Quantitative risk assessment of norovirus transmission in food establishments: evaluating the impact of intervention strategies and food employee behavior on the risk associated with norovirus in foods

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FDA/CFSAN/OAO/DRDA
FDA/CFSAN/OFS/RFPS

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Today’s Outline

• What is a risk assessment? How can it help us?
• Why we did a risk assessment on NoV from infected food employees in food establishments, and what can it tell us?
• How we developed the risk assessment.
• Results of the risk assessment.
• Using risk assessments to solve food safety problems at retail.
Risk Assessment

• A powerful public health tool that facilitates the application of science to policy—provides the “informational bridge” between data & decisions

• A process to describe what we know and how certain we are of what we know.

Answers 4 key questions:

• What can go wrong?
• How likely is it to occur?
• What are the consequences?
• What factors can influence it?
Risk Assessment

- Does not provide “the answer”
- Provides an analysis of contributing factors and options for use in regulatory decisions and for reducing the risk to public health
- Describes uncertainty in risk estimates and variability of response
Risk Assessment

• Tells us where the probability of contamination is highest in the food system being evaluated, and which methods are most effective in preventing or reducing food contamination & subsequent foodborne illness.

• Another advantage of quantitative risk assessments allows for evaluation of potential mitigation by using the “what if” scenario in the model.
  • Change baseline model inputs and measure impact on resulting risk estimates
Risk Assessment: Then and Now

1906 – Dining room of “poison squad”: A direct approach to assessing risk

Risk Assessment modeling techniques
Why a Risk Assessment on NoV Transmission in Food Establishments?

- No single preventive measure can eliminate the risk of foodborne norovirus from a symptomatic food employee.
- Need for better understanding of how effective Food Code intervention strategies are when used individually or in combination to reduce or prevent the incidence of norovirus foodborne illness.
- Need for consideration of actual practices and level of compliance to determine current intervention impact and any need for policy modification.
Norovirus Background

- Leading cause of foodborne illness globally
- Characterized by a sudden onset of vomiting, diarrhea, and abdominal cramps with a duration of 1-3 days

- Large amounts of virus shed during symptoms
  - $10^{12}$ Genome Equivalent Copies (GEC) NoV / g of feces
  - $8 \times 10^5$ GEC NoV / ml of vomit
  - Viral shedding duration in adults lasts 20-30 days

- Infectious dose low or very low (?)
  50% human infectious dose = 18 NoV particles
  (Teunis et al., 2008)
Food employees play a significant role in norovirus foodborne outbreaks

- Restaurants are the most common setting (64%) of food preparation reported in outbreaks in the U.S. (Hall et al., 2014).

- Most foodborne outbreaks linked to food establishments are traced to food employee contamination of Ready-To-Eat (RTE) food (FAO/WHO 2008, Patel et al., 2009, Hall et al., 2013a, Hall et al., 2013b)
Discrete Event Model

Identification of norovirus pathways from source to food in food establishment

Science Based Prevention Strategies (Food Code), e.g.

- Hand Washing
- Glove Use
- Exclusion/Restriction of food employee
- Food-Contact & Non-Food-Contact Surface Disinfection
- Restroom Cleaning Frequency
- Touchless faucets and doors in restroom

Relative impact of individual and combined strategies

Impact of compliance with strategies

Risk Assessment
Setting

Contamination of the door handle and the faucet

Aerosolization in the restrooms during vomit and diarrheal events

Food Employee #1 is (was) sick

Food Employee #2 not sick but may be asymptomatic

Food Employee #3 not sick may be asymptomatic, doesn’t prepare food, touches NFCS every 10 minutes

3 Food Contact Surfaces
e.g.: cutting board, knives, Food prep surface

3 Non Food Contact Surfaces
e.g. microwave door handle, refrigerator door, cash register

Customer

8 hour shift
5 shifts, 2000 servings,
Monte Carlo integration (1,000,000 food establishments)
Dose Response model

**Probability of Infection | Dose**
Teunis et al, 2008

*High probability of infection at low dose (low ID$_{50}$)*

**Probability of Illness | Infection, Dose**
Teunis et al, 2008

*Low probability of illness at low dose*

-> expect many infected but few people sick

**Validity of NoV Dose Responses?**
limited data from experimental infections

**Alternative output provided in this study:**
Proportion of servings with >0 NoV, with >100 NoV or with > 1,000 NoV
Persistence of norovirus on surfaces

Meta-Analysis:
16 articles – 138 curves

Data:

**Virus**
- Nov: GI / GII
- FCV
- MNV1
- MS2
- Tulane

**Method**
- Plaque assay
- Real-time RT-qPCR

**Temperature**
- Room
- Refrigerated

**Surface**
- Hard surface
- Human skin
- Vegetables
- Leafy
- Meat

Mixed model – normalized to norovirus:
Log-Linear persistence model
Time for 1 log$_{10}$ reduction
Disinfection (18 articles – 249 observations)

- **Disinfectant**
  - Quaternary ammonium
  - Sodium hypochlorite
  - Ethanol
- **Method**
  - Plaque assay
  - Real-time RT-qPCR
  - TCID50
- **Surface**
  - Hard surface
  - Hand
- **Wet / Dry**
- **Application time**

- **Virus**
  - Nov : GI / GII
  - FCV
  - MNV1
  - MNV99
  - MS2
  - Tulane

Surface to surface Transfer Model (10 articles – 420 observations)

- **Virus**
  - Nov : GI / GII
  - FCV
  - MNV1
  - MNV99
  - MS2
  - Tulane
  - HAV
- **Method**
  - Plaque assay
  - Real-time RT-qPCR
- **Surface**
  - Hard surface
  - Hand
  - Gloves
  - Knife
  - Vegetables
  - Meat
- **Wet / Dry**
- **Contact time**
- **Initial Level**

Hand Washing (16 articles – 50 observations)

- **Virus**
  - Nov : GI / GII
  - FCV
  - MNV1 / MNV99
  - MS2
  - Tulane
  - HAV
  - Rotavirus
  - Poliovirus
- **Method**
  - Plaque assay
  - Real-time RT-qPCR
  - TCID50
- **Wash time**
- **Soap / No Soap**

*Note: Some observations may be marked with an asterisk.
# Food Employee Behavior

**Visits to the Restroom, Glove Use, # Hand Contacts w/ Food, Handwashing Compliance**

<table>
<thead>
<tr>
<th>Restrooms</th>
<th>Symptomatic</th>
<th>Asymptomatic Shedders (15%)</th>
<th>Not sick</th>
<th>Description</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit-Defecation per shift</td>
<td>+++</td>
<td>Once per day</td>
<td>Once per day</td>
<td>Poisson(4.5) while sick on day 0 Divided / 2 each day while sick</td>
<td>Arias et al. 2010</td>
</tr>
<tr>
<td>Vomit</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>1-3 times / shift</td>
<td>CDC Guidelines document 2011</td>
</tr>
<tr>
<td>Shedding Nov / g</td>
<td>Yes</td>
<td>Yes</td>
<td>0</td>
<td>Pert(4, 8, 10) log(<em>{10}) NoV/g Reduction of 1 log(</em>{10}) / week</td>
<td>Lee et al, 2007; Chan et al, 2006; Atmar et al, 2008</td>
</tr>
<tr>
<td>Aerosol contamination</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>2,420 NoV (+/- 1,200) per m(^3) +1,100 NoV per m(^3) if vomit</td>
<td>Barker et Jones, 2003, Tung-Thomson et al. 2015</td>
</tr>
<tr>
<td>Auto-contamination (Hand)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Pert(-8, -3, -1) log(_{10}) g of feces</td>
<td>Lin et al. 2003</td>
</tr>
</tbody>
</table>

**Graphs:**
- **Stools, per shift**
  - mean: 4.5
- **Concentration NoV in feces**
  - mean: 0.05
- **Symptoms duration**
  - mean: 49 h, sd: 40 h

(Arias et al, 2010)
**Food Employee Behavior**

**Wear gloves** - Green et al. 2005 (Table 2)

<table>
<thead>
<tr>
<th>Wear gloves</th>
<th>Translated in model* (%)</th>
<th>sample</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>0</td>
<td>91</td>
<td>33.6</td>
</tr>
<tr>
<td>Sometimes</td>
<td>50</td>
<td>28</td>
<td>14</td>
</tr>
<tr>
<td>Almost Always</td>
<td>90</td>
<td>35</td>
<td>12</td>
</tr>
<tr>
<td>Always</td>
<td>100</td>
<td>109</td>
<td>40.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>263</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

*Values assumed in the model but not given in Green et al. 2005

**Wash Hands** - Restrooms Berry et al. 2014
- 90% if Defecation
- 65% if Urinal

**Food worker engages in food assembling sequence:**
- Wash hands 41%, CDC EHS-Net
- Change Gloves 50%, CDC EHS-Net

**During food assembling sequence (Stals et al. 2013, Mokhtari and Jaykus, 2009)**
- Number of Food <-> FCS Contacts = 2
- Number of Hand <-> FCS Contacts = 2
- Number of Hand <-> Food Contacts = 2
- Number of Hand <-> Non Food Contacts = 1
Food employee behavior

