Economic Evaluation of Outbreak Responses of Pertussis, Tuberculosis and Fungal Meningitis in New River Valley, Virginia

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Protecting You and Your Environment
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Conflict of interest: None

- We declare that we have no conflict of interest, and we comply with the American Public Health Association Conflict of Interest and Commercial Support Guidelines.

Learning objectives

- Identify the costs and epidemiological benefits of outbreak responses of pertussis, tuberculosis and fungal meningitis in New River Valley, Virginia.
- Evaluate the incremental cost-effectiveness ratio for each of the disease outbreak responses.
- Compare the incremental cost-effectiveness ratios to prioritize the limited resources of the local health department among different interventions.

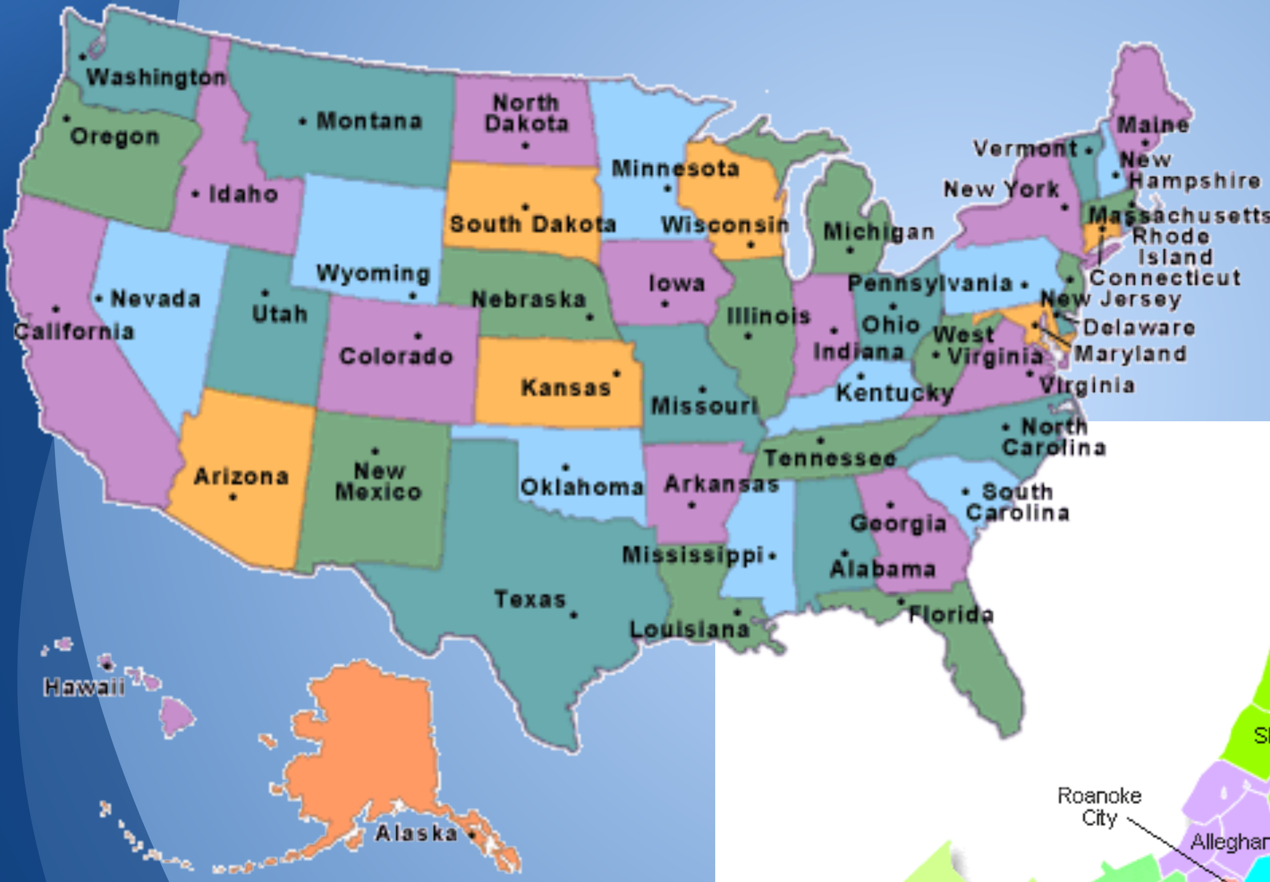
Study objective

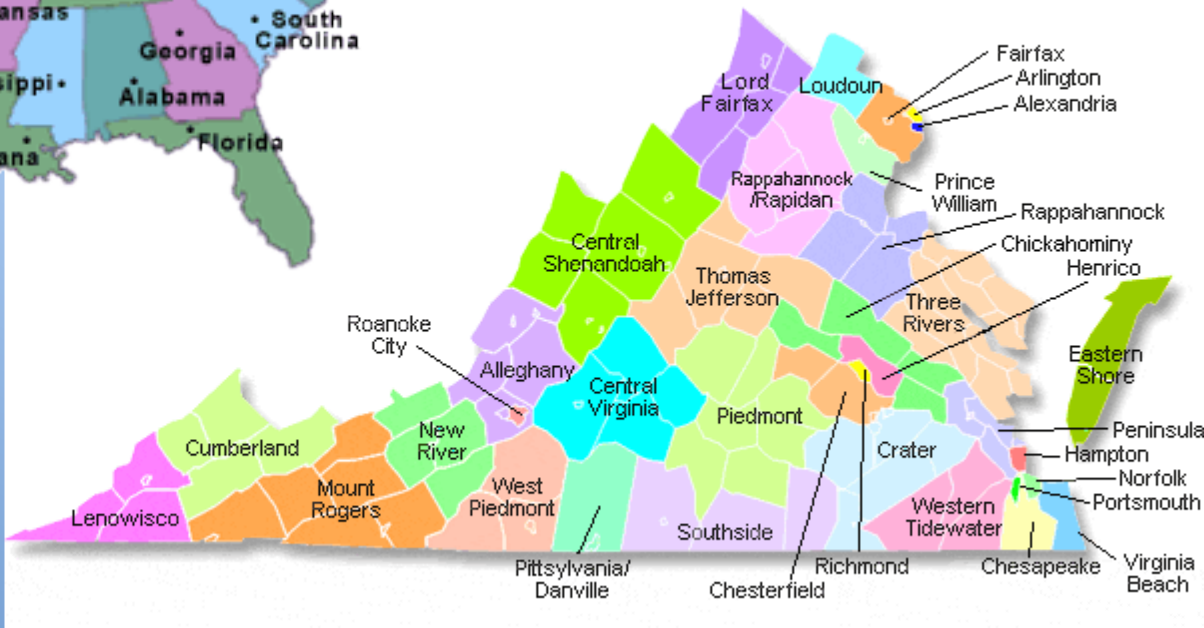
- To conduct cost-effectiveness analysis of infectious disease interventions and assist in prioritization of limited public health resources.

- New River Valley, Virginia, USA
  - Infectious disease outbreaks
    - Pertussis
    - Tuberculosis
    - Fungal meningitis

