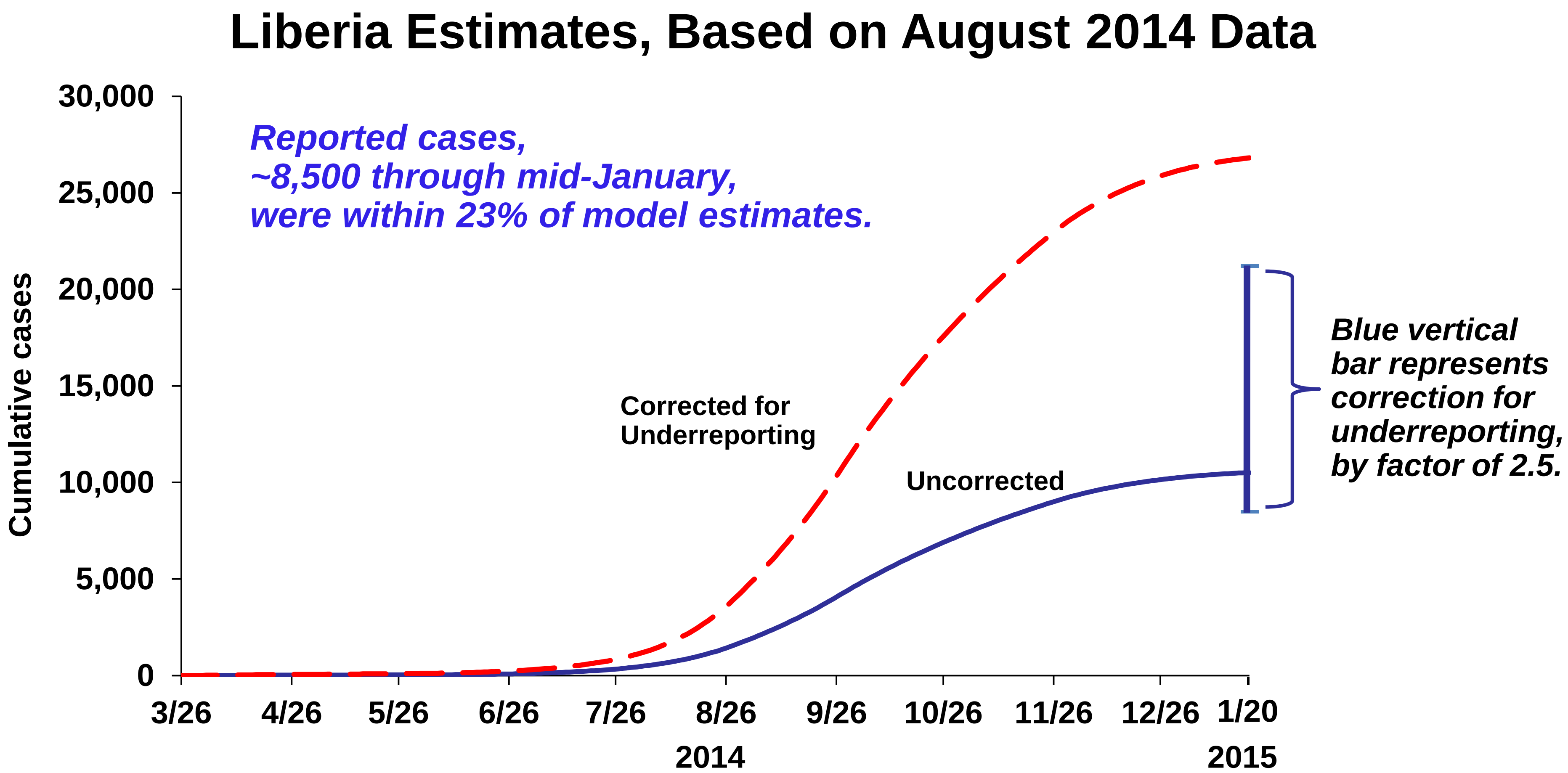
Response Time Matters –
Cases Could Triple For Every Month of Inaction

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

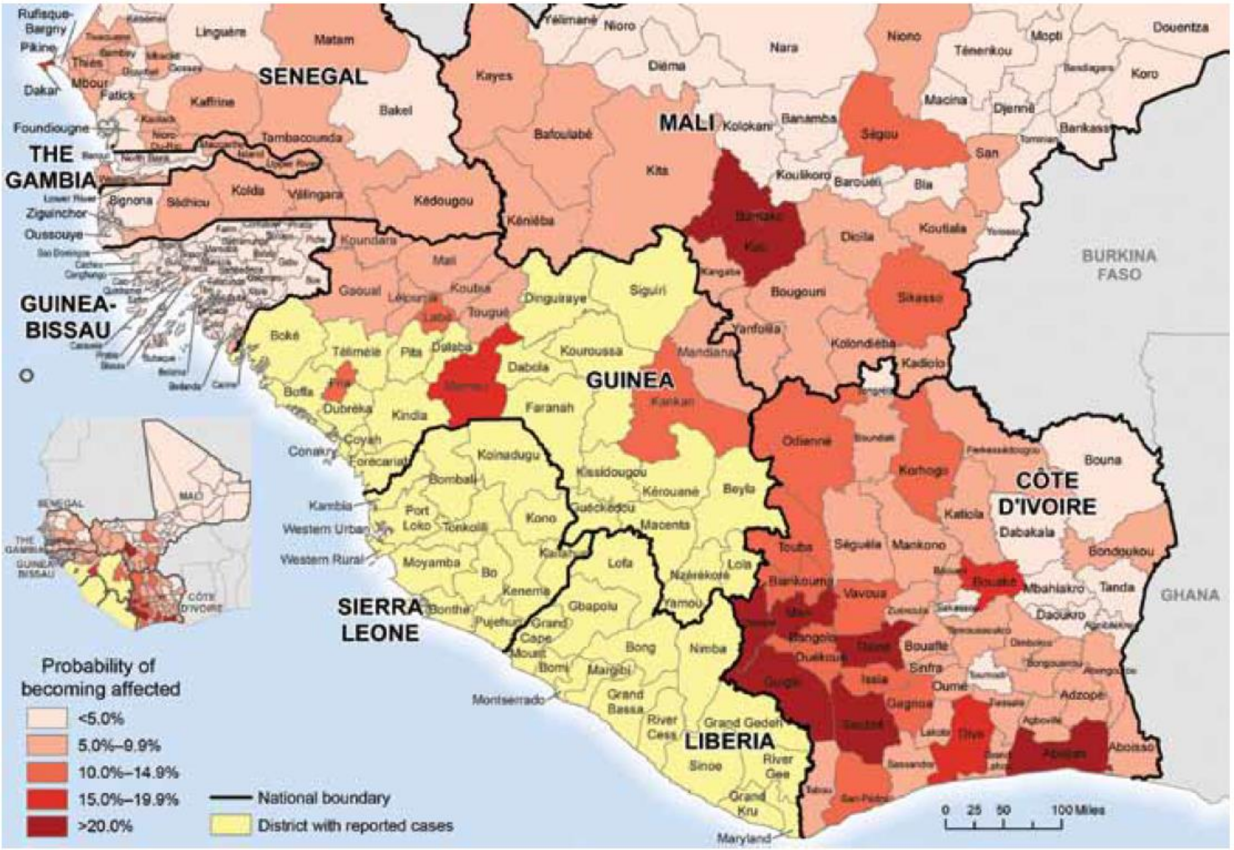


Frieden TR, Damon IK. Emerg Infect Dis. 2015 Nov

DISPATCHES

Regional Spread of Ebola Virus, West Africa, 2014

Gabriel Rainisch, Manjunath Shankar,
Michael Wellman, Toby Merlin, Martin I. Meltzer



Rainisch G, Shankar M, Wellman M, et al. Emerg Infect Dis. 2015 Mar

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
to aid public health officials to estimate the cost of Integrated Disease Surveillance and Response (IDSR) systems

FluWorkLoss – http://www.cdc.gov/flu/pandemic-resources/tools/index.htm
to estimate the potential number of days lost from work due to an influenza pandemic

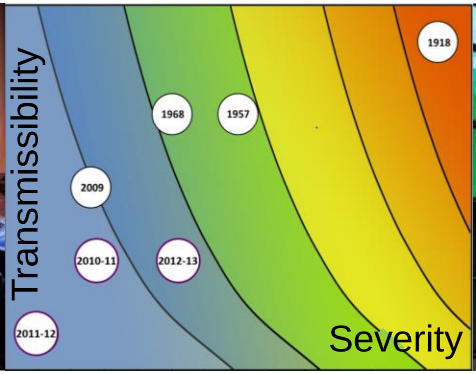
MedCon – http://emergency.cdc.gov/planning/medcon/
to estimate the baseline medical care requirements of a displaced population following a disaster

EbolaResponse – http://stacks.cdc.gov/view/cdc/24900
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

