Epidemiology for strategic control of Neglected Zoonoses

Presented at
FAO-APHCA/OIE/USDA Regional Workshop on
Prevention and Control of Neglected Zoonoses in Asia
July 16, 2015
Obihiro, Japan

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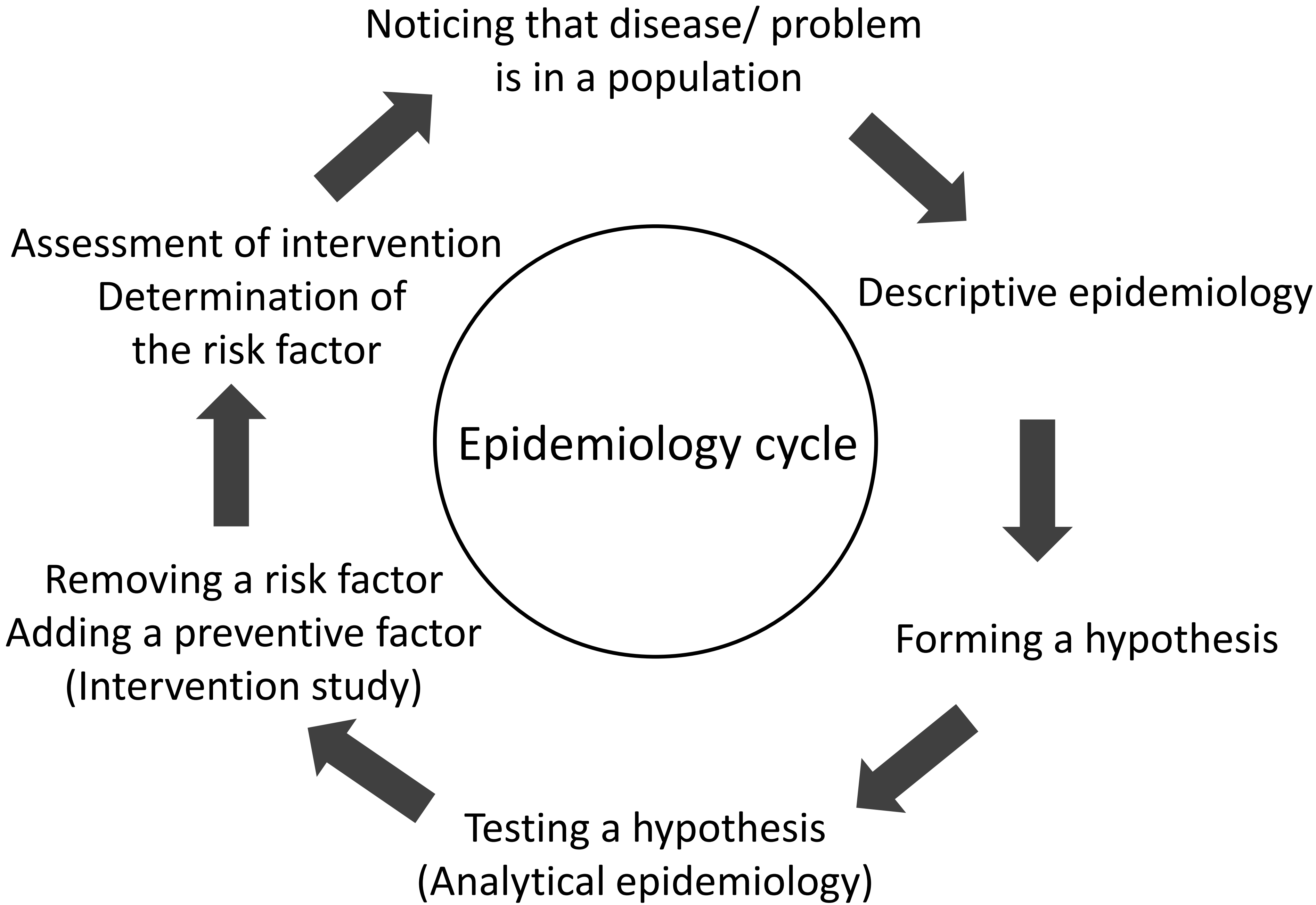
OIE Joint Collaborating Centre
for Food Safety

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

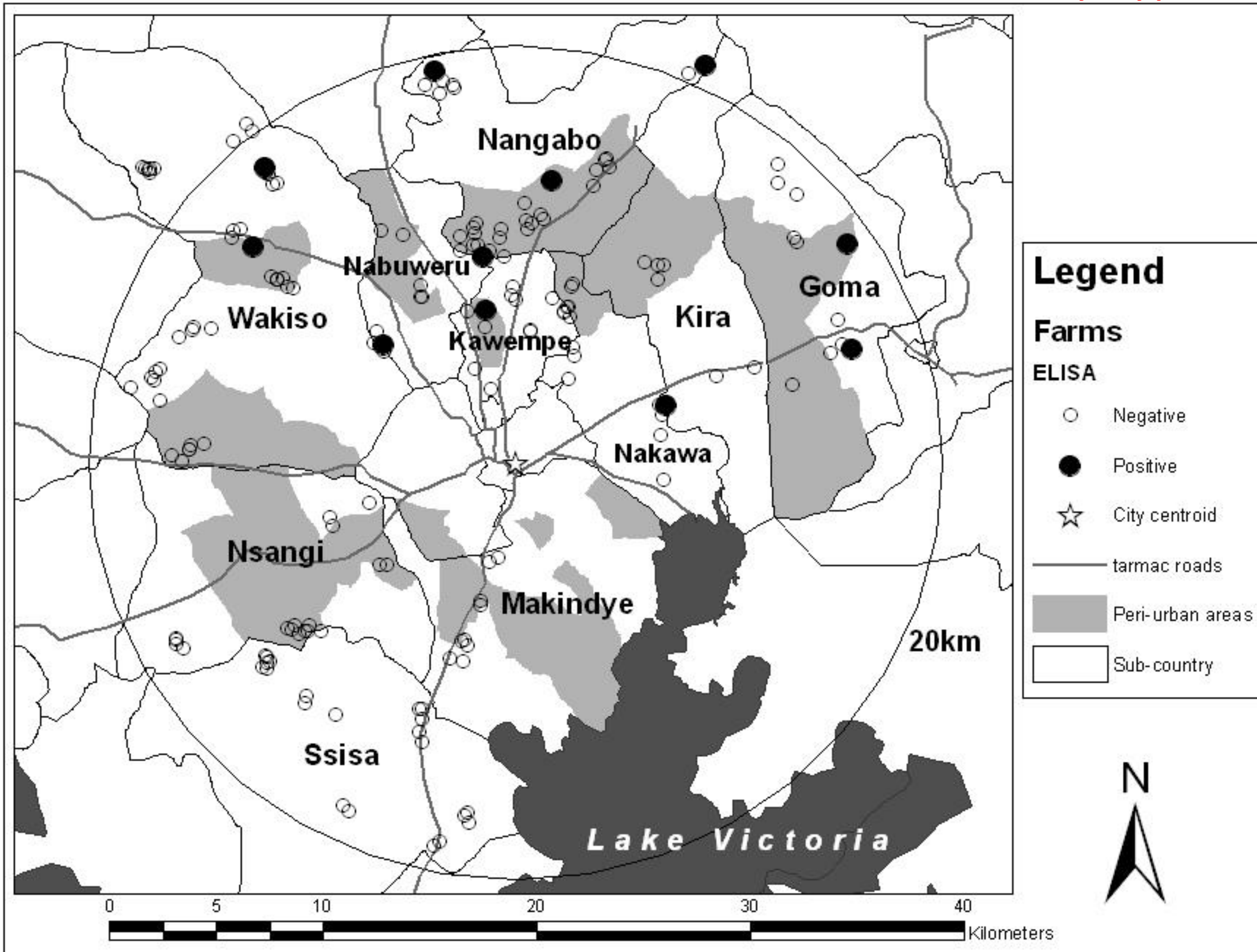
- Tool box to tackle with ‘invisibility’, ‘limited resources’, ‘fragmented responsibility’, and ‘needs of prediction’
  - Epidemiology cycle
  - Inter-disciplinarity
  - Risk-based surveillance
  - Risk assessment
  - Mathematical modelling
  - Animal Health Economics


Noticing that disease/ problem
is in a population
Descriptive epidemiology
Forming a hypothesis
Testing a hypothesis
(Analytical epidemiology)
Removing a risk factor
Adding a preventive factor
(Intervention study)
Assessment of intervention
Determination of
the risk factor
Epidemiology cycle

Brucella infected farms in Kampala, Uganda

Makita K. (2009) PhD Thesis. The University of Edinburgh.

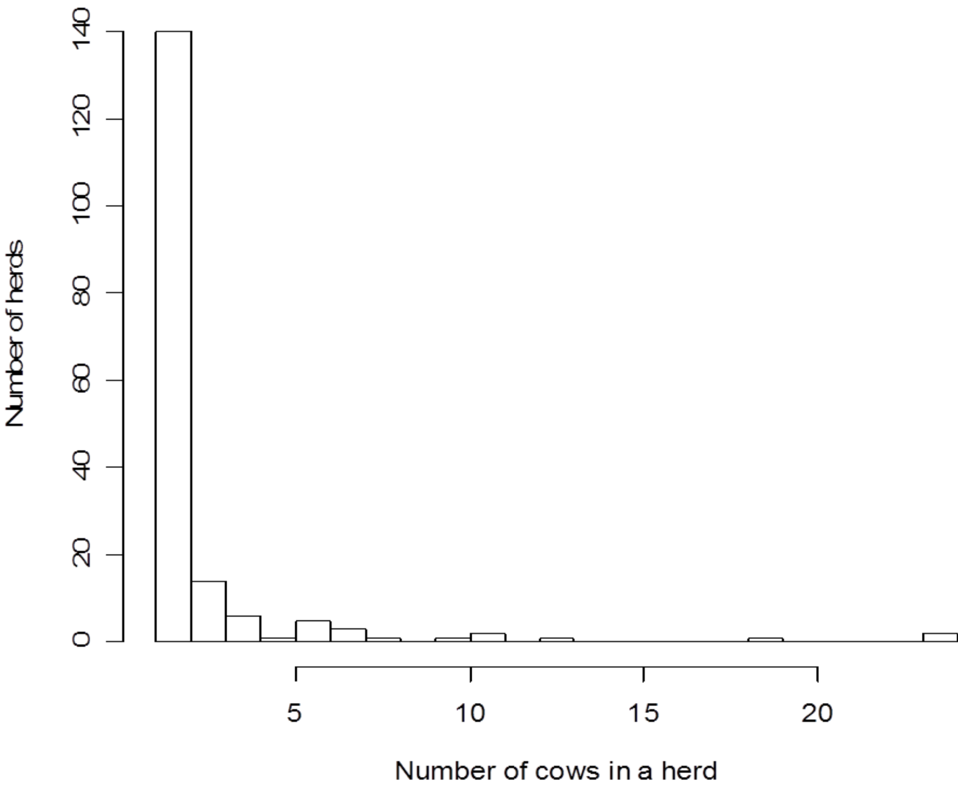
Any hypothesis?



