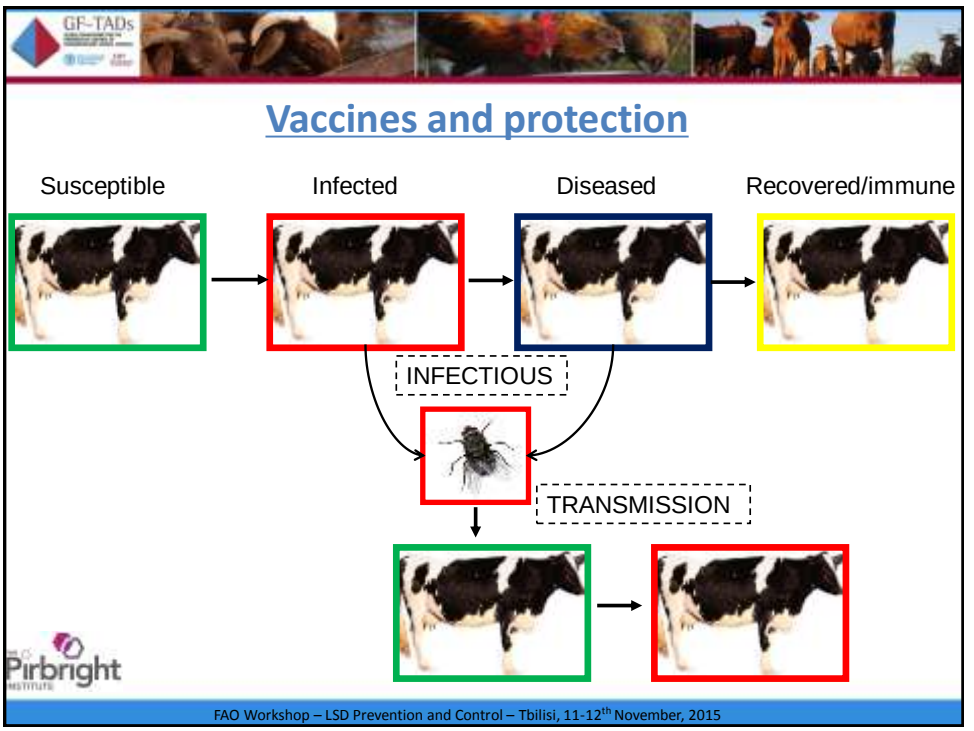
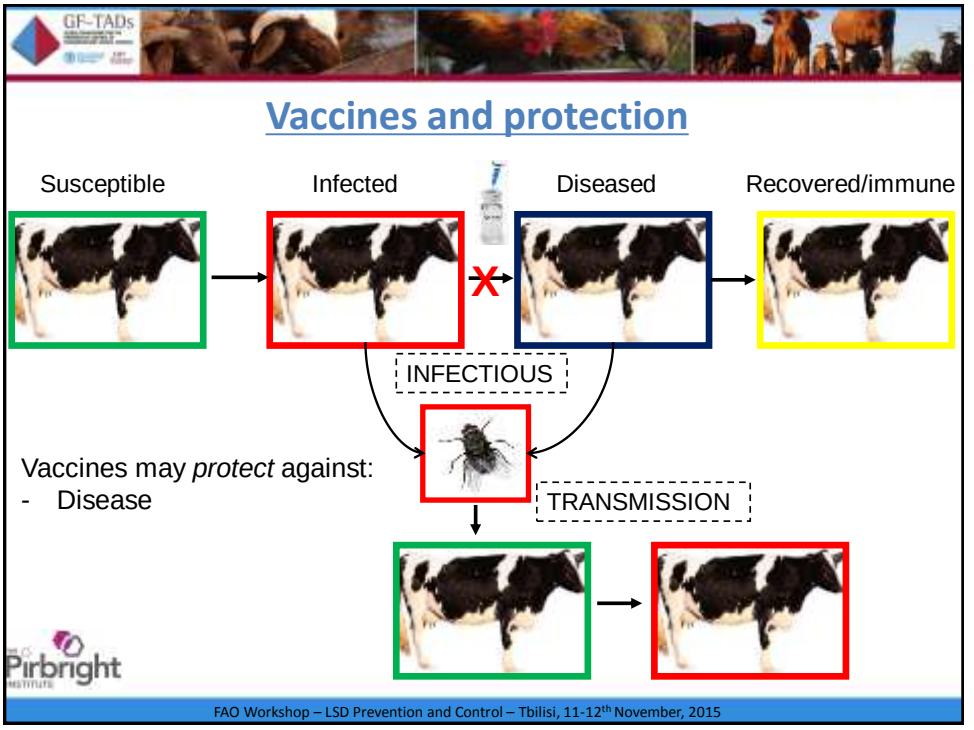
Role of vaccination and the evaluation of LSD control programmes

