Core 3:
Epidemiology and Risk Analysis

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* Purpose: Collect and analyze population data on HuNoV disease burden, including epidemiologic attribution, risk, and costs

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* Collaborators: NC State, Arizona State, U of Cincinnati, FDA, FoodNet, VA, NVSN, CHOA
Core 3: Activities

* 3.1: Develop and apply quantitative risk models
* 3.2: Estimate economic burden of foodborne HuNoV outbreaks
* 3.3: Estimate endemic HuNoV disease burden
* 3.4: Estimate epidemic HuNoV disease burden
* 3.5: Prepare preliminary HuNoV epidemiologic attribution model
Activity 3.1: Development of Quantitative Risk Model

* **On-line Predictive Tool to Investigate Mitigation Alternatives for Norovirus (NorOPTIMAL)**

* Flexible, customizable web-based model designed to
  * Identify opportunities for interventions
  * Evaluate efficacy of different risk reduction strategies
  * Inform research study design
  * Incorporate latest research results
  * Support development of epidemiological attribution model
  * Communicate the nature and magnitude of risk
  * Provide valuable teaching tool for outreach activities
Activity 3.1: Progress to Date on NorOPTIMAL

* Conducted comprehensive review of modeling approaches and selected the agent-based modeling (ABM) approach
* Developed flexible Web-based mathematical engine that can run different ABMs and scenarios
* Developed customizable graphical user interface to define scenarios, parameterize model, and analyze results
* Identified model scenarios for development, e.g., vomiting events, food handling, leafy greens
* For scenarios of interest, began a) data development on risk factors, and b) refinement of ABM algorithms
Activity 3.1: Viral Shedding Patterns from Archived Human Challenge Specimens

* Norwalk virus stool titers peak around $10^{10}$ genome equivalent copies (GEC)/g stool between 5 and 10 days post-challenge, then decline
  * Asymptomatic infections result in a slower decline in titer than do symptomatic infections
  * Virus can be detected in stool up to 35 days post-challenge
* Snow Mountain virus stool titers peak at $10^9$ GEC/g stool around day 5, with sharper increases and decreases than seen with Norwalk
  * For most Snow Mountain infections, stool titers are below detection by day 10, however one subject had detectable virus at day 25
Activity 3.1: NorOPTIMAL Planned Activities

- Continue to develop ABM framework and design, e.g., integrate person-to-person transmission models
- Identify data needs for additional risk factors, linking specific needs to NoroCORE research components
- Complete development of version 1.0 of NorOPTIMAL for pilot testing (e.g., analytics, reporting)
- Begin development of Bayesian approach to “scale” results of ABM local, regional, and national levels
- Create data inputs for the epidemiological attribution model component
**Activity 3.2: Economic Burden of Foodborne HuNoV Outbreaks**

* **Progress to date:**
  * Collected qualitative data on foodborne HuNoV outbreaks through key informant interviews
  * Estimated outbreak costs from direct health care, value of lost labor, facility rehabilitation and closure
  * Conducted consumer survey on knowledge of foodborne disease (see poster)

* **Planned analyses:**
  * Estimate contribution of secondary spread
  * Develop mathematical models to refine estimates
Challenges to Estimating HuNoV Disease Burden

* No national case-based reporting
* No rapid, sensitive clinical assays widely available
* Most gastroenteritis patients do not seek medical care and even fewer submit stool specimens
* Specific coding for HuNoV in administrative data is insensitive and unreliable
* Outbreak reporting is passive, highly variable, and represents small fraction of overall disease burden
Activity 3.3: Approaches to Estimate Endemic HuNoV Disease Burden

* Direct testing
  * Active healthcare-based surveillance for gastroenteritis patients
  * Passive laboratory-based surveillance of routinely submitted specimens
  * Serosurvey of archived NHANES specimens
    * 7 VLPs in development (see poster)
    * Currently developing ELISA panel for serosurvey

* Indirect modeling of national datasets
Activity 3.3 Direct Testing: Active Healthcare-Based Surveillance

* New Vaccine Surveillance Network (NVSN)
  * Year-round, active, population-based surveillance for acute gastroenteritis
  * Hospital and emergency departments (ED)
  * 2008–2009: children <5 years old in 3 sites (completed)
  * 2012–: children <11 years old in 7 sites
    * TN will enroll children <18 years old and also include outpatient clinics
Activity 3.3 Direct Testing: Passive Laboratory-Based Surveillance

