Training Exercise: Research Translation to Address One Health Challenges

Using Research to Strengthen Zoonotic Disease Prevention and Control Capabilities in Indonesia

This training exercise was developed by Gryphon Scientific in collaboration with the Airlangga Disease Prevention and Research Center, University of Minnesota College of Veterinary Medicine, and International Federation of Biosafety Associations.

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Training Exercise Overview

Motivation for the Training

- **Research translation** plays a critical role in the development of evidence-based policies and programs for preventing, detecting, and responding to infectious diseases.
- A **One Health** approach to combating zoonotic diseases can strengthen **prevention** of and enable more rapid **detection** of and **response** to zoonotic disease threats.
  - One Health is a multi-sectoral, interdisciplinary approach that involves the collaborative efforts of multiple sectors and disciplines to achieve the best health for people, animals, and the environment.
- Research translation to address zoonotic disease challenges is complex given the diversity of stakeholders involved and the multi-sectoral nature of the challenges and solutions.

Goals of the Training

- **Overarching Goal:** Build participants' skills in translating research to enhance capabilities for preventing, detecting, and responding to zoonotic disease threats in Indonesia.
  - **Learning Goal 1 |** Evaluate if and how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - **Learning Goal 2 |** Recognize key factors that support cross-sectoral communication about how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.

Learning Goal 1: Objectives

- **Learning Goal 1** | Evaluate if and how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
- *After completing this training, participants will be able to:*
  - Describe at least three applications of the research findings in the scientific literature provided to public health and veterinary policy.
  - Identify at least three limitations of the research methodology and findings in the scientific literature provided that weaken their application to public health and veterinary policy.
  - Identify at least three examples of health systems barriers that may prevent, limit, or delay translation of the research findings in the scientific literature provided to public health and veterinary policy.

Learning Goal 2: Objectives

- **Learning Goal 2** | Recognize key factors that support cross-sectoral communication about how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
- *After completing this training, participants will be able to:*
  - Define research translation in a One Health context.
  - Identify key stakeholders and their roles in research translation for preventing, detecting, and responding to zoonotic diseases.
  - Identify at least three challenges and potential solutions for two-way communication between researchers and policymakers during research translation to address zoonotic disease challenges.

Overview of Training Materials

Training activity	Purpose
Communication Pathways Mapping Activity	To identify, map, and analyze communication pathways between institutions involved in research translation to zoonotic disease challenges in Indonesia
Case Study Exercises on anthrax and highly pathogenic avian influenza	To use published research conducted in Indonesia to identify and assess potential applications of research to public health and veterinary policy and practice in Indonesia
Using the One Health Research Translation Framework in Your Work Activity	To identify opportunities to promote research translation to address zoonotic disease challenges in your work and build your professional One Health research translation network

These activities focus on the translation of *applied research* and *surveillance* findings to *community-level* challenges in public and animal health.

Training Outcomes

- Build workforce capabilities in the translation of local research to enhance national capabilities for preventing, detecting, and responding to zoonotic disease threats.
- Strengthen One Health research translation networks including researchers and policymakers from the public health and veterinary sectors.

Ground Rules for Participation

1. Ask the facilitator to clarify questions about the background information on research translation, case study publications, and activity instructions.
2. In all workshop activities, be willing to contribute your ideas and experiences and actively engage in group discussions.
3. Interact with one another in a way that encourages open communication and exchange of ideas. For example, listen to everyone's ideas respectfully.

Guide to Your Participant Packet

Your participant packet includes the following components:

- Introductory and background information to be used as a reference during and after the training:
    - Introduction to training
    - Glossary of key definitions
    - One Health Research Translation Framework
- Activity worksheets:
    - Communication pathways mapping activity
    - Anthrax and HPAI case studies
    - Using the One Health Research Translation Framework in your work
- Appendices:
    - Additional references on research translation
    - Additional space for note-taking

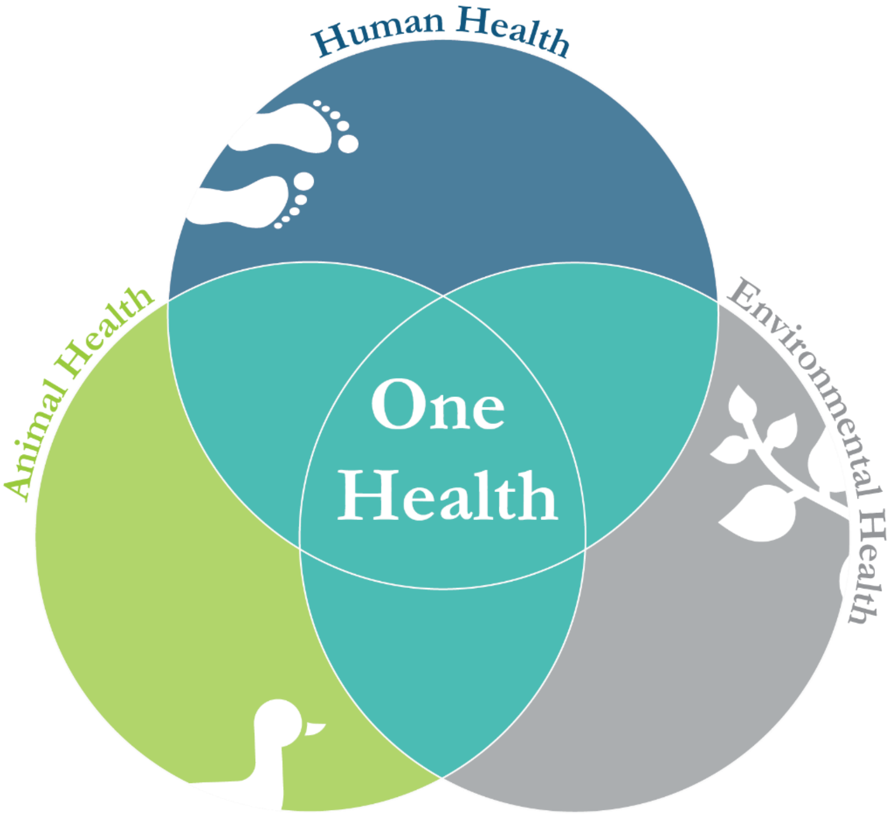
Research Translation and One Health Concepts: Key Definitions

Definitions: One Health Concepts

One Health

A multi-sectoral, interdisciplinary approach that:

- Recognizes that the health of people, animals, and the environment is interconnected, and
- Encourages the collaborative efforts of multiple sectors and disciplines working locally, nationally, and globally to address shared health threats and achieve the best health for people, animals, and environment.



Definitions: One Health Concepts

Sector

Whether the mission and primary area of responsibility of an academic, professional, government, or other organization relates to human, animal, or environmental/ecosystem health

- <u>Multi-sectoral</u>: Involving participation of more than one sector

Discipline

A branch of knowledge, instruction, or learning (for example, economics, virology, epidemiology, law, clinical medicine)

- <u>Interdisciplinary</u>: Involving actions occurring between or among more than one discipline, resulting in the synthesis of perspectives and information to achieve integration of knowledge
- <u>Multisectoral/multidisciplinary</u>: Involving participation of more than one sector and/or more than one discipline; here, refers to including multiple entities across the human-animal-environment interface to jointly address health in a way that is more effective, efficient, or sustainable than might be achieved by one sector acting alone

Definitions: One Health Concepts

One Health Stakeholder	Any individual or group that: • Is involved in preventing or managing a health threat at the human-animal-environment interface (such as researchers or policymakers), or • Affects, is affected by, or perceives themselves to be affected by such a health threat, including those that may be affected by associated risk management measures (such as community members or farmers)
Health Systems	All public, private, and voluntary entities that contribute to the delivery of human, animal, and environmental health, whether at the local, national, or global scale

Definitions: Biorisk Concepts

Biorisk	The combination of the likelihood and consequences of an adverse event involving biological materials following unintentional exposure, accidental release or loss, diversion, theft, misuse, or intentional release
Biorisk Management	The systems, processes, and practices used to identify, assess, control, and monitor biosafety and biosecurity risks posed by working with, storing, transporting, or disposing of biological materials in the laboratory or field

Definitions: Biorisk Concepts

Biosafety	The use of containment principles, technologies, and practices implemented to prevent unintentional exposure to or accidental release of biological materials from a laboratory or field study
Biosecurity	The measures taken to protect, control, and account for biological materials to prevent their loss, diversion, theft, misuse, or intentional release from a laboratory or field setting

Definitions: Research Translation Concepts

Research Application	The use of research findings to modify existing or inform the development of new programs, policies, practices, products or services for preventing, detecting, or responding to zoonotic diseases
Policy	Laws, regulations, administrative actions, strategies, and other decisions, plans, and practices of governments and other institutions formulated to direct actions in pursuit of specific societal goals • Policymaker: Any individual with the authority and responsibility to influence the development, implementation, enforcement, monitoring, and/or evaluation of policies at the local, national, or regional levels

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International Federation of Biosafety Associations

Definitions: Research Translation Concepts

Research Translation	A dynamic and iterative process of applying research findings that includes synthesis, dissemination, exchange, and application of knowledge to improve health systems
Two-way Communication	Ongoing, bi-directional communication between: • *Researchers* and *policymakers* about research findings that could be applied to health systems challenges and health systems needs that could be informed by research; • *Human, animal, and environmental health stakeholders* about the cross-sectoral effects of health system challenges and potential research applications

Definitions: Research Translation Concepts

Pillar

Steps in the One Health Research Translation Framework are categorized into three *pillars*: research evidence, policy, and integration.

- The *research evidence* pillar focuses on the generation and evaluation of research evidence;
- The *policy* pillar focuses on understanding health systems challenges that could be informed by research and implementing research applications;
- The *integration* pillar focuses on integrating research and policy perspectives to inform the development of research applications that are locally relevant, beneficial, and effective.

Definitions: Research Translation Concepts

Research Translation in a One Health Context

A dynamic and iterative process involving collaborative efforts between the human, animal, and environmental health sectors to apply research findings to address shared health threats at the human-animal-environment interface

Key features include:

- Consideration of how information from multiple sectors can inform research applications;
- Evaluation of the cross-sectoral effects of research applications; and
- Refinement of research applications to maximize cross-sectoral benefits.

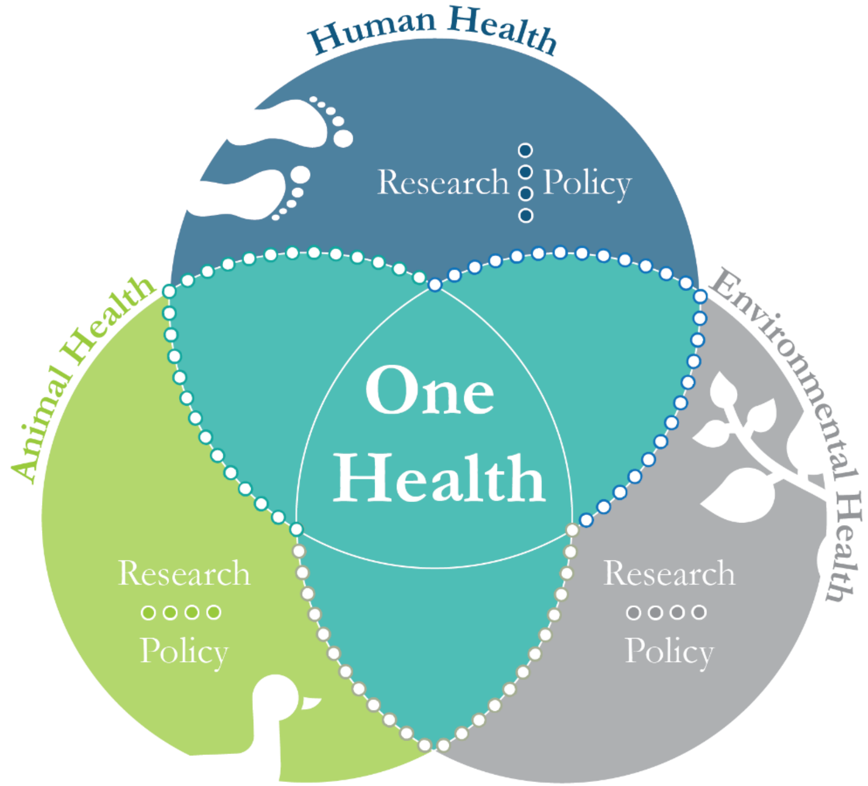
Overview of the One Health Research Translation Framework

One Health Research Translation Framework: Overview

- The **One Health Research Translation Framework** provides a structure for analyzing how research evidence can be applied to improve human, animal, and environmental health systems.
  - The Framework expands on other research translation frameworks to consider multi-sectoral effects and help identify the particular challenges and opportunities for research translation in a One Health context.
- Goals of the framework include:
  - *Conceptual goals*: Understand and explain factors influencing research translation to One Health challenges.
  - *Operational goals*: Describe and guide the process of translating research to policy and practice.
- This framework will guide the case study exercise and other training activities.

Importance of Communication Supporting Research Translation in a One Health Context

Research translation to address One Health challenges requires communication between diverse stakeholder groups.

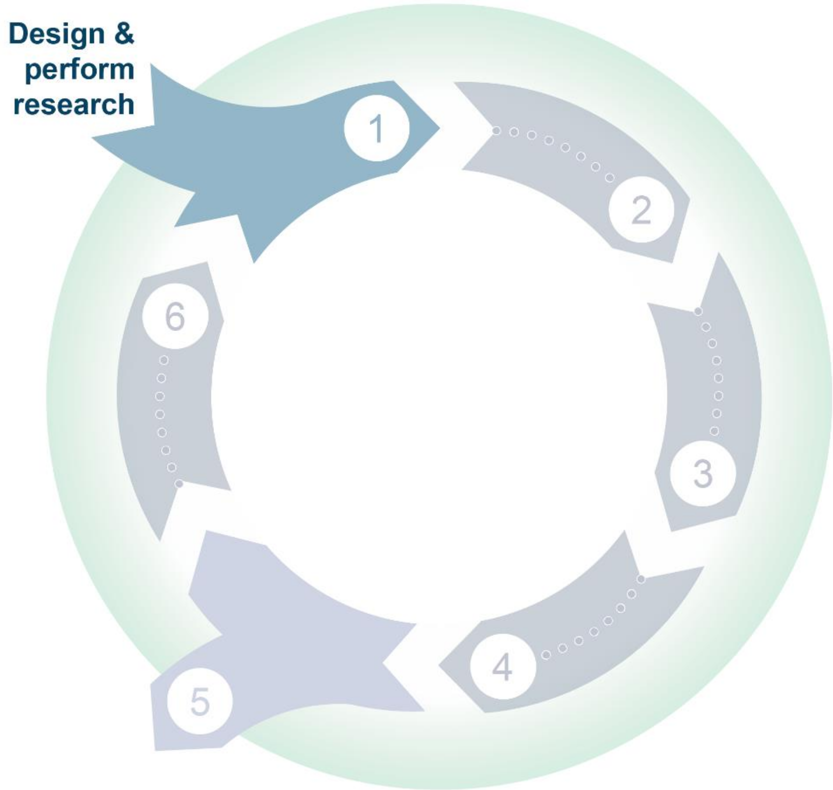


Two axes of communication across stakeholders:

○○○ ○○○ ○○○ Cross-sector communication among human, animal, and environmental health sectors

●●● ●●● ●●● Cross-pillar communication between researchers and policymakers

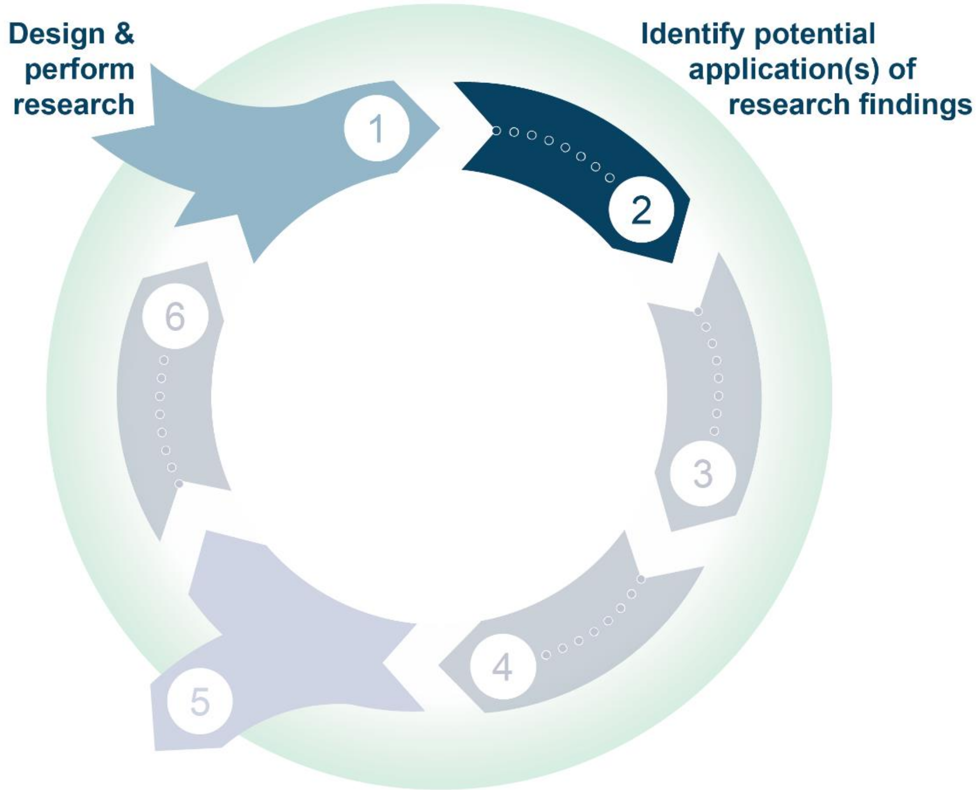
Research Translation Cycle: Step 1



- **Cyclical and iterative process for designing research applications that are locally relevant, effective, and beneficial**
- **Step 1 description:** Design and perform research to address gaps in scientific knowledge about zoonotic diseases.

Light blue: primarily involves researcher input/activities

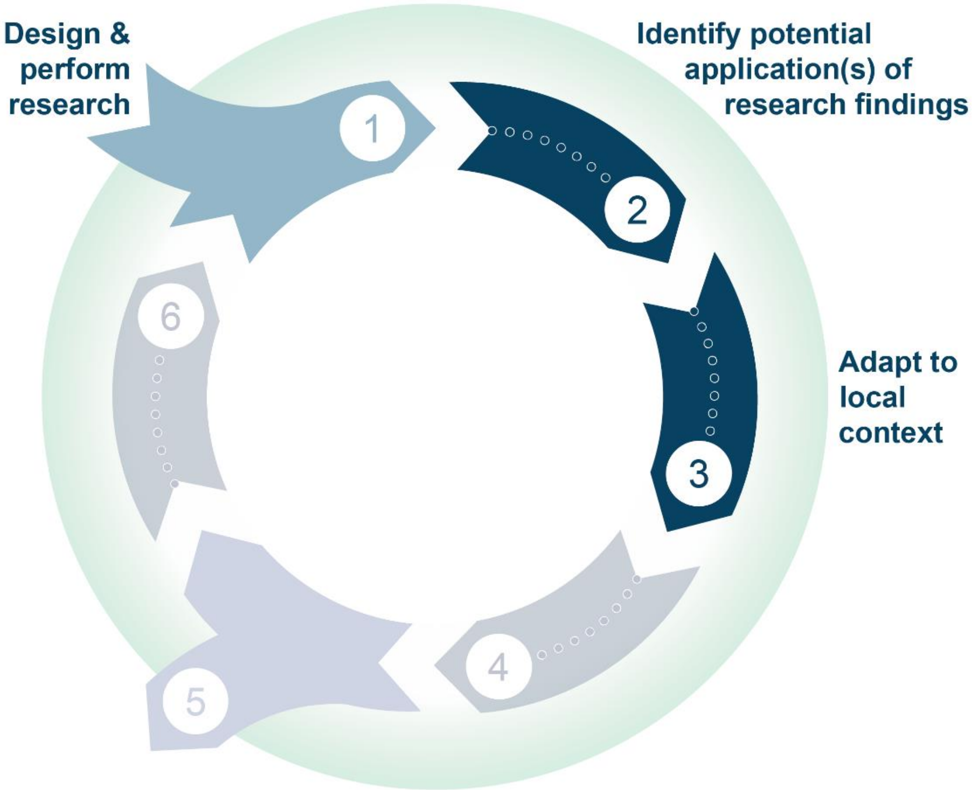
Research Translation Cycle: Step 2



- **Step 2 description:** Identify applications of the research findings (Step 1 output) to policies and programs for preventing and controlling zoonotic diseases.
- Consider ways in which the research could strengthen existing policies and programs or help the development of new policies/programs.