New River Valley

New River Health District



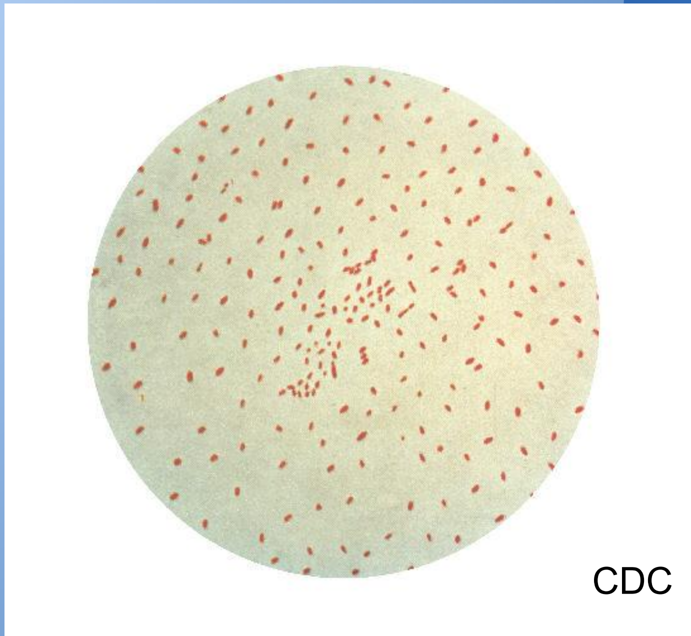


Pertussis

2011 outbreak

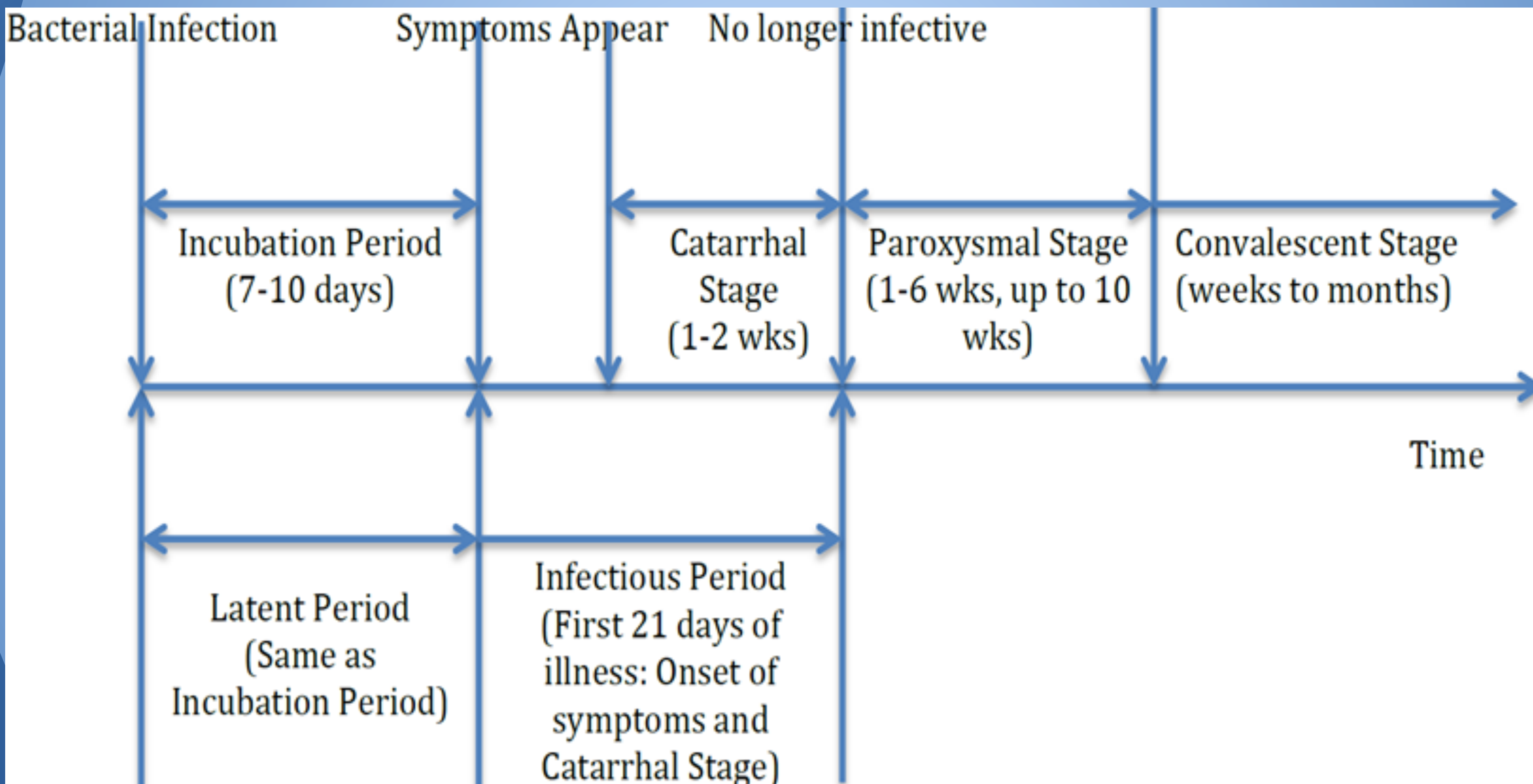
Pertussis

- Bacteria
  - bordetella pertussis
- Symptoms
  - whooping cough
  - fever
- Transmission
  - air-borne



CDC

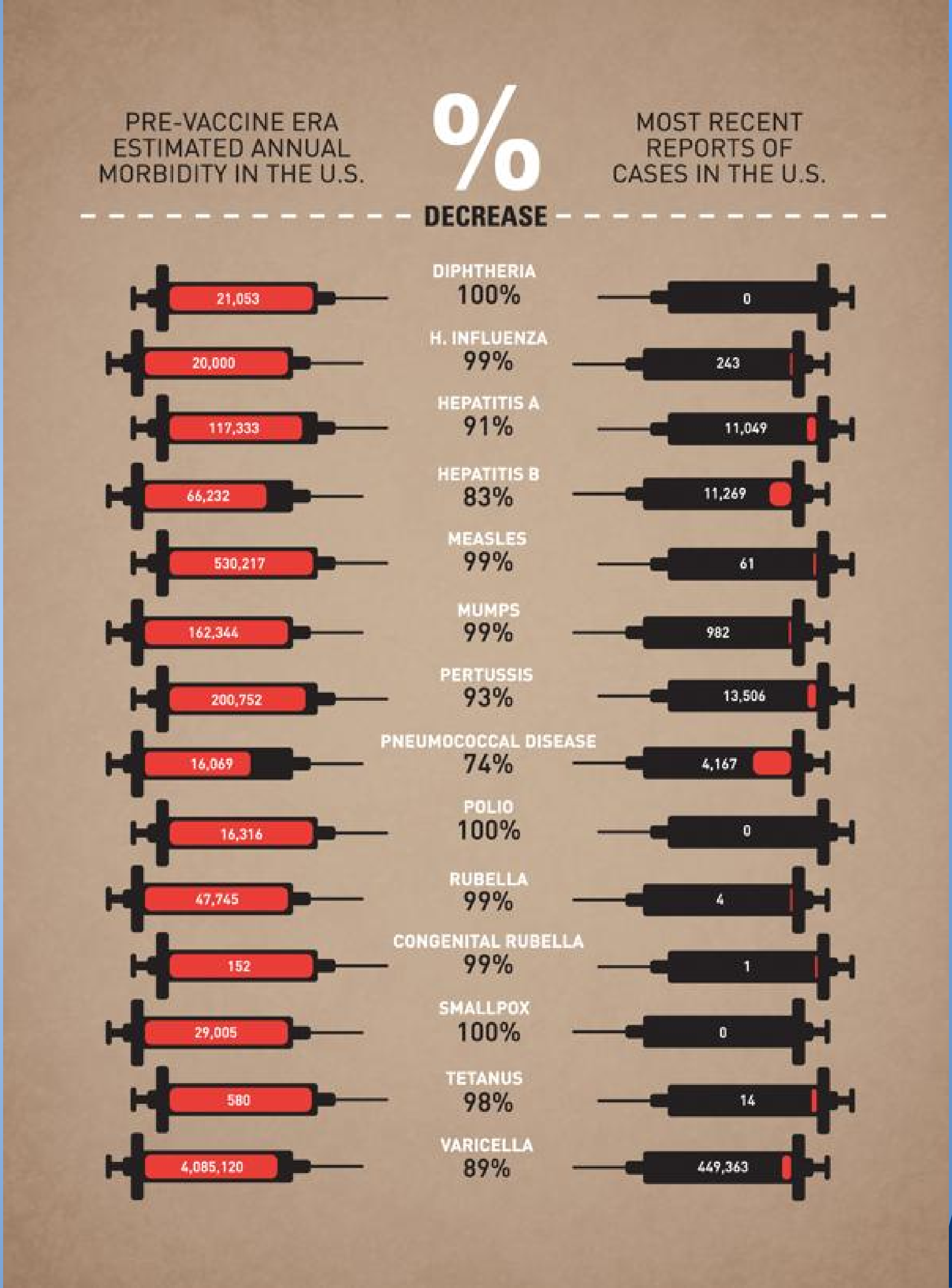
Pertussis infection timeline



Vaccine

- DTaP vaccine
  - Diptheria
  - Tetanus
  - Pertussis

Vaccines



PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY IN THE U.S.
% DECREASE
MOST RECENT REPORTS OF CASES IN THE U.S.
21,053
DIPHTHERIA 100%
0
20,000
H. INFLUENZA 99%
243
117,333
HEPATITIS A 91%
11,049
66,232
HEPATITIS B 83%
11,269
530,217
MEASLES 99%
61
162,344
MUMPS 99%
982
200,752
PERTUSSIS 93%
13,506
16,069
PNEUMOCOCCAL DISEASE 74%
4,167
16,316
POLIO 100%
0
47,745
RUBELLA 99%
4
152
CONGENITAL RUBELLA 99%
1
29,005
SMALLPOX 100%
0
580
TETANUS 98%
14
4,085,120
VARICELLA 89%
449,363

Basic reproduction rate - R_o

- R_o
  - Average number of secondary cases caused by the primary case in a susceptible population

- Epidemic
  - $R_o > 1$
- Endemic
  - $R_o = 1$
- Elimination
  - $R_o < 1$
- Eradication
  - $R_o = 0$