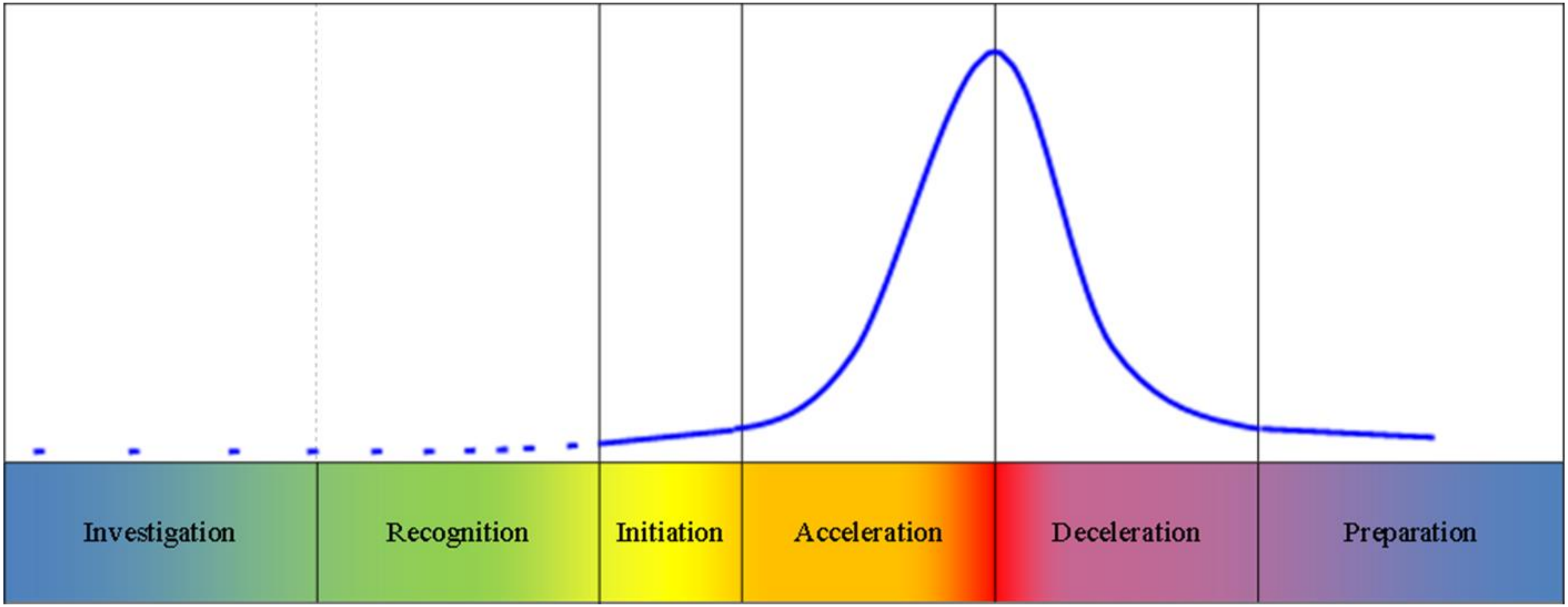


Daniel B. Jernigan, MD, MPH

Director, Influenza Division

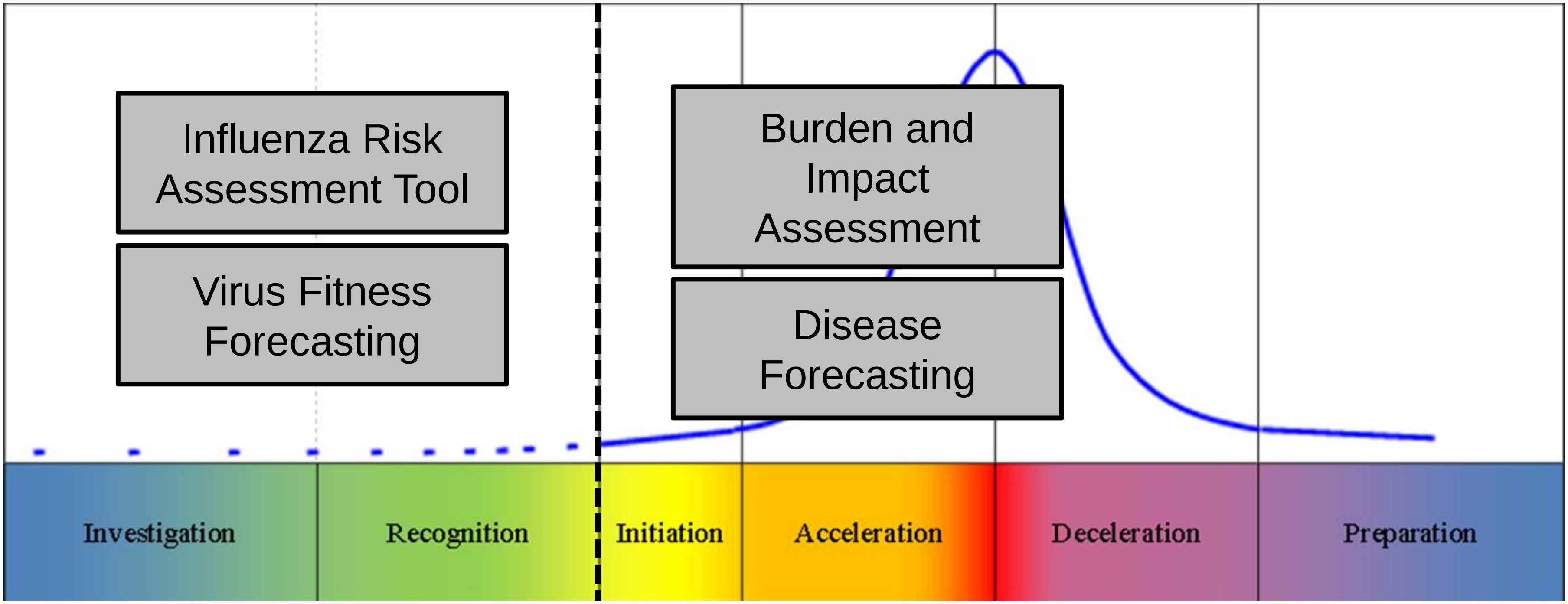
National Center for Immunization and Respiratory Diseases

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

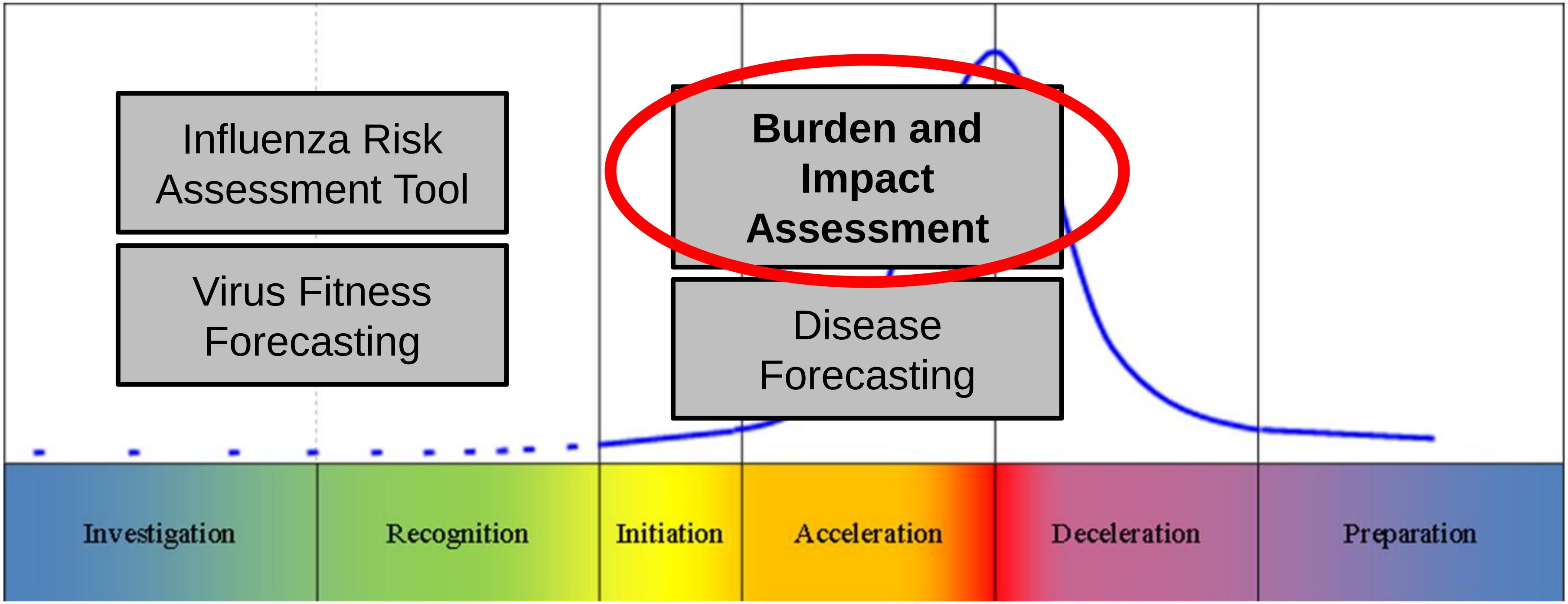


Holloway R, Rasmussen S, Zaza S, et al. MMWR Recomm Rep. 2014 Sep

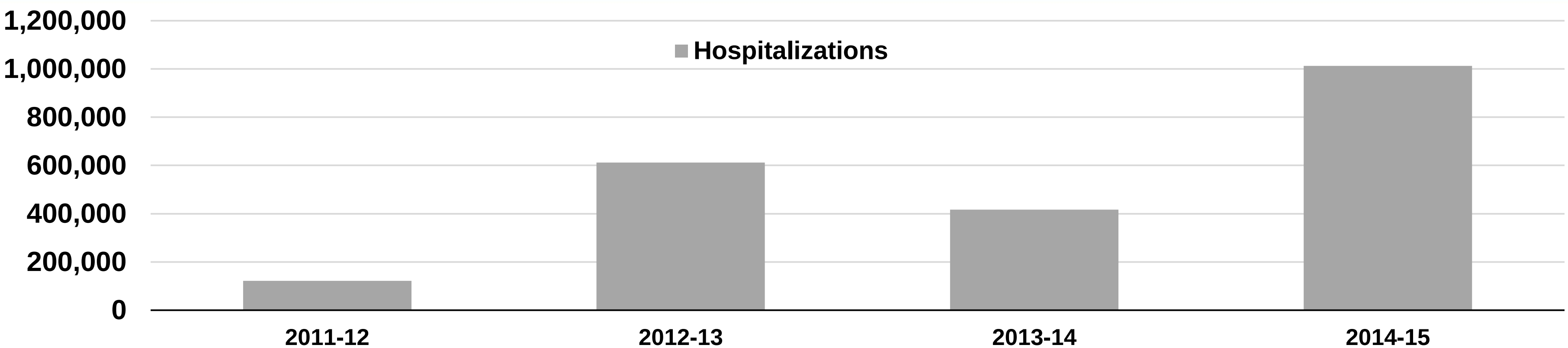
Organizing Framework for Use of Risk Assessment and Modeling Tools Before and After Emergence

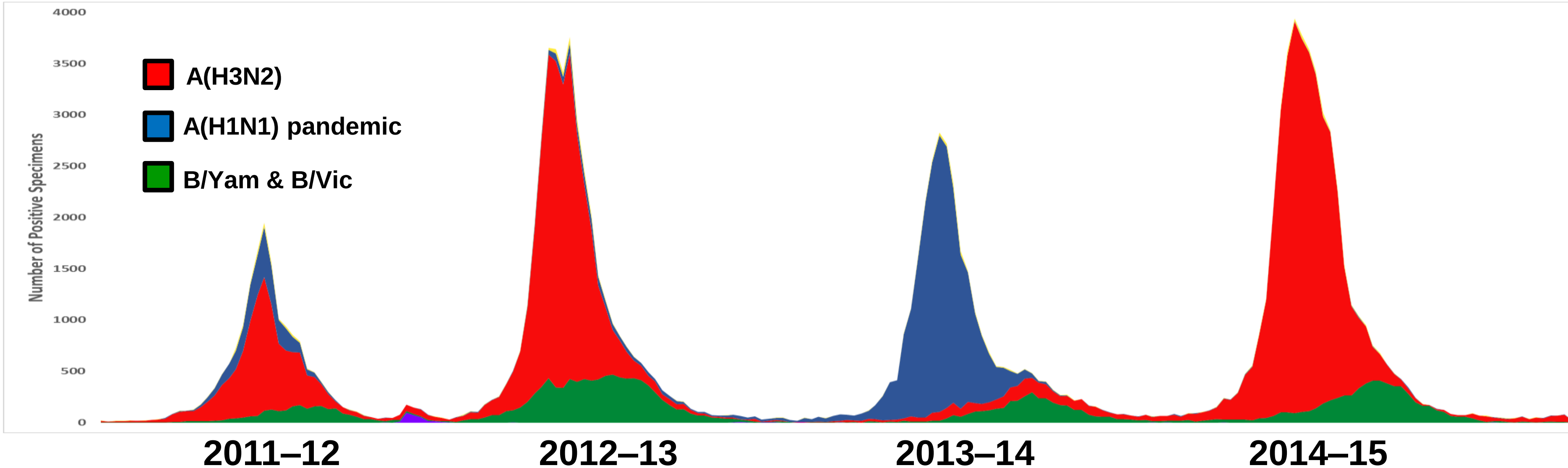


Organizing Framework for Use of Risk Assessment and Modeling Tools Before and After Emergence