Light blue: primarily involves researcher input/activities
Dark blue: joint input of researchers and policymakers is critical

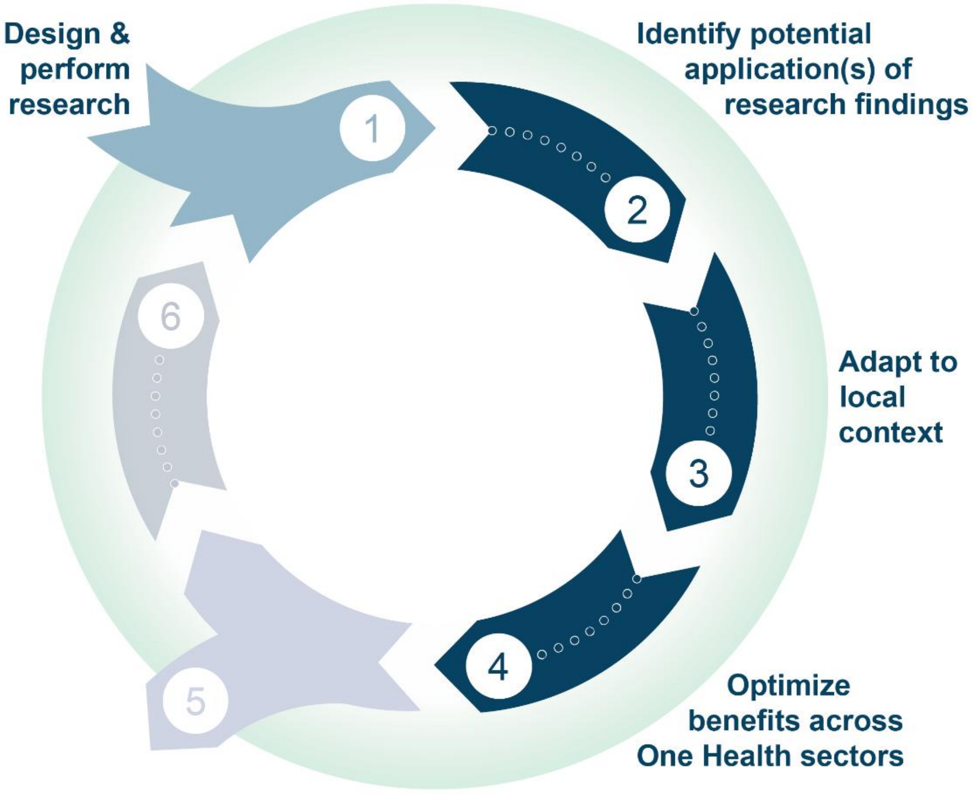
Research Translation Cycle: Step 3



- **Step 3 description:** Adapt the research application (Step 2 output) to the needs, culture, and health systems of the target jurisdiction(s).

Light blue: primarily involves researcher input/activities
Dark blue: joint input of researchers and policymakers is critical

Research Translation Cycle: Step 4



- **Step 4 description:** Adapt the research application (Step 3 output) to maximize its benefits to all One Health sectors by:
  - Considering effects on other sectors, and
  - Incorporating relevant research findings and resources from each sector.

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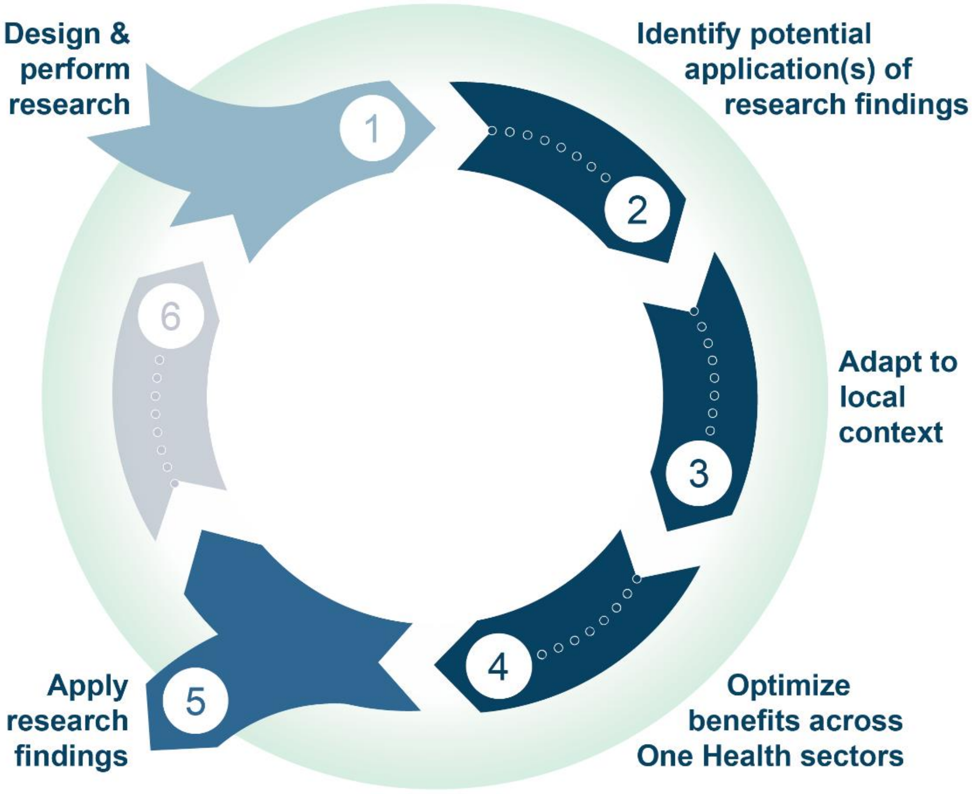
Dark blue: joint input of researchers and policymakers is critical

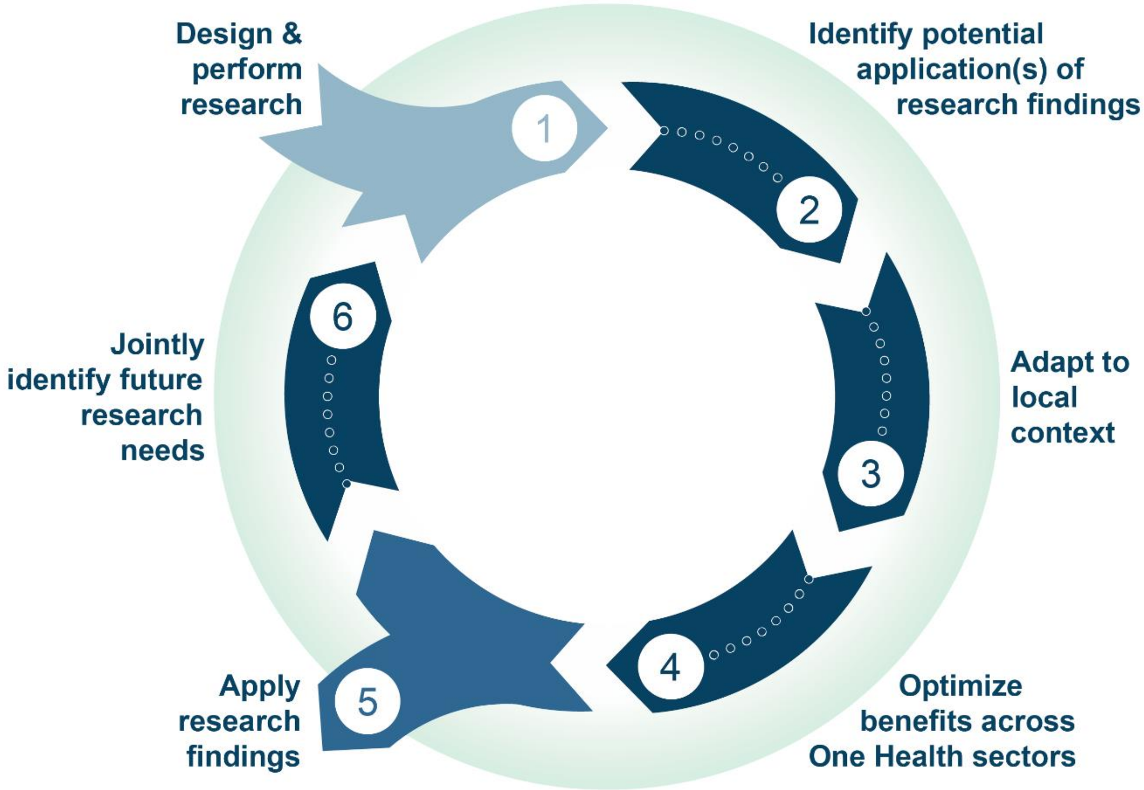
Research Translation Cycle: Step 5



- **Step 5 description:** Implement research application (Step 4 output).
- Involves additional steps (implementation, monitoring, evaluation) that are not captured in this research translation cycle.

Light blue: primarily involves researcher input/activities
Dark blue: joint input of researchers and policymakers is critical
Intermediate blue: primarily involves policymaker input/activities

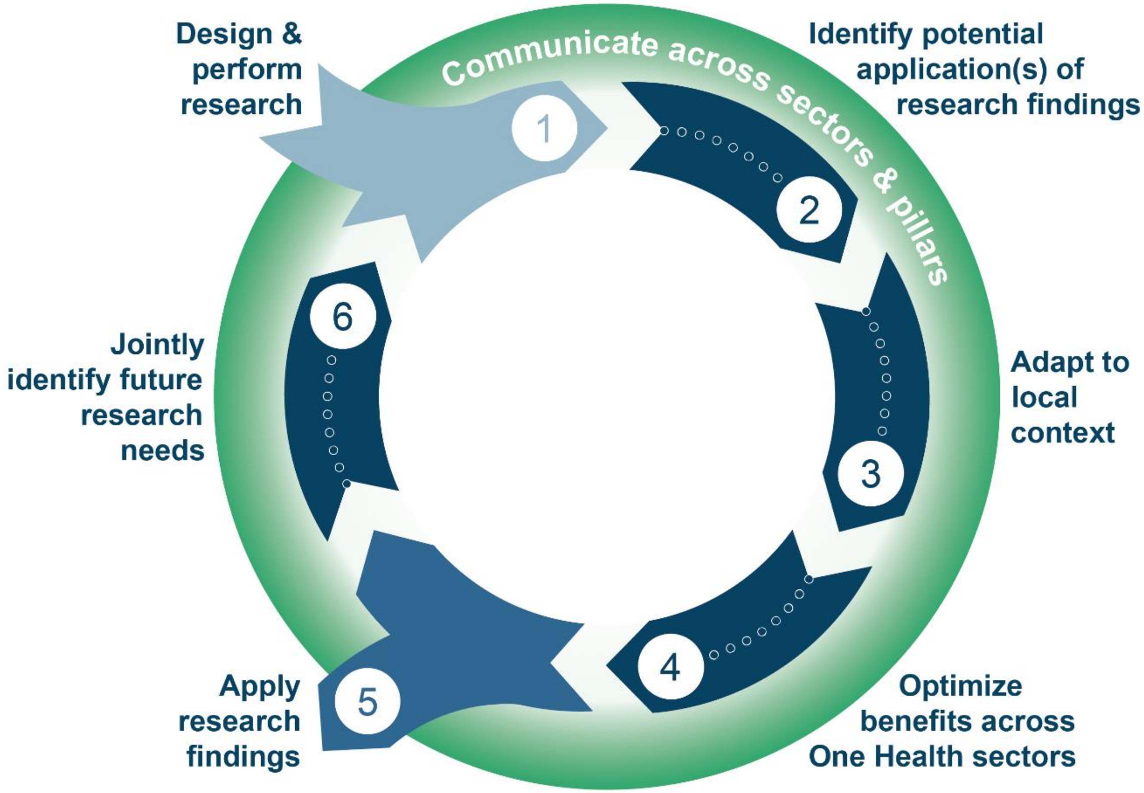
Research Translation Cycle: Step 6



- **Step 6 description:** Synthesize information about outstanding scientific knowledge gaps and zoonotic disease challenges to identify and prioritize research needs.
- After Step 6, researchers design and perform studies to address the identified research needs (Step 1), beginning the cycle anew.

Light blue: primarily involves researcher input/activities
Dark blue: joint input of researchers and policymakers is critical
Intermediate blue: primarily involves policymaker input/activities

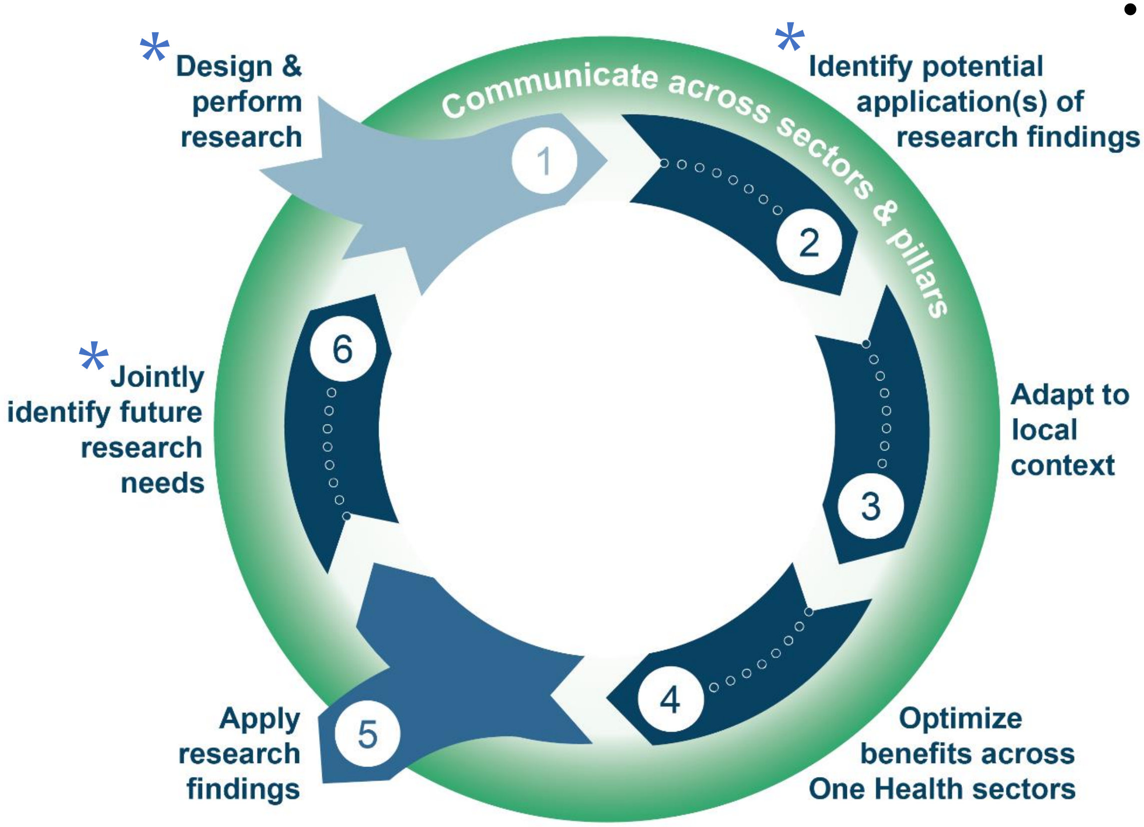
Research Translation Cycle: Communication



- **Communications thread description:** Communicate about research findings and needs.
- Communication across sectors and between researchers and policymakers supports research translation.
- Involving all relevant stakeholder groups throughout the cycle is critical.

Light blue: primarily involves researcher input/activities
Dark blue: joint input of researchers and policymakers is critical
Intermediate blue: primarily involves policymaker input/activities

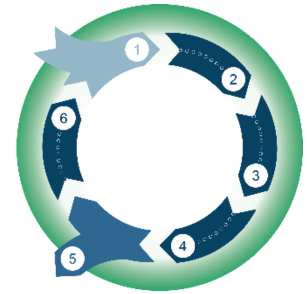
Research Translation Cycle Entry Points



- One Health stakeholders can enter the research translation cycle at multiple points:
  - **Step 1:** The design and conduct of studies to address priority research needs that have already been identified.
  - **Step 2**: The identification of applications of research that has already been conducted.
  - **Step 6:** The identification of research needs to address health systems challenges.

* Entry point for research translation cycle

One Health Research Translation Framework: High Level Structure



Integration Pillar

Communicate about research findings & needs

2

3

4

5

Synthesizes knowledge and experience of researchers and policymakers about research and local health systems to apply research findings in a locally relevant, effective, and beneficial manner.

Research Evidence Pillar

1

Draws from scientific literature and researchers' experience to enable assessment of the relevance and strength of research findings as they relate to polices and programs for preventing and controlling of zoonotic diseases.

Policy Pillar

5

Draws from policymakers' knowledge and experience to enable evaluation of health system needs and the governance structures, current practices, and prevailing culture in public, animal, and environmental health systems that influence research translation to One Health challenges.

Communications Thread

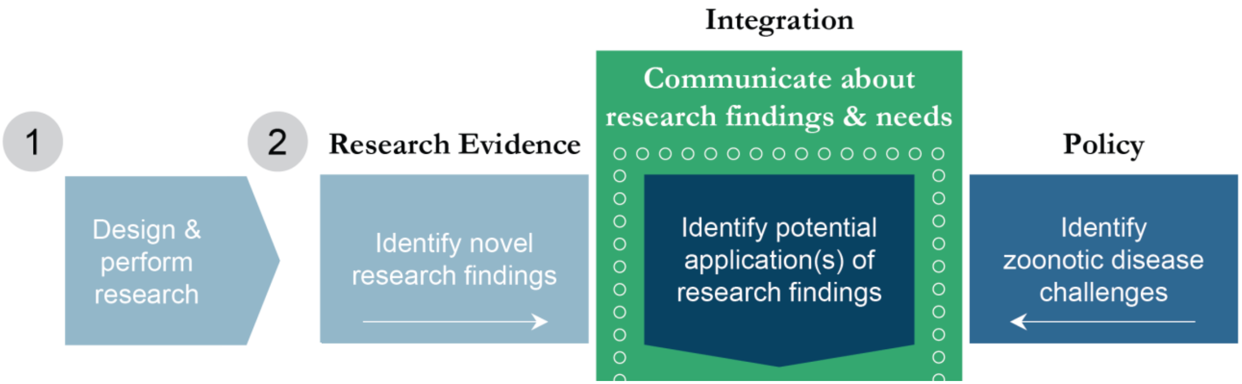
Involves two-way communication and information sharing between researchers and policymakers and across sectors about research findings, applications, and health systems needs to support Integration pillar concepts and activities.

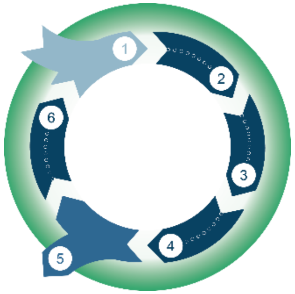
Integration of Research and Policy Perspectives in Research Translation

1

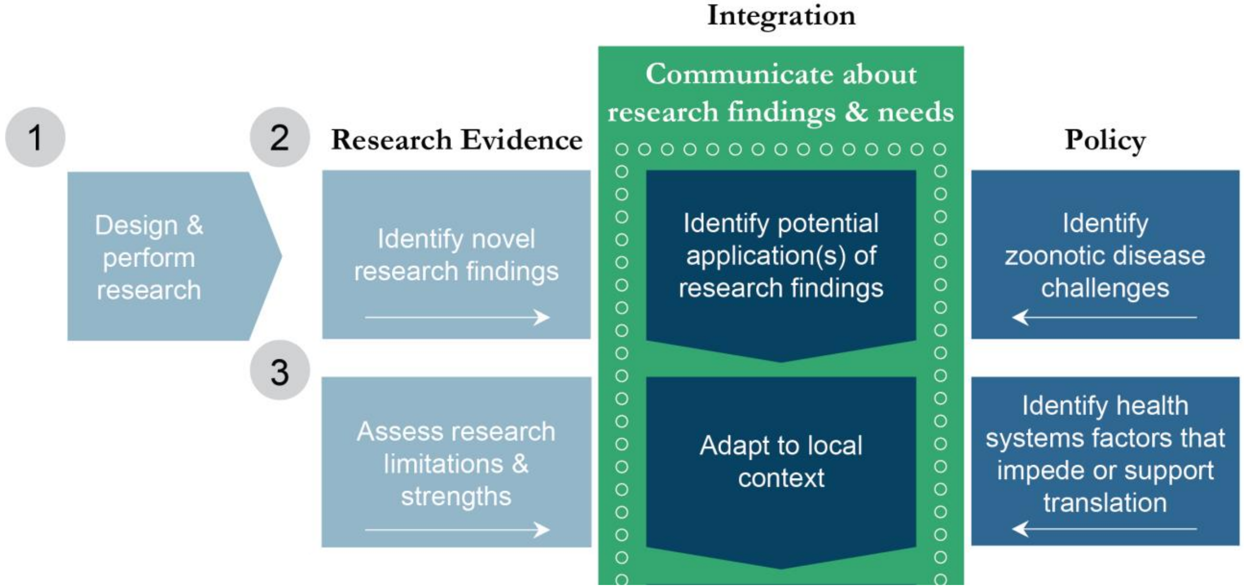
Design & perform research

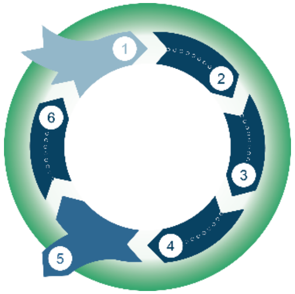
Integration of Research and Policy Perspectives in Research Translation