Herd size and *Brucella* sero-positivity

Makita et al. (2011) BMC Veterinary Research 7:60.
Makita K. (2009) PhD Thesis. The University of Edinburgh.

Any hypothesis?



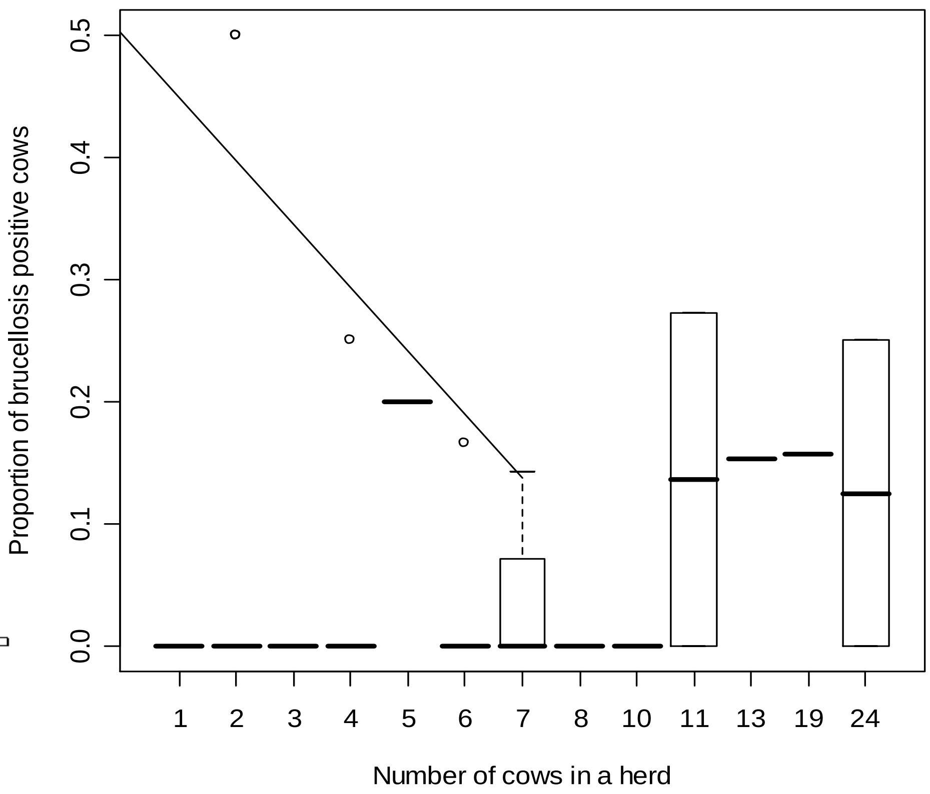
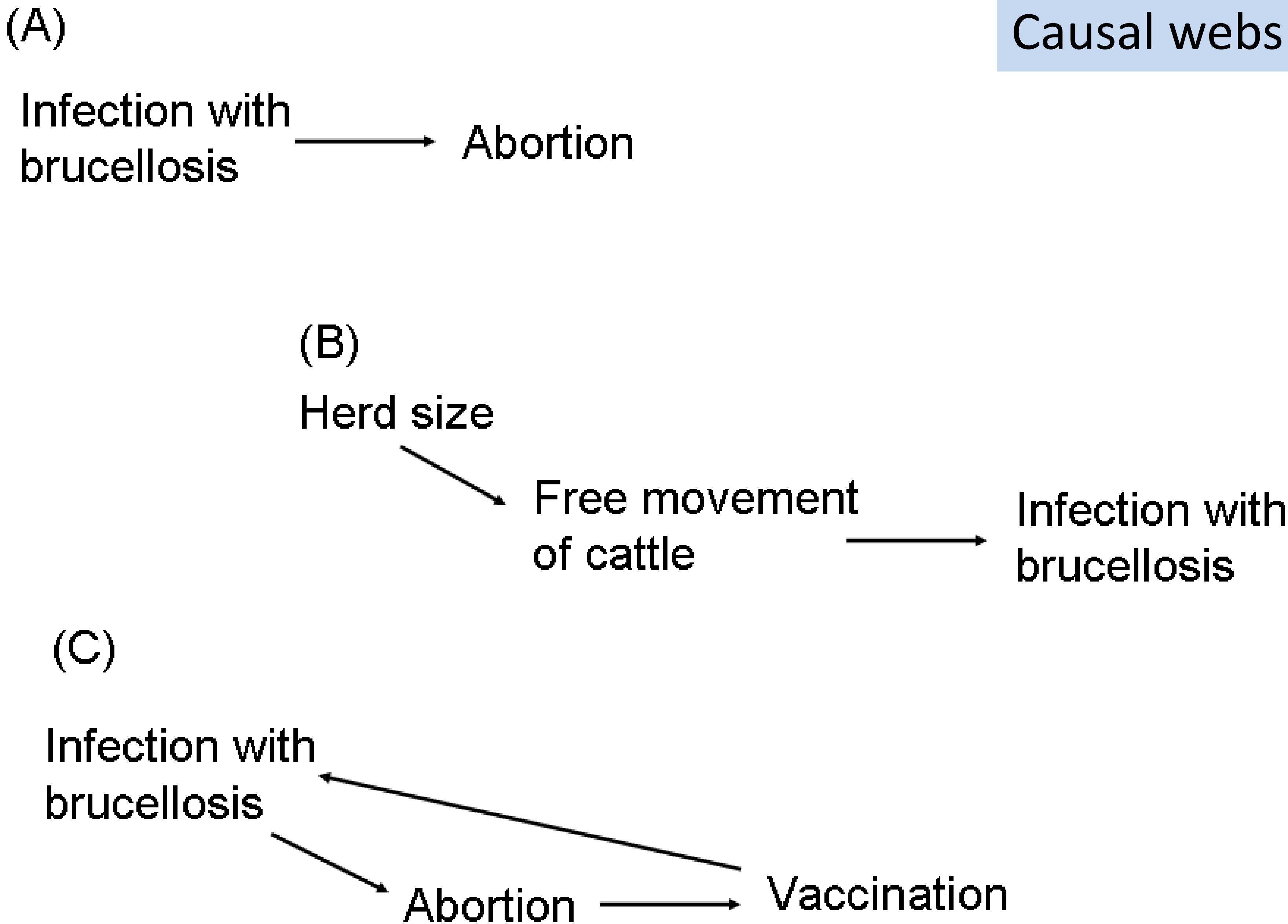


Table 3 Univariate analysis for brucellosis at the herd level

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

* Likelihood ratio test result

Causal webs

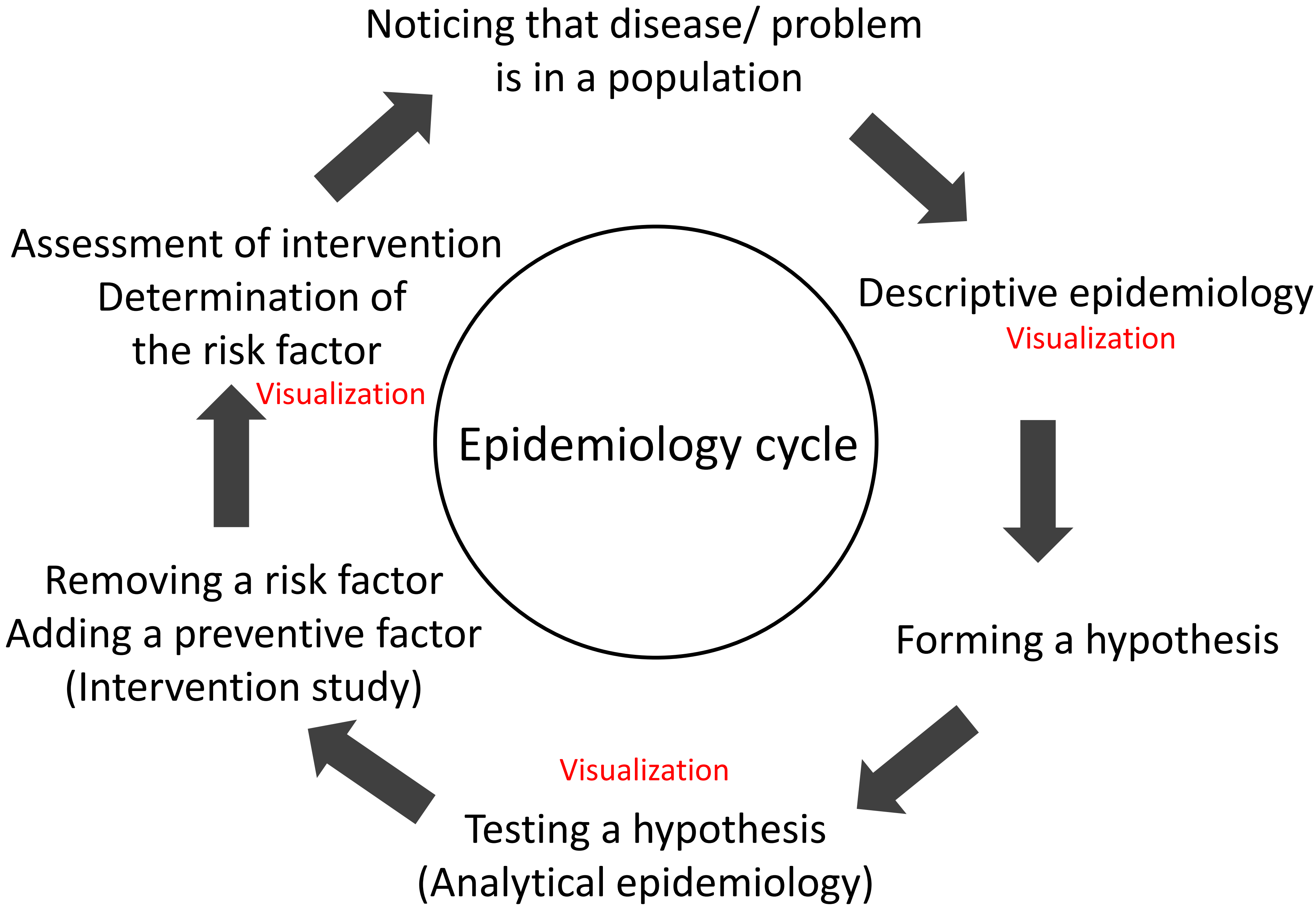


(A)
Infection with brucellosis
Abortion
(B)
Herd size
Free movement of cattle
Infection with brucellosis
(C)
Infection with brucellosis
Abortion
Vaccination