Estimated Hospitalizations
Influenza Surveillance 2011–2015





Reed C, Chaves SS, Kirley P, et al. PLoS One, 2015 Mar
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

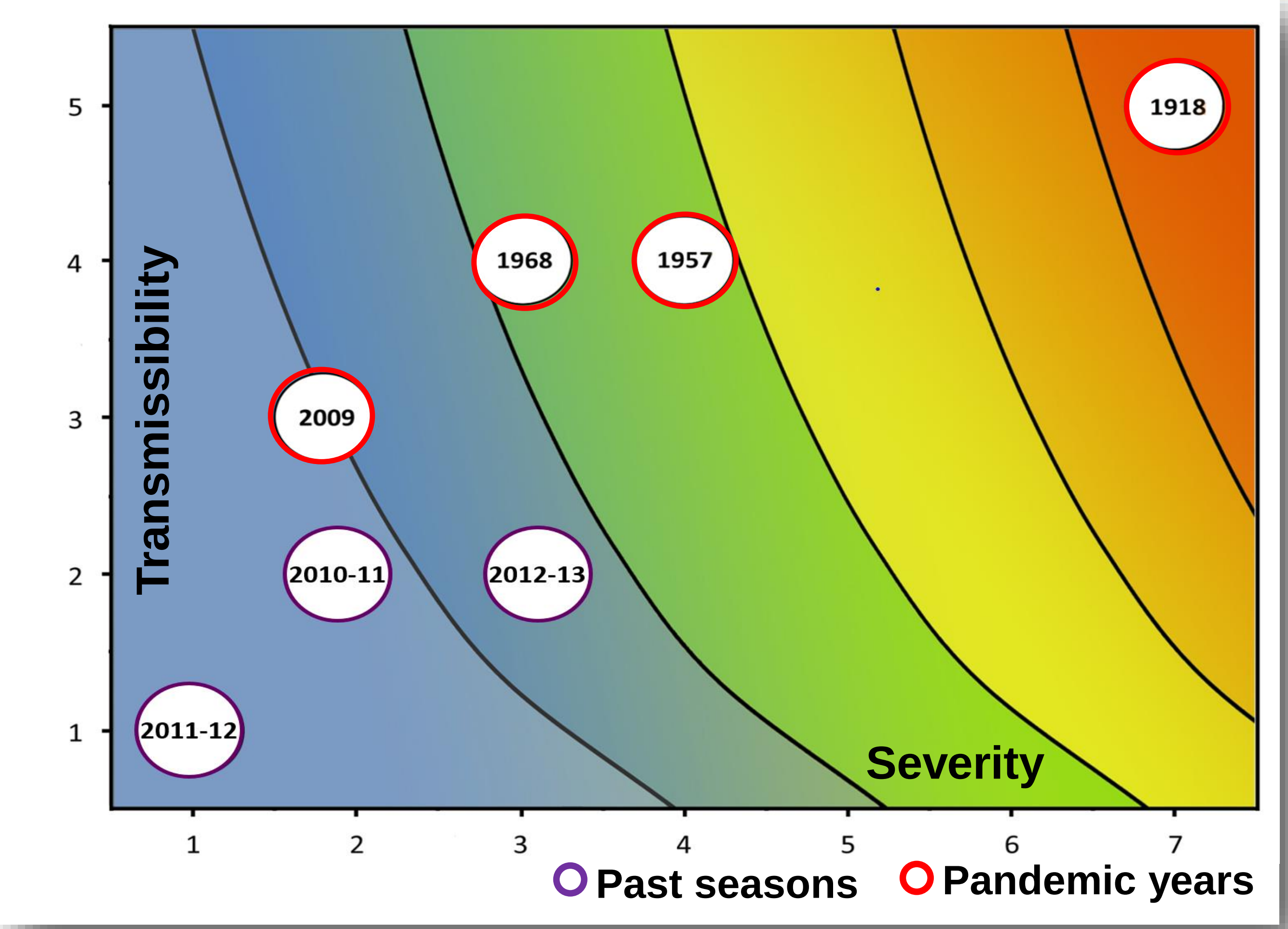
Estimation and Impact Modeling

- **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

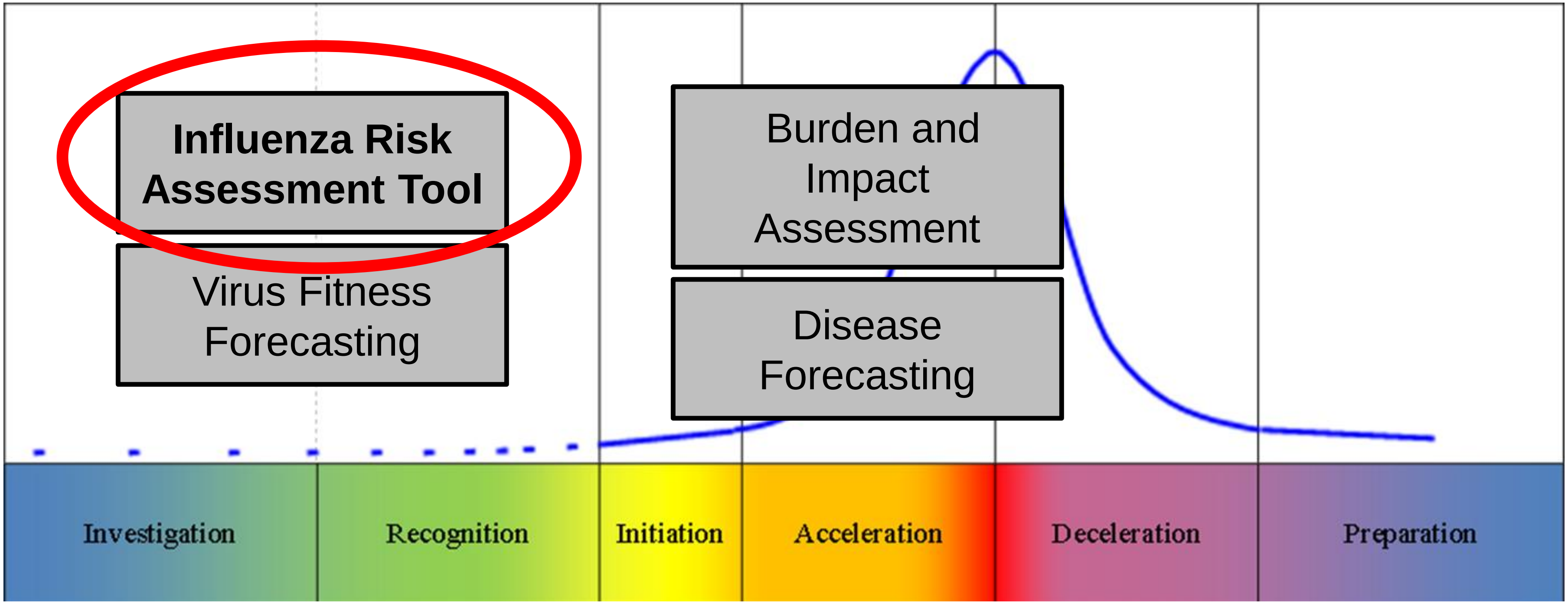
Pandemic Severity Assessment Framework

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

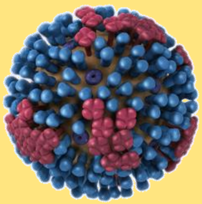


Reed C, Biggerstaff M, Finelli L, et al. Emerg Infect Dis. 2013 Jan

Influenza Risk Assessment Tool



Ten Elements Evaluated in Influenza Risk Assessment Tool (IRAT)

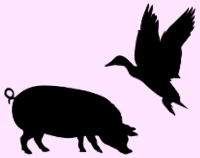


Virus

1. Genomic variation
2. Receptor binding
3. Transmission in laboratory animals
4. Antivirals and treatment options

Population

5. Existing population immunity
6. Disease severity and pathogenesis
7. Antigenic relationship to vaccine candidates



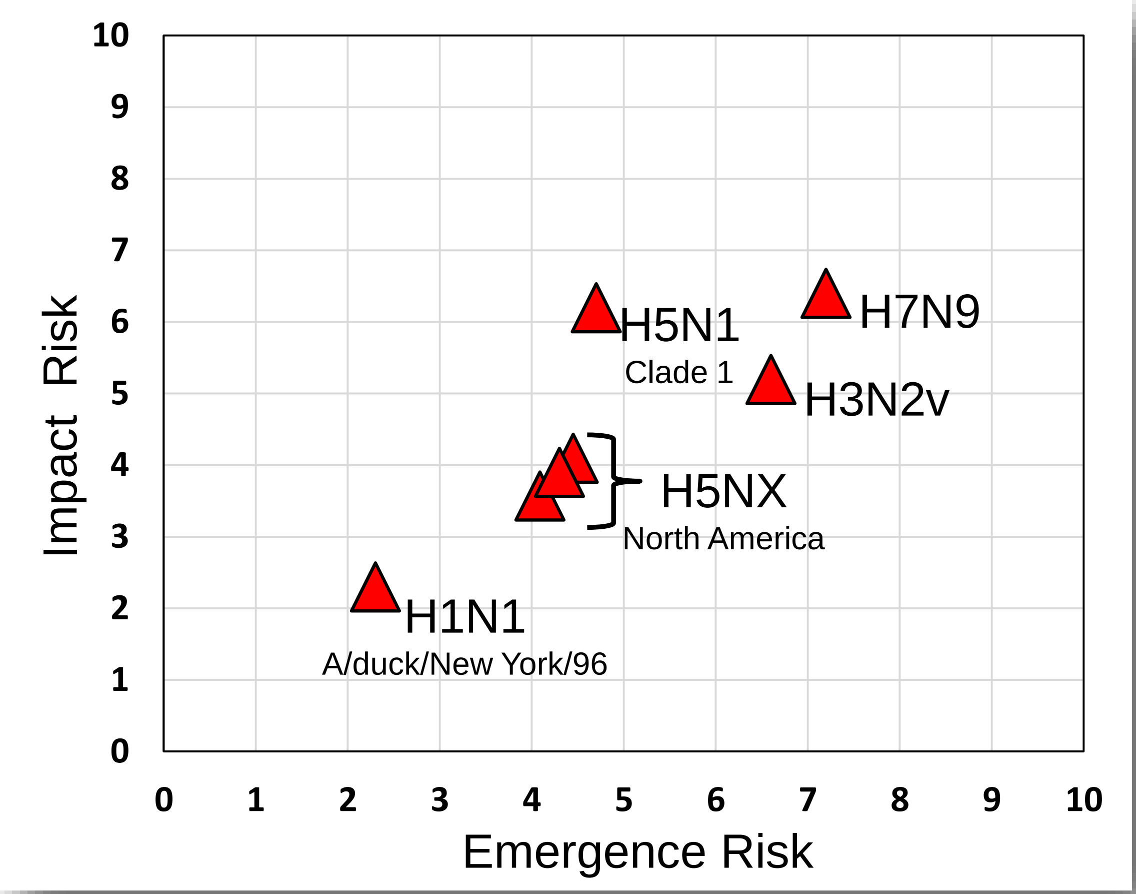
Ecology

8. Global geographic distribution
9. Infection in animals, human risk of infection
10. Human infections and transmission

IRAT: Influenza Risk Assessment Tool. http://www.cdc.gov/flu/pandemic-resources/tools/risk-assessment.htm
Trock SC, Burke SA, Cox NJ. Avian Dis. 2012 Dec