Integration of Research and Policy Perspectives in Research Translation





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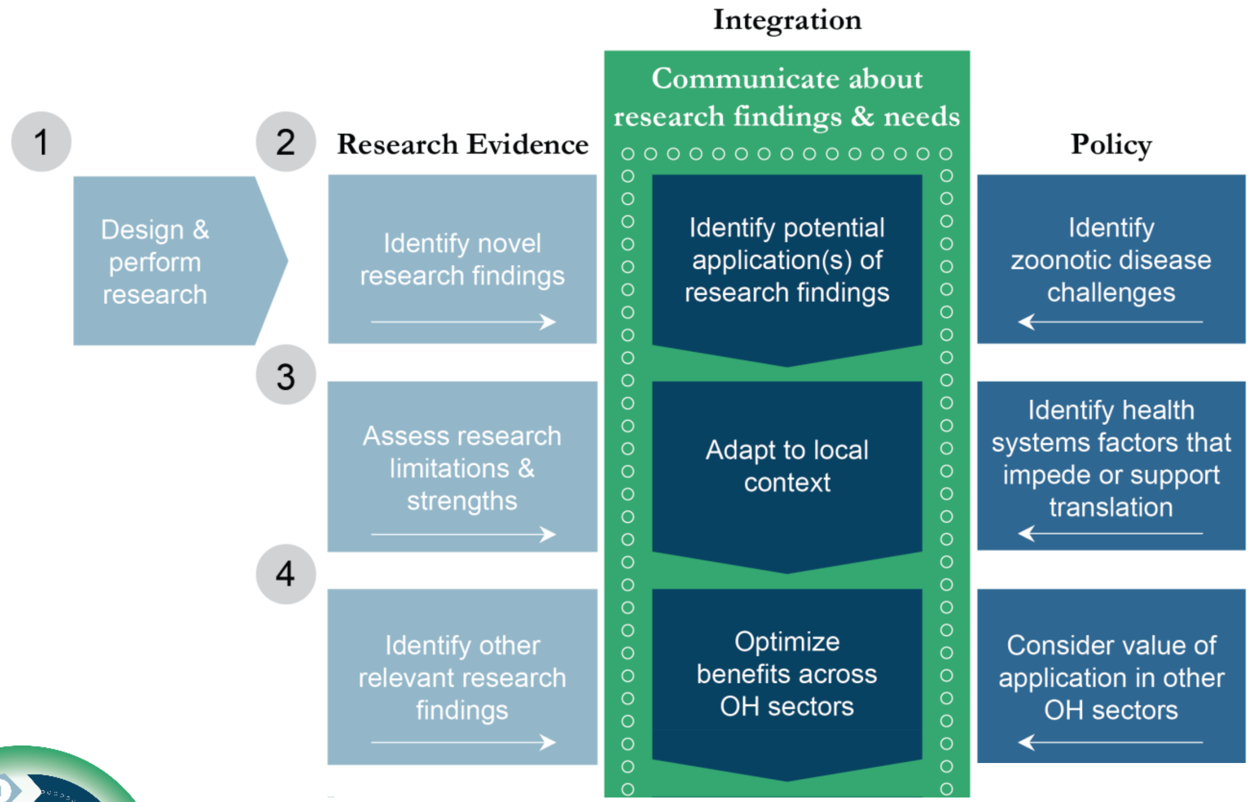

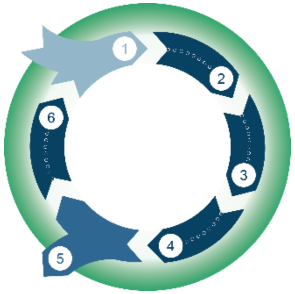

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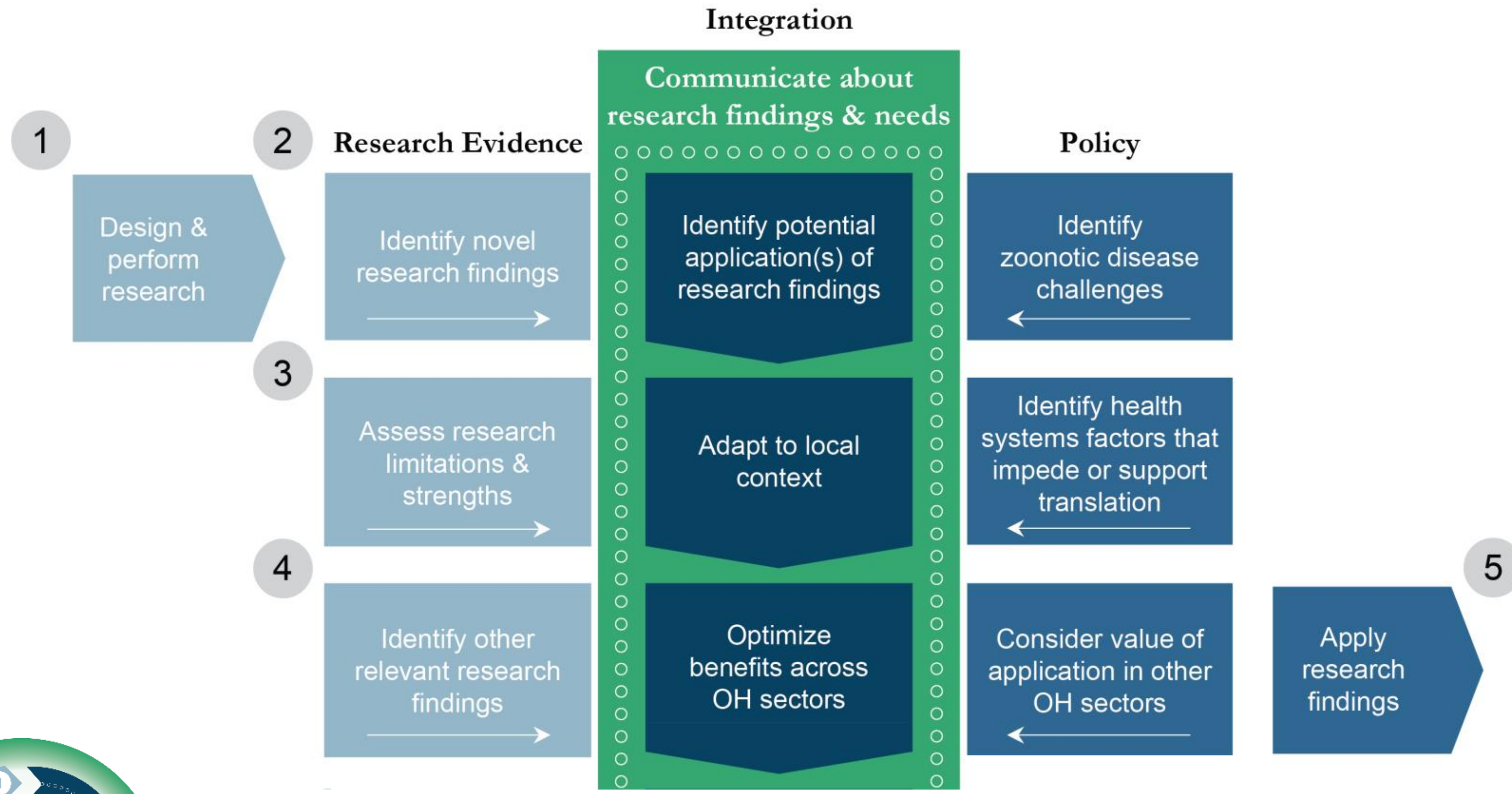

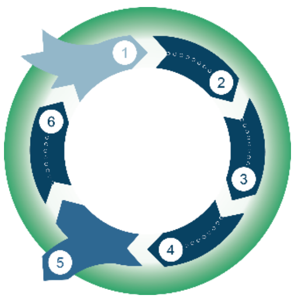

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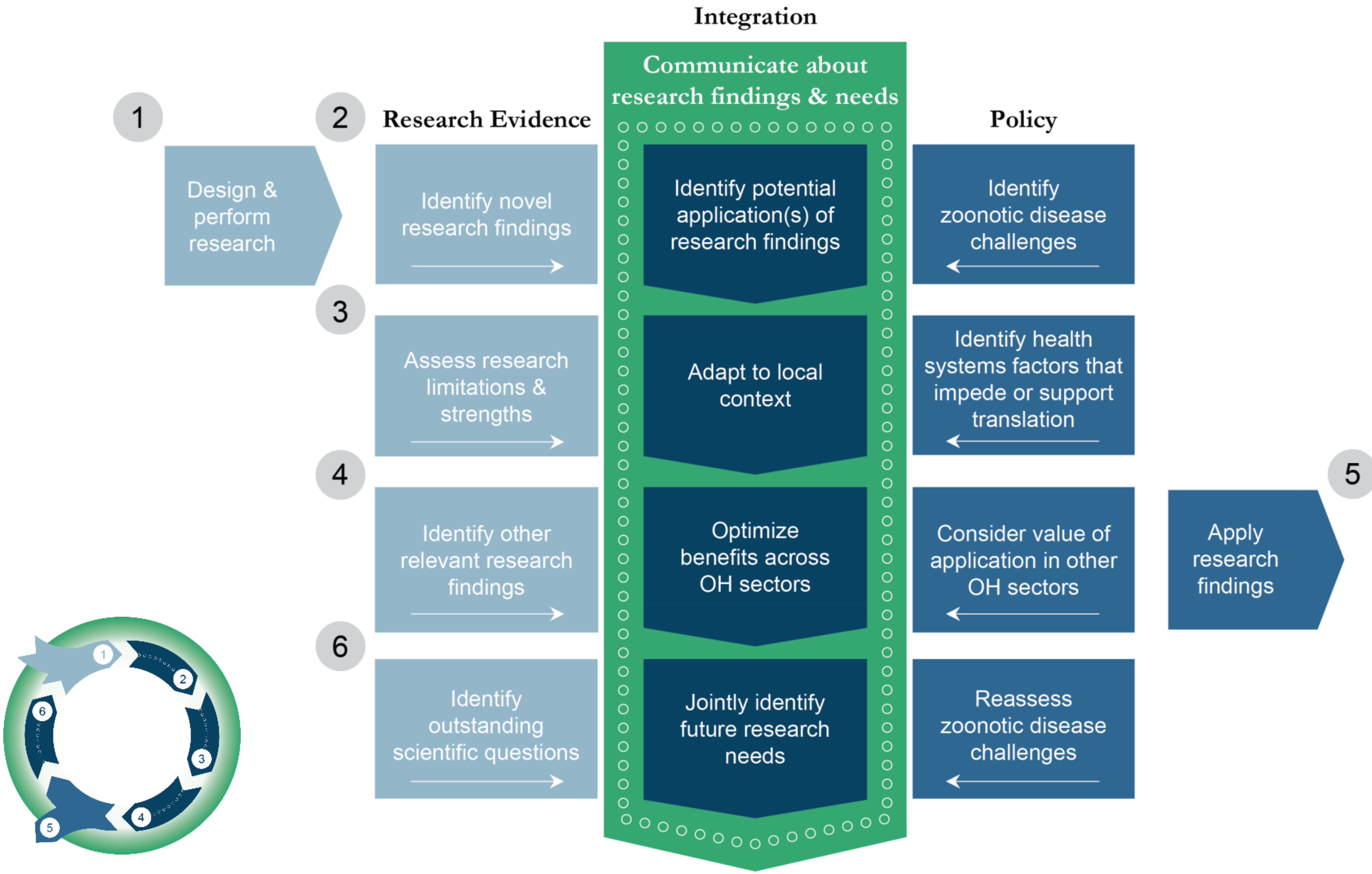


Questions?

Mapping Communication Pathways for Research Translation to Address One Health Challenges

Goals of Activity

- Purpose:
  - To identify, map, and analyze communication pathways between institutions involved in research translation to enhance capabilities for preventing, detecting, or responding to zoonotic diseases in Indonesia.
- *Learning goal*: Recognize key factors that support cross-sectoral communication about how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - *Objective*: Identify key stakeholders and their roles in research translation for preventing, detecting, and responding to zoonotic diseases.
  - *Objective*: Identify at least three challenges and potential solutions for two-way communication between researchers and policymakers during research translation to address zoonotic disease challenges.

Overview of Activity

- This activity uses a systems mapping approach to explore the communication networks needed to support research translation to zoonotic disease challenges in Indonesia.
- You will:
  - Identify institutions from the research, public health, animal health, and environmental health sectors that participate in research translation, including institutions that *conduct* research and that *use* research to inform policy and practice;
  - Characterize their roles in the research translation process;
  - Map communication pathways between institutions, including existing and desired pathways; and
  - Describe potential challenges to and solutions for communication between institutions.

Activity Demonstration: Emerging Zoonotic Disease

1. List relevant institutions

MOH, Directorate of Zoonoses

MOA, Directorate General of Health

Universities

Veterinary Research Center (BBALITVET)

Activity Demonstration: Emerging Zoonotic Disease

1. List relevant institutions
2. Determine the role of each institution
   - Symbols used to designate sector and research vs policy activities

MOH, Directorate of Zoonoses
□ ◇

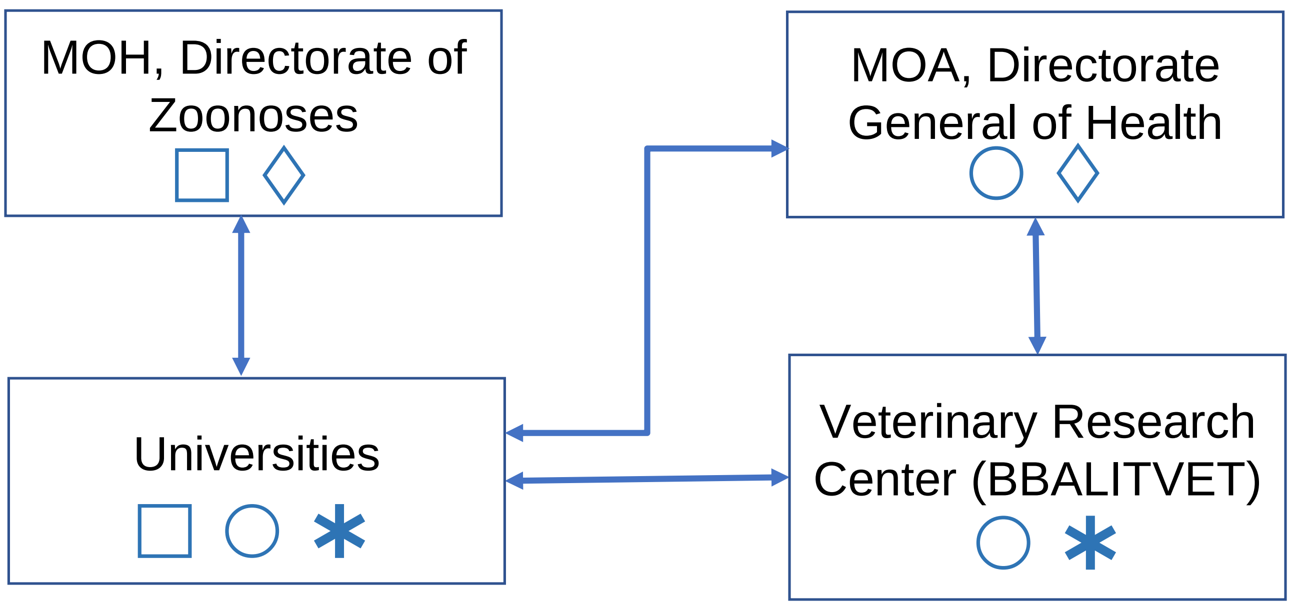
MOA, Directorate General of Health
○ ◇

Universities
□ ○ ✱

Veterinary Research Center (BBALITVET)
○ ✱

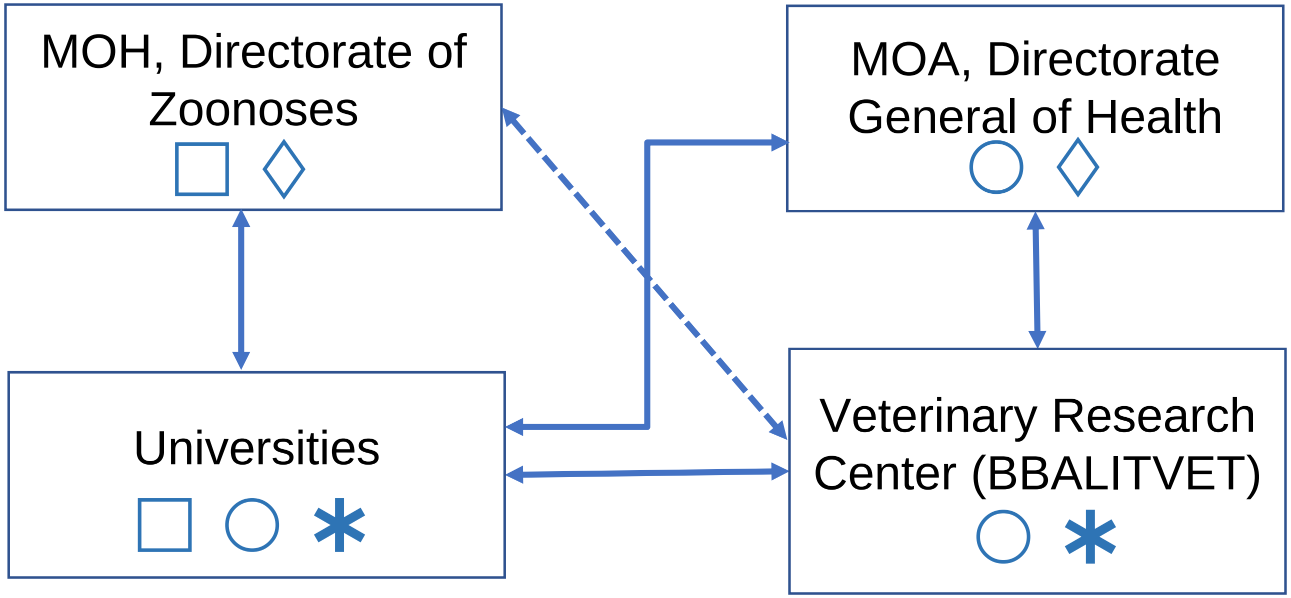
Activity Demonstration: Emerging Zoonotic Disease

1. List relevant institutions.
2. Determine the role of each institution.
   - Symbols used to designate sector and research vs policy activities
3. Draw existing communication pathways between institutions (solid lines).



Activity Demonstration: Emerging Zoonotic Disease

4. Discuss communication challenges and potential solutions.
5. Draw desired communication pathways between institutions (dotted lines).



Activity Instructions

- Participants will split into small groups of 5 – 9 people.
- Refer to the **Participant Worksheet: Mapping Communication Pathways for Research Translation to Address One Health Challenges** in your Participant Packet.
    - This worksheet provides detailed instructions, questions for consideration during the activity, and space to record your notes.
- Facilitators will lead the mapping process.
    - If you have questions about the purpose of a step or the meaning of questions in the worksheet, ask your facilitator for clarification.
- At the end of the activity, small groups will reconvene to compare maps and share highlights from the small group discussions.

Summary Discussion: Share and Compare Communication Pathways Maps

- Consider the communication maps created by other small groups:
  - How are communication pathways at different governance levels similar or different?
  - How are the challenges and potential solutions at different governance levels similar or different?
- Each group will share one or two interesting or surprising things they learned about communication and One Health.

Case Study: Anthrax in Indonesia

Overview of Case Study Exercise

- Purpose:
  - To use published research on anthrax conducted in Indonesia to explore research translation to public health and animal health systems.
- Using the One Health Research Translation Framework, you will:
  - Identify and analyze potential applications of research findings in the literature provided to policies and programs for preventing and controlling anthrax.
  - Describe communication pathways supporting the proposed research applications.

Learning Goals and Objectives

- *Learning goal*: Evaluate if and how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - Describe at least three applications of the research findings in the scientific literature provided to public health and veterinary policy.
  - Identify at least three limitations of the research methodology and findings in the scientific literature provided that weaken their application to public health and veterinary policy.
  - Identify at least three examples of health systems barriers that may prevent, limit, or delay translation of the research findings in the scientific literature provided to public health and veterinary policy.
- *Learning goal*: Recognize key factors that support cross-sectoral communication about how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - Define research translation in a One Health context.

Case Study Outline

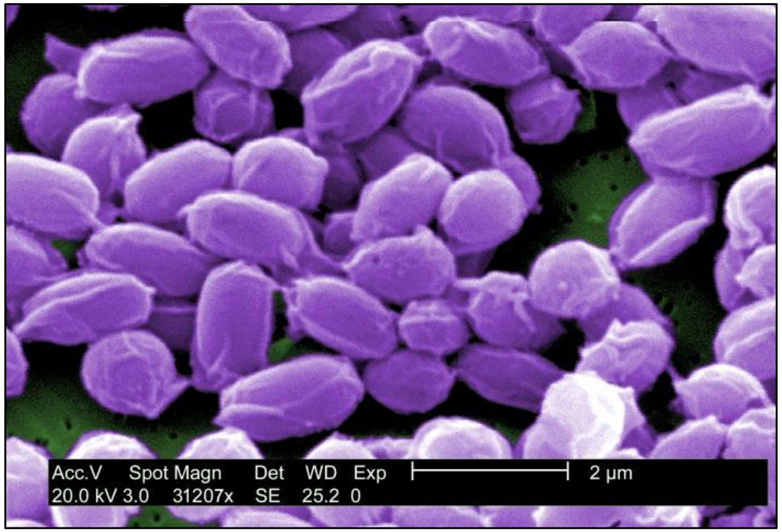
- **Part 1:** Introduction to anthrax in Indonesia
- **Part 2:** Introduction to selected publications
- **Part 3:** Research translation discussion
  - Conducted in small groups
- **Part 4:** Summary discussion
  - Small groups reconvene

Case Study: Anthrax

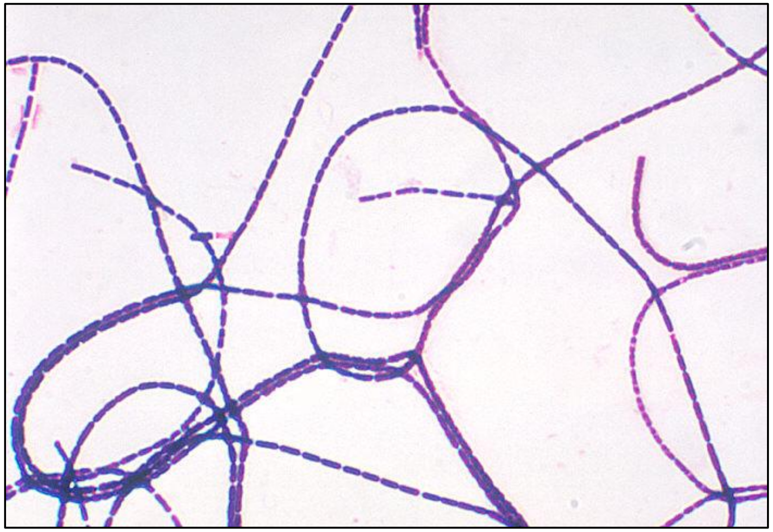
Introduction to Anthrax in Indonesia

Introduction to Anthrax

- Zoonotic disease caused by the bacteria *Bacillus anthracis*
  - Gram-positive, non-motile, rod-shaped bacteria
  - Genus *Bacillus*, *Bacillus cereus* group
    - *Bacillus cereus* group also includes *B. cereus*, a human food-borne pathogen, and *B. thuringiensis*, which is not pathogenic to humans.
  - Natural infections in animals occur primarily in herbivores, including cattle, goats, sheep, horses, and swine.