Dr Nick Lyons

FAO Workshop: LSD prevention and control
Tbilisi, Georgia, 11th November 2015

The Pirbright Institute




GF-TADs
Vaccines and protection
Susceptible
Infected
Diseased
Recovered/immune
INFECTIOUS
Vaccines may *protect* against:
- Disease
TRANSMISSION
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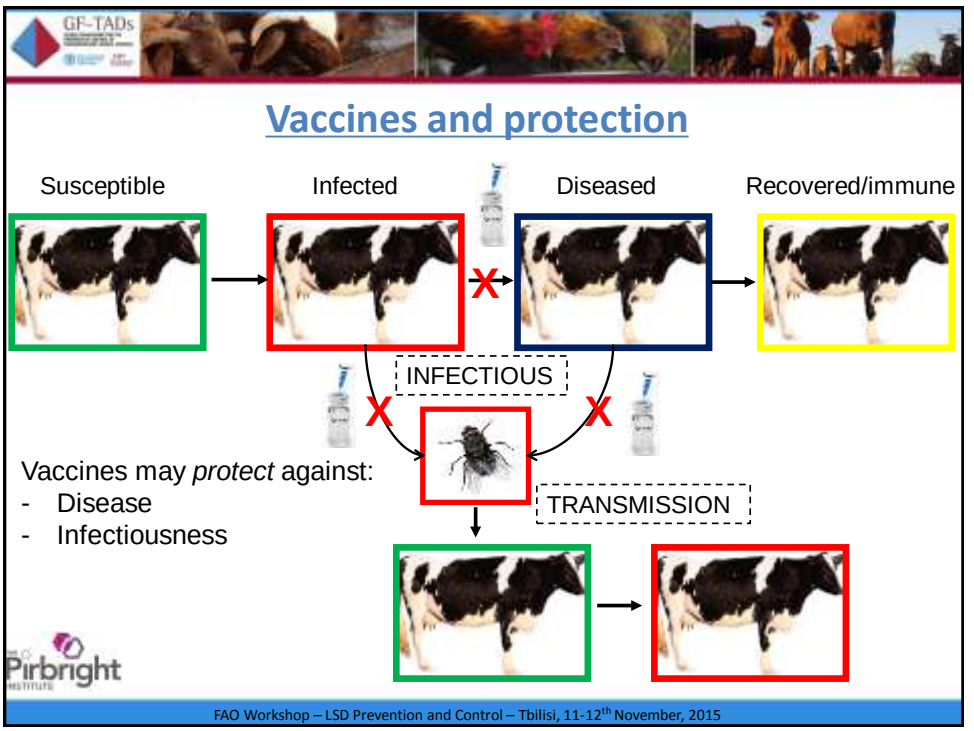
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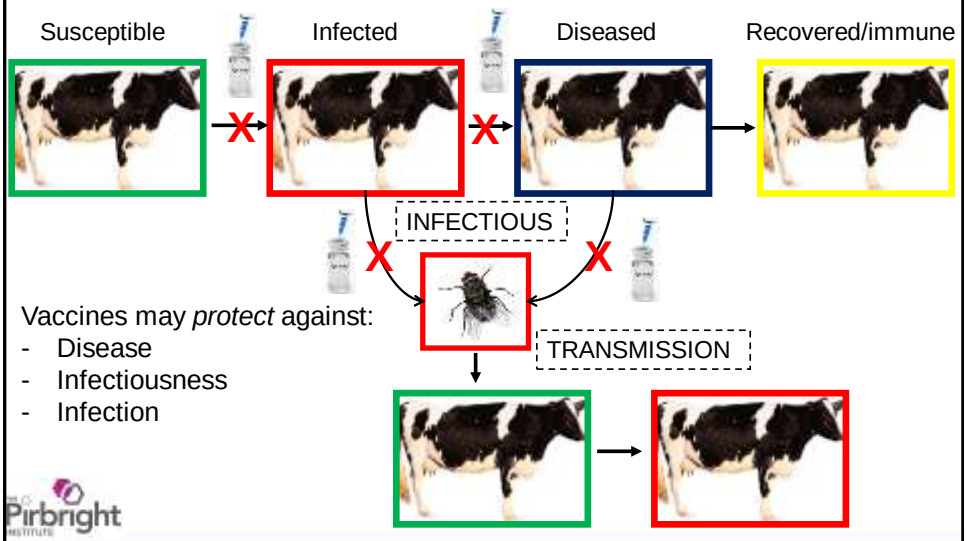
Vaccines and protection