CDC Influenza Risk Assessment of Emerging Novel Influenza Viruses

- **CDC routinely conducts risk assessments on emerging novel influenza viruses**
  - Assess risk of emergence
  - Assess impact, if emerges



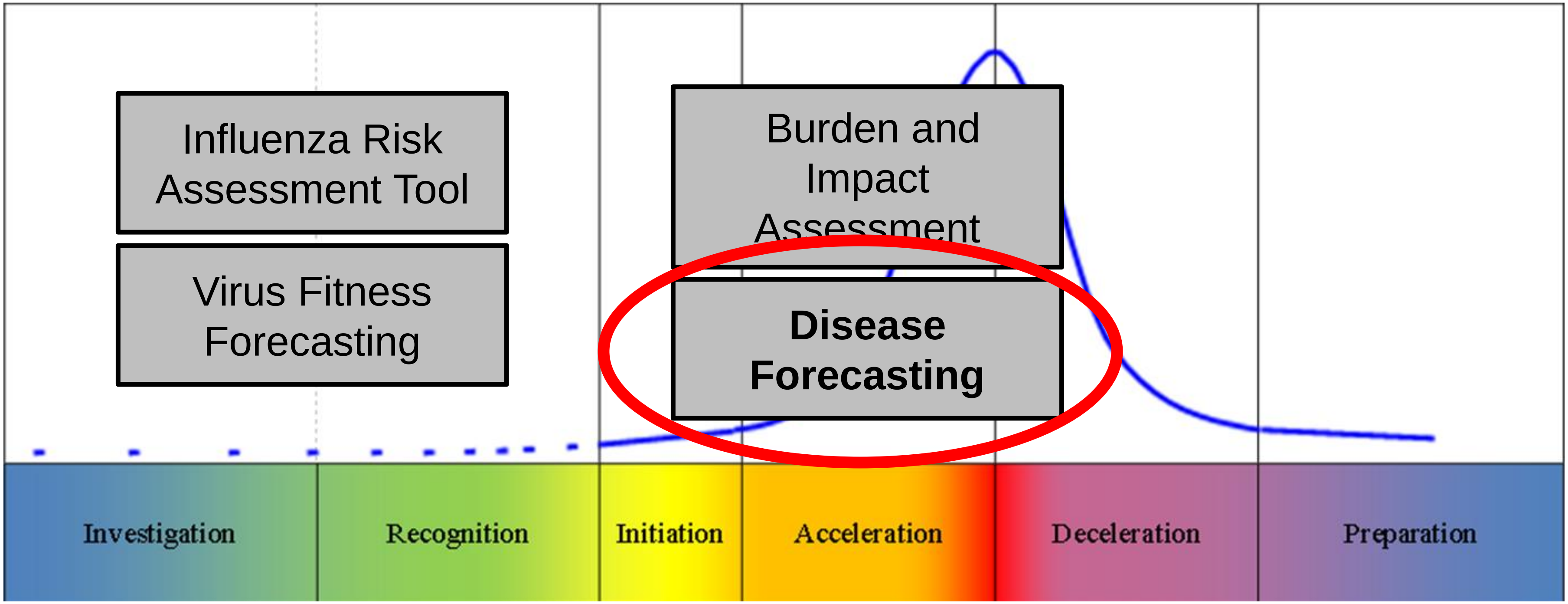
IRAT: Influenza Risk Assessment Tool. http://www.cdc.gov/flu/pandemic-resources/tools/risk-assessment.htm
Trock S, Burke S. CDC Unpublished Data for H5NX Assessment
Trock S, Burke S, Cox N. Avian Dis. 2012 Dec

CDC Influenza Risk Assessment Tool (IRAT)

- **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

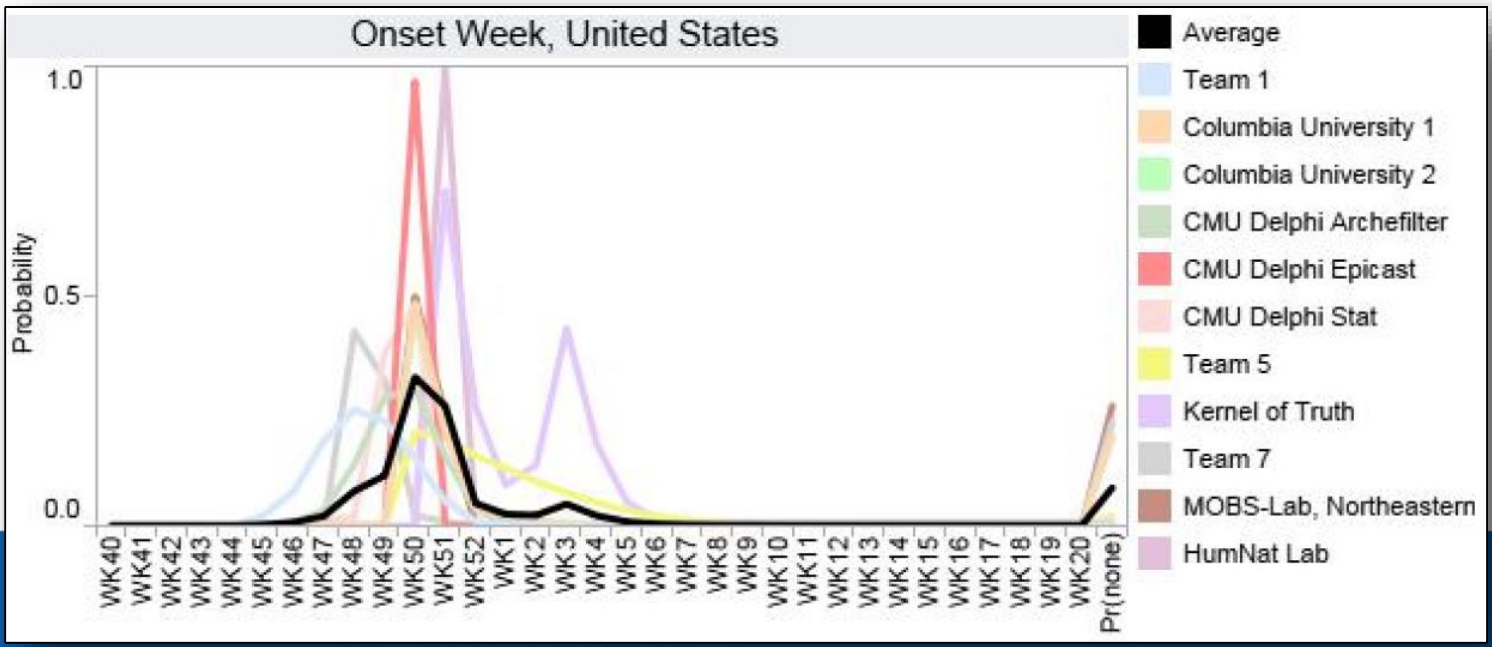
IRAT: Influenza Risk Assessment Tool. http://www.cdc.gov/flu/pandemic-resources/tools/risk-assessment.htm

Disease Forecasting



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**



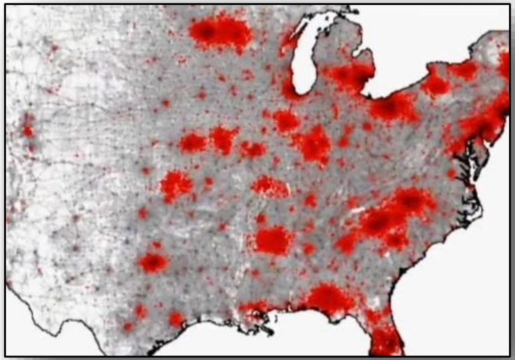
Biggerstaff, Reed, and Influenza Division Applied Research and Modeling Team

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

MIDAS

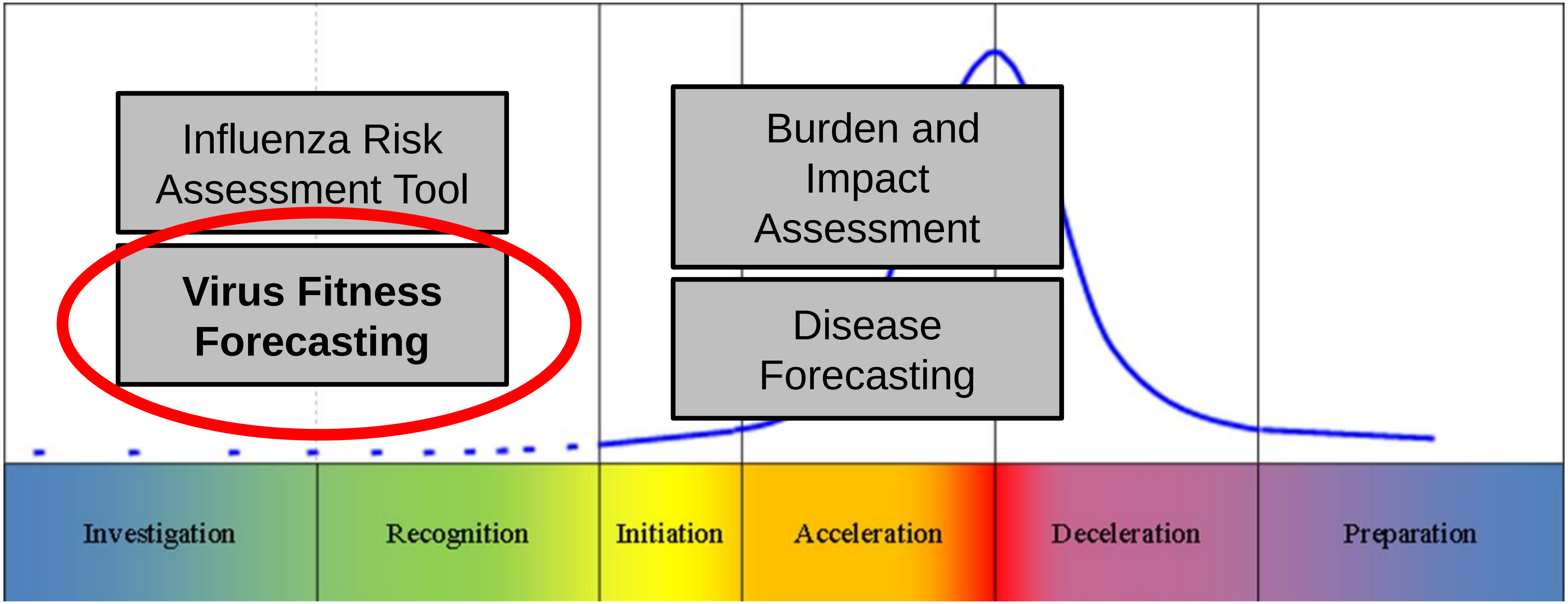
Funded by the National Institutes of Health



