Epidemiology for strategic control of
Neglected Zoonoses

Presented at
FAO-APHCA/OIE/USDA Regional Workshop on
Prevention and Control of Neglected Zoonoses in Asia
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Motivation

• Problem of Neglected Zoonoses
  – Neglected because they are ‘invisible’

  – Cannot be controlled because ‘resource is limited’

  – Cannot be controlled because ‘responsibility is fragmented’

  – Persistency – ‘prediction’ is needed to plan long-term policy
Overview

- Tool box to tackle with ‘invisibility’, ‘limited resources’, ‘fragmented responsibility’, and ‘needs of prediction’
  - Epidemiology cycle
  - Inter-disciplinarity
  - Risk-based surveillance
  - Risk assessment
  - Mathematical modelling
  - Animal Health Economics
Noticing that disease/problem is in a population

- Descriptive epidemiology
- Forming a hypothesis (Analytical epidemiology)
- Testing a hypothesis (Intervention study)
- Assessment of intervention
- Determination of the risk factor
- Removing a risk factor
- Adding a preventive factor (Intervention study)

Epidemiology cycle

Inter-disciplinarity
Risk-based surveillance
Risk assessment
Mathematical modelling
Animal Health Economics
Brucella infected farms in Kampala, Uganda

Any hypothesis?
Herd size and *Brucella* sero-positivity

Makita et al. (2011) BMC Veterinary Research 7:60.

Any hypothesis?
<table>
<thead>
<tr>
<th>Factors</th>
<th>Infected herds</th>
<th>Healthy herds</th>
<th>Prevalence (%)</th>
<th>Prevalence ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urbanicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Urban</td>
<td>4</td>
<td>50</td>
<td>7.4</td>
<td>$x^2 = 0.59^*$</td>
<td>0.743</td>
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<tr>
<td>Peri-urban</td>
<td>2</td>
<td>47</td>
<td>4.1</td>
<td>df = 2</td>
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<tr>
<td>Rural</td>
<td>5</td>
<td>69</td>
<td>6.8</td>
<td>df = 2</td>
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<tr>
<td>Free-grazing</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free-grazing</td>
<td>7</td>
<td>26</td>
<td>21.1</td>
<td>6.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Restricted</td>
<td>4</td>
<td>140</td>
<td>2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>4</td>
<td>57</td>
<td>6.6</td>
<td>$x^2 = 0.47^*$</td>
<td>0.790</td>
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<tr>
<td>Cross</td>
<td>3</td>
<td>61</td>
<td>4.7</td>
<td>df = 2</td>
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</tr>
<tr>
<td>Indigenous</td>
<td>4</td>
<td>48</td>
<td>7.7</td>
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<td></td>
</tr>
<tr>
<td>Insemination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bull</td>
<td>8</td>
<td>121</td>
<td>6.2</td>
<td>0.90</td>
<td>1</td>
</tr>
<tr>
<td>AI</td>
<td>3</td>
<td>45</td>
<td>6.3</td>
<td></td>
<td></td>
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<tr>
<td>Vaccination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccinated</td>
<td>2</td>
<td>7</td>
<td>22.2</td>
<td>3.76</td>
<td>0.10</td>
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<tr>
<td>Not vaccinated</td>
<td>9</td>
<td>159</td>
<td>5.4</td>
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<td></td>
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<tr>
<td>Abortion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aborted</td>
<td>4</td>
<td>21</td>
<td>16.0</td>
<td>3.06</td>
<td>0.052</td>
</tr>
<tr>
<td>Not aborted</td>
<td>7</td>
<td>145</td>
<td>4.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bought-in cattle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7</td>
<td>119</td>
<td>5.6</td>
<td>0.61</td>
<td>0.716</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>40</td>
<td>7.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent fever</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exist</td>
<td>1</td>
<td>16</td>
<td>5.9</td>
<td>0.86</td>
<td>1</td>
</tr>
<tr>
<td>Not exist</td>
<td>10</td>
<td>150</td>
<td>6.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Likelihood ratio test result
(A) Infection with brucellosis → Abortion

(B) Herd size → Free movement of cattle → Infection with brucellosis

(C) Infection with brucellosis
   Abortion → Vaccination
Multivariable analysis
(Generalized Linear Model)

• Risk factors
  – Herd size
    • OR 1.3 (95%CI: 1.1-1.5), p<0.001
  – Recent abortion
    • OR 4.1 (95%CI: 1.0-17.6), p=0.059

• Confounder
  – Free-grazing
    • OR=2.7, p=0.2
    • Removal of the factor from the model changes estimate of herd size by 20%

Brucellosis is causing abortion in large-scale farms which have lands for free-grazing
Noticing that disease/problem is in a population

Assessment of intervention

Removal of a risk factor

Adding a preventive factor (Intervention study)

Determination of the risk factor

Visualisation

Descriptive epidemiology

Forming a hypothesis

Testing a hypothesis (Analytical epidemiology)

Inter-disciplinarity

Risk-based surveillance

Risk assessment

Mathematical modelling

Animal Health Economics
Inter-disciplinary and trans-disciplinary approaches

Example of disciplines:
Medicine, Veterinary Medicine, Environmental Sciences, Socio-economics
Joint field activities among Medicine, Veterinary Medicine and Anthropology

- Safe food fair food project in Mali (ILRI) -

Human brucellosis diagnosis (Medicine)

Brucellosis diagnosis of cattle (Veterinary)

Learning food culture and farming (Anthropology)
Joint field activities among Medicine, Veterinary Medicine and Anthropology
- Safe food fair food project in Mali (ILRI) -

Shared responsibility!
Shared costs!

Human brucellosis diagnosis (Medicine)

Brucellosis diagnosis of cattle (Veterinary)

Learning food culture and farming (Anthropology)
Surveillance

• Systematic and continuous collection, analysis, and interpretation of data, closely integrated with the timely and coherent dissemination of the results and assessment to those who have the right to know so that action can be taken. (A dictionary of Epidemiology 5th Ed. 2008)
Active surveillance
- Active collection of data for a specific purpose

Passive surveillance
- Report-based

Authority

Field
Risk-based surveillance

- Set a priority
- Allocate resources effectively and efficiently
- Selecting hazard and/or sub-population
Animal source foods

- Two-thirds of human pathogens are zoonotic – many of these transmitted via animal source food
- Animal source food is a single most important cause of food-borne disease
- Many food-borne diseases cause few symptoms in animal host
- Many zoonotic diseases controlled most effectively in animal host/reservoir
Dominance of informal markets in developing countries

“Absence of structured sanitary inspection”
Informal ≠ Illegal
Codex Alimentarius Commission

Food safety risk analysis

A tool for decision-making under uncertainty

*Risk is a probability of occurrence of a scenario and its size of impact (Vose, 2008)
Food safety risk analysis in informal marketing system

Participatory methods
Codex Alimentarius Commission
Risk assessment framework (CAC/GL-30 (1999))
Value chain

Producers ↔ Middle men ↔ Consumers

Money flows from Producers to Middle men and then to Consumers.
Actors in informal milk sales in Kampala, Uganda

- Shop with a bulk cooler
- Shop with a small refrigerator
- Boiling centre
- Trader with cans on a bicycle
- Roadside vendor
- Roadside vendor

• Plus milk retail shop without refrigerator and dairy farmers selling at farms
Quantitative dairy value chain in Kampala, Uganda

Brucellosis example (Uganda)

Sources of the risk by production areas

- Nakasongola: 2.6%
- Kayunga: 4.1%
- Peri-urban Kampala: 7.0%
- Urban Kampala: 15.9%
- Mbarara: 70.3%
Brucellosis example (Uganda)

Sources of the risk by milk sellers

- Bulk cooler: 62.7%
- Farm gate: 15.1%
- Small refrigerator: 12.8%
- Bicycle: 7.3%
- Roadside vendor: 1.1%
- Without refrigerator: 1.0%
### Brucellosis example (Uganda)

#### Control options (90% of enforcement)

<table>
<thead>
<tr>
<th>Control options</th>
<th>Reduction</th>
<th>Inputs</th>
<th>Feasibility</th>
<th>Negative impact</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not to take any option</td>
<td>0.0</td>
<td>None</td>
<td>High</td>
<td>Risk remains</td>
<td>Not recommendable</td>
</tr>
<tr>
<td>Construct a boiling centre in Mbarara</td>
<td>62.3</td>
<td>A boiling centre, legislation, fuel</td>
<td>Middle-high</td>
<td>Price up</td>
<td>Recommendable</td>
</tr>
<tr>
<td>Construct boiling centres in peri-urban Kampala</td>
<td>75.4</td>
<td>Boiling centres, legislation, fuel</td>
<td>Middle</td>
<td>Price up</td>
<td>Recommendable</td>
</tr>
<tr>
<td>Enforce milk shops to boil milk or to buy boiled milk</td>
<td>68.9</td>
<td>Legislation, fuel, facilities, enforce</td>
<td>Very low</td>
<td>Price up, many shops cannot afford</td>
<td>Not recommendable</td>
</tr>
<tr>
<td>Ban of farm gate milk sales</td>
<td>12.3</td>
<td>Legislation, enforcement</td>
<td>Low</td>
<td>Alternative sales may not boil</td>
<td>Single measure does not change the risk</td>
</tr>
<tr>
<td>Ban of urban dairy farming</td>
<td>14.8</td>
<td>Legislation, enforcement</td>
<td>Middle</td>
<td>Livelihood of urban farmers, milk supply</td>
<td>Not recommendable</td>
</tr>
<tr>
<td>Ban of milk sales by traders with a bicycle in urban areas</td>
<td>6.6</td>
<td>Legislation, enforcement</td>
<td>High</td>
<td>Livelihood of traders, alternative transport may not boil</td>
<td>Single measure does not change the risk</td>
</tr>
<tr>
<td>Ban of roadside milk sales</td>
<td>0.8</td>
<td>Legislation, enforcement</td>
<td>High</td>
<td>Livelihood of traders, alternative transport may not boil</td>
<td>Single measure does not change the risk</td>
</tr>
<tr>
<td>Ban of milk sales at shops without a refrigerator</td>
<td>0.8</td>
<td>Legislation, enforcement</td>
<td>High</td>
<td>Livelihood of traders, alternative transport may not boil</td>
<td>Single measure does not change the risk</td>
</tr>
</tbody>
</table>
Sensitivity analysis
(From *S. aureus* food poisoning example)

Sensitivity Tornado

- Initial bacteria population
- Temperature
- Prob. *SA* has SE genes
- Prob. farmers boil
- Prob. consumers boil
- Store milk 3,4 days
- Contamination, farm
- Contamination, farm
- Consume on day 0
- Prob. centres boil
- Contamination, centre
- Store milk 1,2 days


*It provides efficient control options*
Advantage of participatory risk assessment

- Speed
- Affordability
- Flexibility in application
- Understanding of culture
- Best control option
- Potential to change behavior
Infectious disease modelling

- Basic reproduction number \((R_0)\)
  - Total number of individuals directly infected by a single infected individual, when introduced to totally susceptible population
  - \(R_0 < 1\)  Infection dies out
  - \(R_0 = 1\)  Infection is maintained
  - \(R_0 > 1\)  Infection takes over
$R_0$ as a communication tool

- Example of Ebola epidemiology
SIR model and calculation of $R_0$

\[ S \rightarrow I \rightarrow R \]

- **S**: Susceptible
- **I**: Infectious
- **R**: Recovered

SIR model
SIR model and calculation of $R_0$

\[ \frac{dS}{dt} = -\beta SI \]
\[ \frac{dI}{dt} = \beta SI - \alpha I \]
\[ \frac{dR}{dt} = \alpha I \]
Modelling disease dynamics

sir <- function(time, state, parameters) {
  with(as.list(c(state, parameters)), {
    dS <- -beta * S * I
    dI <- beta * S * I - gamma * I
    dR <- gamma * I
    return(list(c(dS, dI, dR)))
  })
}

......
In the case of endemic diseases

-Modelling deaths-

\[ \frac{dS}{dt} = -\beta SI + \mu N - \mu S \]
\[ \frac{dI}{dt} = \beta SI - \alpha I - \mu I \]
\[ \frac{dR}{dt} = \alpha I - \mu R \]
SIR model and calculation of $R_0$

$$\beta SI = (\alpha + \mu)I$$
$$\beta/(\alpha + \mu)*S = 1$$

$R$ (Effective reproductive ratio) = $\{\beta/(\alpha + \mu)\}*S$
SIR model and calculation of $R_0$

$R_0 = \frac{\beta}{(\alpha + \mu)} \times N$

*In case all individuals are susceptible ($S_0 = N$)*
Effect of vaccination against rabies
Final size simulation (Hokkaido, Japan)

Vaccination coverage
- 0%
- 51.7%
- 80%

Proportions exceeding two cases per introduction of a rabid dog into Japan

Kadowaki, H., Makita, K. et al. In preparation
Application of mathematical modelling in Neglected Zoonoses control

• Finding effective control options
  – Modelling is flexible
  – Solving parameters
  – Changing values of parameters to see how much $R_0$ changes
Economic effects of disease

- **Direct costs**
  - Destroys resources through mortality
  - Lowers efficiency e.g. through reduced feed conversion
  - Reduces quantity and quality
  - Costs from avoiding disease

- **Indirect costs**
  - Zoonoses
    - Sub-optimal exploitation of resources due to adoption of production models to disease situation e.g. trypanotolerant cattle with low milk production

- **Disease**

Source: McInerney (1996)
Eg. Cost comparison for *S. aureus* mastitis control
(Comparison of two dipping products)

Product A: cheap but many cases

Product B: expensive but fewer mastitis

Makita K, Yamamoto H, et al. (2013)
Journal of Veterinary Epidemiology
Epidemiology can provide solutions to...

- Problem of Neglected Zoonoses
  - Neglected because they are ‘invisible’
  - Cannot be controlled because ‘resource is limited’
  - Cannot be controlled because ‘responsibility is fragmented’
  - Persistency – ‘prediction’ is needed to plan long-term policy
• Thank you for your attention!

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