Vaccines may *protect* against:
- Disease
- Infectiousness
- Infection

Vaccines and protection

- Vaccines may protect against → Disease, Infection, Infectiousness
- Examples: Polio – OPV vs IPV
  Tuberculosis – BCG
  FMD – killed vaccines

- Protective effects are not necessarily absolute…..
- Animals that have less severe disease may be less infectious…

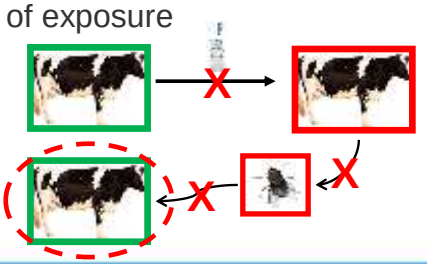
Direct versus *Indirect* protection

Direct protection – does the vaccine protect the individual that is vaccinated

Direct versus *Indirect* protection

Direct protection – does the vaccine protect the individual that is vaccinated

Indirect protection – does vaccination protect those that are not vaccinated due to reduced transmission in whole population and so reduced risk of exposure



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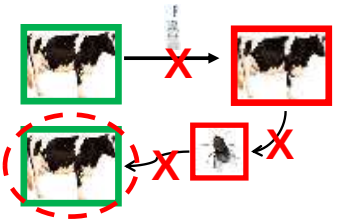
Direct versus *Indirect* protection

- **Indirect protection** – reduced disease in unvaccinated individuals due to reduced transmission in whole population reducing the risk of exposure



- So called **"herd effect"**
- Vaccine must reduce infectiousness
- These combined effects inform our understanding of the "herd immunity threshold" (i.e. the coverage needed to control infection)

Herd immunity threshold

- What level of **vaccine coverage** is required to control (and possibly eliminate) infection?
- Depends on the **force of infection** (i.e. rate of transmission) within a population which determines Rn (the **effective reproduction number**)
- This will vary ***between*** and ***within*** populations
- High transmission areas (**risk hotspots**) need higher vaccination coverage so need to be identified and targetted

Vaccine evaluation – *efficacy* versus *effectiveness*

- Important to have consistent definitions to evaluate vaccines

Vaccine efficacy = 1 – Incidence in vaccinated population / Incidence in unvaccinated population

1. Performed under ideal conditions
2. Assumes equal exposure risk of vaccinated and unvaccinated groups
3. Usually through a randomised controlled trial

Vaccine *efficacy* versus *effectiveness*

Vaccine effectiveness = 1 – Incidence in vaccinated population / Incidence in unvaccinated population

1. Performed under field conditions
2. Assumes equal exposure risk of vaccinated and unvaccinated groups
3. Usually by observational studies (and so need to adjust for exposure risk in analysis
4. Usually lower than the vaccine efficacy

- ***Addresses the question*** - how effective is your vaccination policy? (Rather than how efficacious is the vaccine…)