DHS: Department of Homeland Security
DoD: Department of Defense
ORNL:Oak Ridge National Laboratory

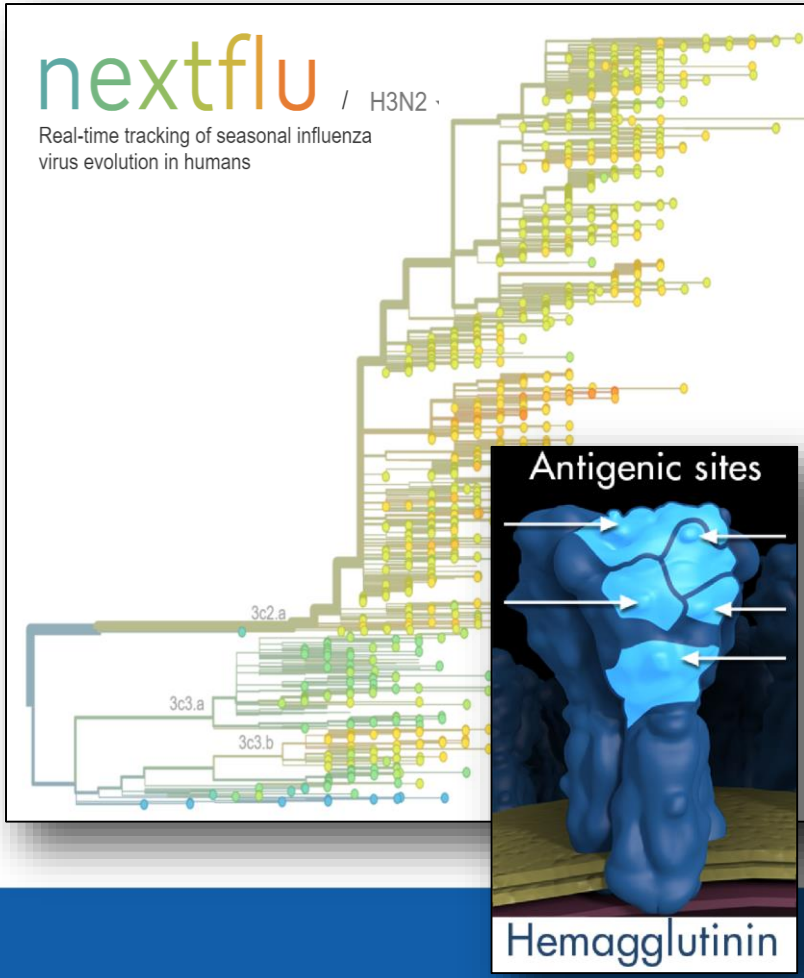
ARDA: Biomedical Advanced Research & Development Authority
LANL: Los Alamos National Laboratory
https://www.nigms.nih.gov/research/specificareas/MIDAS/Pages/default.aspx

Virus Fitness 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**



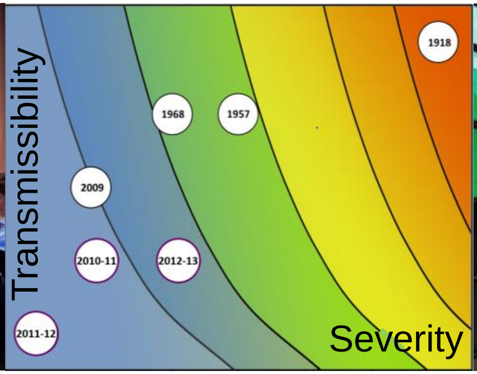
http://www.nextflu.org/H3N2/1y/

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

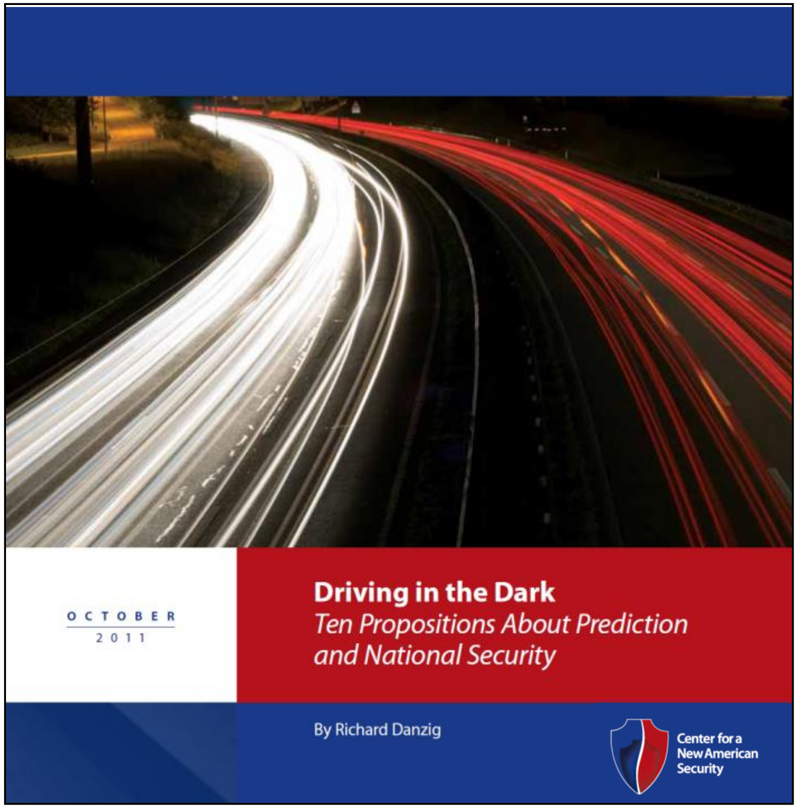
Biomedical Advanced Research and Development Authority

Office of the Assistant Secretary for Preparedness and Response

Models as Tools for Decision Making

"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



Richard Danzig, *Driving in the Dark: Ten Propositions about Prediction and National Security* Center for a New American Security, 2011

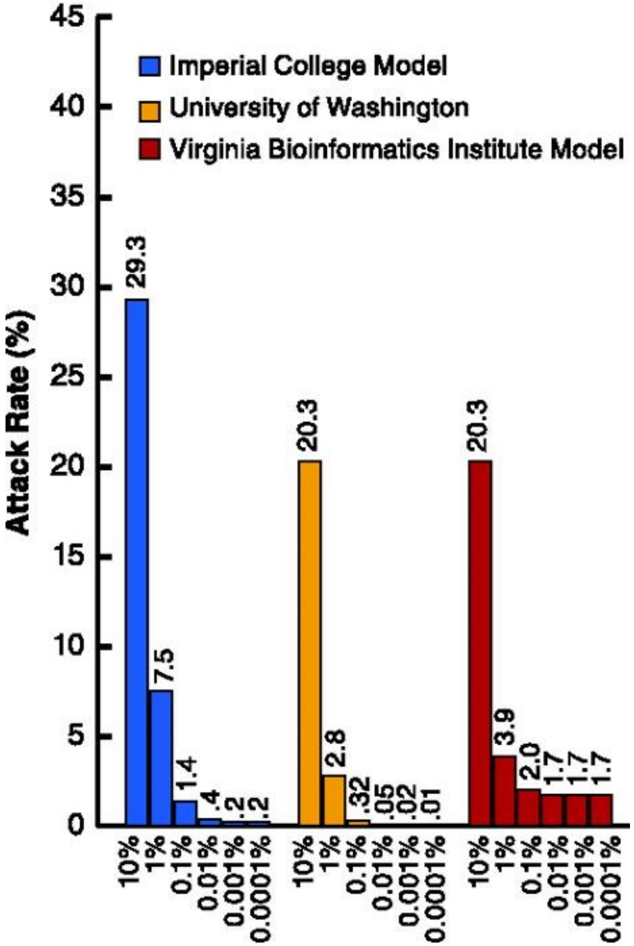
Decision Makers Need to Recognize Limitations of Models

- **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



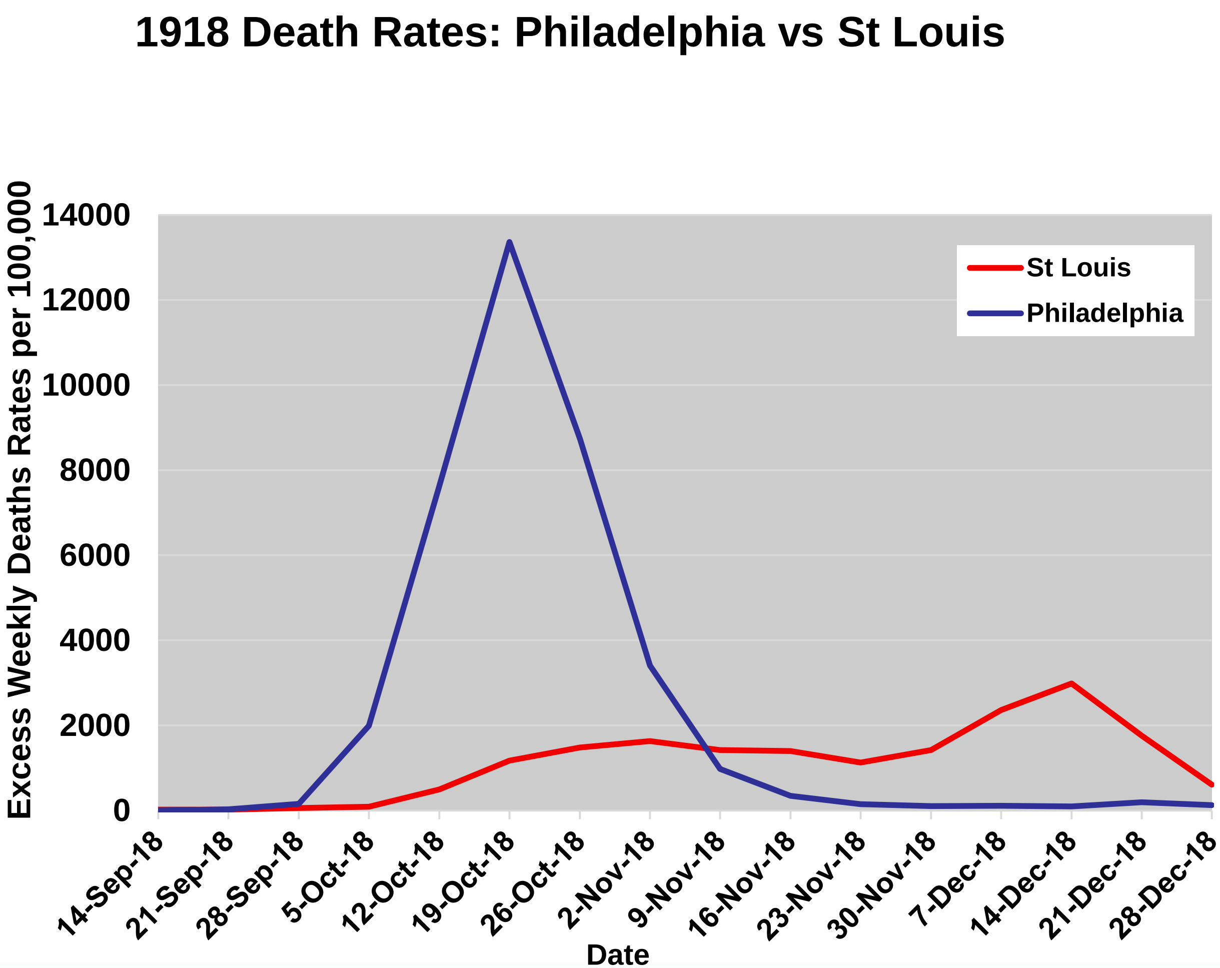
Percent infected before measures started