Endospores from the Sterne strain of *Bacillus anthracis*
Photo credit: CDC/Laura Rose



Chains of Gram-stained *Bacillus anthracis* bacteria
Photo credit: CDC/Dr. James Feeley

Anthrax Transmission Cycle

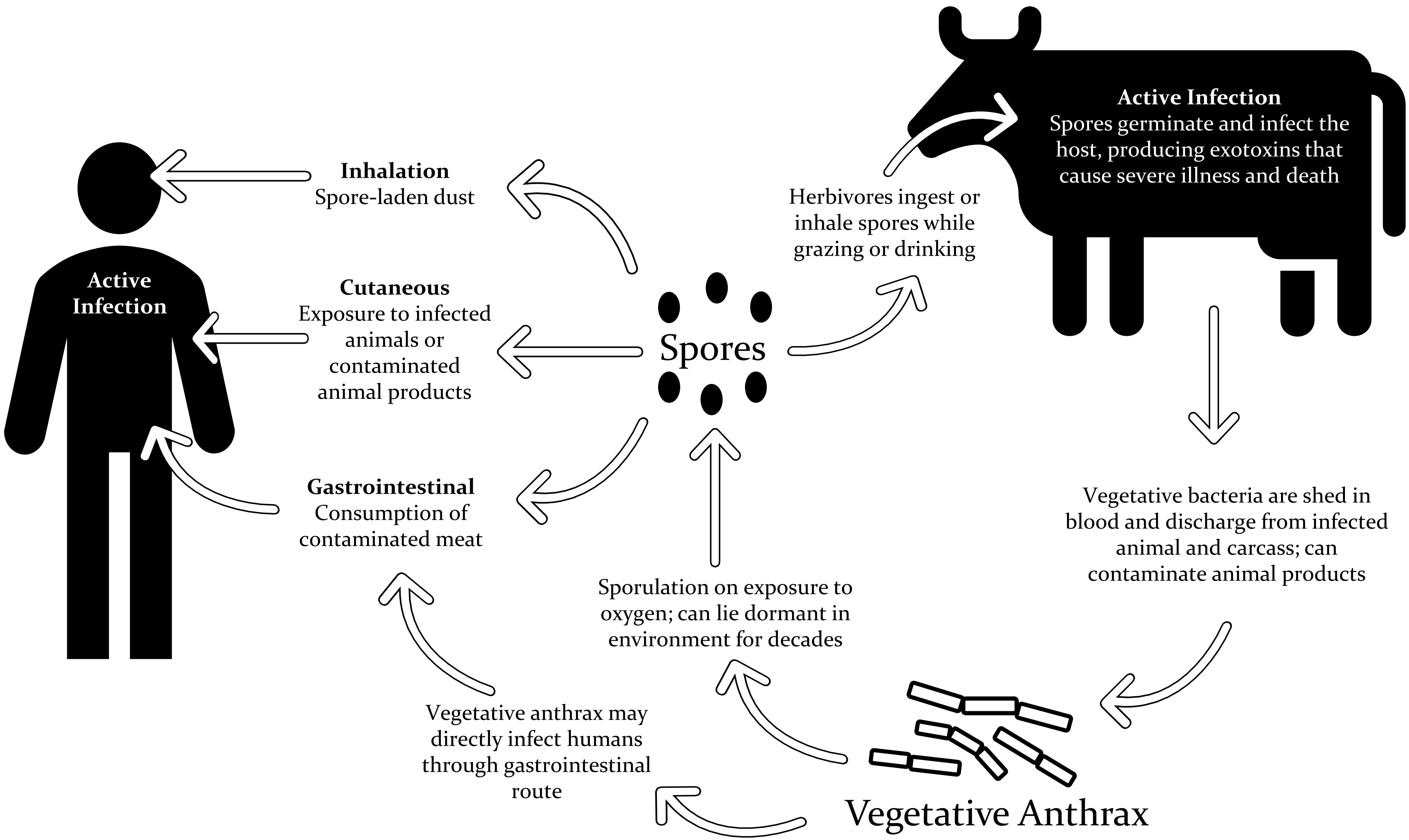


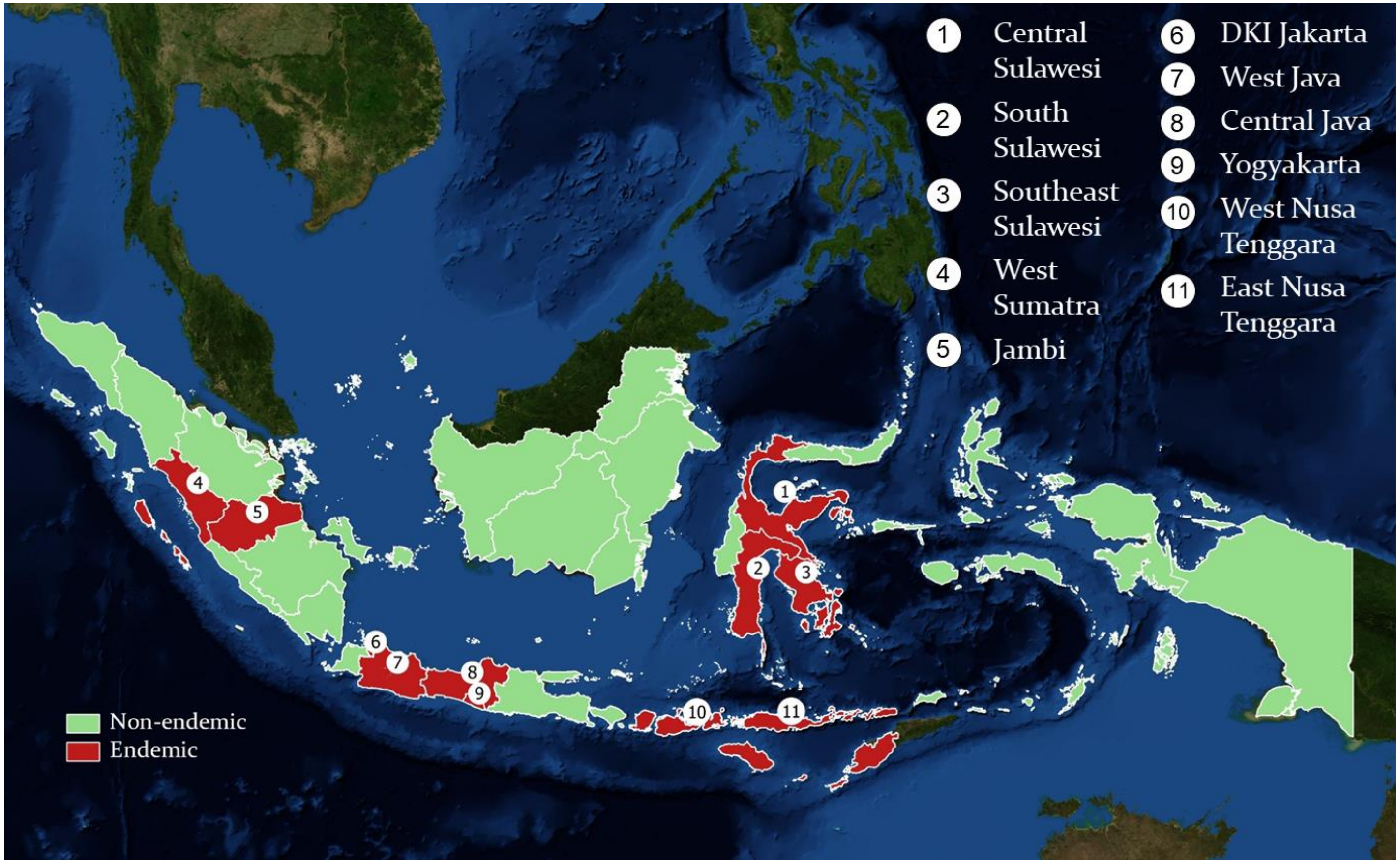
Image adapted from CDC (https://www.cdc.gov/anthrax/basics/index.html) and WHO EMRO (http://www.emro.who.int/fr/health-topics/antrhax/Page-1.html)

Anthrax in Indonesia

Anthrax is considered a priority zoonotic disease by the Ministries of Health and Agriculture and is listed as a Strategic Transmitted Animal Disease (PHMS) by the Directorate General of Animal Husbandry & Animal Health

- *Public health burden*: 308 human cases and 11 deaths reported to the MOH between 2008 – 2017

Provinces endemic for anthrax (2016)



Control Of Anthrax With One Health Approach. Workshop on Anthrax: Strengthening Outbreak Detection, Reporting, and Response Using a One Health Approach. Depok, Indonesia. January 23, 2018. Funded by U.S. Department of State Biosecurity Engagement Program. Implemented by Health Security Partners, INDOHUN, and Ministry of Agriculture Republic of Indonesia.

Economic Impacts of Anthrax in Indonesia

- *In animals,* economic losses arise from disease effects on animals and the cost of responding to outbreaks:
  - Animal death
  - Loss of income from animal products
  - Costs of vaccination and control programs
  - Consequences for regional, national, and international trade
- *In humans,* economic losses arise from:
  - Medical care and treatment costs
  - Lost productivity and lost wages due to illness

Anthrax in Livestock

- Symptoms: Vary by species; often include bloody discharge, bloating, respiratory distress, and sudden death
  - Symptom onset rapid and difficult to detect; sudden death is often the only indication of infection
- Diagnosis: Identification of *B. anthracis* in blood or tissue samples by culturing or rapid tests (such as PCR)
- Transmission routes: Inhalation or ingestion of anthrax spores in contaminated soil, water, plants, or feed
  - Gastrointestinal anthrax caused by ingestion of spores is most common.
- Control strategies:
  - Surveillance, vaccination, and proper disposal of carcasses
  - Revaccination of livestock after outbreaks is important because protection may diminish over time and spores may persist in the environment for many years.
  - A live-attenuated vaccine (Sterne 34F2) is available in Indonesia.

Anthrax in Humans

- Presentation of anthrax depends on the route of exposure
- Three common presentations of anthrax:
  - **Cutaneous anthrax (most common in Indonesia):**
    - Transmission: Direct dermal contact through handling infected animals or contaminated animal products, including carcasses and hides
    - Symptoms: Painless blister or bump which progresses to a black, ulcerated eschar

Cutaneous anthrax lesion on patient forearm

  - **Inhalational anthrax:**
    - Transmission: Inhalation of *B. anthracis* spores, often in association with the textile or tanning industries or from environmental dust
    - Symptoms: Non-specific syndrome with symptoms such as fever, chills, drenching sweats, fatigue, non-productive cough, and vomiting
      - Nearly always fatal once severe symptoms develop
  - **Gastrointestinal anthrax:**
    - Transmission: Ingestion of contaminated meat from an infected animal
    - Symptoms: Nausea, fever, vomiting, and severe bloody diarrhea

Photo credit: CDC/James H. Steele

Anthrax in Humans

- Diagnosis:
  - Diagnosis of inhalational and gastrointestinal anthrax is difficult because symptoms are non-specific.
  - Multiple diagnostic tests can be used to confirm anthrax infection in Indonesia:
    - Isolation/culture of *Bacillus anthracis* (most reliable)
    - PCR amplification of *Bacillus anthracis* from blood/body fluids
    - Immuno-detection of anthrax toxin in blood
    - Serological detection of antibodies (retrospective diagnosis only)

Bacillus anthracis bacterial colonies following isolation

- Treatment and prevention:
  - All types of anthrax can be treated with antibiotics.
  - Antibiotics can also be used for post-exposure prophylaxis when exposure to anthrax spores is known or suspected.
  - A human vaccine has been developed but is not available in most countries, including Indonesia.

Photo credit: CDC/Megan Mathias and J. Todd Parker

Anthrax Control in Indonesia

<u>Control relies on three central approaches</u>:

1) Livestock vaccination:
   - Pusat Veterinaria Farma (Pusvetma), the government-contracted manufacturer of animal vaccines in Indonesia, produces Anthravet, a live vaccine based on the Sterne 34F2 strain.
   - Vaccination is recommended every 6 months for susceptible herds in endemic areas; following outbreaks, two rounds of vaccination are required for affected herds.
2) Surveillance:
   - Surveillance networks identify suspected human and livestock cases, which may prompt investigation and intervention.
     - Human cases are often sentinels for animal cases; investigation into livestock may be initiated following a human case.
     - Government-led vaccination of animals in the immediate area is undertaken after an outbreak is identified.
3) Education:
   - Government efforts aim to increase community awareness and recognition of anthrax and empower communities to reduce the risk of transmission.
     - For example, education on anthrax symptoms and prevention in humans and livestock

Challenges for Anthrax Control in Indonesia

- Livestock vaccination challenges:
  - Vaccination programs are difficult to implement in remote/mountainous regions.
  - Farmers may not complete subsequent rounds of vaccination.
- Surveillance/control challenges:
  - Animal markets and cattle trading play a role in transmission:
    - Farmers may try to sell meat from dead animals to reduce economic losses, which creates a risk of human consumption of contaminated meat.
    - Infected animals and contaminated meat are difficult to track and remove from the market, potentially allowing the disease to spread.
  - Late reporting and under-reporting of human or animal cases makes detection of outbreaks challenging.
- Education challenges:
  - High-risk practices related to animal rearing, slaughtering, and food consumption are difficult to change.

References

1. *Anthrax*. Centers for Disease Control and Prevention. https://www.cdc.gov/anthrax/basics/index.html
2. Perkins, N; Patrick, I; Patel, M; Fenwik, S. *Assessment of zoonotic diseases in Indonesia*. Australian Centre for International Agricultural Research. 2007.
3. Turnbull, Peter Charles Bruce, ed. *Anthrax in humans and animals*. World Health Organization, 2008.
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Case Study: Anthrax

Introduction to Selected Publications

Handlers of Susceptible Animals and their Products have a High Risk of Being Infected With Cutaneous Anthrax in Endemic Areas

Chaerul Basri, Nuning Maria Kiptiyah

Jurnal Veteriner Desember 2010; Vol. 11 No. 4 : 226-231

Background

- The Bogor Regency in West Java is endemic for anthrax.
  - Human anthrax infections have occurred regularly since 2000.
  - Between 2001-2007, the Bogor District Health Office reported 97 humans cases of anthrax disease with 8 deaths (~8% case fatality rate).
- Studies conducted in other regions have found that a history of contact with susceptible animals, such as raising livestock, holding cattle, and slaughtering animals, increases the risk of cutaneous anthrax.
- Little is known about specific risk factors for cutaneous anthrax in Indonesia.

Study Goal and Methodology

Study Goal:

- Identify risk factors associated with cutaneous anthrax in Bogor Regency

Methodology:

- Observational epidemiological study with case control design
  - Structured interviews about contact history with vulnerable animals and animal products
- Study population: 153 adults age 20-50 residing in 4 sub-districts endemic for anthrax in Bogor Regency: Babakan Madang, Cibinong, Citeureup, and Sukaraja
  - 51 cases: identified through case surveillance reports from local Puskesmas
  - 102 controls: residents in same district as cases
  - All cases occurred between 2003 – 2007
- Data analysis:
  - Bivariate analysis with Chi-squared test
  - Multivariate analysis with logistic regression

Key Findings: Bivariate Analysis

Table 1. Factors of history of contact with animals and animal products related to the occurrence of skin type anthrax disease in Bogor District

Risk Factor	Case N = 51		Control N = 102		Value P	OR†	95% CI
	N	%	N	%			
Contact History with Animals							
Feeding / drinking							
No	24	47,1	84	82,4		1	
Yes	27	52,9	18	17,6	0,000*	5,250	2,482-11,107
Holding animals							
No	12	23,5	76	74,5		1	
Yes	39	76,5	26	25,5	0,000*	9,500	4,331-20,837
Slaughtering animals							
No	43	84,3	99	97,1		1	
Yes	8	15,7	3	2,9	0,007*	6,140	1,553-24,266
Contact History with Animal Products							
Handle meat							
No	31	60,8	96	94,1		1	
Yes	20	39,2	6	5,9	0,000*	10,323	3,805-2,007
Handle skin							
No	40	78,4	97	95,1		1	
Yes	11	21,6	5	4,9	0,003*	5,335	1,742-16,342

- In the bivariate analysis, all behaviors studied showed a statistically significant correlation with cutaneous anthrax.

Key Findings: Multivariate Analysis

Table 3. The final model of multivariate multiple logistic regression analysis on the research of factors related to the incidence of skin type anthrax disease in Bogor Regency

No	Variables	B	pWald	OR	95% CI
1	Holding vulnerable animals	0,9472	0,0000	6,648	2,914-15,167
2	Handle meat	0,8355	0,0025	5,318	1,801-15,702
	Constants	- 0,1857	0,5069		

- The multivariate analysis identified two variables as important for predicting the incidence of cutaneous anthrax: holding vulnerable animals and handling the meat of vulnerable animals.
- People who participate in these behaviors are approximately 5-6 times more likely to suffer cutaneous anthrax than those who do not.

Author Conclusions

- A variety of behaviors that involve contact with livestock or livestock products increase the risk of cutaneous anthrax in humans.
  - Holding animals and handling meat were the highest-risk behaviors identified in the study.
  - A different study on risk factors for cutaneous anthrax conducted in Kazakhstan also identified these behaviors as high-risk.
- In endemic areas, the general public should avoid holding susceptible livestock or use personal protective equipment, especially gloves.
- Communities should not accept meat from livestock that has been slaughtered due to illness, and community members that handle meat regularly should practice good hygiene and sanitation measures.

Cost Benefit Analysis and Strategy of Anthrax Control at Sumbawa Island, Province Of West Nusa Tenggara

Erwin Kusbianto, Eko Sugeng Pribadi, Abdulgani Amri Siregar

Jurnal Veteriner Desember 2012; Vol. 13 No. 4: 378-388

Background

- Anthrax is endemic to Sumbawa Island and poses a challenge for efforts to increase livestock production.
  - Economic losses from anthrax are high, arising from vaccination costs, medical expenses, livestock deaths, decreased productivity, and decreased reproduction.
- The anthrax vaccination program on Sumbawa Island covered only 22 – 39% of cattle and buffalo between 2005 and 2009.
  - This level of vaccination resulted in seropositivity rates ranging from 45% to 76%, which was insufficient to eliminate anthrax from the region.
- Cost-benefit analysis can be used to evaluate the comparative value of different vaccination programs to determine which provides the best economic value and most efficient use of resources.
  - Policymakers can use this information to determine the most appropriate control program.

Study Goal and Methodology

Study Goal:

- Perform cost-benefit analysis of two anthrax control programs for cattle and buffalo in Sumbawa:
    - Control program 1: vaccination coverage <50% (*current level*)
    - Control program 2: vaccination coverage >80%

Methodology:

- Data collection:
    - *Primary data*: inputs and outputs of livestock businesses obtained from interviews with 40 ranchers selected by random sampling
    - *Secondary data*: livestock population data, vaccination costs, vaccination coverage, anthrax cases, cattle prices, livestock yields and other data collected from relevant agencies

Methodology: Vaccination Program Assumptions

- The following assumptions were made about the efficacy of vaccination control programs:
  - Vaccination control program with <50% coverage:
    - Assumed livestock deaths will remain constant over 10 years at 0.01% of the population.
  - Vaccination control program with >80% coverage:
    - Assumed livestock deaths will decrease and approach 0% by year 3.
    - After year 3, herds are assumed to be anthrax-free.
- These assumptions were used when calculating the <u>costs</u> associated with raising livestock and treating ill animals and the <u>income</u> generated from livestock sales over a ten-year timeframe under each vaccination control program.

Methodology: Economic Analysis

- Cost and income data were used to assess the economic value of each program using three different measures:
  - Net present value (NPV): Measurement of profit comparing present values of cash outflows (expenditures) to the present values of cash inflows (earnings from sales) over a period of time
    - Positive NPV = Net gain
    - Negative NPV = Net loss
  - Benefit-to-cost ratio (B/C): Total value of the benefits (NPV) compared to the total value of the costs (expenditures)
    - B/C >1 = Benefits greater than costs
    - B/C <1 = Costs greater then benefits
  - Internal rate of return (IRR): Measure of profit as a percentage of investment
    - Larger IRR = greater return on investment

Key Findings

Table 9. Results of cost analysis of anthrax control benefits for cattle and buffalo in P. Sumbawa

No.	Cattle	Vaccination program	Discount	NPV (Rp.)	B/C ratio	IRR (%)
1	Cow	With coverage <50%	15%	504.541.172	1,18	75
			20%	365.568.489	1,07	75
		With coverage >80%	15%	643.274.236	0,70	55
			20%	456.560.783	0,65	55
2	Buffalo	With coverage <50%	15%	296.631.740	1,72	100
			20%	218.610.483	1,56	100
		With coverage >80%	15%	396.307.569	1,04	77
			20%	290.774.335	0,96	77

- Based on NPV, anthrax control with >80% coverage provides greater income than <50% coverage.
- However, the benefit/cost ratio and IRR is higher with <50% coverage.
    - <50% coverage provides a better profit value than >80% coverage.

Author Conclusions

- Anthrax vaccination benefits the economy of Sumbawa by increasing profits and decreasing losses in livestock production.
  - Both control programs provided positive NPV, meaning that both generate value in the local economy.
- Vaccination coverage of <50% of the livestock population is more cost efficient than coverage of >80%.
  - Control programs with coverage >80% generate more income, but also have much higher costs, resulting in a lower B/C ratio and IRR.
  - Control programs with coverage <50% have lower costs while still generating income, giving a higher B/C ratio and IRR.

Questions or Comments?

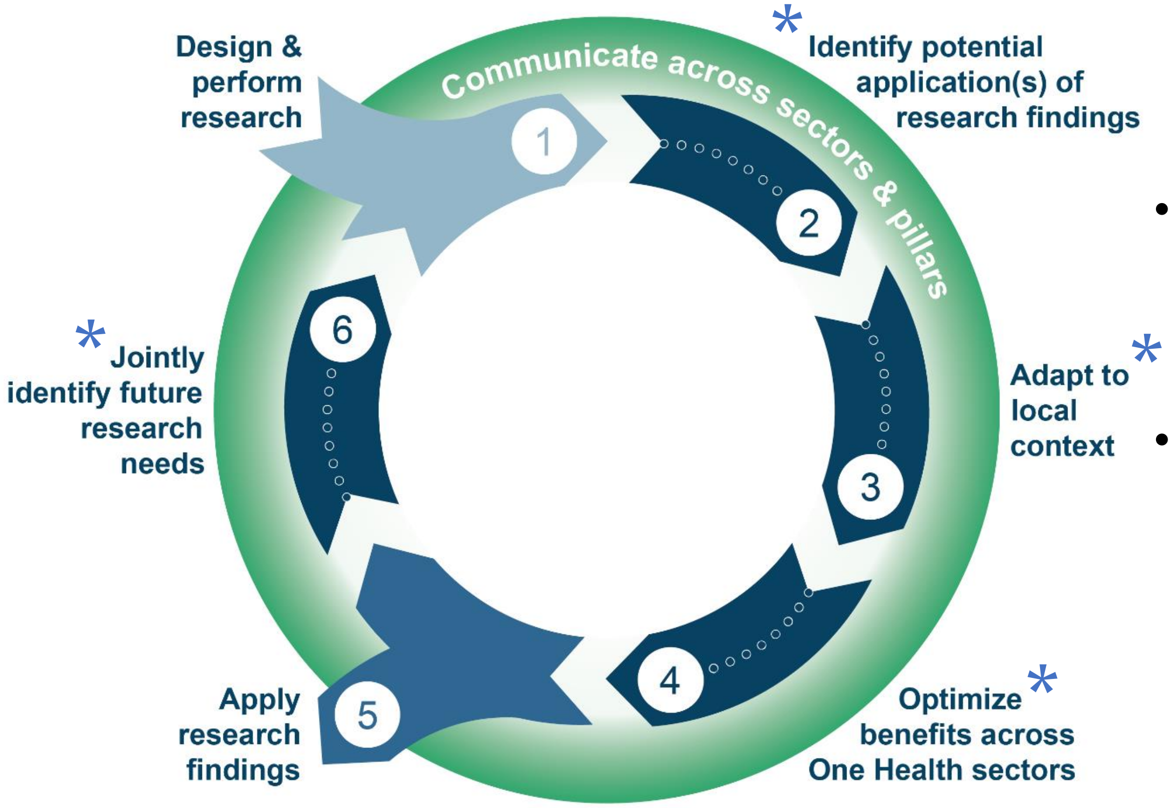
Case Study: Anthrax

Group Discussion

Instructions

- Participants will split into small groups of 6 – 9 people.
- Refer to the **Participant Worksheet: Anthrax Case Study** in your Participant Packet.
  - Structured similarly to the One Health Research Translation Framework
  - Includes discussion questions associated with the Framework steps and space to record your notes
- Facilitators will lead the research translation discussion.
  - If you have questions about the purpose of a step or the meaning of questions in the worksheet, ask your facilitator for clarification.

Structure of Research Translation Discussion



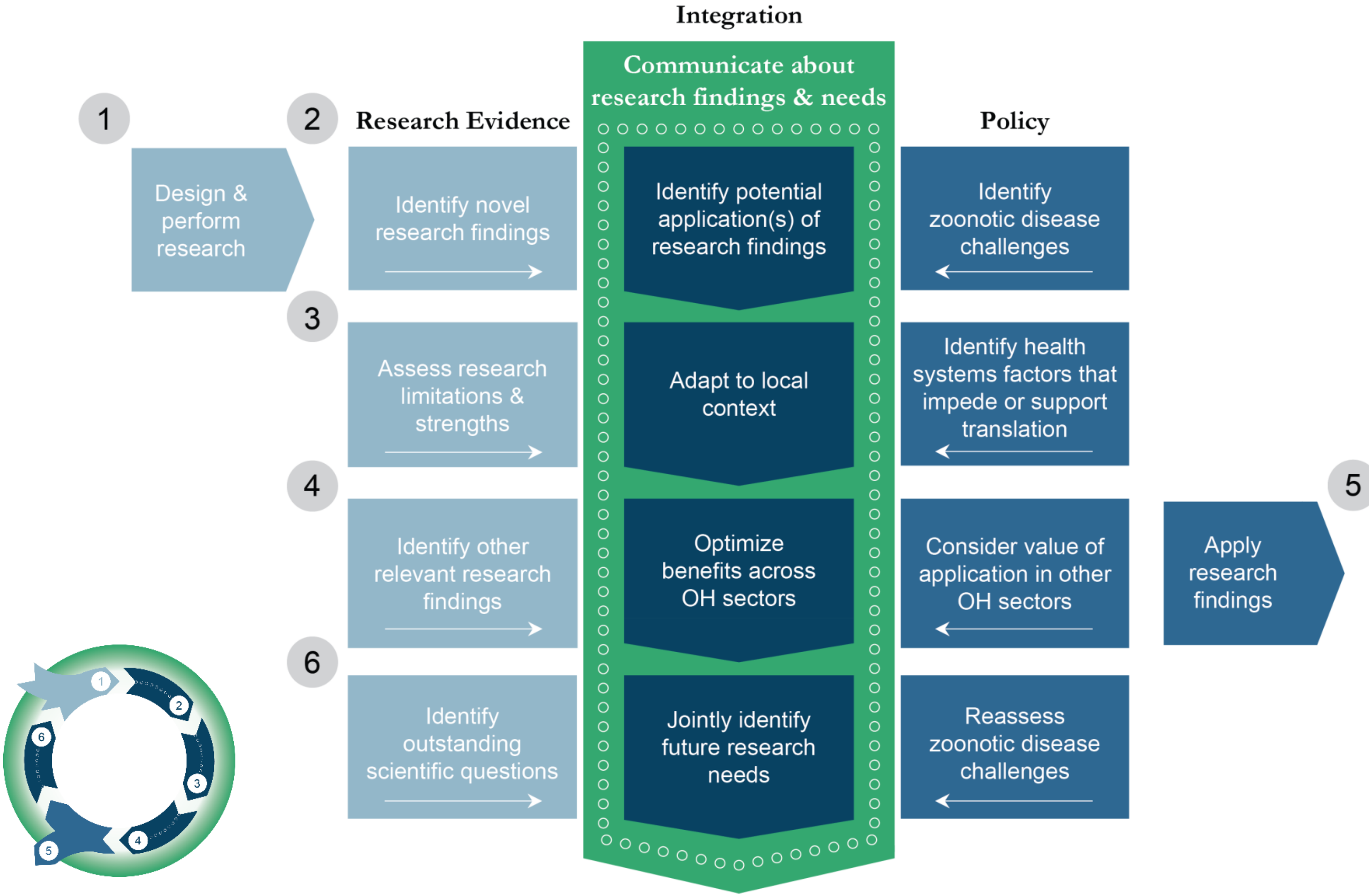
- The research translation discussion will begin at Step 2 because we have selected publications for evaluation.
- The discussion will focus on Steps 2, 3, 4, and 6 of the Framework because joint input from researchers and policymakers is critical for those steps.

* Steps discussed during case study exercise

Participation Guidelines for Case Study Exercises

1. Prior to starting this exercise, participants should have read the case study publications.
2. Ask the facilitator to clarify questions about the background information on research translation, case study publications, and activity instructions.
3. During the case study exercises, focus on understanding and analyzing the potential applications of the research. When critiquing the methodologies or research choices of the authors, focus on how those shortcomings may influence research translation.
4. Be willing to contribute your ideas and experiences and actively engage in group discussions.
5. Interact with one another in a way that encourages open communication and exchange of ideas.

Reference: Framework for Research Translation



Case Study: Anthrax

Summary Discussion

Summary Discussion: Share and Compare Results of Small Group Discussions

Questions to consider:

- What potential applications of the research findings in the selected publications did your group identify?
  - What limitations of the research findings may influence translation?
  - What health systems barriers may prevent, limit, or delay translation of the research findings?
- Did your group identify anything surprising or interesting about research translation and One Health?

CASE STUDY: HIGHLY PATHOGENIC AVIAN INFLUENZA (HPAI) IN INDONESIA

Overview of Case Study Exercise

- Purpose:
  - To use published research on highly pathogenic avian influenza (HPAI) conducted in Indonesia to explore research translation to public health and animal health systems.
- Using the One Health Research Translation Framework, you will:
  - Identify and analyze potential applications of research findings in the literature provided to policies and programs for preventing and controlling HPAI.
  - Describe communication pathways supporting the proposed research applications.

Learning Goals and Objectives

- *Learning goal*: Evaluate if and how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - Describe at least three applications of the research findings in the scientific literature provided to public health and veterinary policy.
  - Identify at least three limitations of the research methodology and findings in the scientific literature provided that weaken their application to public health and veterinary policy.
  - Identify at least three examples of health systems barriers that may prevent, limit, or delay translation of the research findings in the scientific literature provided to public health and veterinary policy.
- *Learning goal*: Recognize key factors that support cross-sectoral communication about how research can be applied to public health and veterinary policy to enhance capabilities for preventing, detecting, and responding to zoonotic diseases in Indonesia.
  - Define research translation in a One Health context.

Case Study Outline

- **Part 1:** Introduction to HPAI in Indonesia
- **Part 2:** Introduction to selected publications
- **Part 3:** Research translation discussion
  - Conducted in small groups
- **Part 4:** Summary discussion
  - Small groups reconvene

Case Study: Highly Pathogenic Avian Influenza

Introduction to HPAI in Indonesia

Avian Influenza Overview

- Influenza A viruses belong to family Orthomyxoviridae.
- Virus characterized by type of surface glycoproteins:
    - Hemagglutinin: HA1-HA18
    - Neuraminidase: NA1-NA11
- 16 HA and 9 NA subtypes known to circulate in wild birds, which are considered a reservoir

Influenza Virus

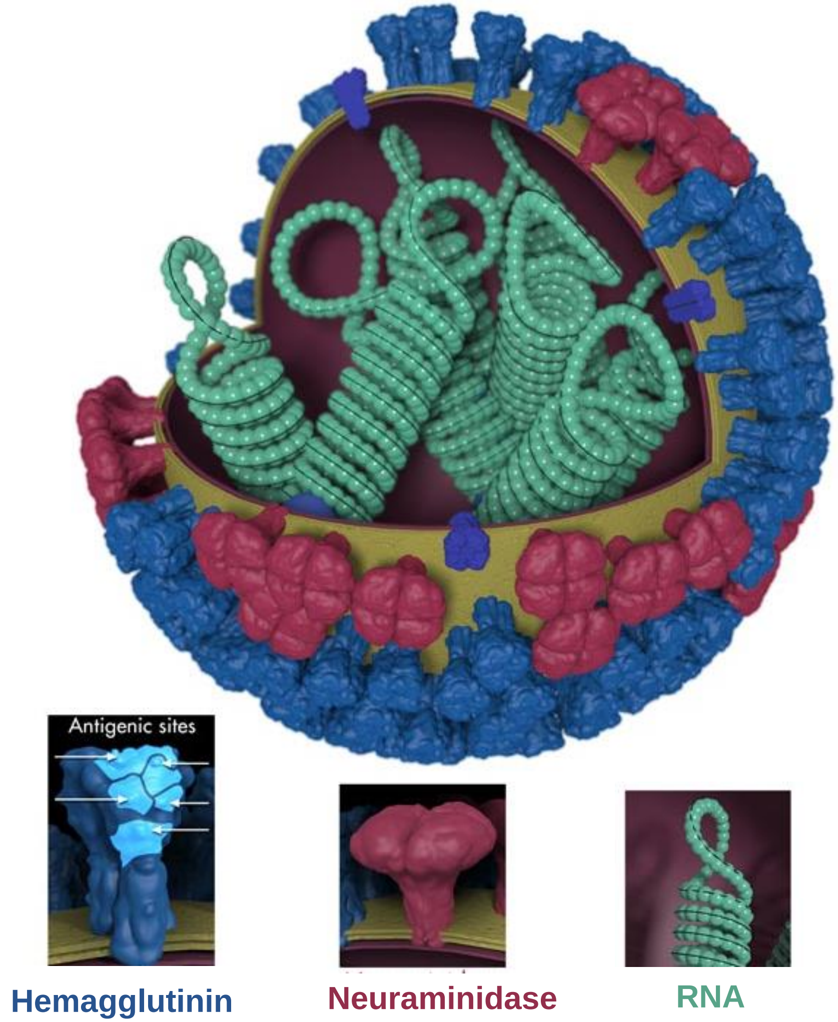
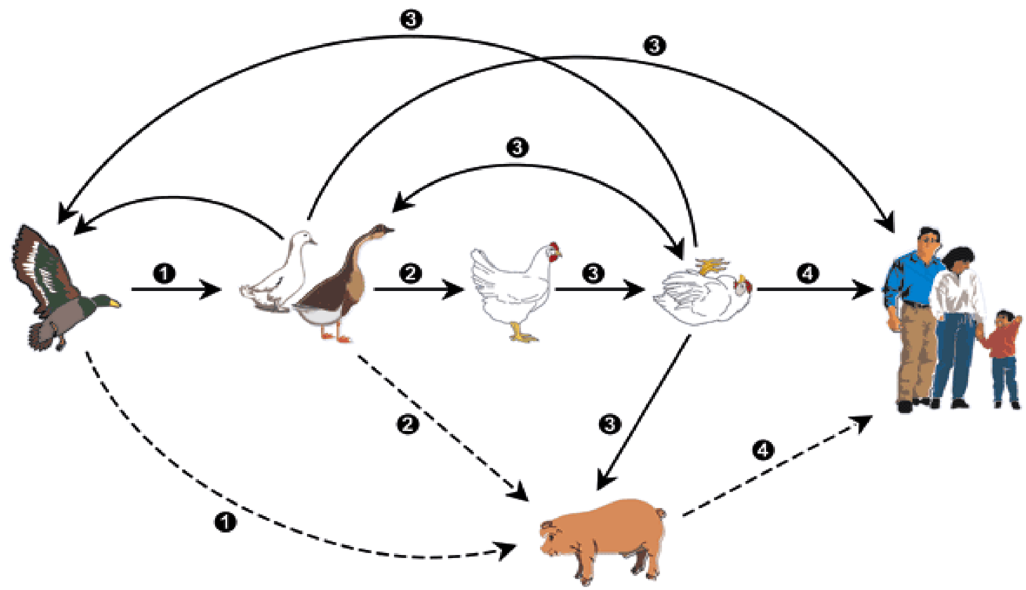


Image credit: National Center for Immunization and Respiratory Diseases (NCIRD), CDC

Avian Influenza in Poultry and Humans

- Multiple avian influenza (AI) subtypes circulate in domestic poultry, including H4, H5, H7, H9, and H10.
- Split into two pathotypes:
  - Low pathogenic AI (LPAI) causes mild illness and few or no symptoms in poultry.
  - Highly pathogenic AI (HPAI) typically causes severe disease with high mortality rates (usually H5 or H7 subtypes).
- Can cross the species barrier to also infect humans (H5, H7, H9 subtypes)

Emergence and transmission of highly pathogenic avian influenza H5N1

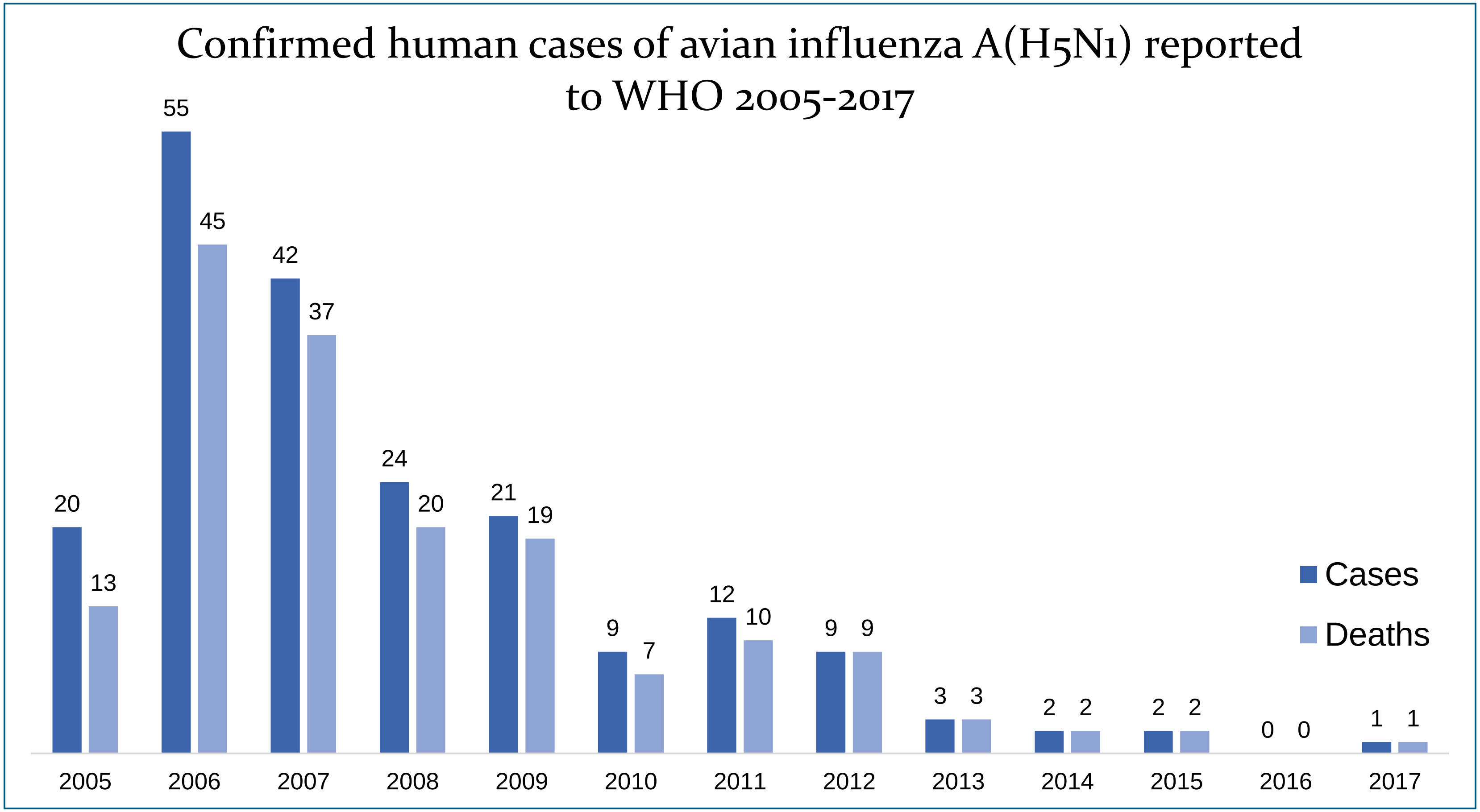


Transmission routes:
- Solid lines: transmission demonstrated
- Dotted lines: transmission postulated but not demonstrated

Opportunities for control:
1) Prevent contact between wild and domestic poultry
2) Prevent contact between domestic waterfowl and gallinaceous poultry
3) Eradicate H5/H7 influenza viruses from gallinaceous poultry
4) Prevent contact between poultry, pigs, and humans and make vaccines and antiviral drugs available

Image credit: Webster, R. G., Hakawi, A. M., Chen, H., & Guan, Y. (2006). H5N1 Outbreaks and Enzootic Influenza. *Emerging Infectious Diseases*, *12*(1), 3-8. https://dx.doi.org/10.3201/eid1201.051024.

Human Cases of HPAI H5N1 in Indonesia



- Indonesia has experienced the highest number of human fatalities from avian influenza A(H5N1) worldwide.
- Between 2005 and 2017, 200 confirmed cases of avian influenza A(H5N1) virus infection and 168 deaths were reported to WHO (fatality rate 84%).

Data source: WHO/GIP, data in HQ as of 2 March 2018

HPAI in Indonesian Poultry

- The first reported outbreak of HPAI H5N1 occurred in 2003.
  - The outbreak likely originated from single introduction of the virus into East Java between November 2002 and October 2003.
- HPAI H5N1 spread rapidly, and 32 of 33 provinces have reported confirmed cases since its introduction.
- HPAI H5N1 is considered endemic in poultry populations.

Introduction of Avian Influenza in Indonesia, September 2003

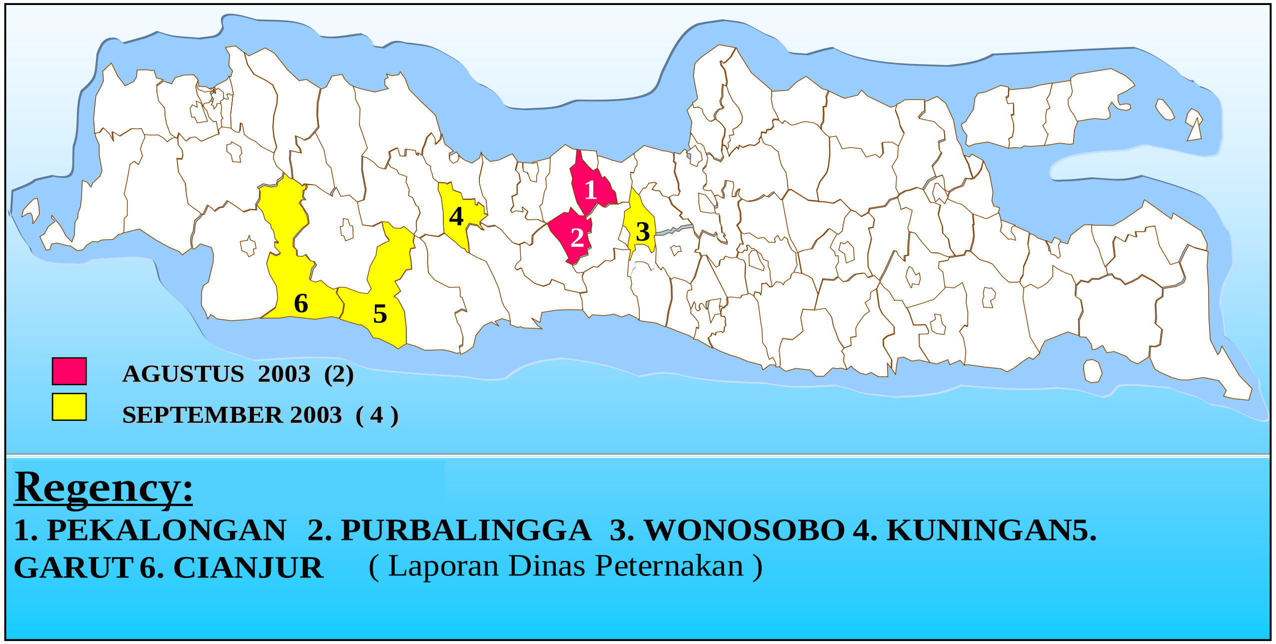


Image credit: Livestock service report, National Committee of Avian Influenza, Directorate General of Livestock and Animal Health

Avian Influenza in Poultry

<u>Transmission routes</u>:

- Poultry infected through contact with infected waterfowl or poultry or contaminated environment
  - Infected birds shed virus in saliva, mucous, and feces.

Drawing blood from a chicken during a One Health simulation in Ketapang, July 2017

<u>Epidemiology</u>:

- Virus circulates in farms, markets, and backyard flocks.
- Poultry movement (local markets, regional import/export) allows virus to spread rapidly.
- Wild birds can introduce new AI strains into poultry populations.

Photo credit: FAO/ECTAD Indonesia

Avian Influenza in Humans

Symptoms:

- May cause disease ranging from mild upper respiratory tract infection to severe pneumonia, acute respiratory distress syndrome, and death

Transmission routes:

- AI is primarily acquired through direct or indirect contact with infected live or dead birds or contaminated environments.
- Circulating AI strains are incapable of sustained human transmission.
  - Limited cases of human-to-human transmission have occurred, generally arising from prolonged, unprotected close contact with infected patients.
  - The first documented human-transmitted case occurred in Indonesia in 2006.

Avian Influenza in Humans

Diagnosis:

- Confirmatory testing and subtyping is performed by molecular methods, virus culture or both.
- Serological tests are useful for estimates of seroprevalence and retrospective diagnosis.

Treatment:

- Antiviral drugs (neuraminidase inhibitors) such as oseltamivir

Prevention and control:

- Protective measures to limit the spread of disease from poultry or contaminated environments to humans include:
    - Personal hygiene (for example, handwashing)
    - Respiratory protection (for example, facemasks)
    - Avoiding potentially contaminated areas and live poultry/carcasses
- Controlling the disease in poultry is critical to decreasing human infection risks.

Economic Impact of HPAI in Indonesia

- HPAI is an economic burden in Indonesia due to:
  - Animal death
  - Widespread disruption of the poultry industry
  - HPAI control program costs
  - National and international trade consequences
  - Lost productivity and lost wages due to human illness and death
  - Medical care and treatment costs
- By 2005, losses from HPAI in Indonesia were estimated at over $170 million.
  - Destruction of approximately 16 million birds
  - Greatest loss among backyard village farmers
  - Estimated 23% of industrial and commercial farm workers lost employment

Government Control Strategy

- In 2004, Indonesia established a nine-point plan for eradicating HPAI H5N1:
  1. Improvement of biosecurity in poultry production sector
  2. Selective culling/infected flock depopulation (compensation scheme implemented in 2011)
  3. Vaccination of poultry in infected and high risk areas
  4. Restriction of movements of poultry and their products (at all times)
  5. Surveillance and tracking
  6. Increasing public awareness
  7. Restocking of poultry following outbreak losses
  8. Stamping out poultry in newly infected areas
  9. Monitoring and evaluation

Ministry of Agriculture, Indonesia
http://www.litbang.pertanian.go.id/berita.php/one/221/

Poultry Vaccination in Indonesia

Selection of poultry vaccines available in Indonesia:

Vaccine	Manufacturer	Seed strain and subtype
BioTek	PT Biotek, Indonesia	A/Turkey/England/N-28/73 (H5N2)
Bird CLOSE 5.1	Shigeta Animal Pharmaceuticals Inc, Indonesia	Based on recombinant virus: HA gene derived from A/chicken/Legok/2003 (H5N1)
Caprivac AI-K	Caprifarmindo, Bandung, Indonesia	A/chicken/West Java/Pwt-Wij/2006 (Pwt) (H5N1)
Gallimune™	Merial, Lyone, France	A/turkey/Wisconsin/1/1968 (H5N9)
Medivac AI	Medion Farma Jaya, Bandung, Indonesia	A/chicken/West Java/Pwt-Wij/2006 (Pwt) (H5N1)
ProTek AI	PT Biotek, Indonesia	A/Turkey/England/N-28/73 (H5N2)
Vaksimune AI	Pt Vaksindo Satwa Nusantra, Indonesia	A/chicken/West Java/ 30/2007 (H5N1), clade 2.1.3.2
Afluvet	Pusat Veteriner Farma (Pusvetma), Indonesia	A/duck/Sukoharjo/BBVW1428-9/2012 (H5N1) clade 2.3.2.1

- Poultry vaccination has been the primary strategy for controlling avian influenza since 2004.
  - Over 20 vaccines have been registered for use in Indonesia.
- In 2011, the Ministry of Agriculture implemented requirements that H5N1 HPAI vaccines use seed strains based on local variants.
- Continuous drift and emergence of new clades lowers vaccine efficacy and poses a challenge for vaccination.

Table adapted from: Tarigan, S., Wibowo, M. H., Indriani, R., Sumarningsih, S., Artanto, S., Idris, S., … Ignjatovic, J. (2018). Field effectiveness of highly pathogenic avian influenza H5N1 vaccination in commercial layers in Indonesia. *PLoS ONE*, *13*(1), e0190947.

Challenges for HPAI Control in Indonesia

<u>Prevention:</u>

- Poor biosecurity at markets, slaughterhouses, and farms (especially backyard farms)
  - Birds suspected to be infected are often improperly disposed of, which may contribute to virus spread.
- Uncontrolled poultry trade and movement
- Inconsistent application of vaccination strategies
- Ineffective risk communication and lack of public knowledge of avian influenza

<u>Detection:</u>

- Limited information on disease prevalence and control efforts from industrial poultry producers
- Lack of reporting or delayed reporting of suspected cases

<u>Response:</u>

- Inconsistent application of culling strategies
- Government compensation rates lower than market value of birds
  - Farmers conceal mortalities that may be caused by HPAI and immediately sell or move surviving birds to prevent economic losses.

References

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4. Tarigan, S., Wibowo, M. H., Indriani, R., Sumarningsih, S., Artanto, S., Idris, S., Ignjatovic, J. (2018). Field effectiveness of highly pathogenic avian influenza H5N1 vaccination in commercial layers in Indonesia. *PLoS ONE*, *13*(1), e0190947.
5. Webster, R. G., Hakawi, A. M., Chen, H., & Guan, Y. (2006). H5N1 Outbreaks and Enzootic Influenza. *Emerging Infectious Diseases*, *12*(1), 3-8. https://dx.doi.org/10.3201/eid1201.051024.
6. WHO/GIP, data in HQ as of 2 March 2018

Case Study: Highly Pathogenic Avian Influenza

INTRODUCTION TO SELECTED PUBLICATIONS

Detection of Avian Influenza H5N1 Subtype in Live Bird Markets around West Java Province

Atik Ratnawati, NLP Indi Dharmayanti

Jurnal Kedokteran Hewan. 2015;19(1)

Background

- Live poultry markets are thought to be a source of HPAI virus infection and to contribute to the spread of HPAI from bird-to-bird and bird-to-human.
  - Poultry in markets come from a variety of sources, and usually little is known about the health status of the poultry or the prevalence of AI in the area of poultry origin.
  - Human cases of HPAI H5N1 in 2011 and 2013 in Bekasi demonstrated that attending bird markets can be a risk factor for infection.
- Previous studies have shown that markets are contaminated with AI H5N1, and AI H5N1 has been detected on a variety of market equipment.
  - Few studies have been published examining the presence of AI H5N1 in poultry in Indonesian live poultry markets.

Study Goal and Methodology

Study Goal:

- Evaluate the presence of H5N1 avian influenza virus in poultry and the environment in several live poultry markets to determine the role of markets as a source of virus transmission

Methodology:

- Sample locations:
    - West Java: 7 randomly selected live poultry markets in 4 districts: Purwakarta (3), Subang (2), Bandung (1), Garut (1)
    - Banten Province: 3 markets in Tangerang Selatan Regency
- Sample types:
    - Cloacal swabs from live birds: 62 pooled samples from 193 birds
    - Environmental samples: 67 swabs from cutting boards, scales, tables, knife handles, and cages
- Sample testing:
    - RT-PCR: screen samples using H5-specific primer first, then test H5-positive samples using an N1-specific primer

Key Findings

Poultry samples

- 9 pools were positive for H5.
- Of these, 6 were positive for N1.

Figure 1. The result of poultry swab amplification with H5 primer.

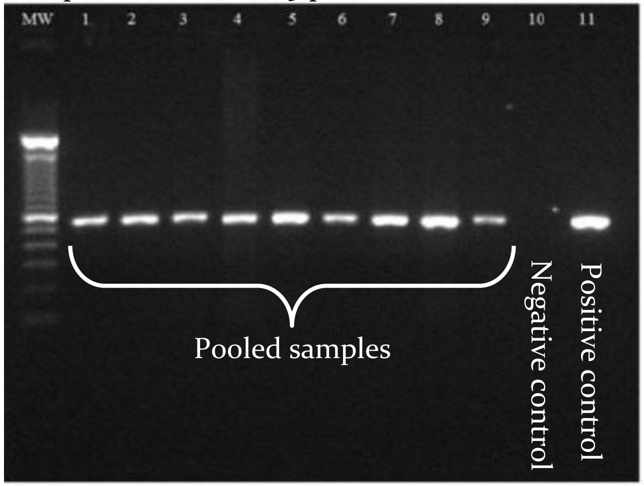
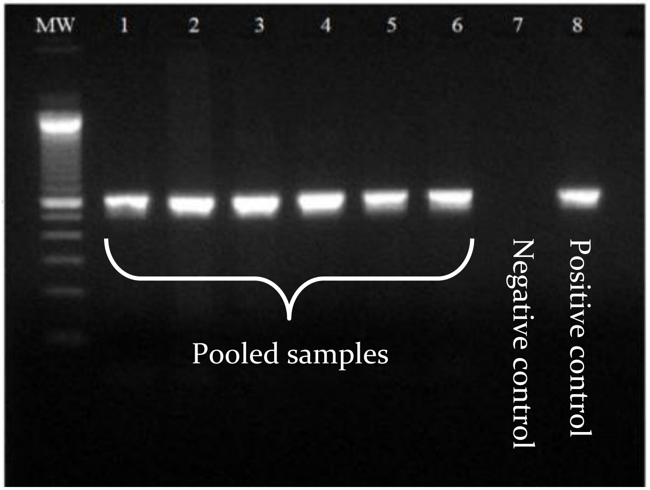


Figure 2. The result of poultry swab amplification with N1 primer.



Environmental samples

- 11 pools were positive for H5.
- Of these, 10 were positive for N1.

Figure 3. The result of environmental swab amplification with H5 primer.

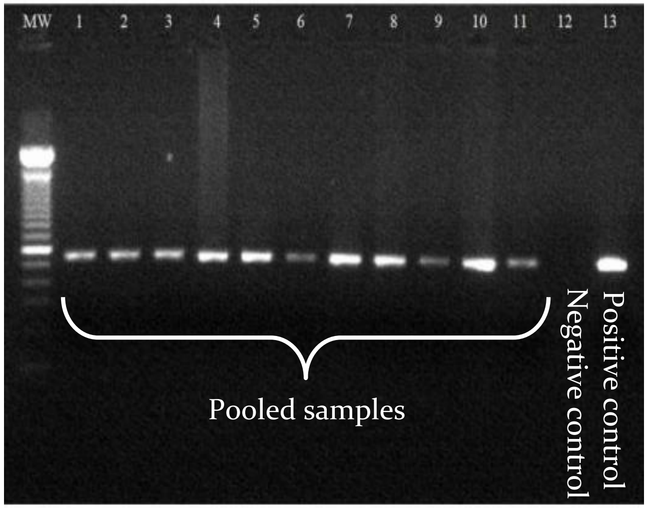
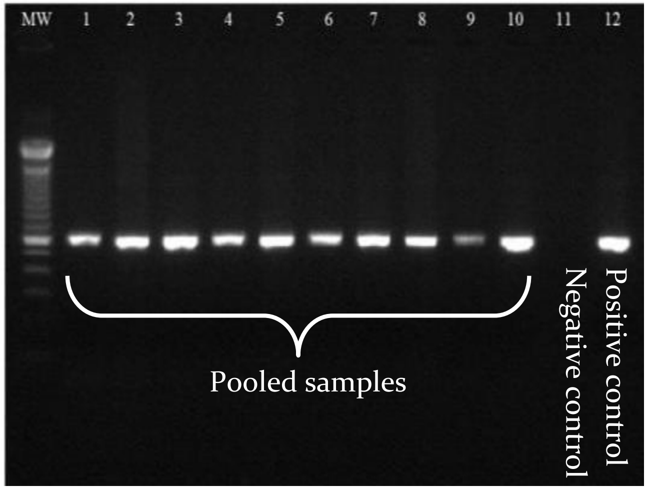


Figure 4. The result of environmental swab amplification with N1 primer.



Key Findings

Table 2. Results of identification of swab samples of cloaca of poultry and environment swabs from live poultry markets in Purwakarta Regency, Subang Regency, Bandung Regency, Garut Regency and South Tangerang Regency using RT-PCR with primers for subtype H5 and N1

Location	Species	Total Samples/ Pool samples	Results RT-PCR			
			H5		N1	
			+	-	+	-
Purwakarta (April 2011)	Poultry	72/23	2	21	2	0
	Environment	6/6	0	6	-	-
Subang (April 2011)	Poultry	65/20	2	18	0	2
	Environment	6/6	0	6	-	-
Bandung (April 2011)	Poultry	15/5	0	5	-	-
	Environment	30/30	1	29	1	0
Garut (April 2011)	Poultry	-	-	-	-	-
	Environment	16/16	6	10	5	1
Tangerang Selatan (April 2011)	Poultry	41/14	5	9	4	1
	Environment	9/9	4	5	4	0

- All poultry markets were contaminated with H5 viruses, though not all samples could be confirmed as AI H5N1.
- AI H5N1 virus was identified in live poultry and on market equipment.

GRYPHON SCIENTIFIC indohun INDONESIA ONE HEALTH UNIVERSITY NETWORK COLLEGE OF VETERINARY MEDICINE UNIVERSITY OF MINNESOTA Driven to Discover International Federation of Biosafety Associations

Author Conclusions

- Live poultry markets can be a source of AI H5N1 transmission.
  - Some poultry in markets are infected with AI H5N1 and can serve as a source of virus transmission to the environment and other birds.
  - The contaminated market environment may infect birds or humans.
- Cleanliness and disinfection of the market environment are important for reducing contamination by AI H5N1 virus.
  - Increased cleanliness can decrease the risk of human infection and virus spread.

Avian Influenza H5N1 Identification in Avian Species Surrounding Avian Influenza H5N1 Human Cases in Bekasi, West Java, 2011

Dyah Ayu Hewajuli, NLP Indi Dharmayanti

Jurnal Veteriner 2014 Vol.15 No.1 pp.68-78

Background

- HPAI outbreaks in poultry are usually found alongside human cases of HPAI.
  - Infected birds may not exhibit symptoms but may shed the virus in feces.
  - Poultry feces containing virus can contaminate the environment, and other birds and humans may be infected directly or indirectly.
- In March 2011, a human case of H5N1 was identified in Bekasi, West Java, and the infection was fatal.

Study Goal and Methodology

Study Goal:

- Test for H5N1 avian influenza in birds in the area surrounding the fatal human case of H5N1 in Bekasi in 2011

Methodology:

- Sample types:
  - <u>Serum</u>: chickens, geese
  - <u>Cloacal swabs</u>: chickens, geese, ornamental birds
  - <u>Environmental swabs</u>: bird cages, market cutting board
- Sample locations:
  - Poultry market, bird shops, and houses near residence of fatal H5N1 case

Sample source	Serum	Cloacal swab	Cage swab	Market cutting board
Chicken	42	15	-	1
Goose	3	1	-	-
Ornamental bird	-	2	45	-
Total	**45**	**18**	**45**	**1**

- Sample testing:
  - Hemagglutination inhibition (HI) for antibodies against H5N1
  - RT-PCR: H5-specific primer and N1-specific primer

Characteristics of Fatal Human Case of H5N1

- The victim regularly visited a live poultry market near the victim's house.
- Many households in the surrounding area keep ornamental birds as pets.
    - Though the victim did not keep ornamental birds, the victim visited in-laws who do.
- Birds in the area did not show symptoms of AI infection.

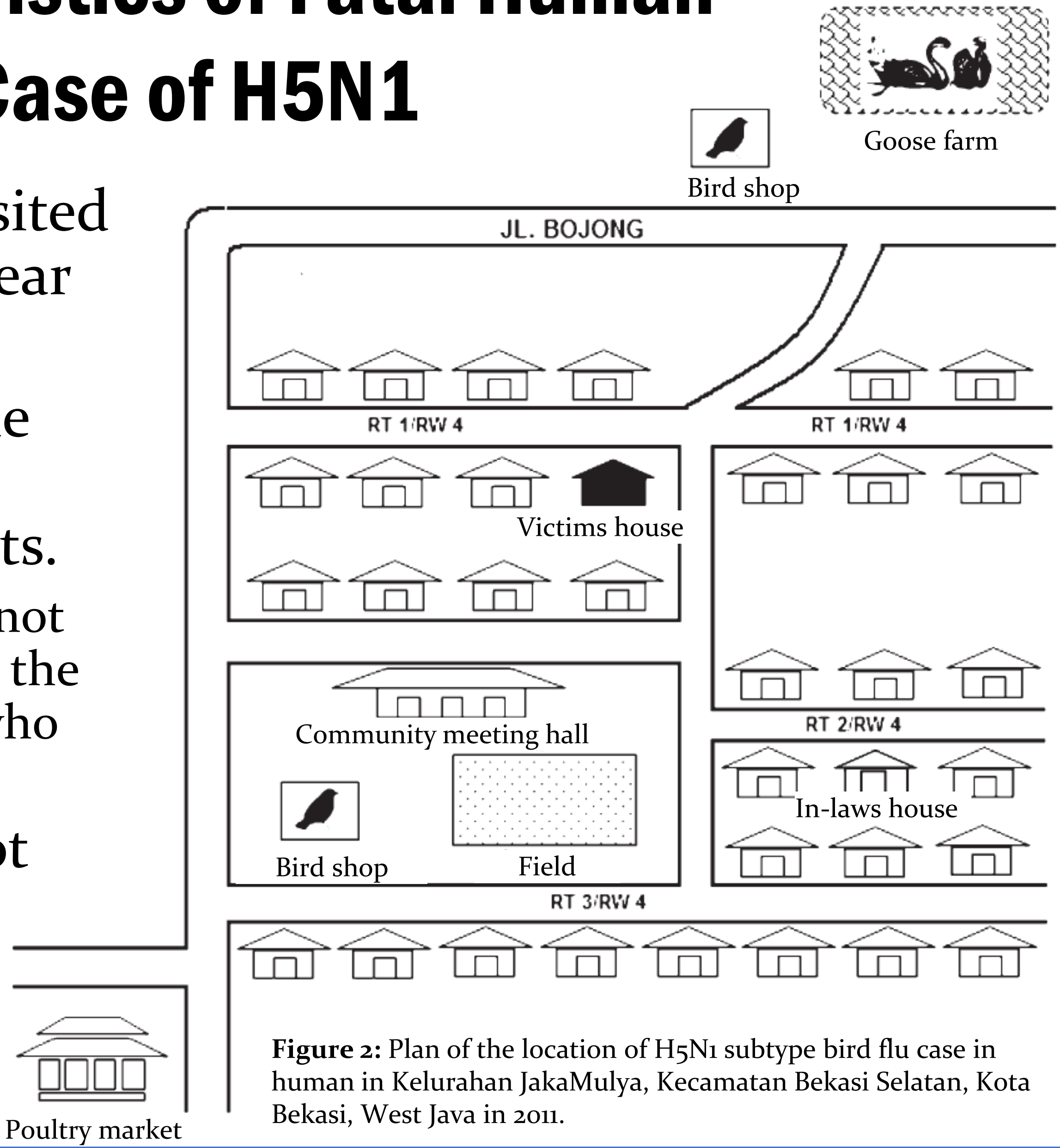


Figure 2: Plan of the location of H5N1 subtype bird flu case in human in Kelurahan JakaMulya, Kecamatan Bekasi Selatan, Kota Bekasi, West Java in 2011.

Key Findings: Serology

Table 2. HI test results of poultry serum samples obtained near a case of H5N1 subtype bird flu in humans in Kelurahan JakaMulya, South Bekasi District, Bekasi City, West Java in 2011

No	Location	Species	Number of Samples	Titer HI (log 2)			
				Neg	<4	4-7	>7
1	Poultry market	Broiler chicken	33	27	2	4	0
		Buras chicken	9	9	0	0	0
2	Jl.Bojong	Goose	3	0	0	3	0
	Total		45	36	2	7	0

- 80% of birds were antibody negative against AI H5N1.
- 2 samples had low antibody titers and 7 samples had moderate antibody titers.
- No samples showed high titers of antibodies against AI H5N1.

Key Findings: RT-PCR

- 7 samples (11.2%) were positive for H5N1:
  - 5 positive samples from chickens in the poultry market and 1 from market cutting board
  - 1 positive sample from neighborhood bird cage
- 26 samples (30.2%) were positive for H5, but negative for N1.
- 36 samples (57.1%) were PCR negative.

Table 3. Result of RT-PCR test of cloacal swabs and cage swabs obtained near a case of H5N1 subtype bird flu in humans in Kelurahan JakaMulya, South Bekasi District, Bekasi City, West Java in 2011

No	Location	Species	Number of samples	RT-PCR Results	
				Subtipe H5	Subtipe N1
1	Poultry market	Ayam Broiler	11	8	2
		Talenan	1	1	1
		Ayam Buras	3	3	3
2	RT1/RW4	Burung Kacer	1	0	0
		Burung Kerocokan	2	1	0
		Burung Decu	2	2	0
		Burung Gondolijo	1	0	0
		Burung Perkutut	3	1	1
		Burung Kenari	1	1	0
		Burung Beo	1	1	0
		Burung Wambi	1	1	0
		Burung Jalak Suren	2	1	0
		Burung Jalak Ijo	1	0	0
		Burung Prenjak	1	0	0
3	RT 2/RW 4	Burung Perkutut	1	0	0
		Burung Anis	1	0	0
4	RT 4/RW 4	Burung Puter	5	1	0
		Burung Kerocokan	2	0	0
		Burung Perkutut	2	2	0
		Burung Kutilang	1	0	0
		Burung Jalak Kebo	2	0	0
		Burung Jalak Nias	1	1	0
		Burung Kacer	3	1	0
		Burung Srindit	1	0	0
		Burung Cucak Biru	1	0	0
		Burung Poksai Mandarin	1	0	0
		Burung Beo	1	0	0
		Burung Tekukur	1	1	0
		Burung Cucak Rawa	1	0	0
5	Jl.Bojong	Ayam Buras	1	0	0
		Burung Puter	1	0	0
		Burung Ciblek	1	0	0
		Burung Kenari	1	0	0
		Burung Kerocokan	1	0	0
		Burung Cucakijo	1	0	0
		Burung Titok	1	0	0
		Angsa	1	0	0
	Total		63	26	7

H5N1 positive samples

Author Conclusions

- AI H5N1 viruses were circulating in birds in the area surrounding a fatal human case of H5N1.
    - Circulation of AI H5N1 in birds can lead to transmission to humans or other birds either directly or indirectly, through environmental contamination.
- Strict biosecurity and sanitation can minimize environmental contamination caused by viral shedding from infected birds, but bird cages in markets and homes are rarely disinfected.
- Cutting boards used in poultry markets can become contaminated if used for butchering infected birds and can pose a risk for virus transmission to humans.
- Efficient control and sanitation programs are needed to prevent virus spread between birds and from birds to humans.

Seroevidence for a High Prevalence of Subclinical Infection With Avian Influenza A(H5N1) Virus Among Workers in a Live-Poultry Market in Indonesia

Kazufumi Shimizu, Laksmi Wulandari, Emmanuel D. Poetranto, Retno A. Setyoningrum, Resti Yudhawati, Amelia Sholikhah, Aldise M. Nastri, Anna L. Poetranto, Adithya Y. R. Candra, Edith F. Puruhito, Yusuke Takahara, Yoshiaki Yamagishi, Masaoki Yamaoka, Hak Hotta, Takako Ustumi, Maria I. Lusida, Soetjipto, Yohko K. Shimizu, Gatot Soegiarto, and Yasuko Mori

J Infect Dis. 2016 Dec 15;214(12):1929-1936.

Background

- Sporadic human infections with HPAI H5N1 pose public health concerns for several reasons:
  - High case fatality rate in patients with severe acute respiratory illness caused by HPAI H5N1
  - Potential adaptation of virus for human-to-human transmission, which could lead to a pandemic
  - Coinfection with avian and human seasonal influenza viruses may allow genetic reassortment, leading to the emergence of a novel influenza virus with pandemic potential
- The prevalence of asymptomatic/subclinical HPAI H5N1 infections in humans is not well understood.
  - Laboratory confirmed cases are usually the most severe cases, and there may be numerous undetected cases with mild or no symptoms.

Study Goal and Methodology (1/2)

Study Goal:

- Examine the seroprevalence of HPAI H5N1 virus infection among live poultry market workers

Sample Collection Methodology:

- Blood and oropharyngeal swab samples were collected from market workers annually between 2012 and 2016.
  - 406 total samples collected
  - Subset of participants recruited for serial sampling over multiple years
  - Control population: Healthy volunteers from East Java
- Cloacal swabs were obtained from sick or dead poultry at live poultry markets, farms, and backyards in East Java.
  - 27,020 birds (chickens, ducks, and turkeys) observed by veterinarian
  - 226 samples collected from birds exhibiting clinical signs of HPAI H5N1 infection

Study Goal and Methodology (2/2)

Sample Testing Methodology:

- RT-PCR on oropharyngeal swab samples and viruses isolated from poultry cloacal swabs to detect:
  - H5 HA of Eurasian AND Indonesia lineages of A(H5N1)
  - H5 of Eurasian lineage A(H5N1) ONLY (to differentiate lineages)
  - M gene of influenza (for detection of all influenza A viruses)
- Hemagglutination-inhibition (HI) assay to detect antibody activity against:
  - H5N1 Eurasian lineage
  - H5N1 Indonesian lineage
  - H3N6 avian influenza
  - Human seasonal H3N2
  - 2009 pandemic H1N1
- All tests involving live A(H5N1) were conducted in a biosafety level 3 laboratory.

Key Findings: Poultry Surveillance

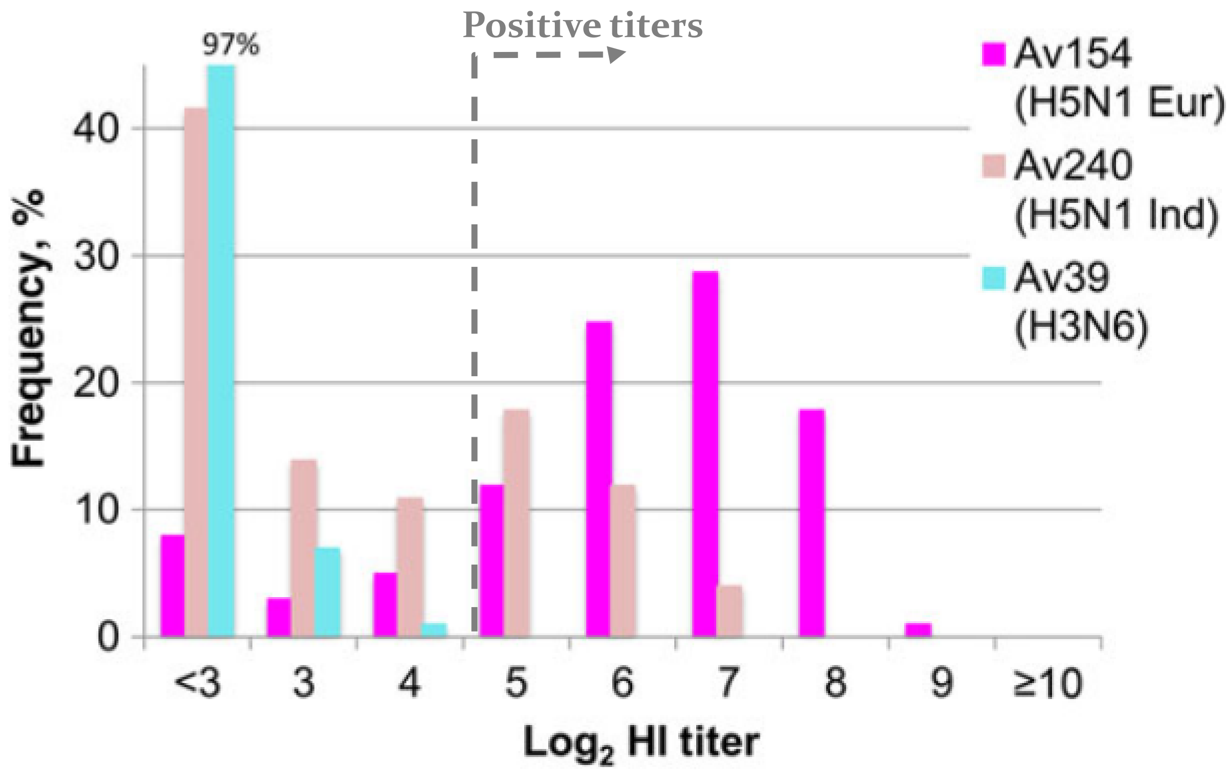
Table 1. Influenza A Virus Isolation From Poultry in East Java, Indonesia

Poultry	Population Observed	Samples Collected	HA-Positive Eggs Harvested	Subtype/Lineage, by RT-PCR		
				H5/Eur	H5/Ind	H3
May–Sep 2013[a]						
Ducks, no.	13 000	56	9	5	0	1
Muscovy ducks, no.	400	22	6	5	0	0
Chickens, no.	1800	42	10	3	0	0
Turkeys, no.	300	2	2	2	0	0
Subtotal, no. (%)	15 500 (100)	122 (0.787)	27 (0.174)	15 (0.097)	0 (0)	1 (0.006)
Jan–Feb 2014[b]						
Ducks, no.	1800	13	7	3	1	1
Muscovy ducks, no.	720	9	2	1	1	0
Chickens, no.	9000	82	46	12	4	0
Subtotal, no. (%)	11 520 (100)	104 (0.903)	55 (0.477)	16 (0.139)	6 (0.052)	1 (0.009)
Overall, no. (%)	27 020 (100)	226 (0.836)	82 (0.303)	31 (0.115)	6 (0.022)	2 (0.007)

- Eurasian lineage H5N1 was detected in 31 samples (0.115% of poultry observed), while Indonesian lineage H5N1 was detected in 6 samples (0.022% of poultry observed).
- HPAI H5N1 was detected more frequently during the 2014 rainy season than during the 2013 dry season.

Key Findings: Human Surveillance (1/3)

Figure 1. Distributions of hemagglutination-inhibition (HI) titers against avian influenza type A viruses among live-poultry market workers.



- Among serum samples from 2014, 84% were positive against Eurasian lineage H5N1 and 34% were positive against Indonesian lineage H5N1 with HI titers >32.
- HPAI H5N1 was not detected in oropharyngeal swabs, but human seasonal H3N2 and 2009 pandemic H1N1 viruses were detected.

Key Findings: Human Surveillance (2/3)

- None of the healthy controls were positive for antibody activity against Eurasian lineage H5N1.
- Approximately 80% of controls and market workers were positive for human seasonal influenza.

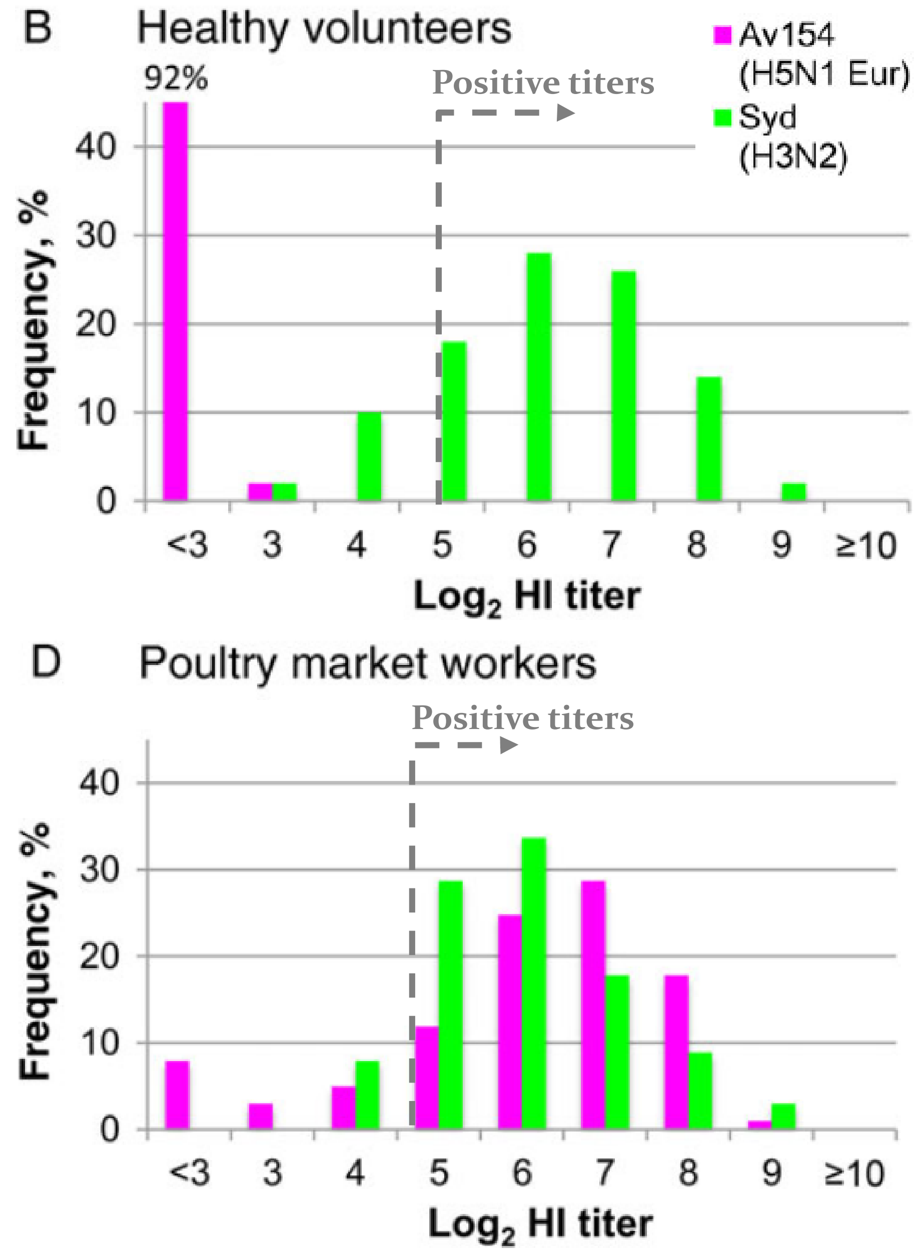


Figure 2. The distributions of hemagglutination-inhibition (HI) titers against influenza A/turkey/East Java/Av154/2013(H5N1) virus Eurasian lineage (Av154[H5N1 Eur]) and seasonal influenza A/Sydney/5/1997(H3N2) virus (Syd[H3N2])

Key Findings: Human Surveillance (3/3)

- Seropositivity against Eurasian lineage H5N1 peaked in 2014.
  - Indonesian lineage H5N1 also peaked in 2014, but at much lower titers.
  - No significant peaks were observed for seasonal influenza viruses.
- The percentage of workers that seroconverted was 44% in 2014, 3% in 2015, and 4% in 2016.

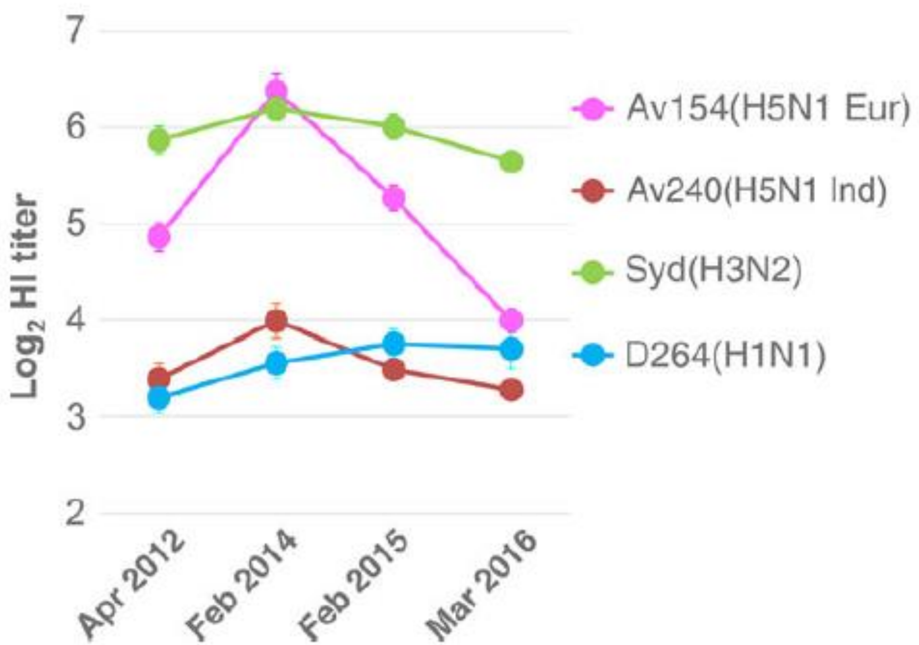


Figure 4. Kinetics of hemagglutination-inhibition (HI) titers against avian and seasonal human influenza A viruses

Author Conclusions

- Eurasian lineage H5N1 virus has previously infected live bird market workers.
  - Seroconversion results suggest a high prevalence of HPAI H5N1 virus infection between 2012 and 2014.
  - Detection of seasonal influenza viruses in swab samples from several market workers means that coinfection may have occurred, underscoring the importance of monitoring for coinfection at live poultry markets.
- H5N1 infections were likely mild or asymptomatic.
  - Antibody titers against H5N1 decreased after a year, which is indicative of asymptomatic infection.
  - No participants were hospitalized with severe respiratory illness and influenza-like illness among participants was not significantly correlated with H5N1 infection.

Field effectiveness of highly pathogenic avian influenza H5N1 vaccination in commercial layers in Indonesia

Simson Tarigan, Michael Haryadi Wibowo, Risa Indriani, Sumarningsih , Sidna Artanto, Syafrison Idris, Peter A. Durr, Widya Asmara, Esmaeil Ebrahimie, Mark A. Stevenson, Jagoda Ignjatovic

PLoS One. 2018 Jan 10;13(1):e0190947

Background

- Vaccination with inactivated avian influenza vaccines has been shown to have beneficial effects for poultry flocks, including prevention of clinical signs and mortality and reduction in the number of infected birds.
  - Factors that influence vaccination outcome include type and quality of vaccine, vaccination schedule, dose, and method of administration.
- Currently, no single regime is recommended for HPAI vaccination of commercial poultry in endemic areas of Indonesia.
  - Although the majority of commercial poultry layers in Indonesia are vaccinated, the field effectiveness of vaccines remains unknown.

Study Goal and Methodology

Study Goal:

- Evaluate through longitudinal sampling the level and duration of AI H5N1 vaccine induced immunity in commercial layer flocks

Methodology:

- Study population: 16 medium-sized commercial flocks (Sector 3) in West Java (8) and Yogyakarta (8)
  - 25 birds selected randomly from each flock
- Longitudinal surveillance: Blood samples drawn at 18, 28, 38, 48, 58, and 68 weeks old

Vaccination regimes used by farms could be grouped into three categories:

Regime	# times vaccinated before 19 weeks old	# times vaccinated after 19 weeks old
Regime A (n = 8)	2-3	-
Regime B (n = 2)	2	1
Regime C (n = 6)	3-4	2-3

- Sample testing: Tested for antibody levels against multiple Indonesian H5N1 strains using haemagglutination inhibition (HI) test

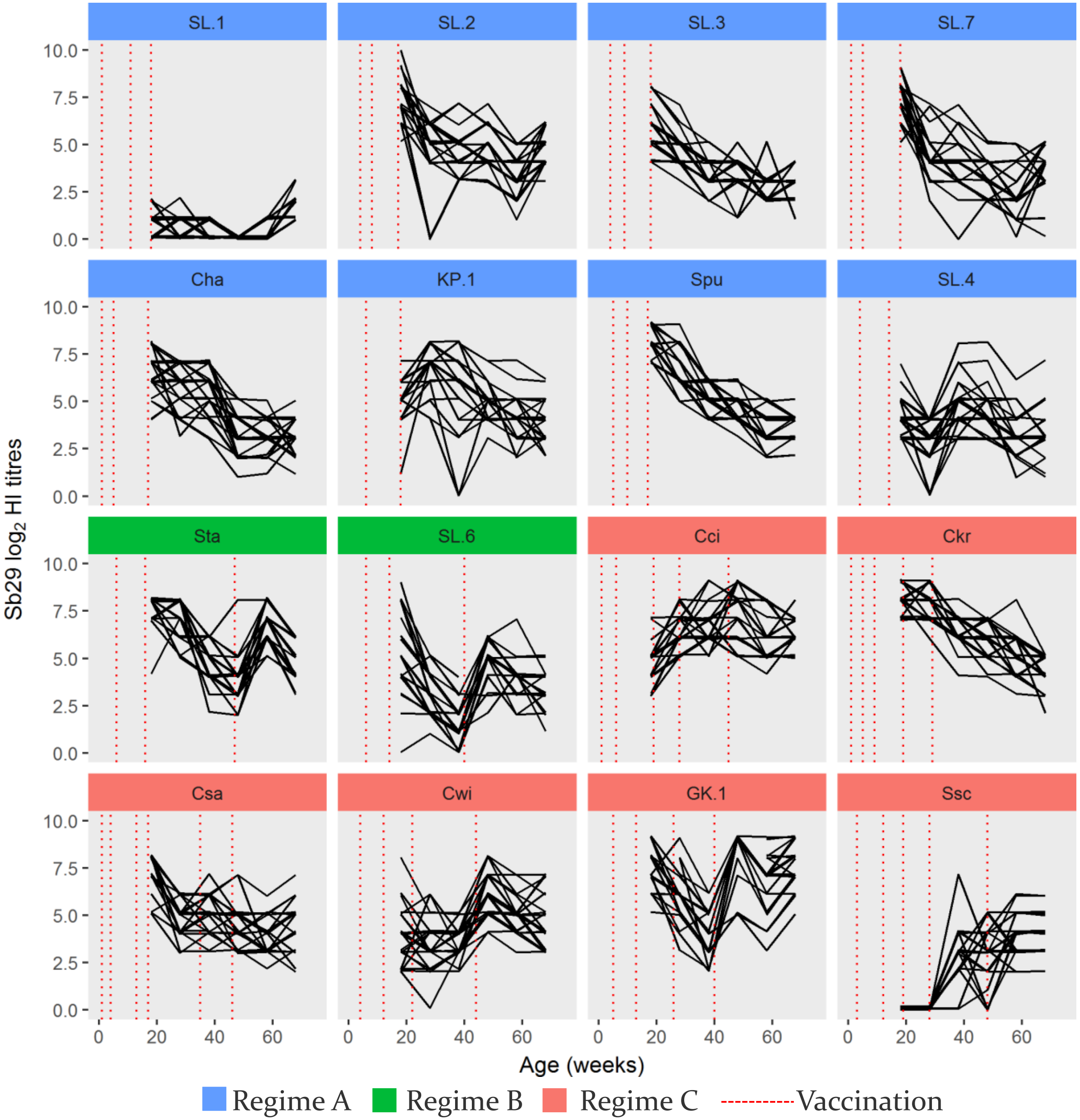
Methodology: Challenge Study

- At the conclusion of longitudinal surveillance, 22 birds from a regime A flock and 24 from a regime C flock were experimentally infected with HPAI H5N1.
  - Challenge virus: HPAI A/chicken/West Java/Subang-29/2007 (H5N1)
  - Experiment conducted in biosafety level 3 experimental facility
  - Morbidity and mortality monitored in each flock
  - Blood samples collected before and after infection for determination of H5N1 antibody levels using HI assay
- Control birds were not available because unvaccinated birds pose a risk to flocks and could not be kept on commercial farms.

Key Findings

- Titers for regime A flocks were significantly lower compared with titers from regime B and C flocks.
- Titers varied significantly between flocks within each regime.
- One regime A flock did not respond to vaccination (SL.1).

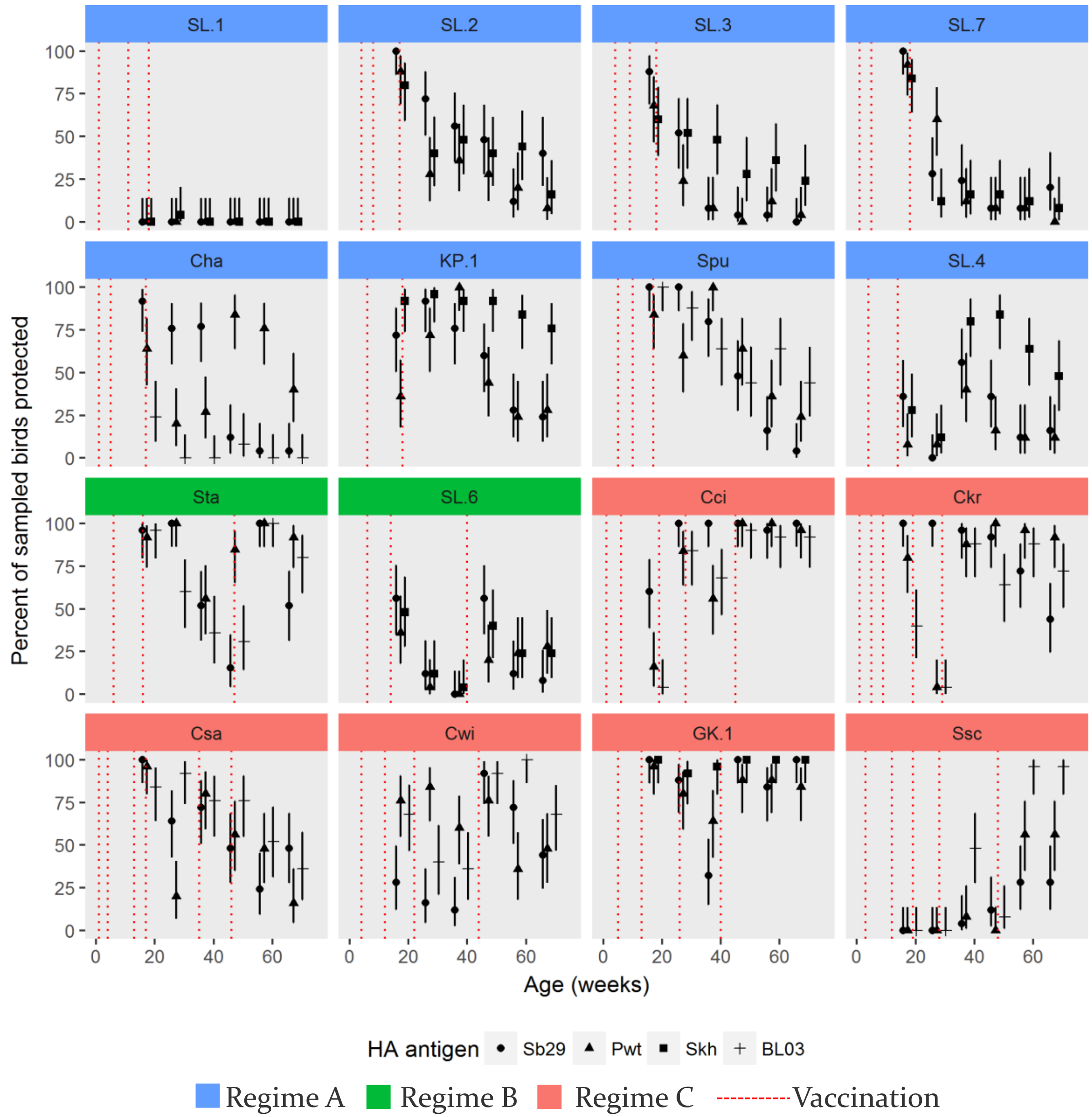
Fig 1. Hemagglutination inhibition (HI) titers against Sb29 H5N1 hemagglutinating antigen in vaccinated birds.



Key Findings

- Duration of protective immunity was variable between flocks.
- The majority of flocks were protected at 18 wo (>60% of birds with protective level of antibodies), but the number of protected birds decreased sharply after 18 weeks in almost all flocks.
- Only 2 flocks from regime C remained protected at 68 weeks.

Fig 2. Proportion of vaccinated birds with protective hemagglutination inhibition (HI) titers of ≥4log2.



Key Findings: HPAI H5N1 Challenge

Outcome	Regime A	Regime C
Birds infected	92%	54%
Mortality rate	75%	50%
Mean time of death	7.5 days	7.5 days

- The number of birds infected upon challenge was significantly lower in regime C birds than regime A birds.
  - Mortality rates did not differ significantly between flocks.
- The majority of surviving birds had protective levels of antibodies at the time of infection, while the majority of birds that died did not.

Author Conclusions

- AI H5N1 vaccination had variable outcomes, including vaccine failure, and was largely ineffective in providing long-lasting, protective immunity.
  - The field effectiveness of vaccination differed across all flocks, and no vaccine or vaccination strategy was consistently effective.
  - Birds vaccinated using Regime A, the most common vaccination strategy in Indonesia, were protected until 38 weeks old, but Sector 3 layers are generally kept until 80 to 100 weeks old.
- In general, the number of vaccinations correlated with antibody level: regime A had the fewest vaccinations and lowest titers, regime C had the most vaccinations and highest titers.
  - Vaccinating flocks 3 – 4 times before and 2 – 3 times after 19 weeks old could give longer-lasting protection.
  - Monitoring antibody levels in vaccinated flocks could inform the timing of re-vaccination for more effective responses.

Questions or Comments?

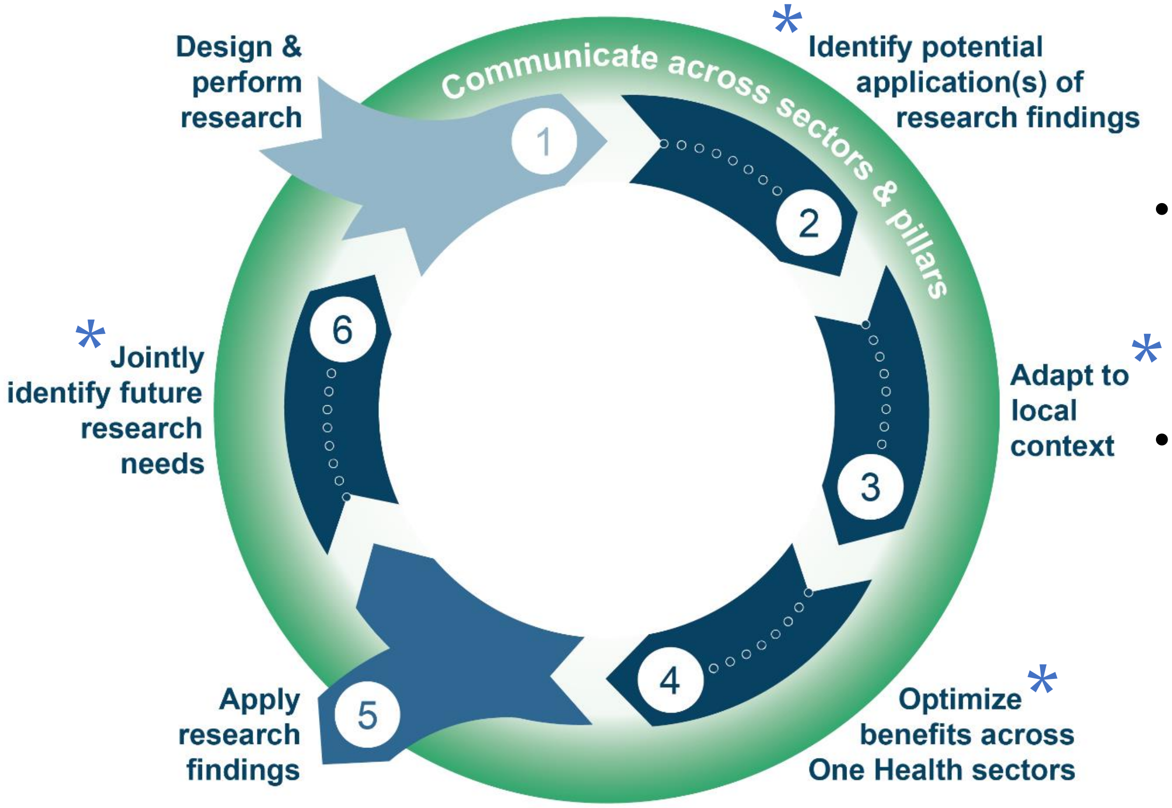
Case Study: Highly Pathogenic Avian Influenza

Group Discussion

Instructions

- Participants will split into small groups of 6 – 9 people.
- Refer to the **Participant Worksheet: Highly Pathogenic Avian Influenza Case Study** in your Participant Packet.
  - Structured similarly to the One Health Research Translation Framework
  - Includes discussion questions associated with the Framework steps and space to record your notes
- Facilitators will lead the research translation discussion.
  - If you have questions about the purpose of a step or the meaning of questions in the worksheet, ask your facilitator for clarification.

Structure of Research Translation Discussion



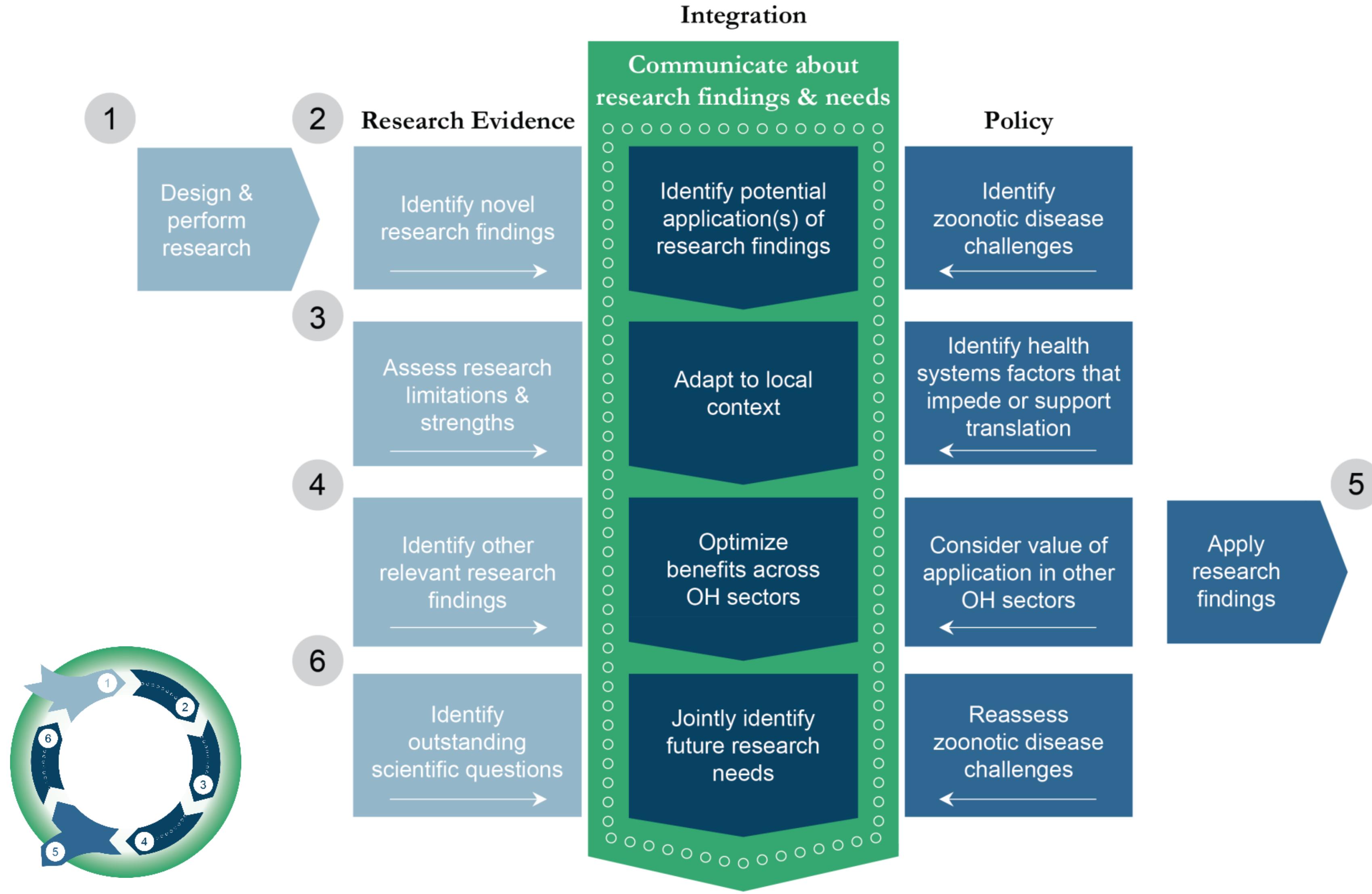
- The research translation discussion will begin at Step 2 because we have selected publications for evaluation.
- The discussion will focus on Steps 2, 3, 4, and 6 of the Framework because joint input from researchers and policymakers is critical for those steps.

* Steps discussed during case study exercise

Participation Guidelines for Case Study Exercises

1. Prior to starting this exercise, participants should have read the case study publications.
2. Ask the facilitator to clarify questions about the background information on research translation, case study publications, and activity instructions.
3. During the case study exercises, focus on understanding and analyzing the potential applications of the research. When critiquing the methodologies or research choices of the authors, focus on how those shortcomings may influence research translation.
4. Be willing to contribute your ideas and experiences and actively engage in group discussions.
5. Interact with one another in a way that encourages open communication and exchange of ideas.

Reference: Framework for Research Translation



Case Study: Highly Pathogenic Avian Influenza

SUMMARY DISCUSSION

Summary Discussion: Share and Compare Results of Small Group Discussions

Questions to consider:

- What potential applications of the research findings in the selected publications did your group identify?
  - What limitations of the research findings may influence translation?
  - What health systems barriers may prevent, limit, or delay translation of the research findings?
- What benefits of integrating research and policy perspectives did your group identify?
  - What challenges and potential solutions for cross-pillar communication did your group identify?
- Did your group identify anything surprising or interesting about research translation and One Health?

Final Activity:

Using the One Health Research Translation Framework in Your Work

Activity Overview

- Purpose: To explore how you can use the One Health Research Translation Framework in your work to:
  - Promote research translation to address zoonotic disease challenges as part of your professional responsibilities
  - Build your professional One Health research translation network
- In this activity, you will:
  - Evaluate your role in research translation at your institution
  - Identify research translation opportunities that are relevant to your work
  - Assess communication pathways in your One Health network that could support research translation
- Activity output: preliminary action plan for promoting research translation to address One Health challenges in your work

Instructions

- Participants will split into small groups of 3-4 people.
- Refer to the **Participant Worksheet: Using the One Health Research Translation Framework in Your Work** in your Participant Packet.
  - This worksheet provides detailed instructions, questions for consideration during the activity, and space to record your notes.
- Participants will complete the activity within their small groups.
  - If you have questions about the purpose of a step or the meaning of questions in the worksheet, ask a facilitator for clarification.

Structure of Activity

Activity Step	Format	Time (minutes)
Step 1 | Evaluate your role in research translation	Individual assessment	5-10
Step 2 | Identify opportunities for research translation in your work	Individual assessment	5 – 10
	Small group discussion	15 – 20
Step 3 | Assess communication pathways in your One Health networks	Individual assessment	5 – 10
	Small group discussion	15 – 20
Step 4 | Develop preliminary action plan for promoting research translation in your work	Individual assessment	15-20

Step 1

Activity Step	Format	Time (minutes)
Step 1 | **Evaluate your role in research translation**	Individual assessment	5-10

- Write answers to the worksheet questions on **pages 55-56**.
- Think about research translation activities that **are** or **could be** part of your professional responsibilities.

Step 2

Activity Step	Format	Time (minutes)
Step 2 | **Identify opportunities for research translation in your work**	Individual assessment	5 – 10
	Small group discussion	15 – 20

Individual assessment

- Write answers to the questions in the **left** column of the worksheet on **pages 57-58**.
- Answer **either** the questions for **researchers (page 57**) or **policymakers (page 58**), depending on your experience, roles, and responsibilities.

Small group discussion

- Discuss your answers to the individual assessment with your small group.
- Use the questions in the **right** column to guide your discussion.
- Write comments from the discussion in the notes section on the **right**.

Step 3

Activity Step	Format	Time (minutes)
Step 3 | **Assess communication pathways in your One Health networks**	Individual assessment	5 – 10
	Small group discussion	15 – 20

Individual assessment

- Write answers to the questions in the **left** column of the worksheet on **pages 59-60**.
- Answer **both** sets of questions before small group discussion.

Small group discussion

- Discuss your answers to both sets of individual assessment questions with your small group.
- Use the questions in the **right** column to guide your discussion
- Write comments from the discussion in the notes section on the **right**.

Step 4

Activity Step	Format	Time (minutes)
Step 4 | **Develop preliminary action plan for promoting research translation in your work**	Individual assessment	15-20

- Write answers to the questions on the worksheet on **pages 61-62**.
- These questions require you to evaluate, synthesize and prioritize ideas and discussion from Steps 1 – 3 of this activity.
- Also draw from your experience in the case study exercises and communication pathways mapping activity.