Study designs for vaccine effectiveness

- There are three broad types of study design all with their strengths and weaknesses
  - Cohort study
  - Case-control study
  - Ecological study ("screening method")
- The choice depends on a number of issues including:-
  - Disease epidemiology and expected incidence
  - Availability of records
  - Availability of resources

Vaccine effectiveness – example from Ethiopia

		Vaccination	
		Yes	No
Disease	Yes	274 (16.2%)	23 (25.0%)
	No	1413 (83.8%)	69 (75.0%)
		1687	92

Unpublished data used with permission from Dr Getachew Gari, NAHDIC

Incidence in vaccinated = 274/1687 = 16.2%

Incidence in unvaccinated = 23/92 = 25.0%

Vaccine effectiveness = 1 – (16.2/25.0)
= 1 – 0.65
= 0.35 or 35% (95%CI 3-56%)

Vaccine effectiveness – example from Ethiopia

	Vaccination	
	Yes	No

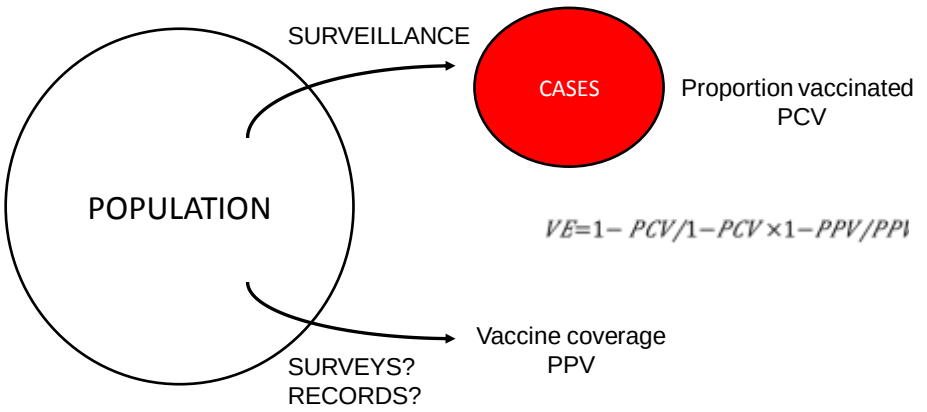
Vaccine effectiveness will often vary in different settings

This estimate is UNADJUSTED for confounders such as age, number of lifetime doses, and previous disease

Vaccine effectiveness = 1 – (16.2/25.0)
= 1 – 0.65
= 0.35 or 35% (95%CI 3-56%)

"Rapid screening method"

("case population" study)



Need the proportion of cases vaccinated (PCV) and the vaccine coverage (PPV)

Effectiveness studies – a few key points

- Confounders - for observational studies it is essential to adjust for exposure risk and previous disease (i.e. age)
- Selection bias – how are areas/farms chosen in the analysis
- Ecological studies - Comparing groups or regions is complicated as it is difficult to say all farms are at equal exposure risk…unless this is adjusted for in the analysis
- Vaccines doses – should consider the total number of lifetime doses, and the timing of the last dose
- Important to consider the impact of maternal immunity

Specific issues with LSD vaccination strategies and evaluation

- **Poor challenge model** (only 50-60% of unvaccinated control animals get disease)
- High level of **subclinical infection**
- **Limited field data** reported for LSD
- Lack of **serology** and no serological correlates of protection
- Limited quantitative understanding of **risk factors** for targeted control measures (e.g. risk based vaccination)

Evaluating other interventions

- Is ***insect control*** a viable addition to vaccination?
- The effectiveness of different interventions for insect contro is likely to be highly variable between different settings depending on:
  - Vector types present
  - Density of different vectors
  - Resistance to insecticides
  - Prevalence of LSDV
- No evidence from field studies of an effect
- Observational studies (for example a cross-sectional survey) would be a good place to start generating evidence

Summary

- Vaccination may protect against disease, infection and infectiousness (all to varying degrees)
- Vaccine effectiveness studies tell us about the performance of a vaccination policy (this is not necessarily expensive to do but should be done using rigorous and repeatable epidemiological methods)
- There is a limited understanding to many aspects of LSD:
  - This limits our capacity for control
  - There is a great need for further research in experimental and field settings

Thank you for your attention
Any questions?

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