- 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

Halloran ME, Ferguson NM, Eubank S, et al. Proc Natl Acad Sci U S A. 2008 Mar

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



- **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
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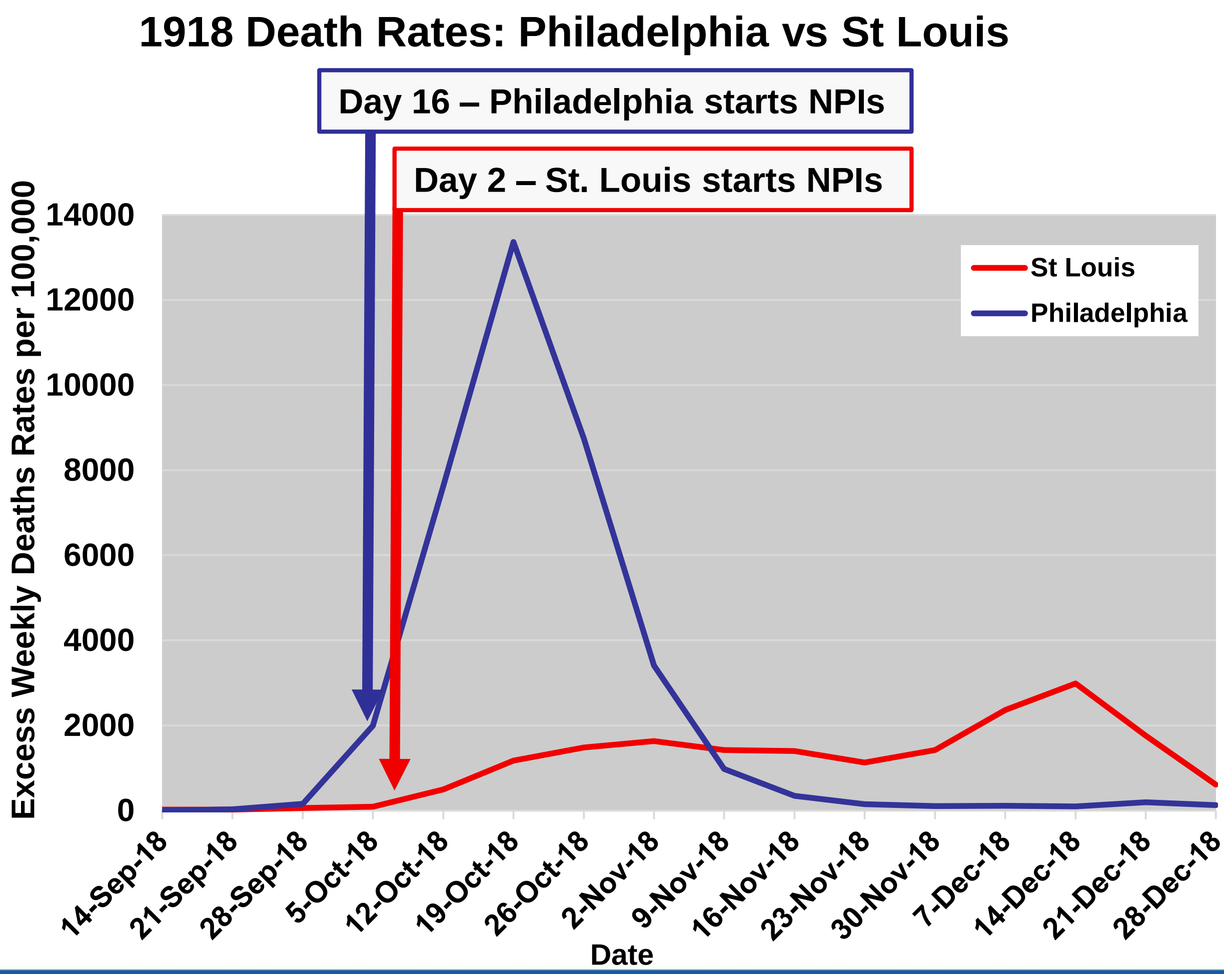

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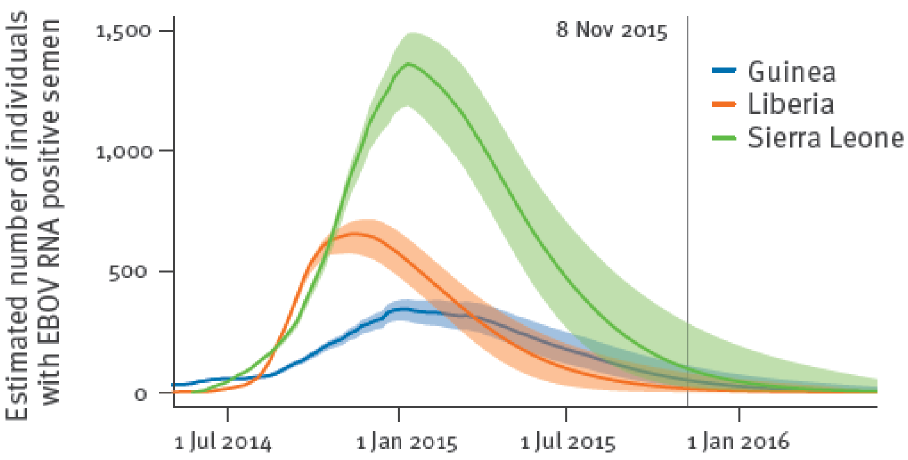
Examples of Ways In Which Models Provide Foresight