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**で in **large-scale** farms which have lands for **free-grazing**


Noticing that disease/ problem
is in a population
Descriptive epidemiology
Visualization
Forming a hypothesis
Visualization
Testing a hypothesis
(Analytical epidemiology)
Removing a risk factor
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(Intervention study)
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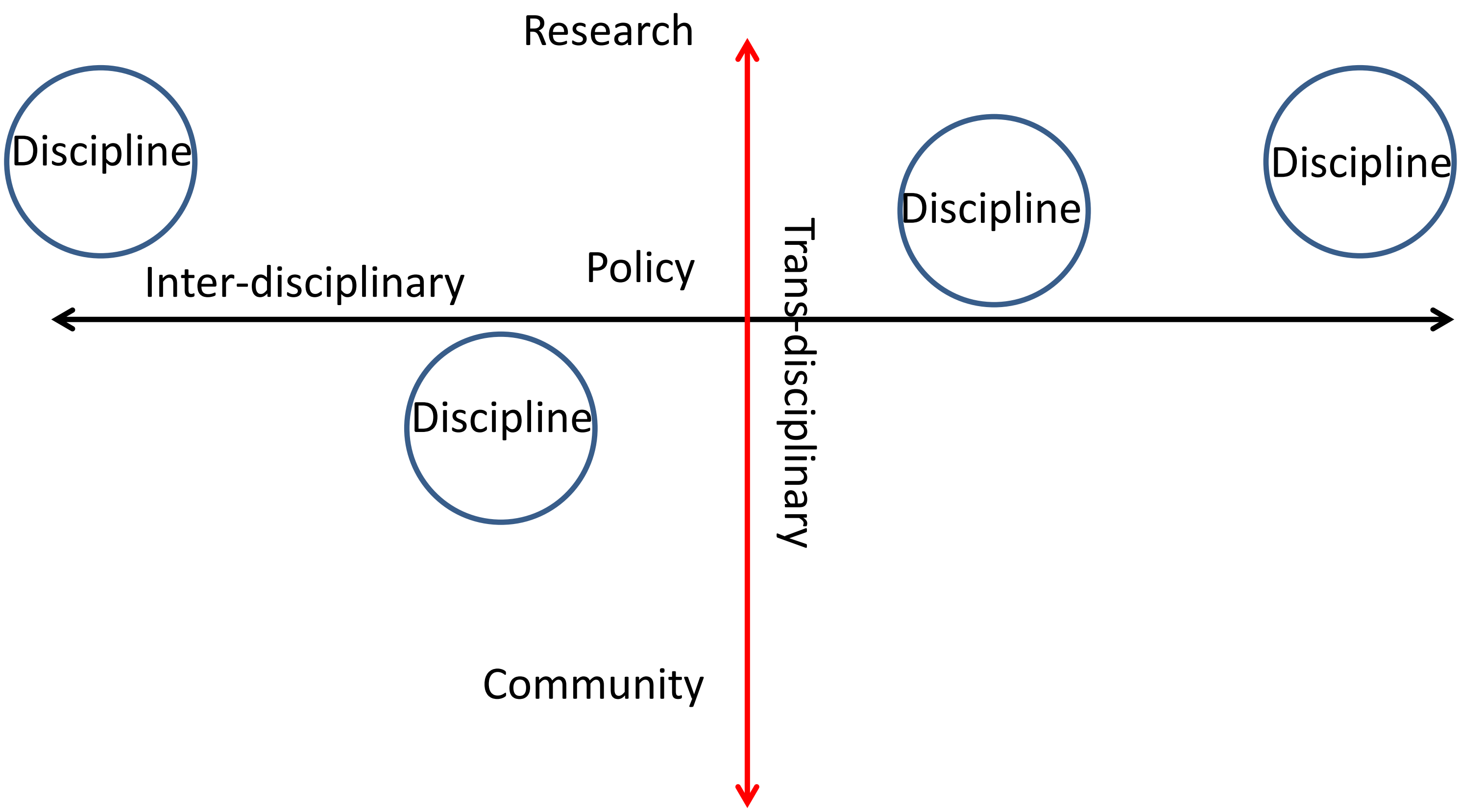
the risk factor
Visualization
Epidemiology cycle

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) -

Brucellosis diagnosis of cattle (Veterinary)

Learning food culture and farming (Anthropology)

Human brucellosis diagnosis (Medicine)

Joint field activities among Medicine, Veterinary Medicine and Anthropology

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

Shared responsibility!

Shared costs!

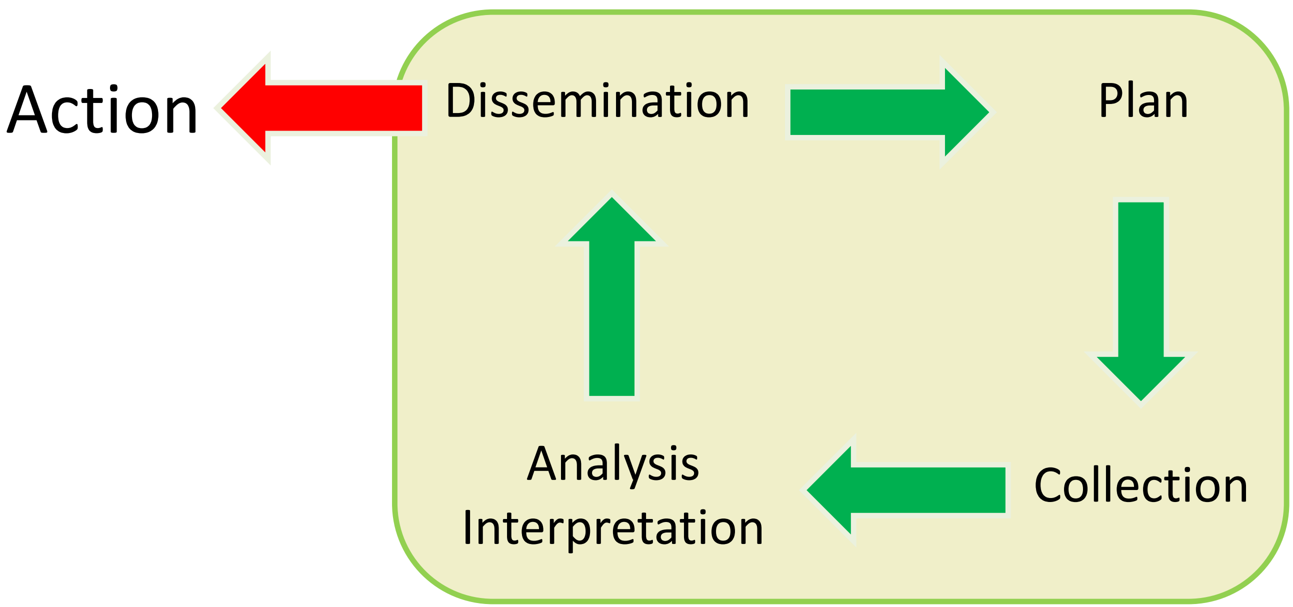
Brucellosis diagnosis of cattle (Veterinary)

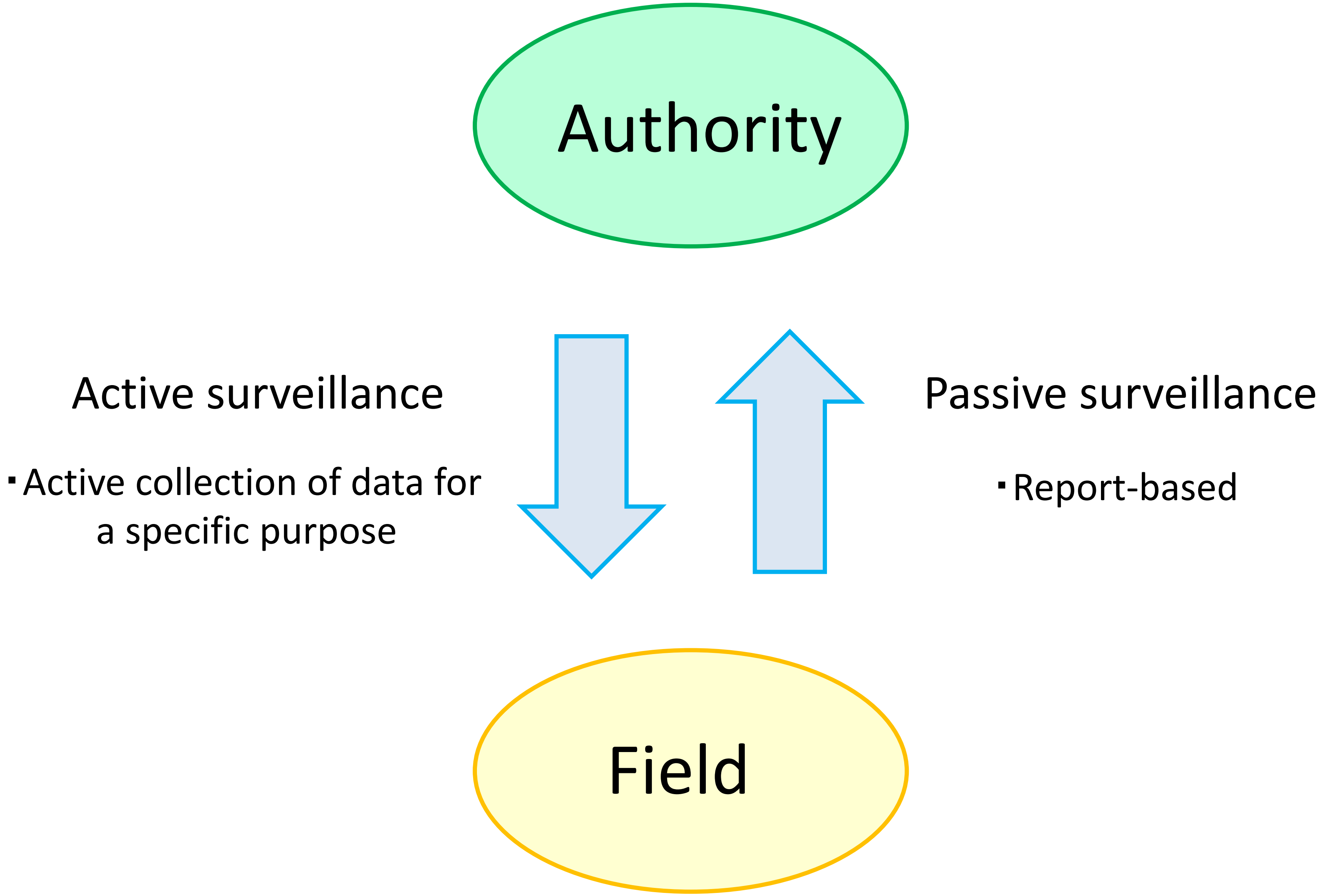
Learning food culture and farming (Anthropology)

Human brucellosis diagnosis (Medicine)

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)




Authority
Active surveillance
・Active collection of data for a specific purpose
Passive surveillance
・Report-based
Field

Risk-based surveillance

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

BMC Health Services Research

BioMed Central

2006, 6:20

Open Access

Debate

Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: Review of current approaches

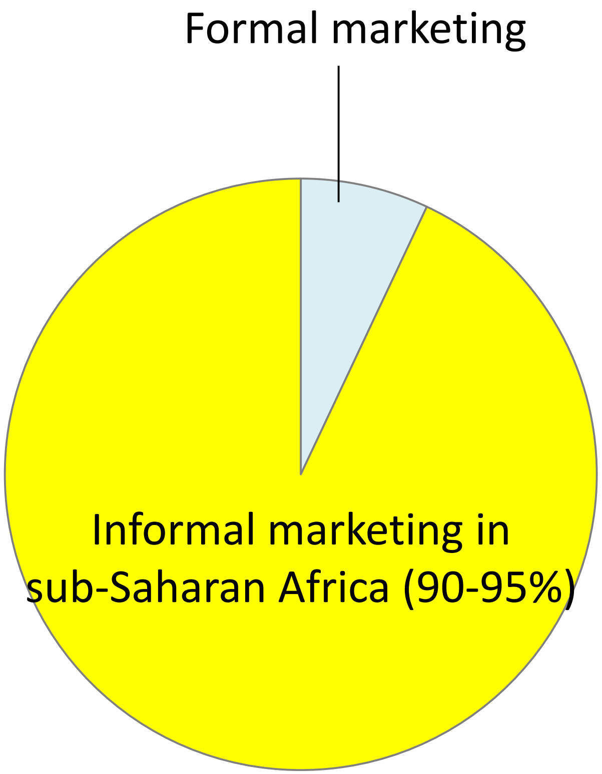
Katharina DC Stärk*[1], Gertraud Regula[1], Jorge Hernandez[2], Lea Knopf[1], Klemens Fuchs[3], Roger S Morris[4] and Peter Davies[5]

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

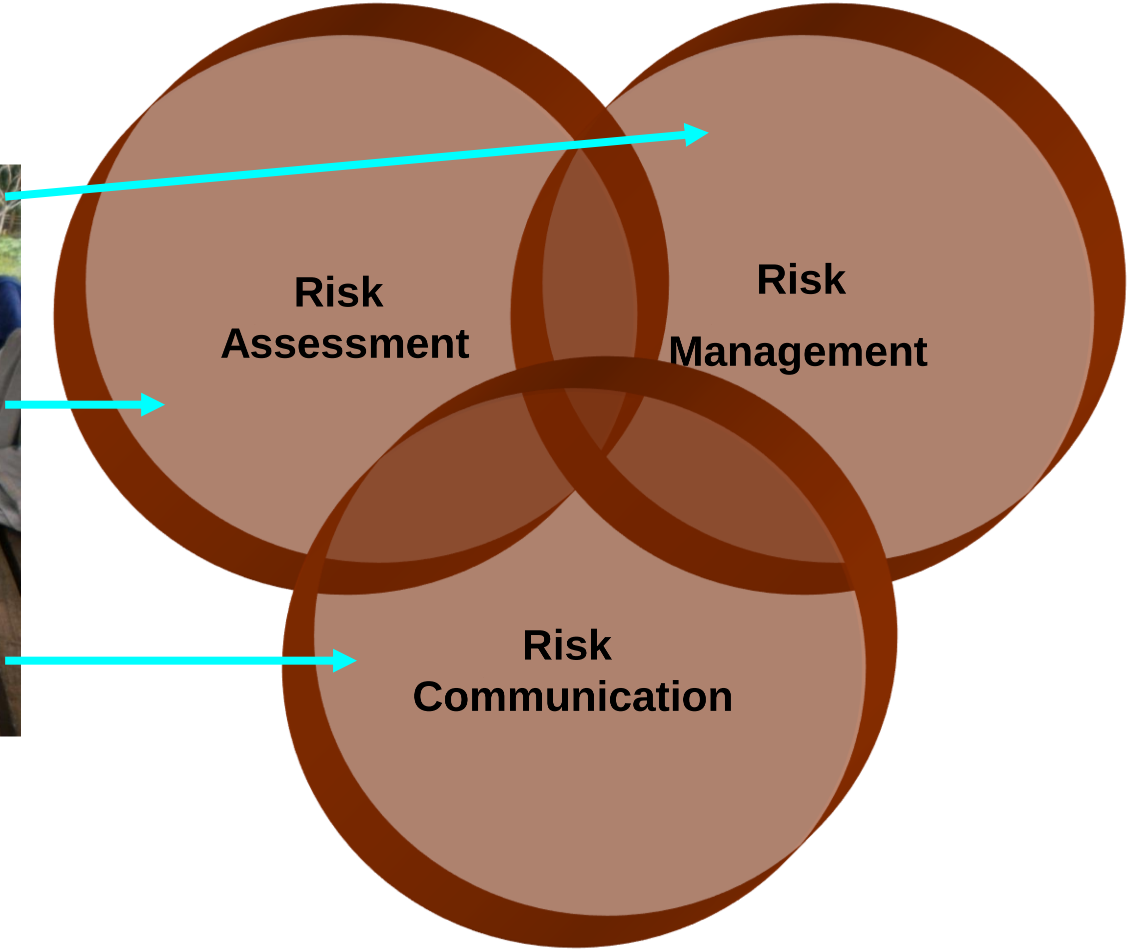
Codex Alimentarius Commossion
Food safety risk analysis
A tool for decision-making under uncertainty

*Risk is a probability of occurrence of a scenario and its size of impact (Vose, 2008)

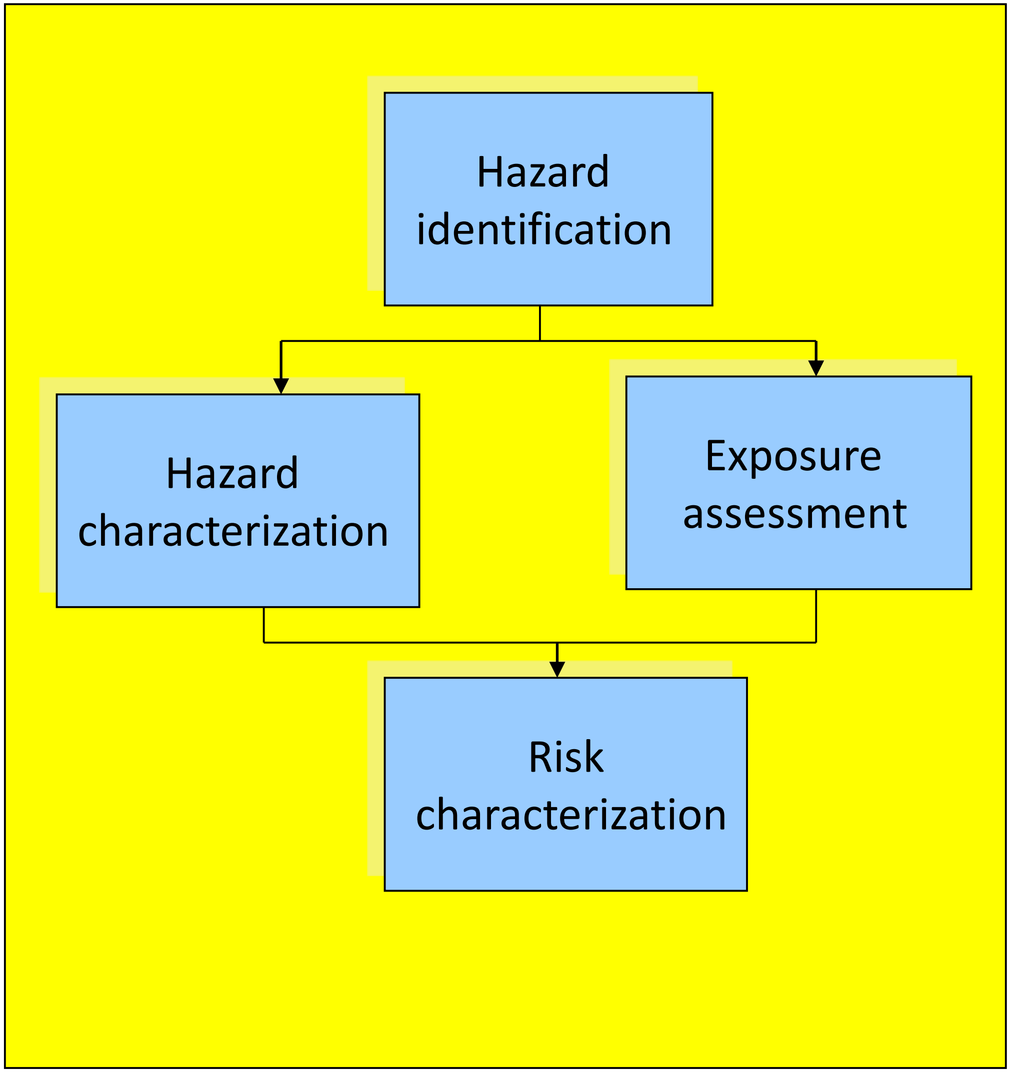
Food safety risk analysis

in informal marketing system

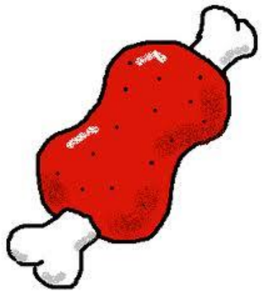
Participatory methods

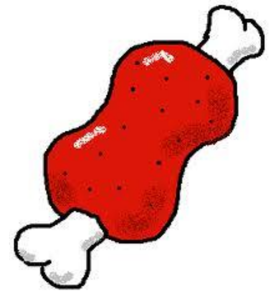


Codex Alimentarius Commission
Risk assessment framework (CAC/GL-30 (1999))



Value chain





Producers → ← Middle men → ← Consumers

Actors in informal milk sales in Kampala, Uganda

Shop with a bulk cooler

Shop with a small refrigerator

Boiling centre

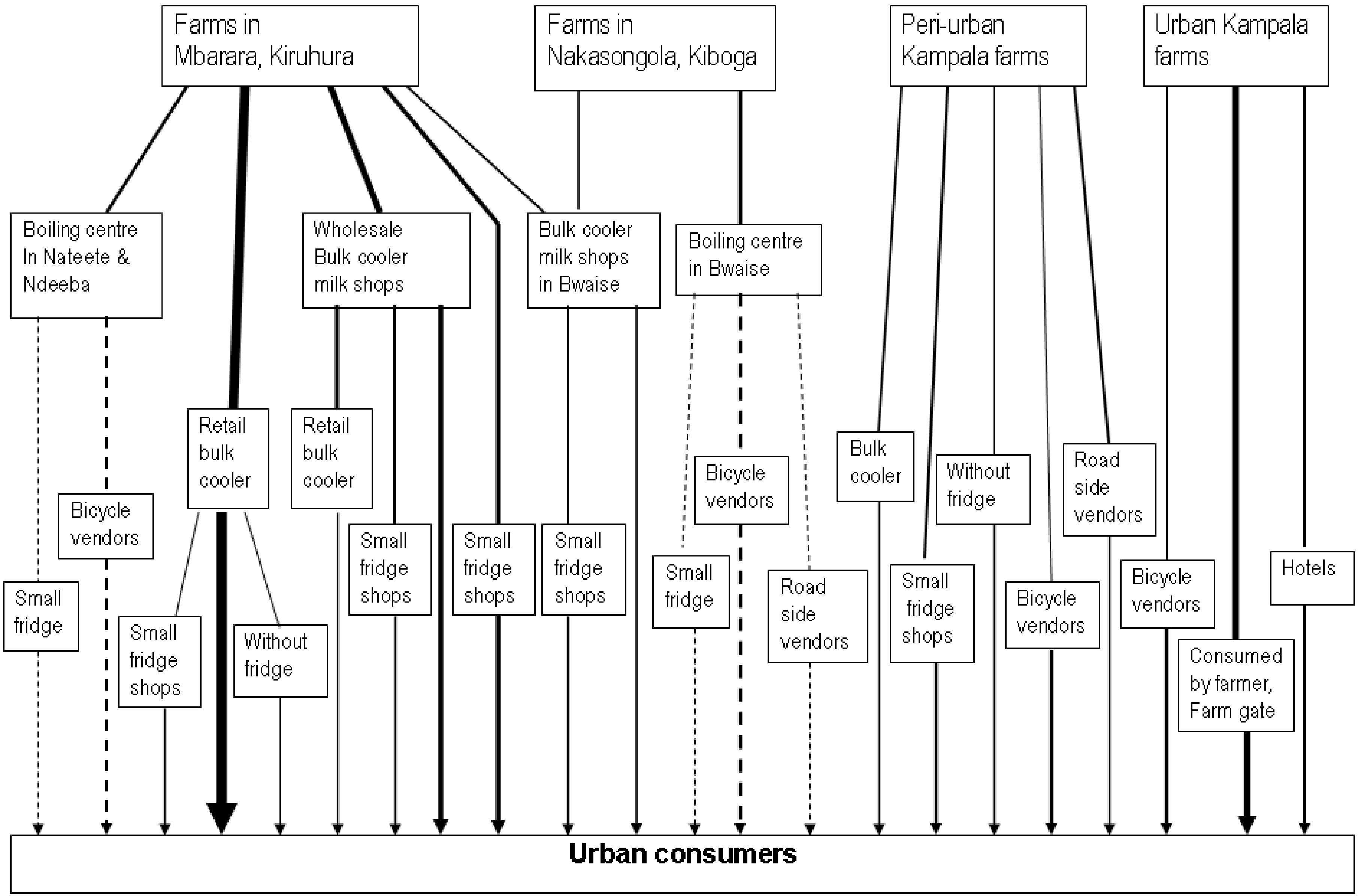
Trader with cans on a bicycle

Roadside vendor

Roadside vendor

- Plus milk retail shop without refrigerator and dairy farmers selling at farms

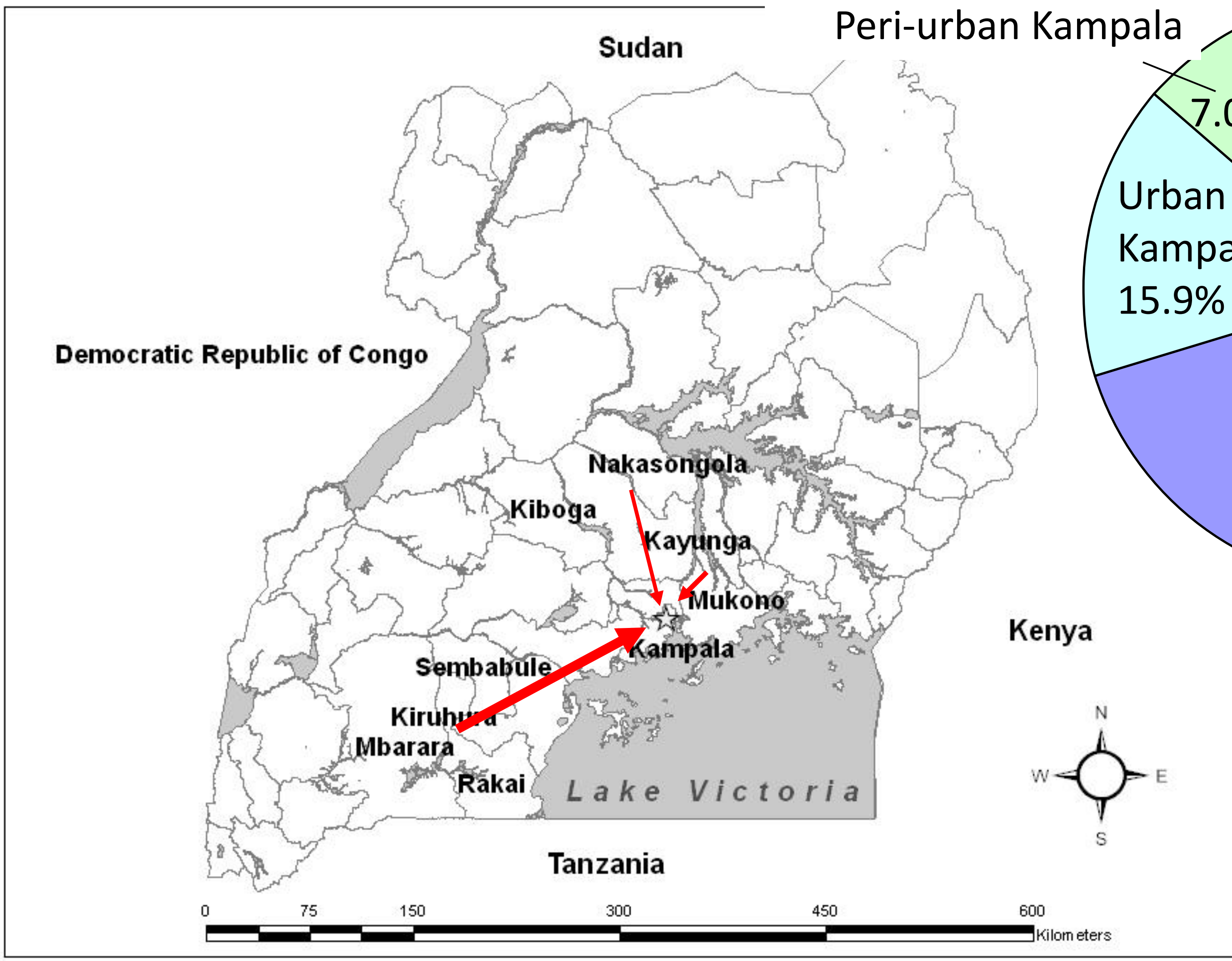
Quantitative dairy value chain in Kampala, Uganda

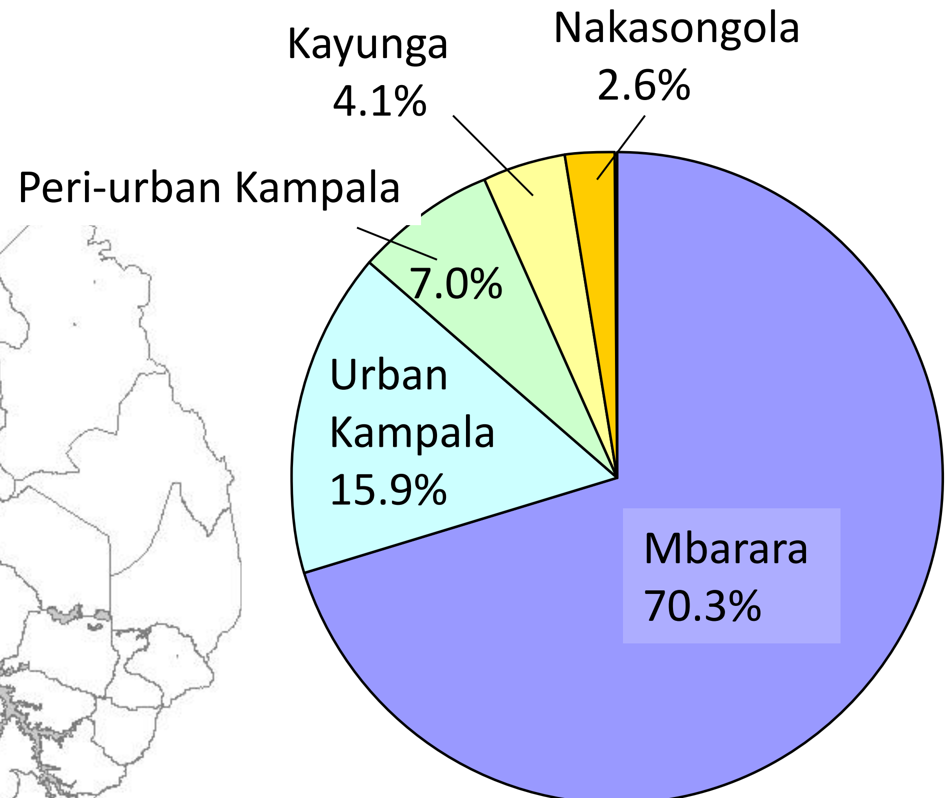


Source: Makita K. et al. (2010). How human brucellosis incidence in urban Kampala can be reduced most efficiently? A stochastic risk assessment of informally-marketed milk. PLoS ONE 5 (12): e14188.

Brucellosis example (Uganda)

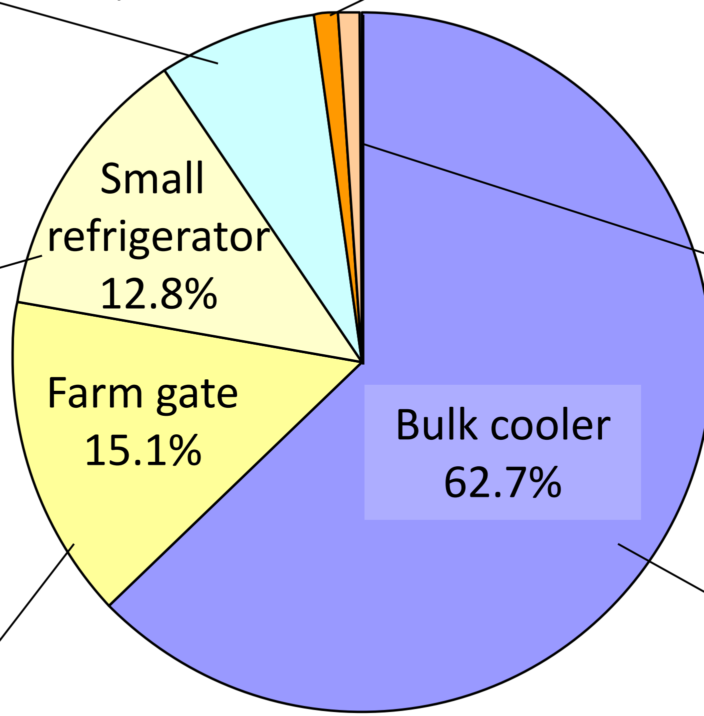
Sources of the risk by production areas





Brucellosis example (Uganda)

Sources of the risk by milk sellers



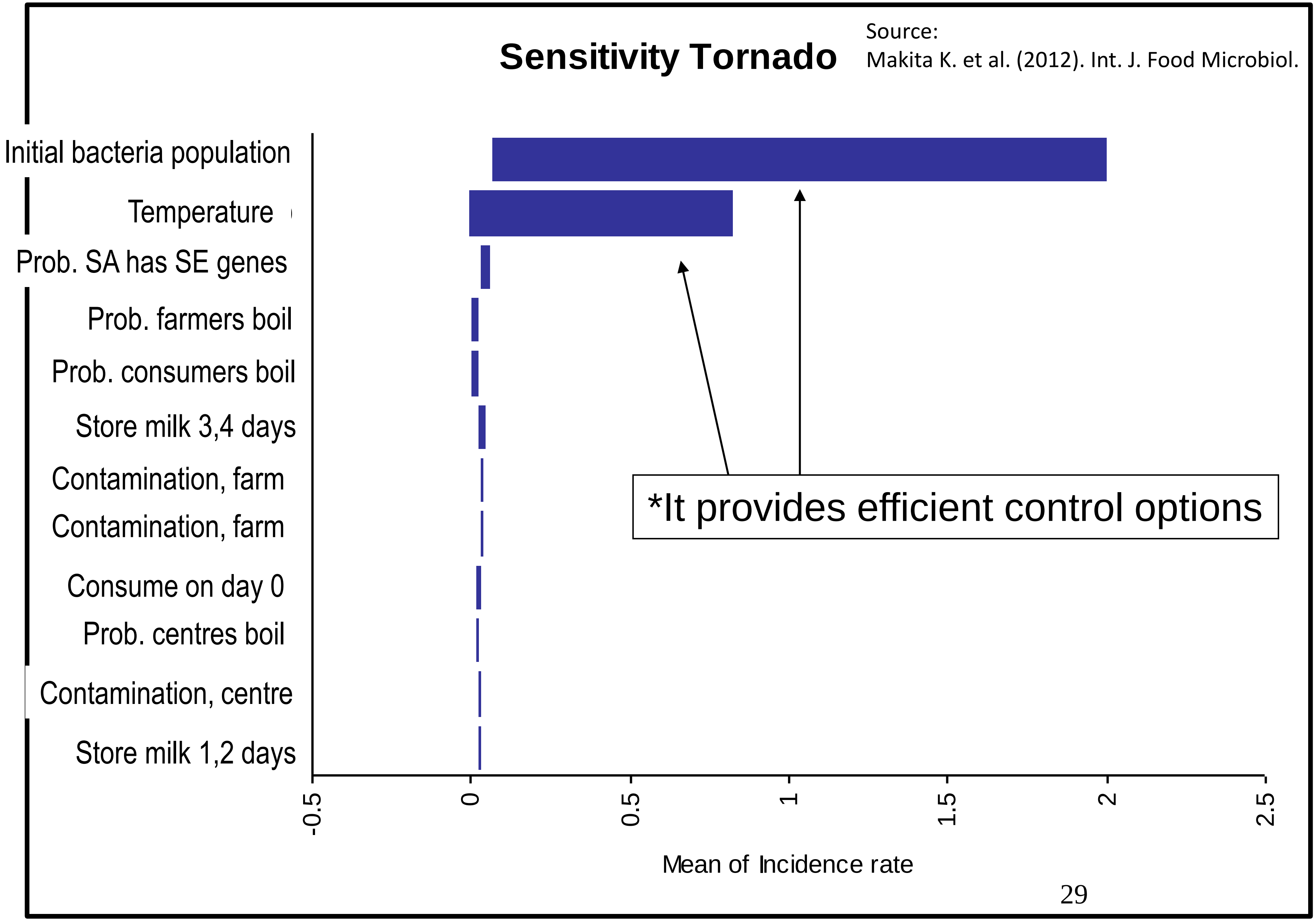
Brucellosis example (Uganda)

Control options (90% of enforcement)

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

Sensitivity analysis

(From *S. aureus* food poisoning example)



Advantage of participatory risk assessment

-Speed

-Affordability

-Flexibility in application

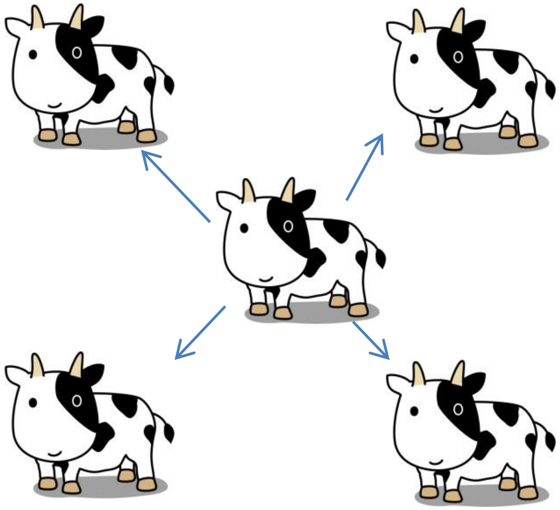
-Understanding of culture

-Best control option

-Potential to change behavior

Infectious disease modelling

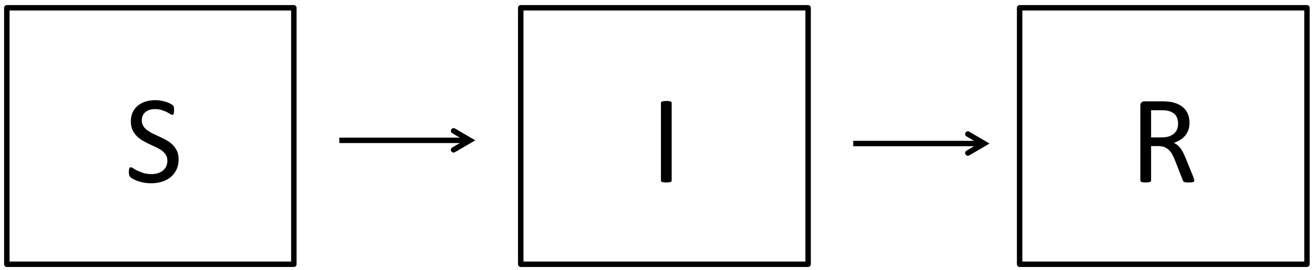
- Basic reproduction number (R_0)
  - Total number of individuals directly infected by a single infected individual, when introduced to totally susceptible population
  - $R_0<1$ Infection dies out
  - $R_0=1$ Infection is maintained
  - $R_0>1$ Infection takes over



R_0 as a communication tool

- Example of Ebola epidemiology
  - Nature (2014 Oct 16)

SIR model and calculation of R_0



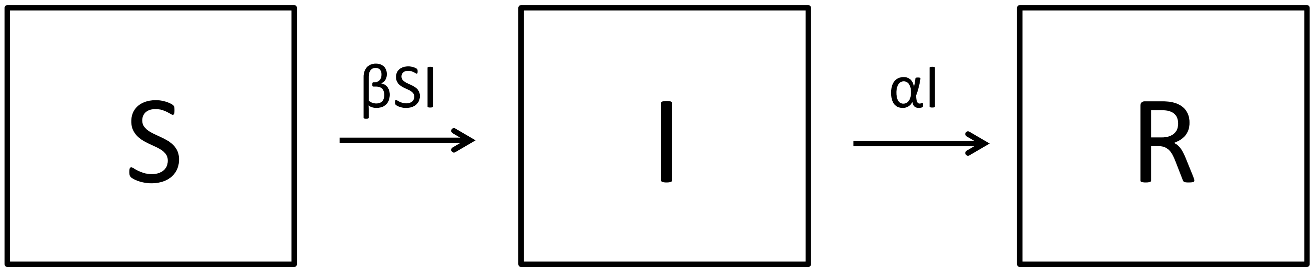
S: Susceptible

I: Infectious

R: Recovered

SIR model

SIR model and calculation of R_0



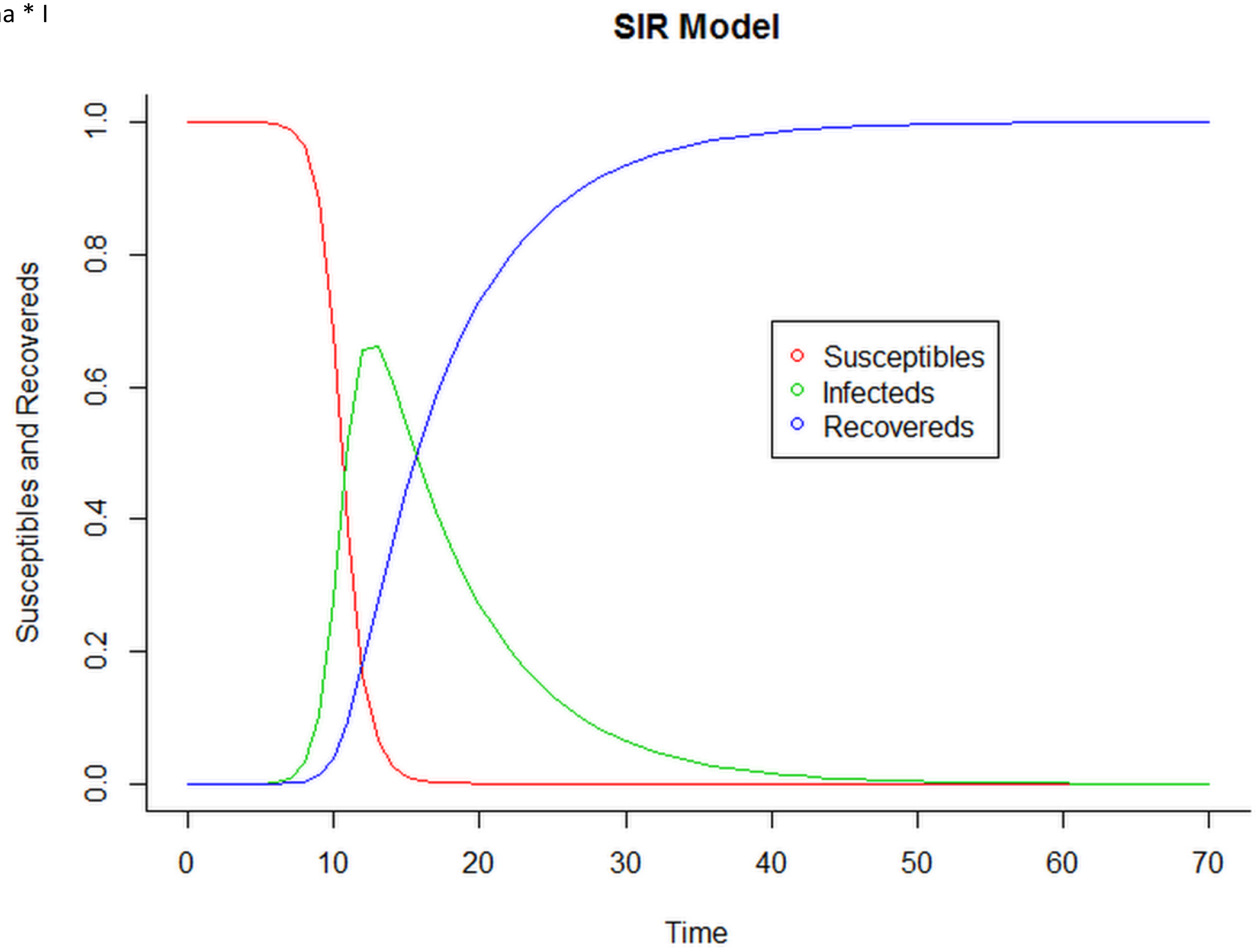
$$dS/dt = -\beta SI$$

$$dI/dt = \beta SI - \alpha I$$

$$dR/dt = \alpha I$$

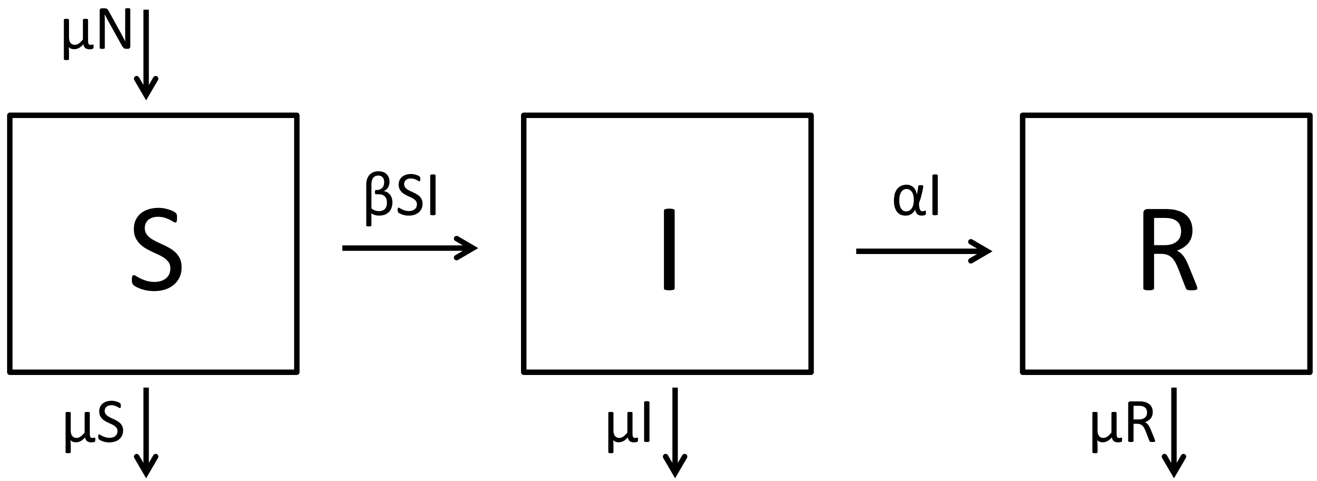
Modelling disease dynamics

```
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-

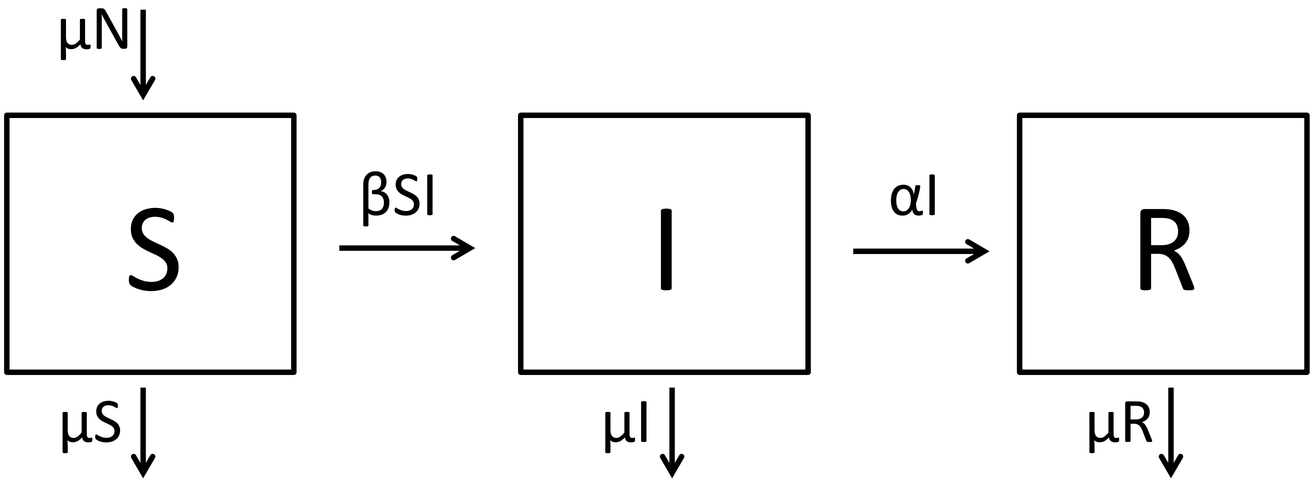


$$dS/dt = -\beta SI + \mu N - \mu S$$

$$dI/dt = \beta SI - \alpha I - \mu I$$

$$dR/dt = \alpha I - \mu R$$

SIR model and calculation of R_0

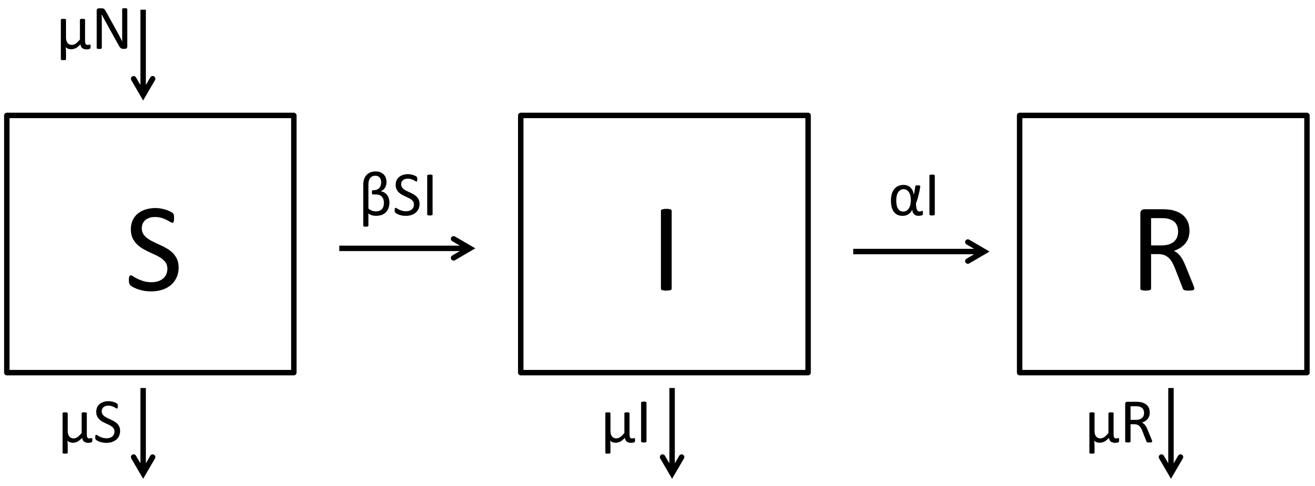


$$\beta SI = (\alpha + \mu)I$$

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

$$R_{\text{(Effective reproductive ratio)}} = \{\beta/(\alpha + \mu)\}*S$$

SIR model and calculation of R_0



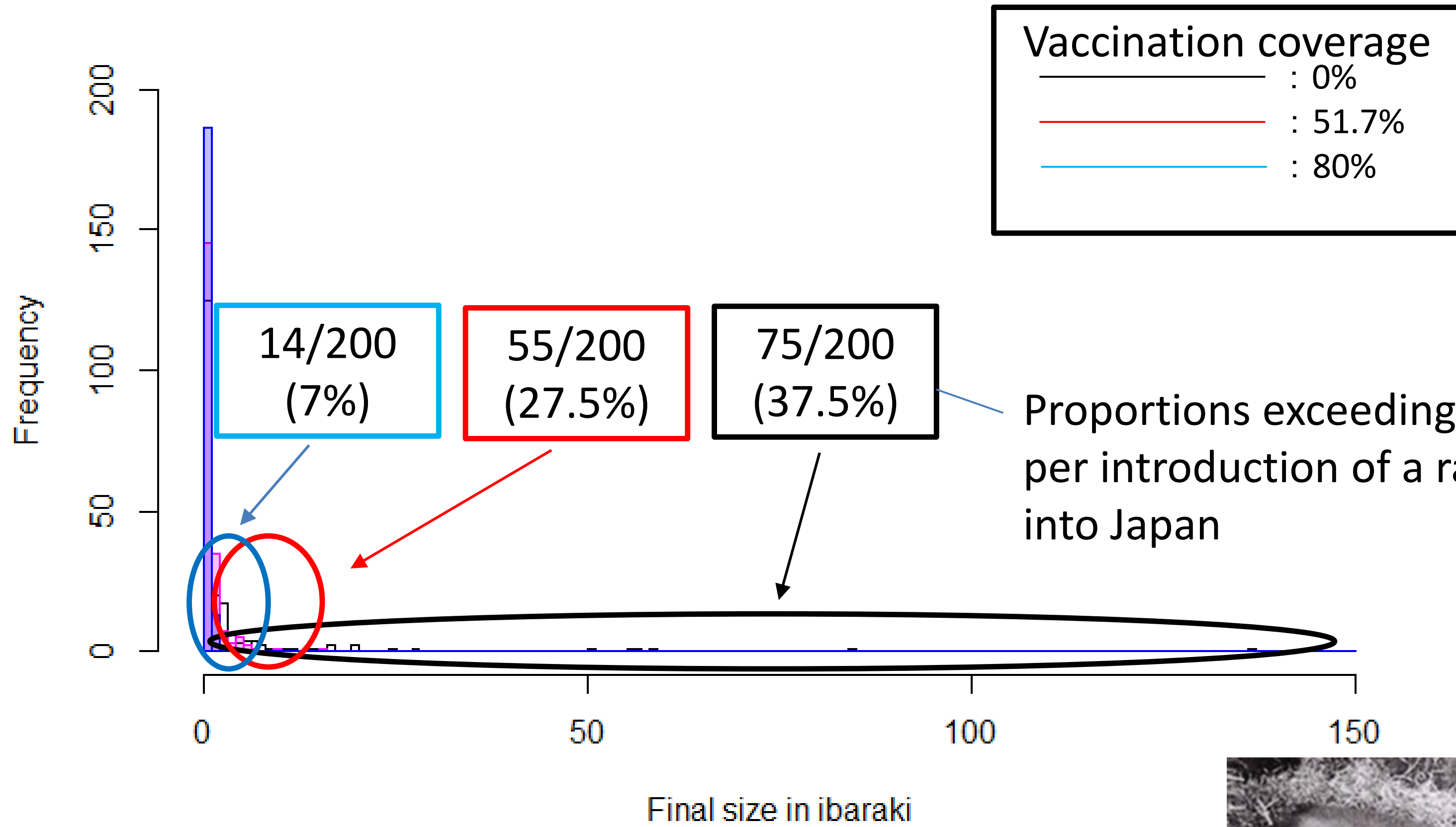
*In case all individuals are susceptible (S_0 = N)

$$R_0 = \{\beta/(\alpha + \mu)\}*N$$

Force of infection

Effect of vaccination against rabies

Final size simulation (Hokkaido, Japan)



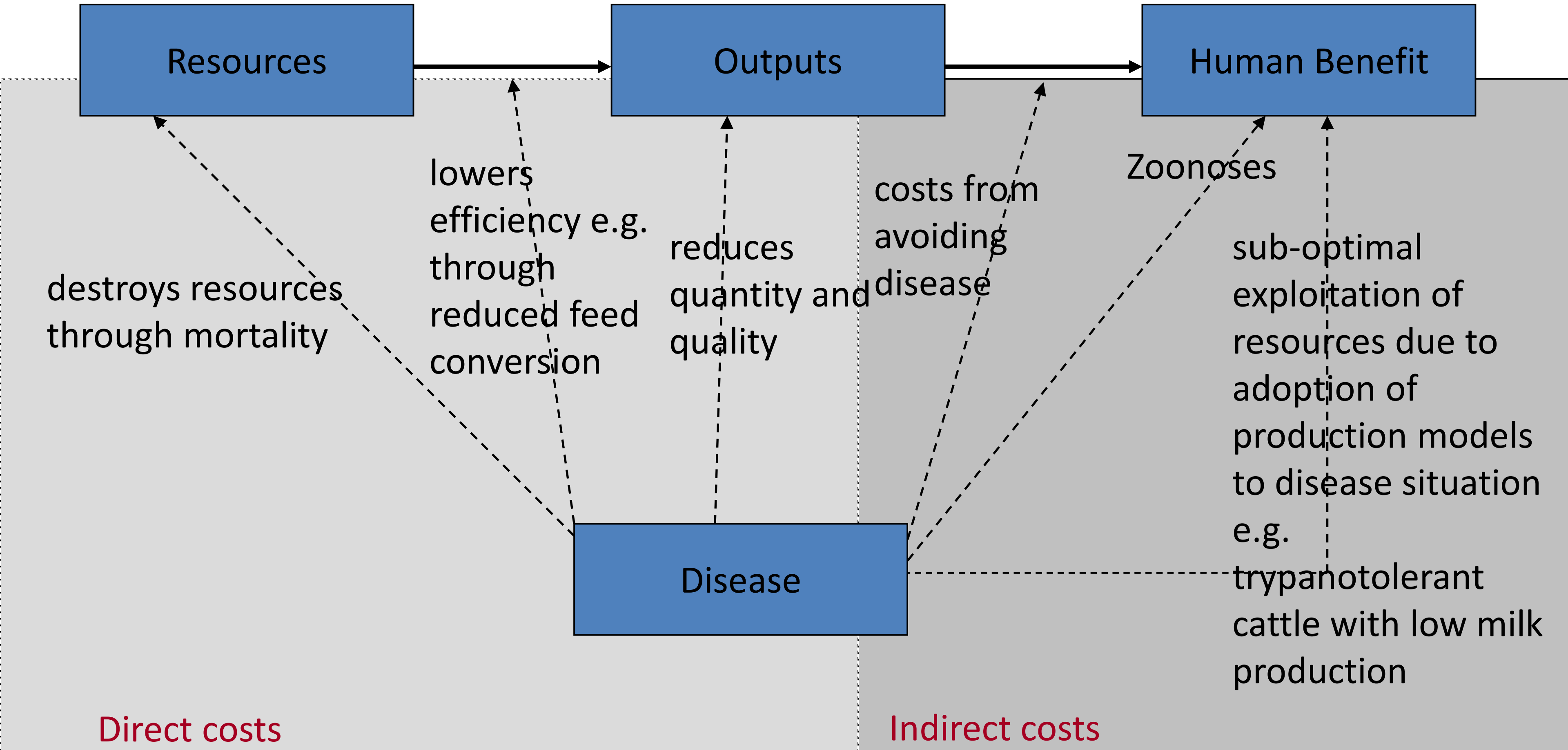
Proportions exceeding two cases per introduction of a rabid dog into Japan

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

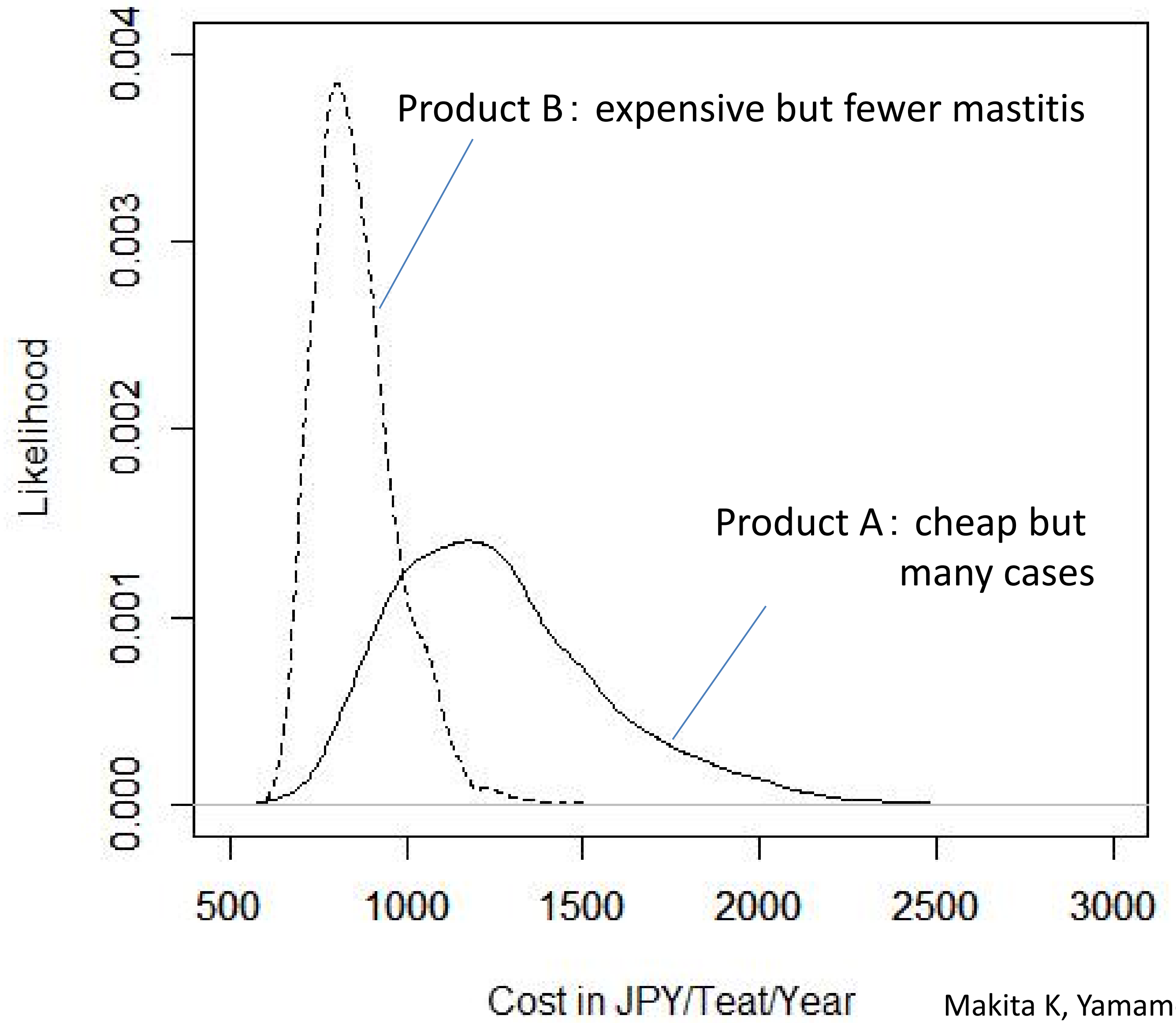
Economic effects of disease



Source: McIneryney (1996)

Eg. Cost comparison for *S. aureus* mastitis control

(Comparison of two dipping products)



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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