Modeling Disease Surveillance and Assessing Its Effectiveness for Detection of Acute Respiratory Outbreaks in Resource-Limited Settings

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Acute Respiratory Infection Epidemic Simulator (ARIES)

Develop model to

– Evaluate acute respiratory illness surveillance in resource-limited settings
– Measure potential benefit of policy decisions and countermeasures

Required features

– Focus on early outbreak stages
– Restrict demographic modeling to features relevant to disease spread
– Include knowledge of existing surveillance capability
– Portability
A U.S. Department of Defense program is underway to assess health surveillance in resource-poor settings and to evaluate the Early Warning Outbreak Reporting System (EWORS).

This program has included several information-gathering trips, including a trip to Lao PDR in September 2006.
Challenges of Surveillance in Resource-Poor Regions

Healthcare access is limited by

- Available transportation
- Lack of trained care providers or insurance/ability to pay for care
- Preference for herbal, spiritual healers
- Lack of modern communication technology

Magnified Threat of Major Epidemics

- Infectious disease outbreaks not uncommon
- Many workers at human-animal interface
- Vaccine, antiviral supplies scarce if available
EWORS Systems
- 35 sites in 4 countries in SE Asia and in 2 sites in Peru
- Daily transfer of patient records from network hospitals to national hub
- Popular at each installation

Initial Application in Lao PDR
- Investigative trip by 6-member EWORS International Working Group
- Interviews at hospitals, National Center for Laboratory and Epidemiology, Ministry of Health, and other government agencies
- Collection of healthcare-seeking behavior information
- Discussions of both theoretical and actual surveillance practices
Key Features of ARIES

• Model is individual-based, but includes only infected and exposed

• Attention limited to the stages of the event before population behavior radically changes

• Assumptions of near-instantaneous detection in published research are unrealistic, especially in resource-limited settings

• Goal is to implement realistic surveillance modeling
Components of ARIES

*Demographic model* generates features relevant to outbreak spread.

*Disease model* simulates progression of disease in infected agents.

*Travel model* simulates agent travel patterns to mimic geographic spread.

*Surveillance model* simulates delays in detection, data entry, data transmission, and epidemiologic investigation.

**Information basis**
census data, population survey reports, site-visit interviews, acquired data from EWORS, area geography, disease model.
Household Model

Accurately estimate household makeup of specified province in Lao

Considerations

- Household size
- Age group and sex
- Preserve census dependency ratios
- Sex of household head for comparison to census distributions
- Pregnancy status

☑ Objectives ☑ Background ☑ Approach & Methods ☐ Validation & Study Design ☐ Results ☐ Conclusions
Disease Model

Disease stages model [Feighner]
- Stage lengths
- Probability of complications
- Percentage of asymptomatic

Disease transmission model [Glass]
- Susceptibility and infectivity are functions of disease stage and age
- Transmission is also dependent on type of contact (household, peer, random)
Disease Stage Model

STAGE 1: Infected, Non-Symptomatic, Non-Contagious

STAGE 2: Infected, Non-Symptomatic, Contagious

Stage 2 > 2 days?

STAGE 3a: Infected, Symptomatic, Contagious

Person Dies?

YES

Dead

Complications?

YES

STAGE 3b: Infected, Symptomatic, Contagious w/Complications

Person Dies?

YES

Complications?

YES

Person Dies?

YES

Recovered

NO

NO

NO
Travel Model

Establish location of an infected individual throughout course of infection

Considerations
- Subdivide province into rural and urban districts
- Update agent locations on time scale of days
- Movement is district-to-district
- Occupation and age influence agent itinerary
- For each new agent location, recompute probabilities of travel to other districts
- Multi-day trips are allowed
Surveillance Model

• To include surveillance in a disease model need to consider both surveillance lag and the effect of surveillance system on surveillance lag

• Model both traditional surveillance and EWORS

• Investigate advantage of proposed EWORS expansion
  – Additional provincial EWORS hospitals
  – EWORS systems in chosen district hospitals
  – Other interventions

• EWORS hospital currently in Luang Prabang District

• Simulations will also be run with an additional EWORS system at Nam Bak

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Surveillance Model

- **Time for Patients to Seek Care**
  - Apx. 1-14 days

- **Effect of Surveillance System**
  - Components of Surveillance System
    1. Time from visit to entry into system
    2. Time from entry to analysis
    3. Time from analysis to review of results
    4. Time from review to investigation
    5. Time from investigation to action
    6. Other, e.g. time variation by site

- **Time for Dr to ID Outbreak**
  - Without Rapid Test
    - Up to 1 week
    - Flu A
  - With Rapid Test
    - 0-1 days H5N1
    - 0-2 days
    - 1-3 days

- **Time for Public Health Response to Start**
  - Dr IDs Outbreak
  - Dr contacts DPH
  - LPH investigates
  - LPH contacts RPH
  - RPH investigates
  - RPH contacts NPH
  - NPH responds

**Effect of Surveillance system depends on:**
1. Design of the system
   - Paper or electronic
   - Data pre-computerized or specially entered
   - Data source & its reporting lag
   - System validity (IT & Epi)
   - Integration of system into surveillance
   - Nodal differences
2. PH Belief in system
3. PH Use of system

**Time for patient to seek care depends on:**
1. Health beliefs & attitudes
2. Income
3. Availability of health care & transportation to it
4. Relationship with HCP
5. Severity of illness
6. Status of patient within household

**Time for patients to seek care depends on:**
1. Health beliefs & attitudes
2. Income
3. Availability of health care & transportation to it
4. Relationship with HCP
5. Severity of illness
6. Status of patient within household
• Serial Interval: 2.6 days (for an effective reproductive rate of about 1.6)
• Household Attack Rate: 0.25
• Fraction of symptomatic cases: 0.67
• Overall case fatality rate: 6%
Three scenarios

- No EWORS system
- EWORS in Luang Prabang
- EWORS in Luang Prabang and Nam Bak

Each scenario - 5 seed cases in single province

- Luang Prabang
- Chomphet
- Nam Bak
- Vieng Kham

100 runs for each scenario/seed province
• Curves show number of new symptomatic cases by day for one of the simulated epidemics.
• Runs start with 5 seed cases in Luang Prabang to increase likelihood of spread.
Rate of Epidemic Spread

Distribution of Days Until an Infection out of District

Seed District
- Luang Prabang
- Chomphet
- NamBak
- Vieng Kham

Day of Outbreak

Objectives  Background  Approach & Methods  Validation & Study Design  Results  Conclusions
Time to Outbreak Identification

- No EWORS
  - Mean = 23.2, Med = 18
  - N = 56

- EWORS in LP
  - Mean = 15.9, Med = 13
  - N = 70

- EWORS in LP & NB
  - Mean = 8.4, Med = 8
  - N = 99

Objectives
Background
Approach & Methods
Validation & Study Design
Results
Conclusions
Outbreak Identification & Reporting

Report Delay to National Public Health

<table>
<thead>
<tr>
<th>Seed Province</th>
<th>Median Number of Days to Report</th>
<th>Mean Number of Days to Report</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No EWORS</td>
<td>EWORS in Luang Prabang</td>
</tr>
<tr>
<td>Luang Prabang</td>
<td>32</td>
<td>3</td>
</tr>
<tr>
<td>Chomphet</td>
<td>32</td>
<td>3</td>
</tr>
<tr>
<td>Nam Bak</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Vieng Kham</td>
<td>15</td>
<td>4</td>
</tr>
</tbody>
</table>

Objectives

Background

Approach & Methods

Validation & Study Design

Results

Conclusions
Conclusions

• Outbreak identification time
  – up to 2-week improvement in median identification time with EWORS system
  – Additional few days’ advantage with district-level system in Nam Bak

• Rate of epidemic spread
  – Probability of out-of-district infection within 3 days > 50% in every scenario
  – Infection reaches town of Luang Prabang within 4 days, regardless of seed district

• Variability among runs

• Effect of rapid test capability at provincial hospital: the median dropped below 6 days, even without EWORS, in each scenario

• Modeling surveillance capability is important
References

Included Modeling Elements

Population details for “agents”
• Age group and sex
• Statistics for rural/urban, north/south/central
• Occupation category from census data
• Travel survey information
• Provincial geography
• SES surrogates
  – Occupation
    – Literacy, education
    – Clean water availability
    – Household income

Disease spread
• Health-care-seeking behavior
• Travel patterns (inter-regional spread)
• Immunocompetence, based on statistics for:
  – Age
  – Pregnancy
  – Nutrition
  – Vitamin A intake
Infected Agent Attributes

– Static attributes (drawn from population data)
  • Age
  • Sex/pregnancy status
  • Family size
  • Peer group size
  • Region / Location (Province)
  • Rural Access to Road, Rural No Access to Road, Urban
  • Occupation
  • Type of Health Care Access

– Dynamic Attributes
  • Disease State
  • Ambulatory
  • Infectiousness
### Modeling Person-to-Person Transmission

<table>
<thead>
<tr>
<th>Contact frequency of link (per day)</th>
<th>3.00</th>
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</thead>
<tbody>
<tr>
<td><strong>Glass Parameters: (between 0 and 1)</strong></td>
<td></td>
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<tr>
<td>$I_D$  Disease infectivity</td>
<td>0.50</td>
</tr>
<tr>
<td>$I_R$  Relative infectivity of disease state</td>
<td>1.00</td>
</tr>
<tr>
<td>$I_A$  Relative infectivity of person</td>
<td>0.50</td>
</tr>
<tr>
<td>$S_P$  Overall susceptibility to disease</td>
<td>0.50</td>
</tr>
<tr>
<td>$S_A$  Relative susceptibility of person</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>Overall Transmissivity Factor</strong></td>
<td>0.06</td>
</tr>
<tr>
<td>exp. dist. mean for transmission time</td>
<td>5.33</td>
</tr>
<tr>
<td>median for transmission time</td>
<td>3.70</td>
</tr>
<tr>
<td><strong>Length of disease state (days)</strong></td>
<td>5.00</td>
</tr>
<tr>
<td><strong>Attack rate (%) for link &amp; disease state</strong></td>
<td>60.84</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Days</th>
<th>Infection Probability</th>
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</thead>
<tbody>
<tr>
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<td>0.3127</td>
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<td>0.4302</td>
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<td>4.0</td>
<td>0.5276</td>
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<tr>
<td>5.0</td>
<td>0.6084</td>
</tr>
</tbody>
</table>

Lao PDR Statistics Related to SES

Key Survey Percentages

- Literacy
- Safe water
- Nearest hospital <4 km away
- Medical practitioner in village
- Villages with 4 essential drugs

Inference of Reporting Delays from Data

Comparison by year:
Ratio of (Visits sent by day)/All Visits

Days Late:

EWORS Data Reporting for 2004

| Hosp | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | Total |
|------|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|------|
| H001 | 0.02 | 0.12 | 0.23 | 0.34 | 0.45 | 0.52 | 0.56 | 0.60 | 0.62 | 0.64 | 0.65 | 0.67 | 0.69 | 0.70 | 0.72 | 0.73 | 0.74 | 0.76 | 0.78 | 18313 |
| H002 | 0.13 | 0.30 | 0.41 | 0.49 | 0.53 | 0.57 | 0.60 | 0.64 | 0.66 | 0.67 | 0.68 | 0.69 | 0.70 | 0.71 | 0.73 | 0.74 | 0.74 | 0.75 | 0.75 | 6921 |
| H003 | 0.10 | 0.28 | 0.40 | 0.46 | 0.50 | 0.53 | 0.54 | 0.54 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 9769 |
| H004 | 0.09 | 0.21 | 0.27 | 0.30 | 0.33 | 0.35 | 0.35 | 0.37 | 0.38 | 0.39 | 0.39 | 0.39 | 0.40 | 0.40 | 0.41 | 0.41 | 0.41 | 0.42 | 0.42 | 5104 |
| H005 | 0.04 | 0.25 | 0.30 | 0.35 | 0.37 | 0.38 | 0.40 | 0.42 | 0.42 | 0.43 | 0.43 | 0.44 | 0.44 | 0.44 | 0.45 | 0.45 | 0.45 | 0.46 | 0.46 | 3616 |
| H006 | 0.10 | 0.19 | 0.22 | 0.25 | 0.27 | 0.29 | 0.30 | 0.31 | 0.32 | 0.32 | 0.33 | 0.33 | 0.33 | 0.34 | 0.34 | 0.35 | 0.35 | 0.36 | 0.36 | 5253 |
| H007 | 0.07 | 0.17 | 0.20 | 0.23 | 0.25 | 0.28 | 0.30 | 0.31 | 0.33 | 0.34 | 0.35 | 0.36 | 0.37 | 0.38 | 0.39 | 0.39 | 0.40 | 0.40 | 0.40 | 5442 |
| All  | 0.07 | 0.20 | 0.29 | 0.36 | 0.42 | 0.46 | 0.48 | 0.51 | 0.52 | 0.53 | 0.54 | 0.55 | 0.55 | 0.56 | 0.57 | 0.58 | 0.59 | 0.60 | 54418 |

EWORS Data Reporting for 2005

| Hosp | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | Total |
|------|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|------|
| H001 | 0.00 | 0.15 | 0.31 | 0.44 | 0.52 | 0.59 | 0.62 | 0.66 | 0.69 | 0.73 | 0.76 | 0.79 | 0.80 | 0.82 | 0.85 | 0.87 | 0.88 | 0.88 | 0.90 | 0.92 | 16661 |
| H002 | 0.29 | 0.59 | 0.72 | 0.81 | 0.85 | 0.88 | 0.91 | 0.94 | 0.96 | 0.97 | 0.98 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 7978 |
| H003 | 0.07 | 0.42 | 0.66 | 0.80 | 0.89 | 0.92 | 0.93 | 0.95 | 0.97 | 0.98 | 0.99 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 16095 |
| H004 | 0.20 | 0.48 | 0.57 | 0.63 | 0.65 | 0.69 | 0.72 | 0.75 | 0.77 | 0.79 | 0.80 | 0.81 | 0.82 | 0.85 | 0.87 | 0.89 | 0.90 | 0.92 | 0.92 | 6067 |
| H005 | 0.05 | 0.60 | 0.73 | 0.89 | 0.92 | 0.94 | 0.96 | 0.98 | 0.98 | 0.99 | 0.99 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 3995 |
| H006 | 0.23 | 0.48 | 0.62 | 0.73 | 0.77 | 0.80 | 0.82 | 0.84 | 0.86 | 0.87 | 0.88 | 0.89 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.94 | 0.94 | 4584 |
| H007 | 0.16 | 0.36 | 0.46 | 0.54 | 0.60 | 0.65 | 0.71 | 0.76 | 0.81 | 0.84 | 0.87 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.95 | 0.96 | 5687 |
| All  | 0.11 | 0.39 | 0.55 | 0.66 | 0.72 | 0.77 | 0.80 | 0.82 | 0.85 | 0.87 | 0.89 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.94 | 0.95 | 0.95 | 0.96 | 60667 |