- **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

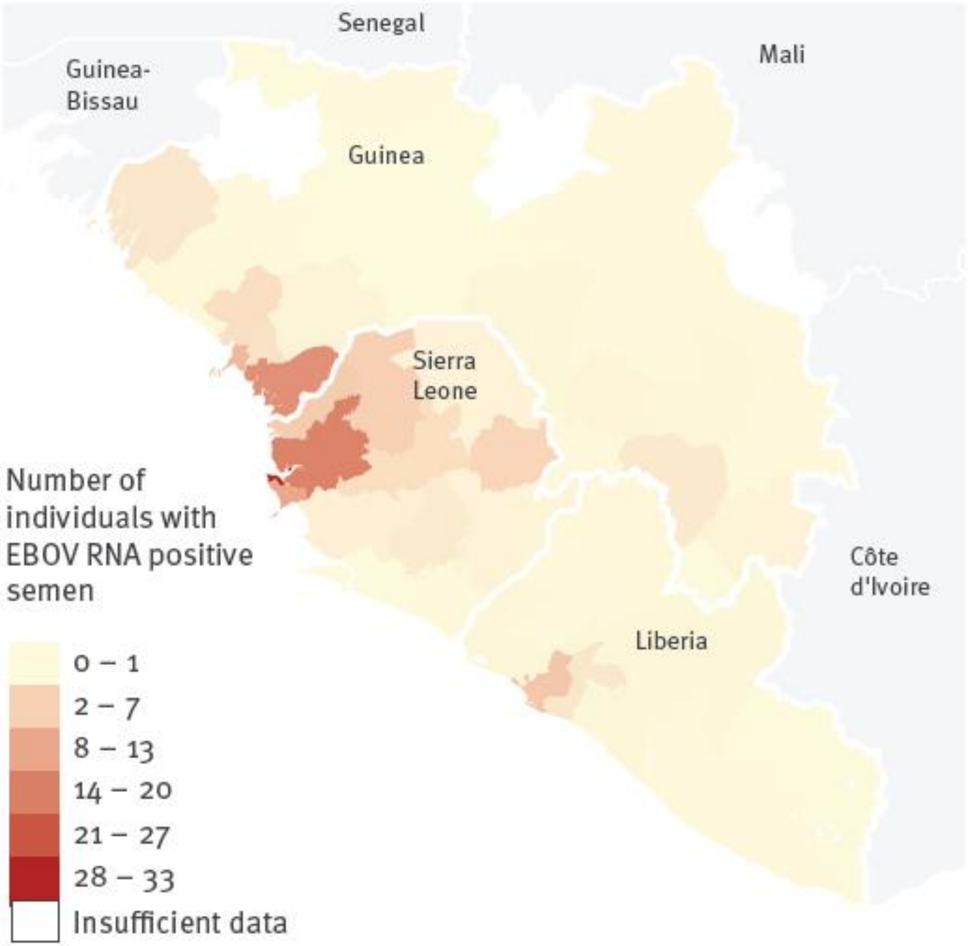
Risk of Sexual Transmission of Ebola



- 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

Eggo RM, Watson CH, Camacho A, et al. Euro Surveill. 2015 Dec

Risk of Sexual Transmission of Ebola



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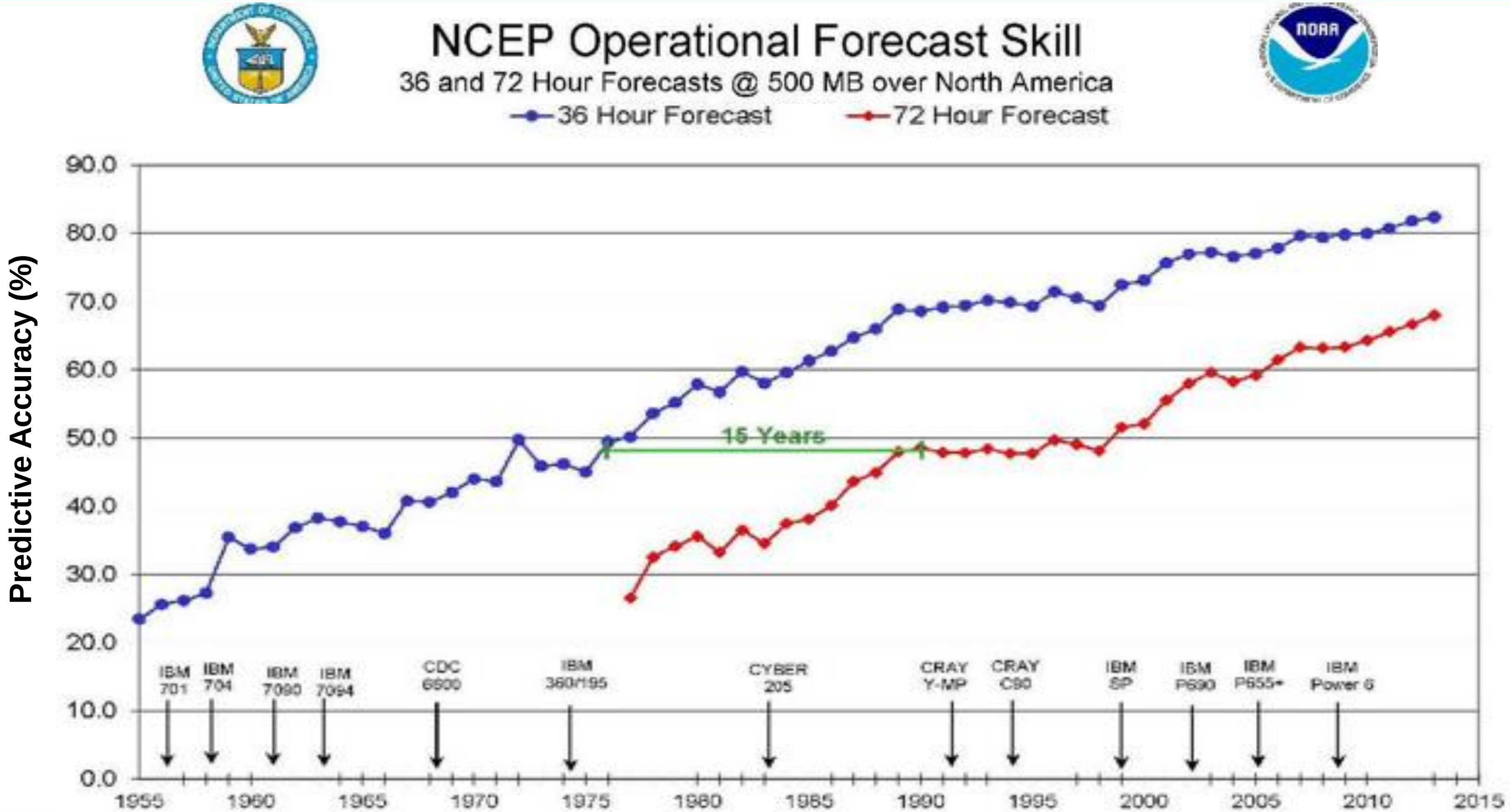
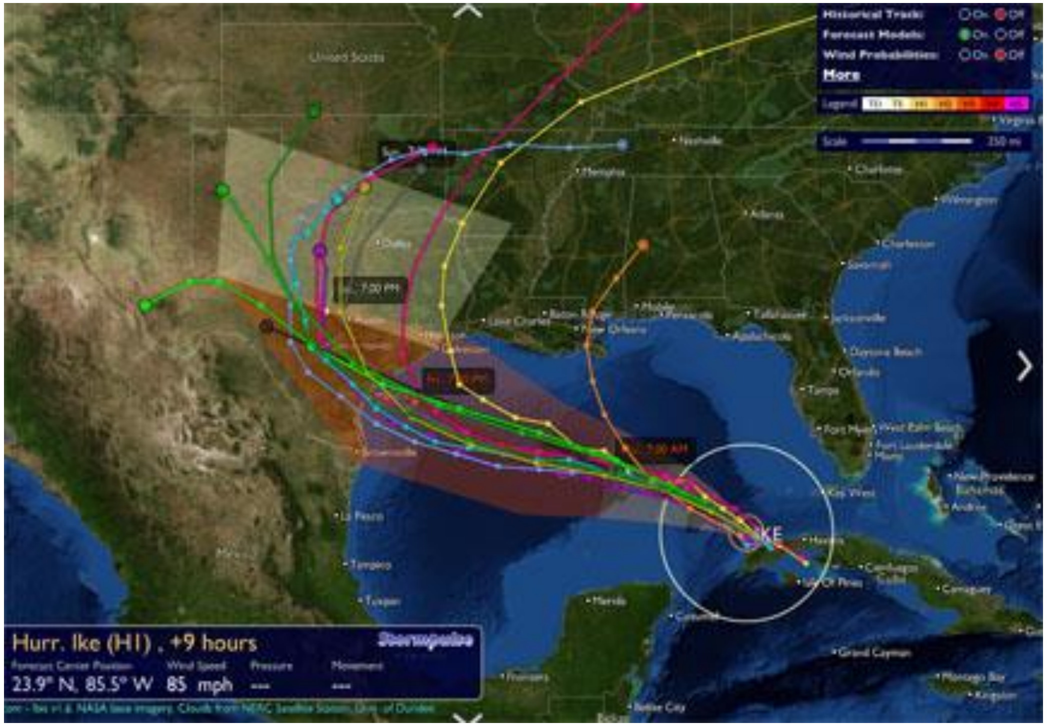
Repeated Comparison of Predict vs. Actual Outcomes Has Improved Accuracy of Models



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

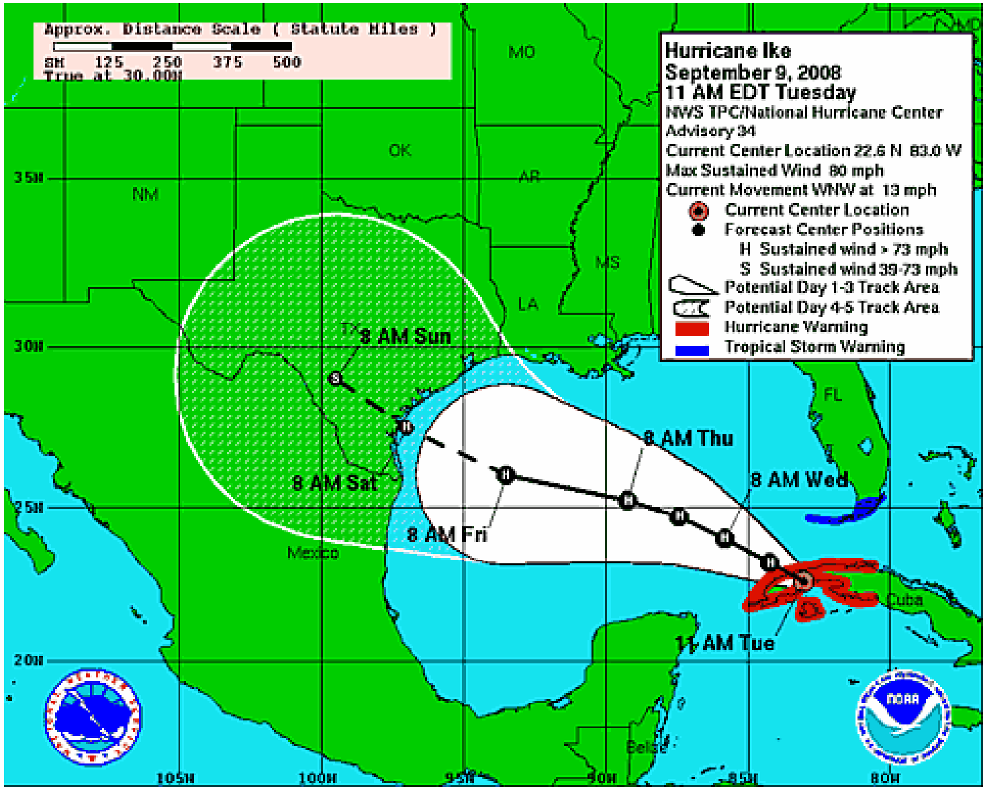


Multiple pathways modeled for Hurricane Ike

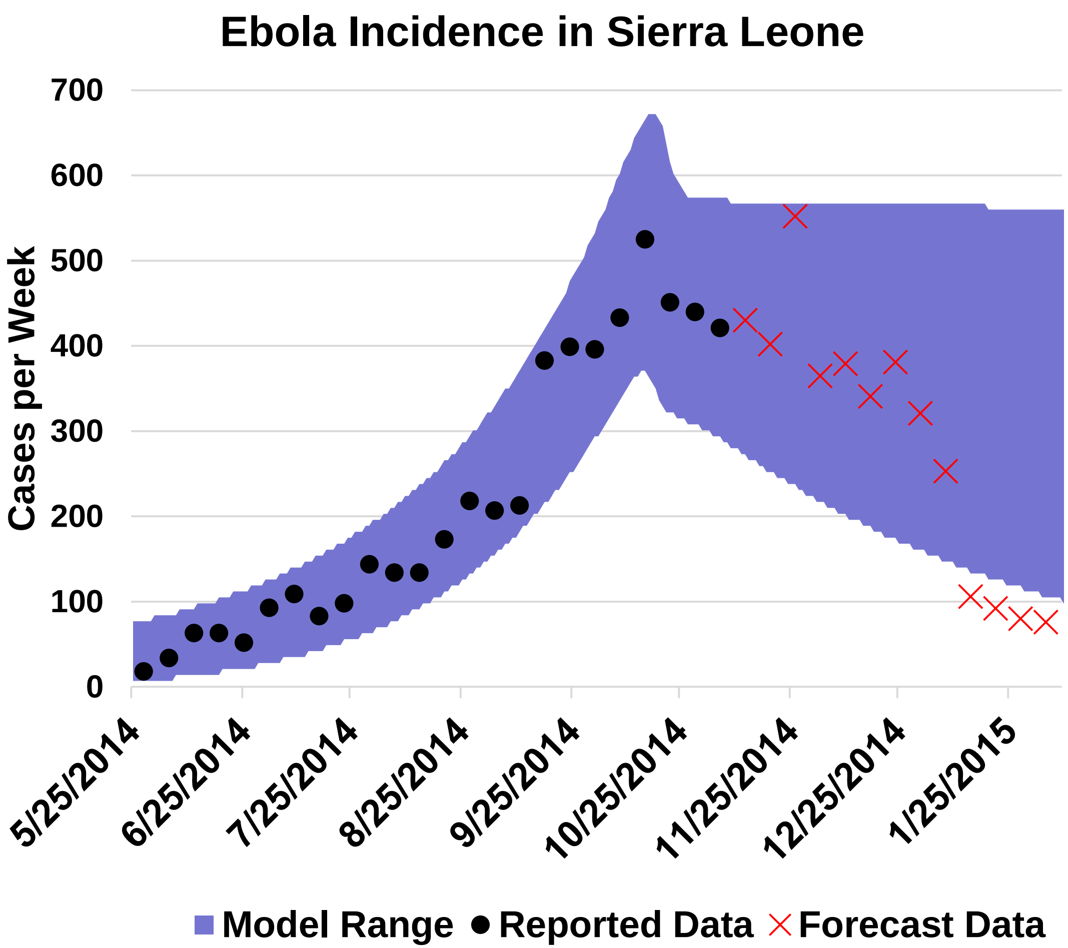
Combining Multiple Predictive Models Shrinks Cone of Error