- Food employee wears gloves
  - Keep wearing gloves?
    - No
      - Change gloves?
        - Yes
          - Trash gloves
          - Wear gloves
        - No
          - Wash hands?
            - Yes
              - Wash hands
              - Trash gloves
            - No
              - Trash gloves
    - Yes
      - New Gloves

- Food employee is bare handed
  - Wash hands?
    - Yes
      - New Gloves
    - No
      - Wear gloves?
        - Yes
          - Wear gloves
        - No
          - Wash hands?
            - Yes
              - Wash hands
              - Wear gloves
            - No
              - Trash gloves

Legend:
- Main events
- Function / action
- Decision?/Loop
- Object
- Object State
- Food employee action transition
  - One direction norovirus transfer
  - Both directions norovirus transfer

Prevalence and level of norovirus [GEC NoV] in food

- time = time + time of the last action
- day = day + 1 – go back to work
- Store = Store + 1

Food employee behavior:
- If available
  - Food employee
    - Food
      - FCS
      - NFCS
      - Gloves/hands
        - Trash gloves
        -戴手套?
          - Yes
            - Wash hands?
              - Yes
                - Wash hands
                -戴手套?
              - No
                - Trash gloves
          - No
            - Wash hands?
              - Yes
                - Wash hands
                -戴手套?
              - No
                - Trash gloves

Legend:
- Main events
- Function / action
- Decision?/Loop
- Object
- Object State
- Food employee action transition
  - One direction norovirus transfer
  - Both directions norovirus transfer

Prevalence and level of norovirus [GEC NoV] in food
Integration

R Code

Run on an High Performance Computer

Parallel computing
(code running on 100 computers simultaneously).
(takes 3h per scenario rather than 300h)

This study used the computational resources of the HPC clusters at the Food and Drug Administration, Center for Devices and Radiological Health (CDRH). Reproducible Risk Assessment: Code available on request.
Food workers are excluded from work **24 h after the end of the symptoms** before coming back to work.

What would be the impact if the food workers were excluded from work **48 h after the end of the symptoms**?
Results: Number of Customers Infected Always Exceeds Number Sick

Example Using Model Results:
Mean # infected/2000 servings vs. Mean # ill / 2000 servings

- 48 hr Exclusion/ Full (100%) Compliance
- 24 hr Exclusion/ Full (100%) Compliance
- 24 hr. Exclusion/ Current (74%) Compliance Levels
- Ill Food Employee /No Exclusion

Mean # Infected Customers/ 2000 Servings
Mean # Sick Customers/ 2000 Servings
Results: Large Store-to-Store Variability
Provided relative to the baseline (# of infected customers)
Baseline scenario represents current practices

Mean over 1,000,000 simulated stores:
Proportion of Food Servings Contaminated (>0 NoV) = 9.7%
Proportion of servings w/ > 1,000 NoV = 0.54%
74 infected customers over 2,000 servings
90% Variability interval: [2.1, 233.7] infected customers
1.7 sick customers over 2,000 servings
90% Variability interval: [0.0, 7.9] sick customers

The outbreaks!
Some over 80%

Proportion of contaminated (>0 NoV) serving after 5 shifts
Results for the alternative scenarios are provided relative to the baseline (>1000 NoV)
Baseline

Restrooms

Food Employee -1

Source (feces/vomit)

Wash

Trash

Food Employee -2

Faucet

Door handle

Wash / Sanitize

Environment

Wash / Sanitize

Food Employee -3

Hands

NFCS

Wash / Sanitize

Food preparation / Assemblage

Hands

Gloves

Wash / Sanitize

Food

Sold

Log_{10} NoV over 5 shifts

Mean number of infected customers: 74 for 2000 servings

Prevalence: 9.7%

Baseline
Full compliance of handwashing in restrooms and in food preparation area, wearing and changing gloves when engaging food preparation

Mean number of infected customers: 42.6 for 2000 servings

Prevalence: 5.7%
No contact with handle and faucet in restrooms

Environment
- Door handle: Wash / Sanitize
- Faucet: Wash / Sanitize

Food Employee -1
- Source (feces/vomit)
- Hands
- Wash
- Gloves
- Food
- Sold

Food Employee -2
- Hands
- NFCS
- Wash / Sanitize
- Food preparation / Assemblage

Food Employee -3
- Hands
- NFCS
- Wash / Sanitize
- Food preparation / Assemblage

Restrooms
- Wash / Sanitize
- Faucet
- Door handle

Prevalence: 7.3%
Mean number of infected customers: 55.8 for 2000 servings
\[ \log_{10} \text{NoV} \text{ over 5 shifts} \]
What is the impact of the compliance with exclusion during active symptoms plus an additional post-symptomatic exclusion period?

<table>
<thead>
<tr>
<th>Scenario #</th>
<th>#1 Baseline</th>
<th>#2</th>
<th>#3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance with exclusion</td>
<td>74%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Duration of the post-symptomatic exclusion period</td>
<td>24h</td>
<td>24h</td>
<td>-</td>
</tr>
<tr>
<td>Simplified description of the scenario</td>
<td>Current compliance Sumner et al. (2011)</td>
<td>Full Compliance</td>
<td>Employee always works while ill</td>
</tr>
</tbody>
</table>
### Results

What if the compliance with the current 24h exclusion after symptom resolution increased?

Increasing compliance with the current 24 hour exclusion would reduce the expected number of infected customers.

<table>
<thead>
<tr>
<th>Compliance with exclusion</th>
<th>100%</th>
<th>74%</th>
<th>74%</th>
<th>84%</th>
<th>0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of the exclusion period after symptom resolution</td>
<td>24h</td>
<td>24h</td>
<td>48h</td>
<td>24h</td>
<td>-</td>
</tr>
<tr>
<td>Simplified description of the scenario</td>
<td>Full Compliance</td>
<td>Baseline</td>
<td>Exclusion extension</td>
<td>Improving compliance</td>
<td>Upper Baseline</td>
</tr>
</tbody>
</table>

Increasing compliance would reduce the expected number of infected customers.
What if the extension of the exclusion time period to 48h leads to a decrease with the compliance?

The public health benefit from extending the exclusion period after symptom resolution may be eliminated or may result in an increase in the burden of illness if compliance decreases.

### Baseline Number of infected customers

<table>
<thead>
<tr>
<th>Scenario #</th>
<th>Baseline</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>#6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance with exclusion</td>
<td>74%</td>
<td>100%</td>
<td>0%</td>
<td>74%</td>
<td>64%</td>
<td>54%</td>
</tr>
<tr>
<td>Duration of the post-symptomatic exclusion period</td>
<td>24h</td>
<td>24h</td>
<td>-</td>
<td>48h</td>
<td>48h</td>
<td>48h</td>
</tr>
<tr>
<td>Simplified description of the scenario</td>
<td>Current compliance (sumner et al. 2011)</td>
<td>Full Compliance</td>
<td>Employee always works while ill</td>
<td>Exclusion extension</td>
<td>Exclusion extension</td>
<td>Exclusion extension</td>
</tr>
</tbody>
</table>
What is the Impact of exclusion period after symptom resolution? What is the impact of extending it to 48 hours?

“Indirect and Direct Transmission Potential of NoV Over Time”

Symptomatic Exclusion Period

Symptom-free Period (shedding)

Highest level of infectivity occurs when symptoms first appear, often with an explosive introduction

Mean disease duration = 49h

Arias et al. (2010)

Adapted from Lopman, B., et al. (2012).
What is the impact of hand washing efficacy, hand washing frequency and frequency of glove changing?

Increasing hand washing efficacy is effective

Full compliance with Food Code recommendations with regard to hand washing and glove-use when engaging food preparation is effective

Increasing hand washing efficacy is effective

%Baseline Number of infected customers

<table>
<thead>
<tr>
<th>Scenario #</th>
<th>#1 Baseline</th>
<th>#7</th>
<th>#8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simplified description of the scenario</td>
<td>Current practices</td>
<td>Hand washing efficacy + $1 \log_{10}$</td>
<td>100% Hand washing and change gloves when engaging food preparation and 100% hand washing in restrooms</td>
</tr>
</tbody>
</table>

100% 58% 62%
What is the impact of contacts between hands and faucet in the restrooms and cleaning frequency in the restrooms?

Removing contacts between hands, faucet and door in the restrooms appears to be effective.

Increasing restroom disinfection frequency has a limited impact on risk reduction.

### Graph

- **100%**
- **75%**
- **97%**

### Table

<table>
<thead>
<tr>
<th>Scenario #</th>
<th>#1 Baseline</th>
<th>#9</th>
<th>#10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simplified description of the scenario</td>
<td>Current practices</td>
<td>Touchless faucet and door in the restrooms</td>
<td>Restrooms are washed and disinfected every 4 hours</td>
</tr>
</tbody>
</table>
Results

<table>
<thead>
<tr>
<th>Compliance with exclusion</th>
<th>Baseline</th>
<th>Restrooms washed every 4 hours</th>
<th>Always wear gloves, don’t necessarily change gloves</th>
<th>24h Restriction, FE-1 doesn’t touch food, less frequent handwashing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusion period</td>
<td>24h</td>
<td>24h</td>
<td>24h</td>
<td>24h</td>
</tr>
<tr>
<td>Percentage</td>
<td>74%</td>
<td>74%</td>
<td>74%</td>
<td>74%</td>
</tr>
</tbody>
</table>

Some interventions are not sufficient by themselves and some could even increase the risk if not properly implemented.
Impact of Compliance with Exclusion

Mean # of Sick Customers & Proportion of Servings Contaminated (% with >0 NoV)/ 2000 Food Servings

- No Comp.- Ill Food Worker Present: 5 Ill, 21.5% contaminated
- 54% Comp.- 48 hr: <2 Ill, 10.5% contaminated
- 64 % Comp.- 48 hr: <2 Ill, 9.7% contaminated
- 74% Comp.-24 hr: <2 Ill, 9.7% contaminated
- 74 % Comp.-48 hr: <2 Ill, 8.9% contaminated
- 84 % Comp.- 24 hr: 1 Ill, 8.7% contaminated
- 100% Compliance- 24 hr: 1 Ill, 7.4% contaminated

Mean # Ill  % Food Servings Contaminated w/ NoV
Mean # of Sick Customers & Proportion of Servings Contaminated (% with >0 NoV)

* Full Compliance w/ Food Code
- Mean # Customers Ill: <1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 4.1%

*Full Compliance w/ Handwashing + NBHC
- Mean # Customers Ill: <1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 5.7%

* Improve Handwashing Efficacy (+ 1 log10 reduction)
- Mean # Customers Ill: <1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 6.1%

* Full Compliance with Exclusion
- Mean # Customers Ill: 1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 7.4%

* Install Touchless Faucets and Door in Restroom
- Mean # Customers Ill: 1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 7.3%

* Improve Exclusion Compliance by 10%
- Mean # Customers Ill: 1
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 8.7%

* Full Compliance w/ Restroom Handwash
- Mean # Customers Ill: <2
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 9.2%

* Wash Restrooms Every 4 hrs
- Mean # Customers Ill: <2
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 9.4%

* Current Compliance Levels w/ Food Code
- Mean # Customers Ill: <2
- Proportion of Food Servings Contaminated w/ NoV/ 2000 Food Servings: 9.7%

* Includes Current Food Code Practices
Excluding symptomatic food employees at the peak of their infectiousness* is the priority to reduce the burden to public health associated with norovirus transmission in food establishments.

*see Lopman et al 2012, Zelner et al. 2013, Teunis 2013

Results support the current recommendations of the FDA Food Code--Better compliance with current Food Code interventions would reduce Nov transmission.
Summary of Results Continued:

3. Handwashing and No Bare Hand Contact are Highly Effective Preventive Strategies in reducing the transmission of NoV.

4. Improving Handwashing Efficacy by Just 1 additional log reduction is also an effective preventive strategy.

5. Eliminating hand-contact in the restrooms between the faucet, door handle and hands is an effective additional preventive strategy to the transmission of NoV & is more effective than washing and sanitizing the restrooms every 4 hours.
Lessons Learned

1. Considering compliance is critical when evaluating the effectiveness of preventive measures

2. Both the efficacy and the level of compliance with an intervention are needed to determine effective control measures, and any improvement in either can have a large impact in reducing NoV foodborne illness

3. More research is needed on Food Employee Behavior/ How to Improve Food Code Compliance
While the general impact of individual interventions may seem intuitive, the net impact of combined interventions along with potential levels of compliance with these interventions are not always what one might assume.
Wrap-Up: Risk Assessments: A New Tool for Retail Food Safety

• **Identifies the problem:** Tells us where to focus our attention
  • Risk Assessments provide a data-driven system to help us analyze large quantities of data with transparency

• **Evaluates potential controls**
  • Helps us focus on areas with greatest likelihood of pathogen contamination and/or growth in food preparation/distribution and,

• **Identifies knowledge gaps:** Helps us prioritize research needs
  • Identifies effective interventions for the reduction of foodborne illness
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For more information, see full report:
• Quantitative Risk Assessment of Norovirus Transmission in Food...

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