* Children’s Hospital of Atlanta
  * HuNoV prevalence in hospitalized pediatric patients
  * Testing complete on >100 patients; planned expansion to aged population

* Veterans Affairs Medical Centers
  * Population-based rates of HuNoV hospital admissions and hospital acquired HuNoV in adults
  * Surveillance in 4 sites since Nov 2011: 5% of 1800 specimens positive thus far

* FoodNet
  * Population-based rates of community and outpatient HuNoV across all ages (surveillance in 4 sites began 2012)
  * Prevalence of HuNoV among sporadic foodborne illness using citizen complaint hotline (1 site since Oct 2011)
Among nosocomial and/or immunocompromised pediatric acute gastroenteritis cases, norovirus is the most prevalent etiology.

* Compared to rotavirus, *C. difficile*, and other bacterial pathogens

* All norovirus cases were GII, predominantly GII.4
Activity 3.3: HuNoV Prevalence in Sporadic Foodborne Illness, MN FoodNet

N=184 complainants (52% HuNoV positive)
Activity 3.3 Indirect Modeling Analyses of HuNoV Burden

* National Center for Health Statistics Multiple-Cause Mortality
  * National incidence of HuNoV-associated deaths based on underlying and contributing causes
  * Completed and published (Hall et al 2012 Clin Infect Dis)

* Commercial, Medicare, & Medicaid healthcare claims (MarketScan)
  * Population-based incidence of HuNoV ED and outpatients visits
  * Completed and in press (see poster)

* National Ambulatory Medical Care Surveys (NAMCS/NHAMCS)
  * Nationally representative samples of office- and hospital-based EDs and outpatient clinics
  * Analysis planned
Activity 3.3: Summary of Recent US HuNoV Disease Burden Studies

* Severe HuNoV-associated disease has been previously underestimated
  * Greatest burden and highest rates of hospitalization and mortality are in the elderly (≥65 years)
  * Burden in young children (<5 years) comparable to that of rotavirus prior to vaccine program

* Highest rates of ED and outpatient visits in young children (<5 years)

* Pronounced winter seasonality with peaks during December-February

* Surges by up to 50% during epidemic years associated with emergence of new variants
Activity 3.3: Updated Annual Burden of HuNoV Disease in US

- 800 Deaths
- 71,000 Hospitalizations
- 414,000 ED Visits
- 1.7 million Outpatient Visits
- 21 million Episodes

[Image of a pyramid with the data mentioned above]
US Norovirus Outbreak Surveillance

* **NORS**
  * Epidemiologic surveillance for all enteric disease outbreaks
  * Data on setting, transmission mode, exposures, demographics, outcomes

* **CaliciNet**
  * Laboratory surveillance using molecular genotyping of outbreak-associated specimens
  * Data on genotypes to identify new strains and potentially link outbreaks
Activity 3.4: Surveillance Enhancements to Estimate Epidemic HuNoV Disease Burden

* Improved NORS data accessibility
  * Data downloaded by state and local users in a variety of file formats and database structures
  * Data from each transmission mode accessed more readily across CDC management teams

* Direct NORS data upload from existing state databases
  * Eliminate double entry by state epidemiologists
  * Improve system acceptability and reporting rates

* Extensive NORS user interface changes

* NORS-CaliciNet data integration
Activity 3.5: Prepare Preliminary HuNoV Epidemiological Attribution Model

* Characterize the national burden of epidemic HuNoV
* Monitor temporal trends and emergent strain impacts
* Identify priority settings and populations for interventions
* Attribution of HuNoV outbreaks by:
  * Modes of transmission (e.g., % foodborne)
  * Setting of exposure and food preparation
  * Food commodities and contamination factors
  * Genotype (through NORS-CaliciNet integration)
Mode of Transmission in HuNoV Outbreaks, 20 States, 2009 (N=613)

- Person-to-person: 78%
- Foodborne: 15%
- Other/Unknown: 7%
- Environmental: 0.2%
- Waterborne: <0.1%
Setting of Food Preparation in Foodborne HuNoV Outbreaks, 2001-2008 (N=2922)

- Restaurant: 62%
- Caterer: 11%
- Private home: 10%
- Banquet facility: 4%
- Grocery store: 4%
- School: 3%
- Nursing home: 3%
- Other: 4%
Foods Implicated* in Norovirus Outbreaks Reported to CDC by Commodity and Point of Contamination, 2001-2008

*Limited to outbreaks with a simple food (consisting of a single commodity) implicated

**Insufficient or conflicting information provided in outbreak report
Questions?

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