- **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**



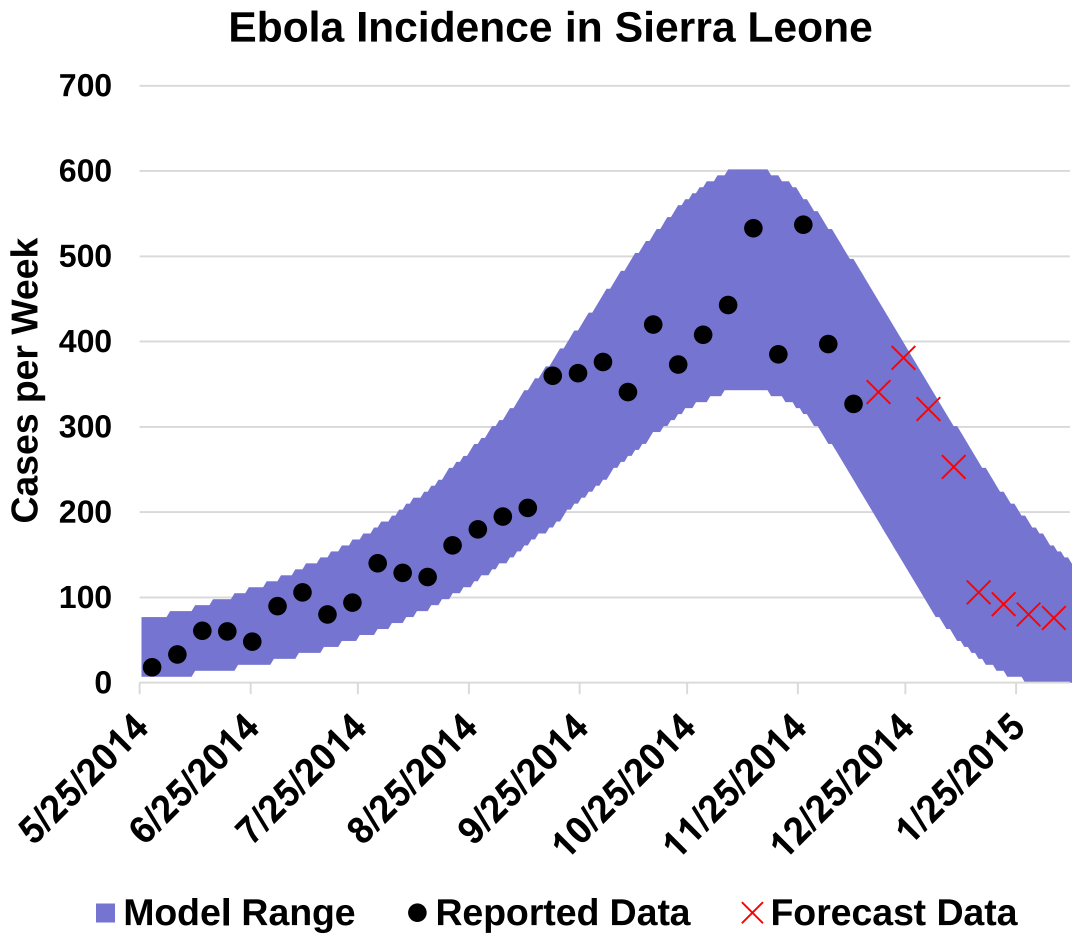
Looking to The Future of Epidemic Forecasting



- 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)

Looking to The Future of Epidemic Forecasting



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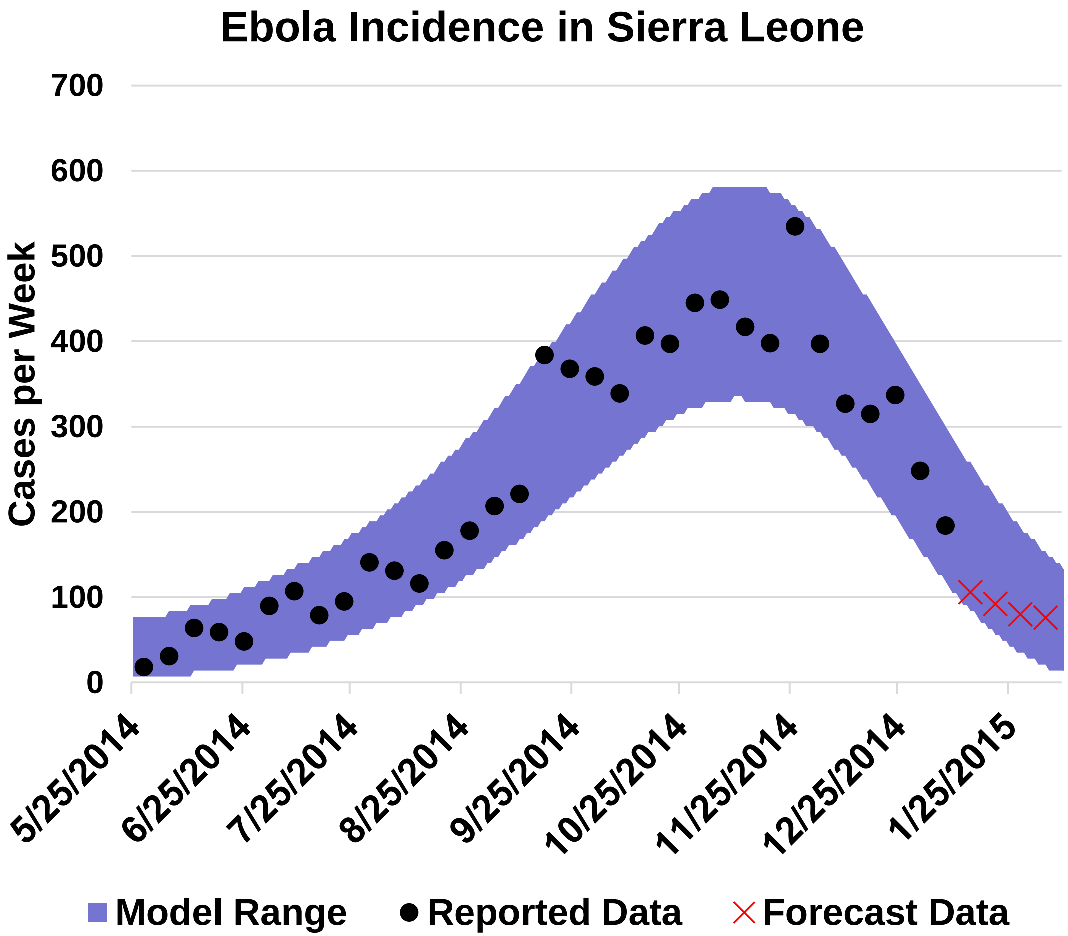

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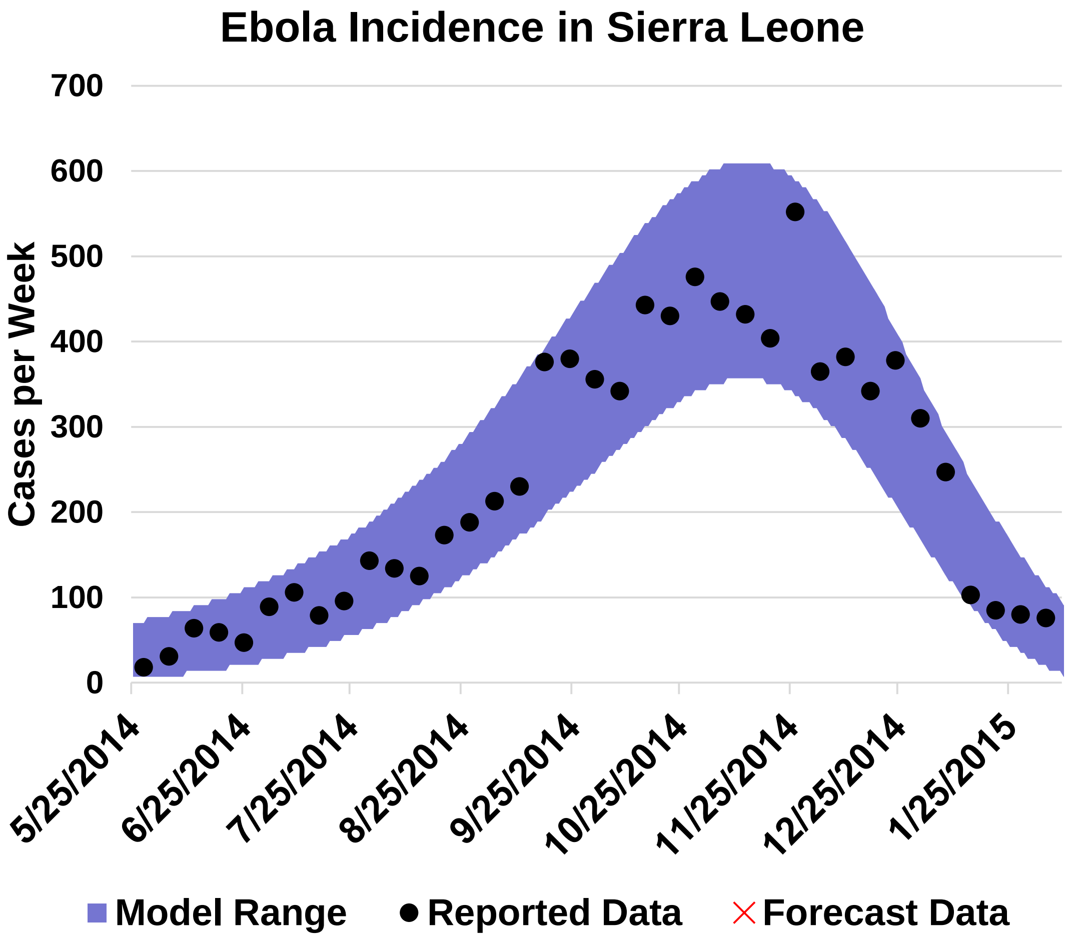

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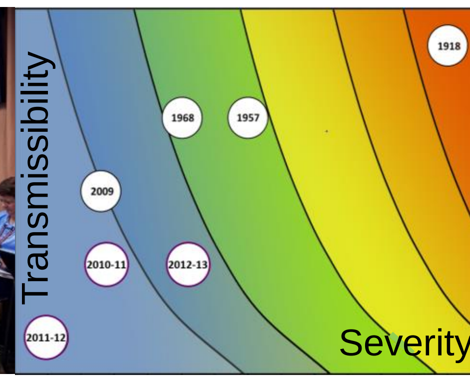
The Prosocial Function Of Modeling: Conduit for Communication

With thanks to Steve Bankes

CDC PUBLIC HEALTH GRAND ROUNDS

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





January 19, 2016

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention