Pandemic Influenza Preparedness: Preparation of a Research Platform to Ensure a Timely Response

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Background
- Pandemic influenza can result in a rapidly escalating epidemiologic pattern in populations with little or no pre-existing immunity.
- Information from public health research can inform strategies to control and prevent pandemic influenza virus infection.
- During the 2009 pandemic, some public health research was not initiated in a timely fashion due to delays related to protocol development, site selection, institutional review board approval, and lack of flexible funding mechanisms.
- Therefore, CDC developed a new research platform to enable rapid initiation of special epidemiological studies in the event of a future influenza pandemic.

Methods
- The Pandemic Preparedness Meta-Project was created in September 2013 to provide a platform to address four objectives:
  - Examine influenza vaccine effectiveness (VE) and uptake;
  - Examine antiviral use and effectiveness (AVE);
  - Describe epidemiologic characteristics of pandemic influenza infection; and
  - Estimate incidence of pandemic influenza infection-associated-hospitalizations and ambulatory care visits.
- Sites were selected to optimize data collection for outpatient and inpatient settings with acute respiratory illness and to establish longitudinal cohorts of pregnant women, healthcare personnel, first responders, and households.

Analytic Framework for Common Objectives

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<tr>
<th>Study Design</th>
<th>Study Domain</th>
<th>Study Population</th>
<th>Analytic Approach to Common Objectives</th>
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<td>MAARI Studies</td>
<td>Inpatient Studies</td>
<td>All hospitalized patients at 6 study sites meeting an H1N1 screening definition</td>
<td>Proportion where laboratory test confirmed cases of influenza are estimated from study denominator</td>
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<td>Ambulatory Care Studies</td>
<td>All patients at 5 study sites seeking care meeting an H1N1 screening definition</td>
<td>Test-negative design components: odds of vaccination between PCR-confirmed cases and estimate fraction vaccinated is estimated from study denominator</td>
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<td>Pregnant Women Studies</td>
<td>All pregnant women at 7 study sites admitted to hospital or seeking care meeting an H1N1 screening definition</td>
<td>Comparing outcome rates in the vaccinated to unvaccinated: 1 – (IRvax/IRunvax)</td>
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<td>Prospicio (Prospective) Studies</td>
<td>Pregnant Women</td>
<td>Study before enrollment criteria for infection and vaccine exposure</td>
<td>Rate where numerator is a count of PCR-confirmed cases and denominator is at-risk person-time</td>
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<td>Early Recoverers of Pandemic Influenza Vaccine (HCR IV)</td>
<td>500 pregnant women at 6 study sites enrolled prior to pandemic virus circulation</td>
<td>Comparing influenza infection incidence rate in those vaccinated that were infected in the Unvaccinated (U/R) to the Vaccinated (V/R)</td>
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<td>Household Studies</td>
<td>1000 households (500 individuals) at 2 study sites enrolled prior to pandemic virus circulation</td>
<td>Not likely possible due to small sample size of enrollees infected with wild-type influenza A(H1N1) virus (yes/no; early/late)</td>
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Geographic Reach of Clinical Partners
- Sites were selected based on their clinical and research capabilities and broad geographic representation.
- Ambulatory sites: Baylor (Houston, TX), Columbia (NYC), Vanderbilt (Nashville, TN), Group Health Cooperative (Seattle, WA), Kaiser Permanente Northern California (KPNC) (Oakland, CA).
- Inpatient sites: Baylor (Houston, TX), Geisinger (Danville, PA), CHOP (Philadelphia, PA) Utah/Intermountain (Salt Lake City, UT).
- Pregnancy sites: Columbia (NYC), University of Pittsburgh Medical Center (UPMC) (Pittsburgh, PA), University of Alabama (UAB) (Birmingham, AL), Baylor (Houston, TX), University of Utah/Intermountain (Salt Lake City), Kaiser Permanente Northern California (KPNC) (Oakland, CA), Kaiser Permanente Northwest (KPNW) (Portland, OR).
- Community sites: Marshfield (WI), University of Utah (Salt Lake City, UT), Olmstead/Mayo (Rochester, MN), Baylor Scott & White (Temple, TX), Kaiser Permanente Northwest (KPNW) (Portland, OR).

Results
- By November, 2015, all preparatory work will be completed.
- 14 sites have been selected for various study components and IRB submissions initiated.
- Protocols and data collection instruments will be finalized; all have shared data elements.
- A common data management system was chosen; implementation and programming have begun.
- Central laboratories were identified.
- Sites and protocols will be maintained in a readiness state in future years.
- Pre-pandemic training of staff will be done to ensure a standardized approach across study sites.
- Limited piloting of study components will be conducted.
- In addition, sub-studies were developed to:
  - Assess immune responses to illness and vaccine, monitor for antiviral resistance, evaluate viral shedding; and collect specimens for genomic studies.

Conclusions/Next Steps
- A comprehensive, flexible, and nimble research study platform is being established for deployment when pandemic influenza emerges in the U.S.
- The Pandemic Preparedness Meta-Project will generate data to inform a timely and appropriate public health response.