Effective reproductive rate

$R \sim R_o * (1 - \text{interventions impact})$

R and vaccination

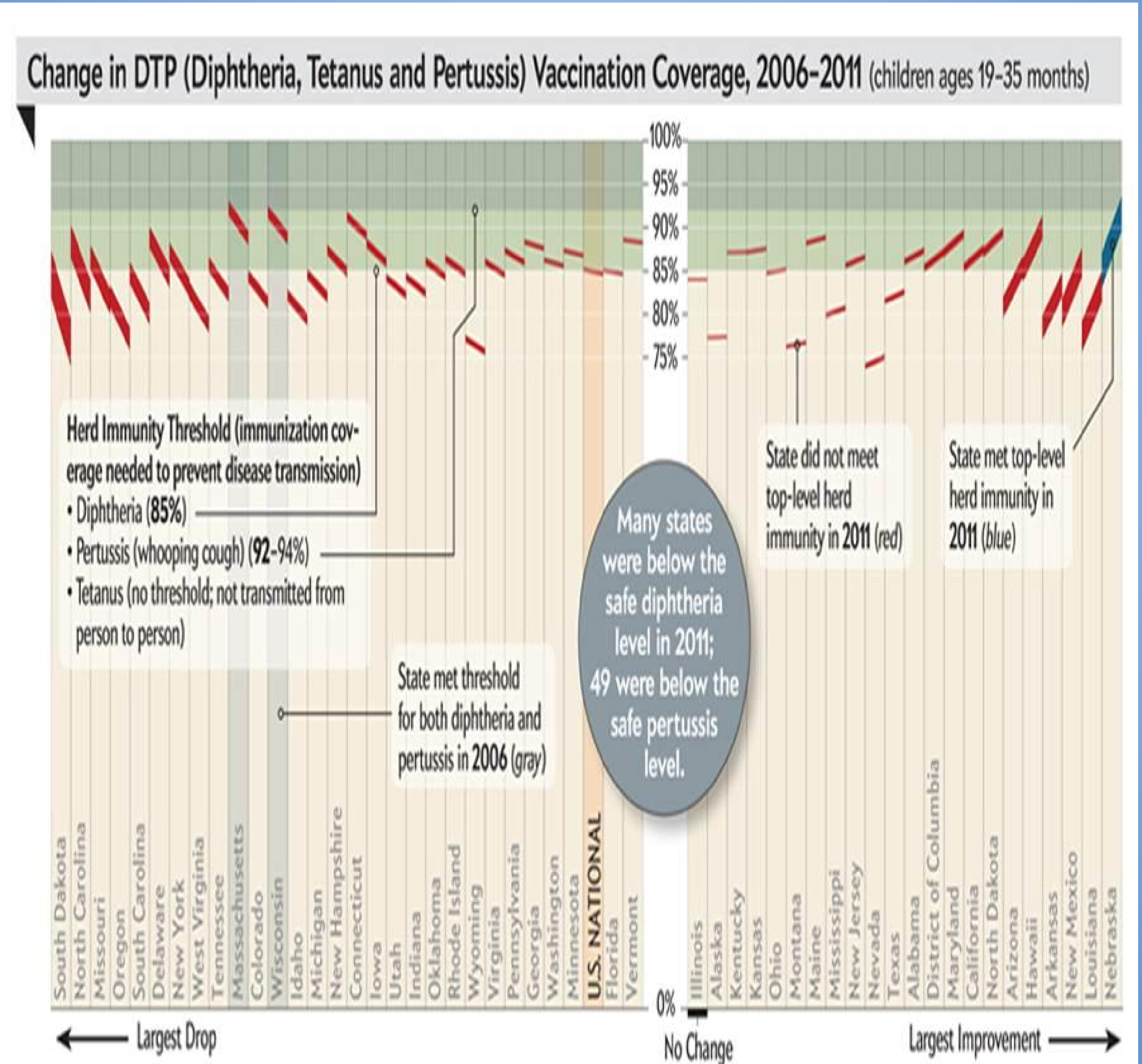
- Elimination
  - $R < 1$

  f = fraction of population that are vaccinated
  $(1 - f)$ = fraction of susceptible population

- For herd immunity
  - minimum fraction/threshold (f_h) of population to be vaccinated
    - $R = Ro\ (1 - f_h) < 1$
    - $f_h > 1 - (1 / R_o)$

- Pertussis
  - Herd immunity ~ (92-94)%

DTaP vaccine



Pertussis incidence - Virginia

Table 1. Pertussis Incidence in Virginia, 2007-2011			
Year	Number of Cases	Rate per 100,000	Number of Outbreaks
2007	128	1.65	6
2008	198	2.55	9
2009	222	2.82	10
2010	384	4.87	10
2011	399	5.06	13

Pertussis outbreak (2011) New River Valley

- 72 cases

- Prime impact
  - private school
    - vaccination rate ~ 0%

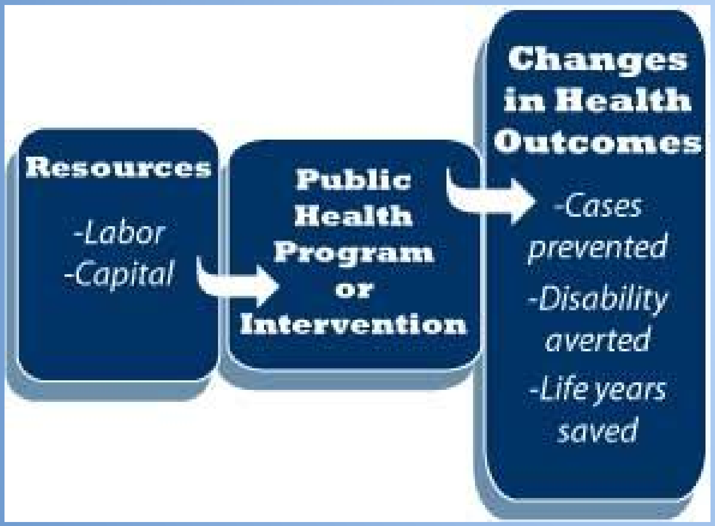
New River Health District Intervention

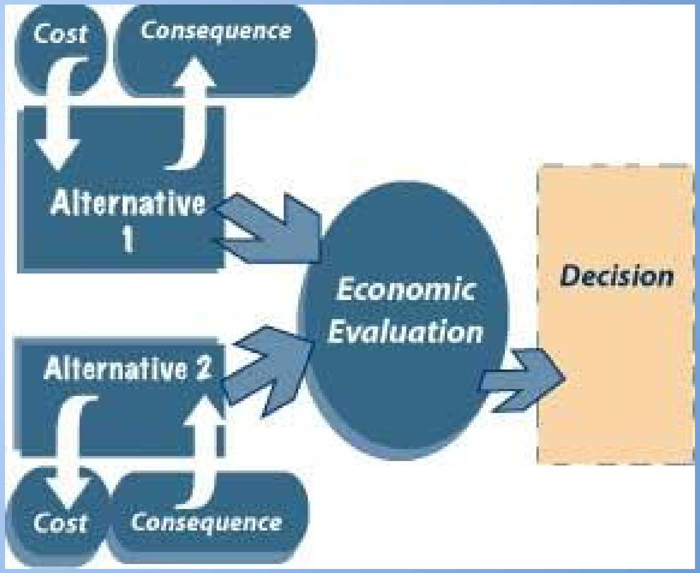
- Vaccination & health education campaigns

- Vaccine clinics
    - school
    - community

Economic evaluation

ICER - Incremental Cost-Effectiveness Ratio





$$ICER = \frac{\text{Cost}_{\text{new intervention}} - \text{Cost}_{\text{control}}}{\text{Effectiveness}_{\text{new intervention}} - \text{Effectiveness}_{\text{control}}}$$

Data sources (cost)

- New River Health District
  - employee hours
  - number of vaccines
  - clinical hours
- US Census Data
  - average salary of various positions
- CDC
  - vaccine price list archive
    - cost of vaccines

Intervention cost

Health Department Costs				
Position	# of	Hours	Hourly Salary + Benefits	Total
Epi	1	200	43.39	8678
Nurse Epi	1	16	35.97	575.52
Planner	1	24	48.71	1169.04
Director	1	45	95.7	4306.5
Clerical	1	26	31.07	807.82
Nurse Manager SR.	1	10	47.6	476
Public Health Nurse	1	12	39.38	472.56
Public Health Nurse Senior	1	16	41.34	661.44
Total State Personell Cost				**17146.88**
Clinical Costs				
Physician	6	122	81	9882
Physicians Assistant	1	24	41.54	996.96
Nurse practitioner	3	74	43.97	3253.78
Nurse	9	208	31.1	6468.80
Nursing Assistant	1	26	11.54	300.04
Medical Assistant	2	52	13.87	721.24
Clerk	9	198	13	2574
LPN	1	26	19.42	504.92
Total Physician cost				**24701.74**
Vaccine Costs				
		# of Vaccines	Individual Vaccine Cost	Total
School Clinic		47	26.26	1234.22
Public Clinic		40	26.26	1050.4
Total Vaccine Clinic Cost				**2284.62**

Summary				
Total State Personell				**17146.88**
Total Medical Cost				**24701.74**
Total Vaccine Clinic				**2284.62**
Total Overall Cost				**44133.24**

DALY, YLL, YLD

- ***DALY***
  - *D*isability *A*djusted *L*ife *Y*ear
- ***YLL***
  - *Y*ears of *L*ife *L*ost due to premature death
- ***YLD*** **(***Y*ears *L*ived with *D*isability)
  - Years of Life Lost due to Disability
    - population: (prevalence) * (disability weight)
      - individual: (years with disability) * (disability weight)

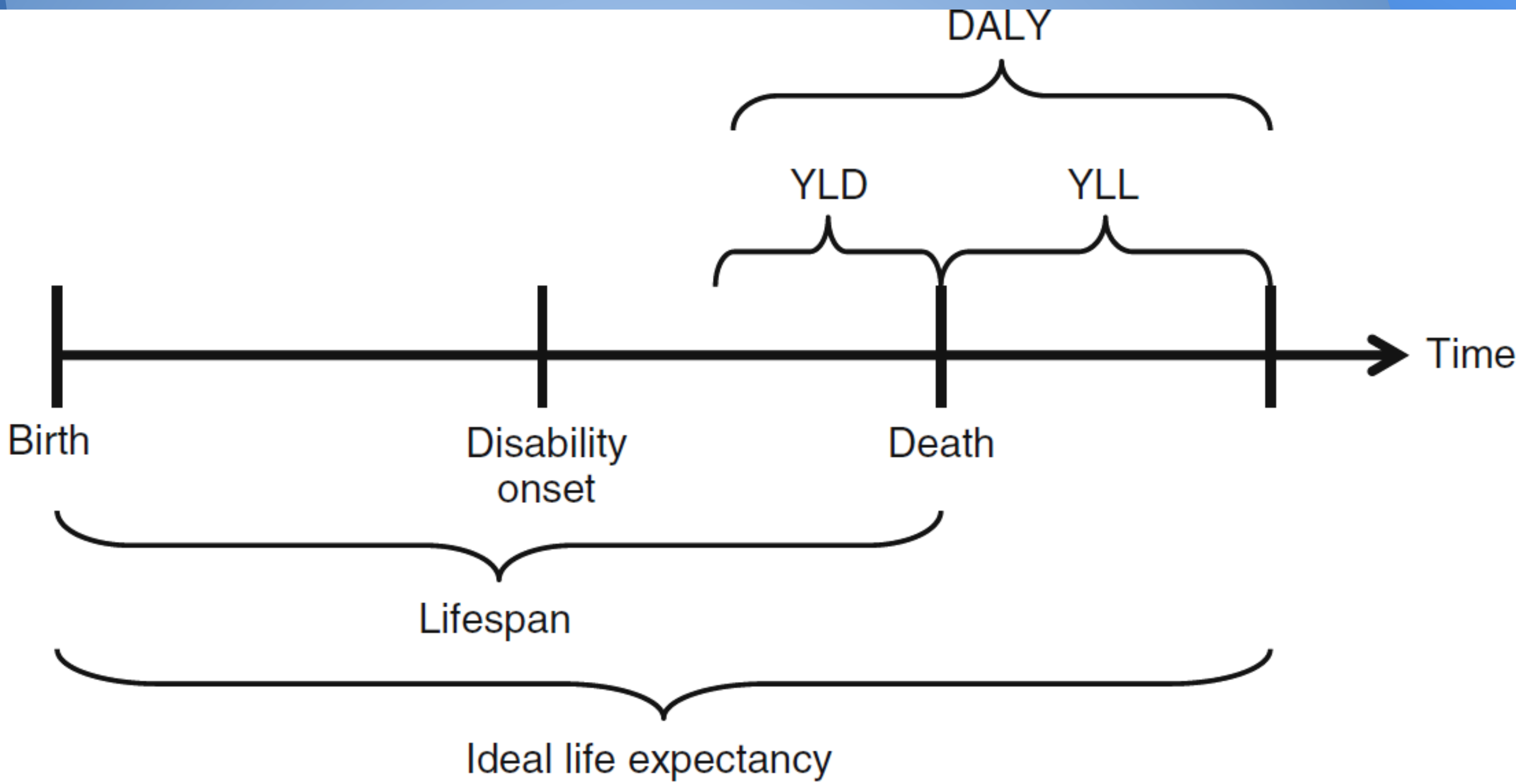
- ***DALY = YLL + YLD***

One DALY equals one lost year of healthy life.

DALY = YLL + YLD

DALY
Disability Adjusted Life Years is a measure of overall disease burden, expressed as the cumulative number of years lost due to ill-healh, disability or early death
=
YLD
Years Lived with Disability
+
YLL
Years of Life Lost
Healthy life
Disease or Disability
Early death
Expected life years

DALY = YLL + YLD



DALY = YLL + YLD
DALY: Disability Adjusted Life Years
YLL: Years of Life Lost due to premature death
YLD: Years of Life Lost due to Disability

DALY = YLL + YLD

LE	=	*Average Life Expectancy*	=	*78.7*
MR	=	*Mortality rate of pertussis worldwide*	=	*.001*
I	=	*Number of Confirmed Cases*	=	*72*
DW	=	*Pertussis Disability Weight*	=	*.137*

Calculation of YLL				
	Average Age	# of Confirmed Pertussis Cases	YL= # cases*(LE-Avg. Age)	YLL= [YL(Adults)*MR] + [YL(Children)*MR]
Adults	36.33	29	1228.73	4.28
Children	7.69	43	3053.43	

Calculation of YLD			
	Duration of illness (years)[L]	YLD= I*DW*L	$YLD_{Averted}$= $YLD_{Possible}$-YLD_{Actual}
YLD_{Actual}	.125	1.23	1.63
$YLD_{Possible}$	.29	2.86	

ICER

$$ICER = \frac{\text{Cost}_{\text{new intervention}} - \text{Cost}_{\text{control}}}{\text{Effectiveness}_{\text{new intervention}} - \text{Effectiveness}_{\text{control}}}$$

Incremental Cost-Effectiveness Ratio

$$\begin{aligned} DALY &= YLL + YLD \\ &= 4.28 + 1.63 \\ &= 5.91 \text{ DALYs} \end{aligned}$$

Cost of Intervention = $44,133.24
Cost of no Intervention = $0

ICER = $44133.24 / 5.91 DALYs

ICER = $7,468 / DALY averted

Tuberculosis

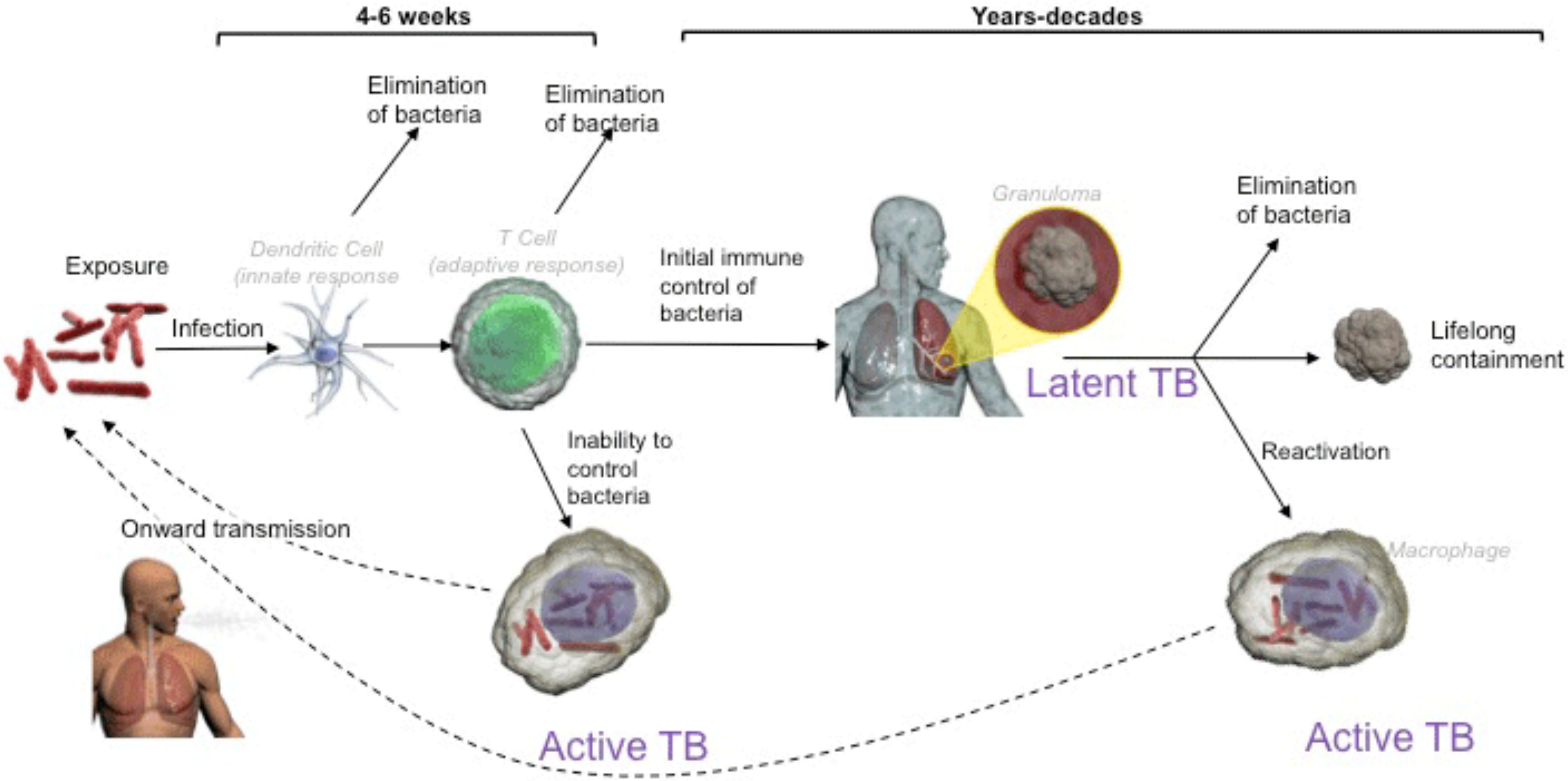
2011 outbreak

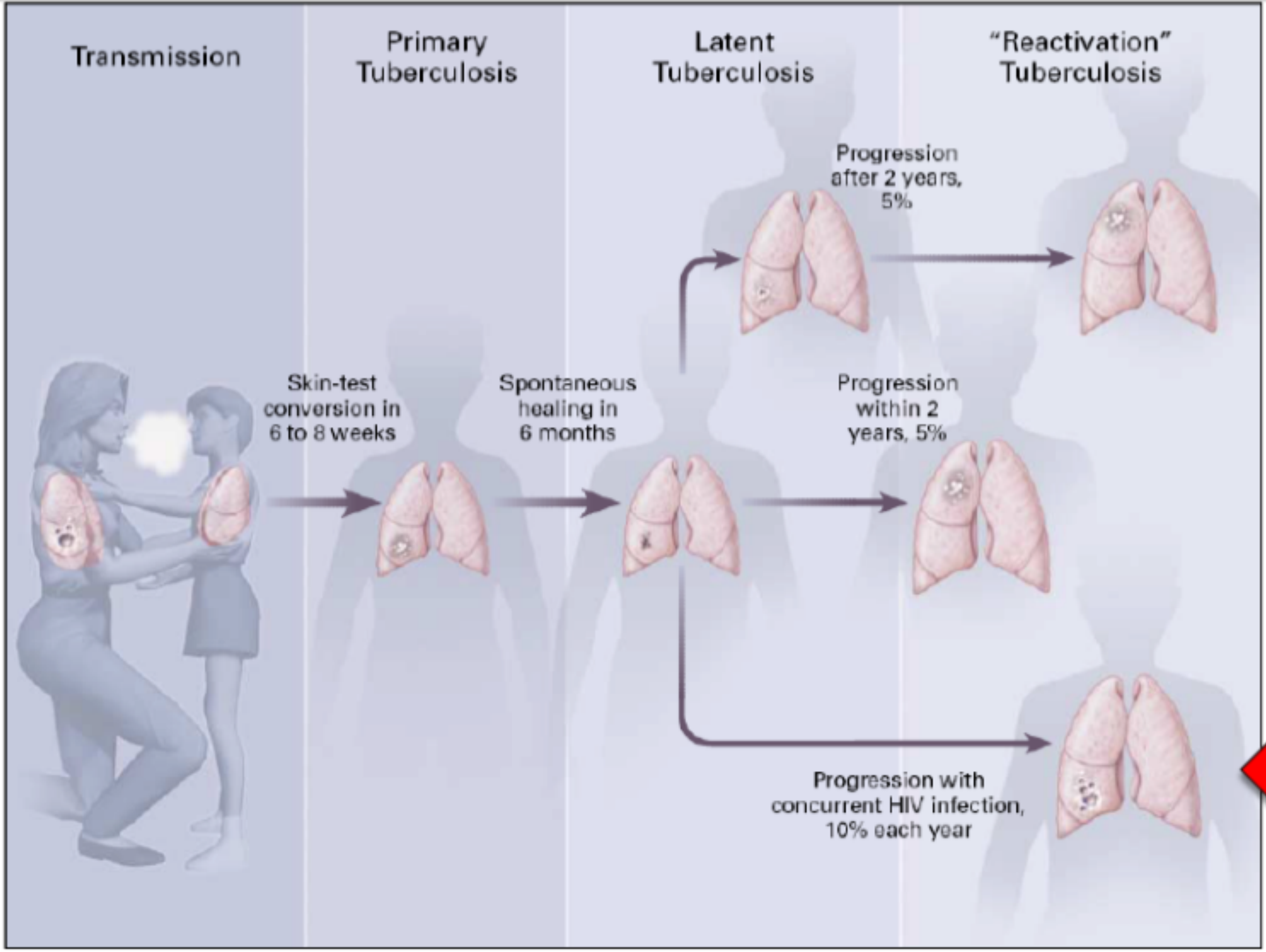
Tuberculosis

- Bacteria
  - Mycobacterium tuberculosis
- Symptoms
  - respiratory problems
- Transmission
  - air-borne

- Latent TB infection
  - ~ ⅓ global
    - asymptomatic
    - non-infectious
- Active TB disease
    - symptomatic
    - infectious

Natural history of TB infection





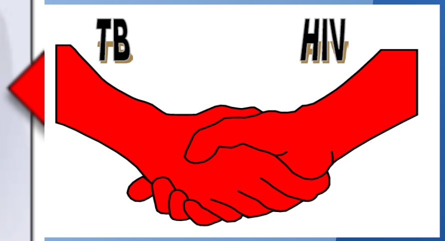


Figure 3. Transmission of Tuberculosis and Progression from Latent Infection to Reactivated Disease.

Among persons who are seronegative for the human immunodeficiency virus (HIV), approximately 30 percent of heavily exposed persons will become infected. In 5 percent of persons with latent infection, active disease will develop within two years, and in an additional 5 percent, progression to active disease will occur later. The rate of progression to active disease is dramatically increased among persons who are coinfected with HIV.

- P Small 2001

Tuberculosis outbreak (2011) New River Valley

- New River Valley jail
  - 1 case
    - 41 year old
    - 6 month history of TB symptoms
    - HIV+
  - admitted to hospital
    - TB and HIV drug treatment
    - isolation

New River Valley Regional Jail

- Inmate population
  - week day
    - 880
  - weekend
    - 930-940
- New inmates
  - ~ (50-60) / week
- Employees
  - ~ 200

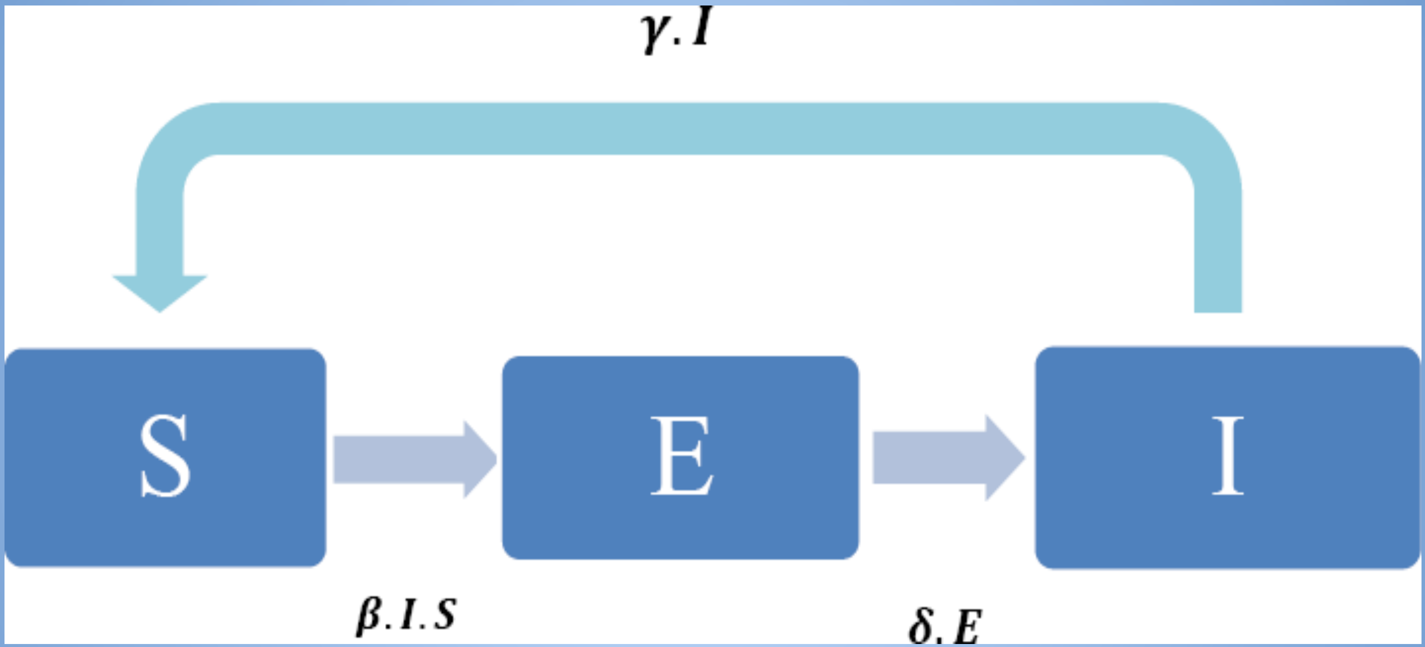
LTBI treatment - 3HP

- 3 month treatment
  - once a week
    - isoniazid
    - rifapentine
- DOT
  - directly observed therapy

LTBI treatment

- 35 inmates
  - PPT+
  - chest x-ray -
  - HIV -
- 28 inmates
  - 3HP treatment
  - 17 completed
- 21 staff
  - PPT+
  - chest x-ray -
  - HIV -
- 10 staff
  - 3HP treatment

SEIS (Susceptibles-Exposed-Infectious-Susceptibles) tuberculosis

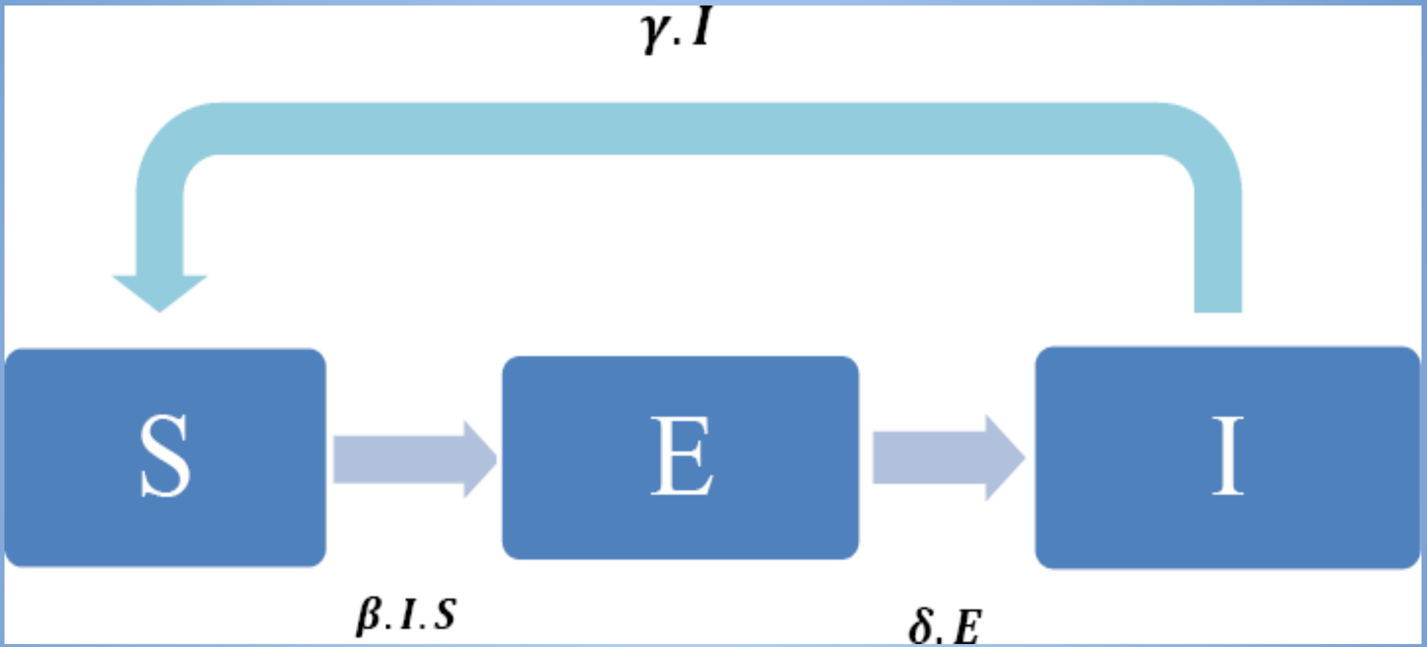


λ = Force of infection

$\lambda . S$

SEIS

tuberculosis

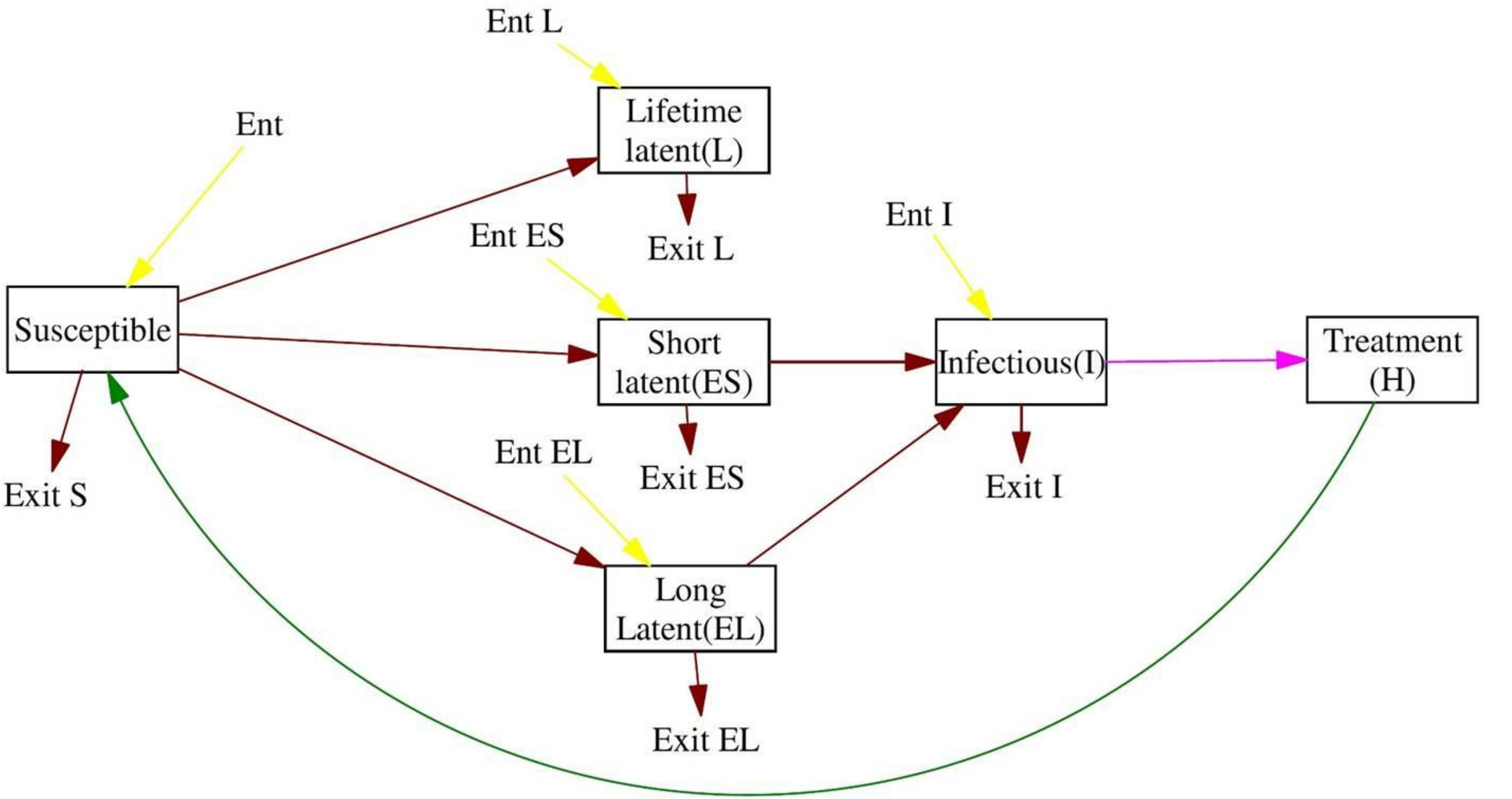


$$\frac{dS}{dt} = -\beta SI + \Upsilon I$$

$$\frac{dE}{dt} = +\beta SI - \delta E$$

$$\frac{dI}{dt} = +\delta E - \Upsilon I$$

TB transmission dynamics



SEIS epidemiological model
(Susceptibles-Exposed-Infectious-Susceptibles)

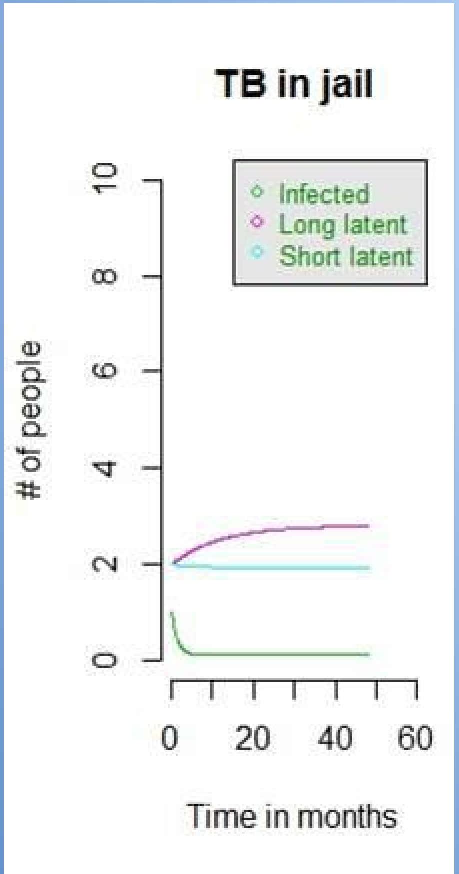
Parameter	Description
λ	Uninfected entry rate
β	Transmission rate
R_1	Exit rate
τ	1/(treatment period)
λ_{E_S}	Short latent entry rate
λ_{E_L}	Long latent entry rate
λ_L	Life time latent entry rate
R_2	1/(diagnosis delay)
P	Fraction of population that may develop active disease
f_S	1/(short latent period)
f_L	1/(long latent period)

Differential Equations

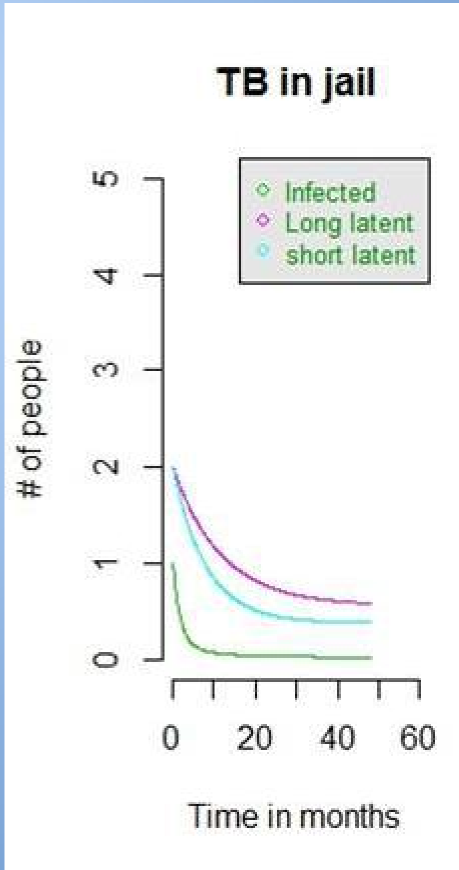
Susceptibles	$dS/dt = \lambda - \beta SI - R_1 S + \tau H$
Short Latent	$dE_S/dt = \lambda_{E_s} + (p/2)\,\beta SI - f_s E_S - R_1 E_S$
Long Latent	$dE_L/dt = \lambda_{E_L} + (p/2)\,\beta SI - f_L E_L - R_1 E_L$
Lifetime Latent	$dL/dt = \lambda_L + (1-p)\,\beta SI - R_1 L$
Infectious	$dI/dt = f_s E_S + f_L E_L - R_1 I - R_2 I$
Hospitalized	$dH/dt = R_2 I - \tau H$

Scenario simulations

- Base-case scenario
  - No TB pre-screening



- Intervention scenario
  - TB pre-screening

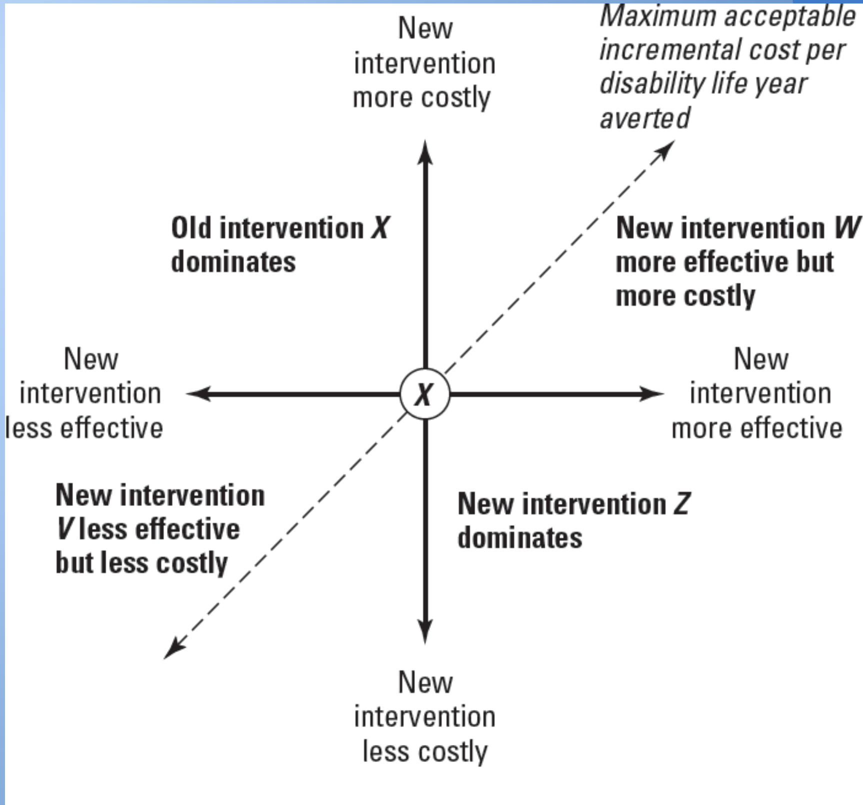


ICER

$$ICER = \frac{\text{Cost}_{\text{new intervention}} - \text{Cost}_{\text{control}}}{\text{Effectiveness}_{\text{new intervention}} - \text{Effectiveness}_{\text{control}}}$$

Incremental Cost-Effectiveness Ratio

ICER = - $15,461 / DALY averted (cost saving)



Comparison of Cost and of Effectiveness between Interventions: Conditions for Dominance

Fungal Meningitis

2012 outbreak

Fungal meningitis

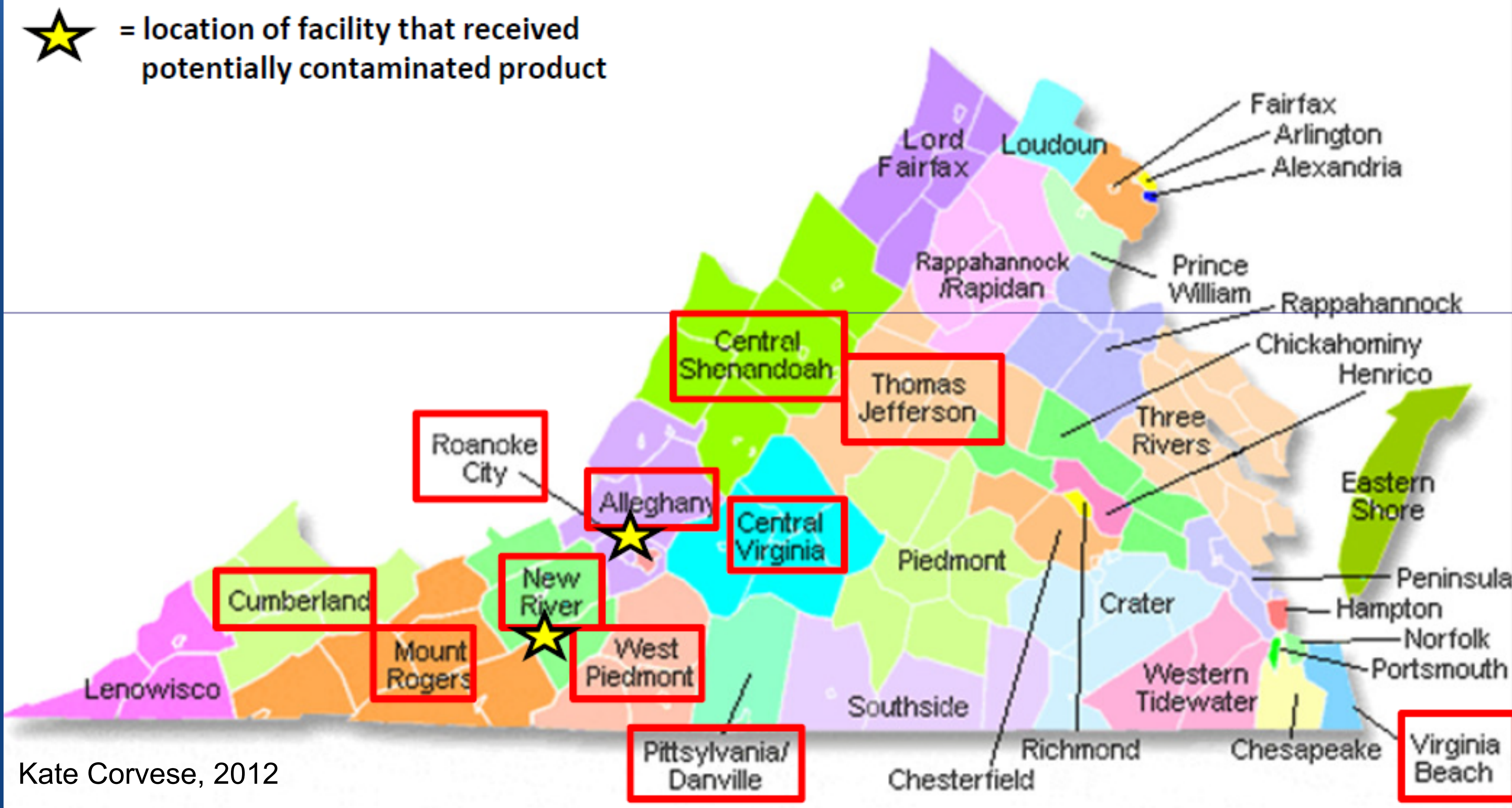
- Fungus
- Symptoms
  - headache
  - stiff neck
  - fatigue
- Transmission
  - non-contagious
- New England compounding center
  - contaminated lots of methylprednisolone acetate
    - used in epidural spinal injections

Fungal meningitis outbreak

- Health facilities
  - 23 states
    - received contaminated lots
  - 20 states
    - 751 cases
    - 64 deaths
- Virginia
  - 54 cases
  - 5 deaths

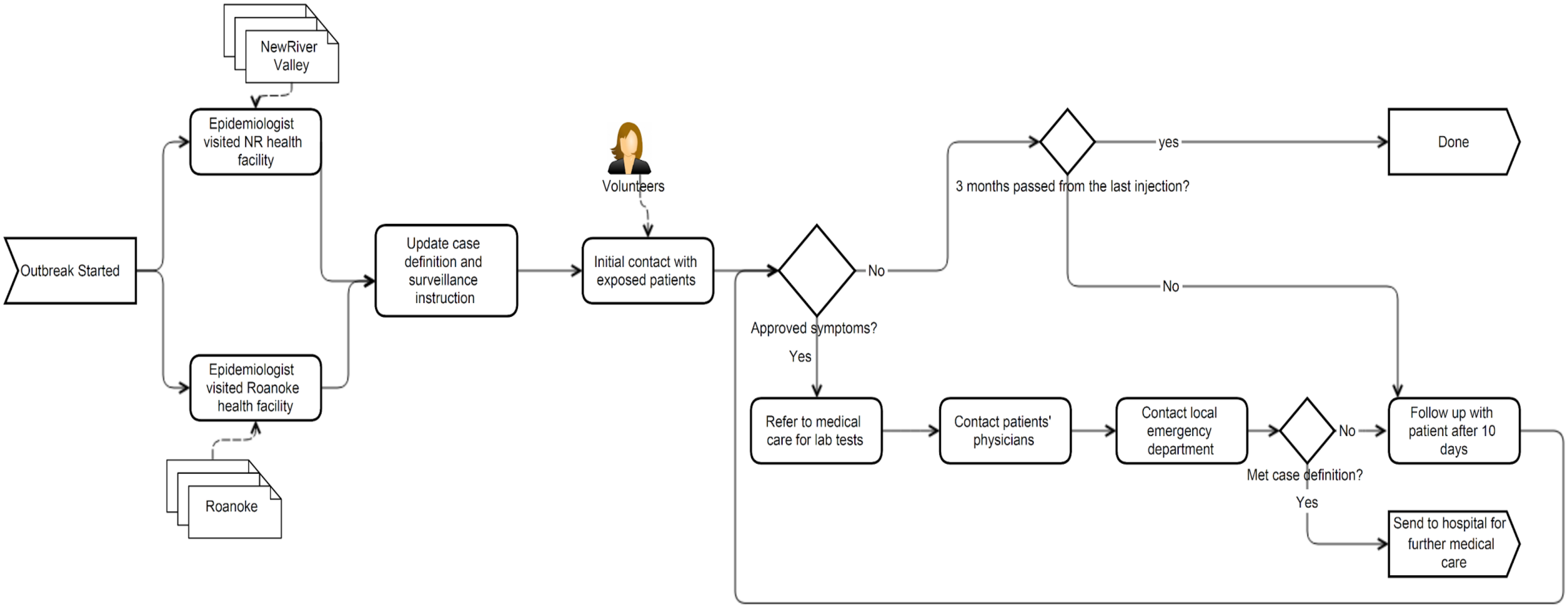
Fungal meningitis outbreak (2012) New River Valley

94 exposed residents

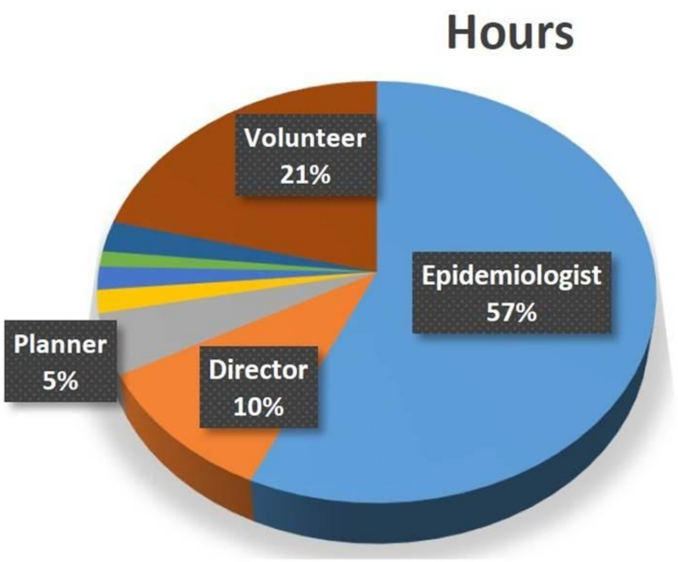


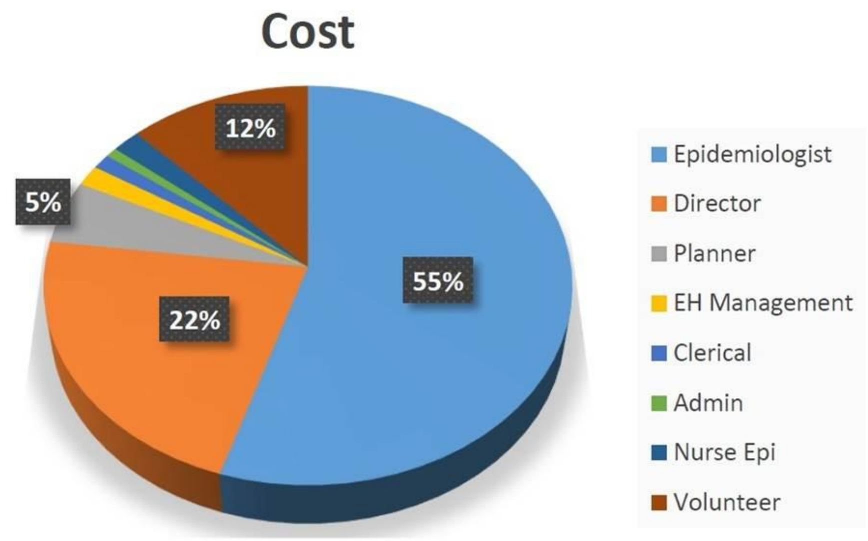
Kate Corvese, 2012

Surveillance process



Time & costs


Hours
Volunteer 21%
Epidemiologist 57%
Planner 5%
Director 10%


Cost
12%
5%
55%
22%
Epidemiologist
Director
Planner
EH Management
Clerical
Admin
Nurse Epi
Volunteer

ICER

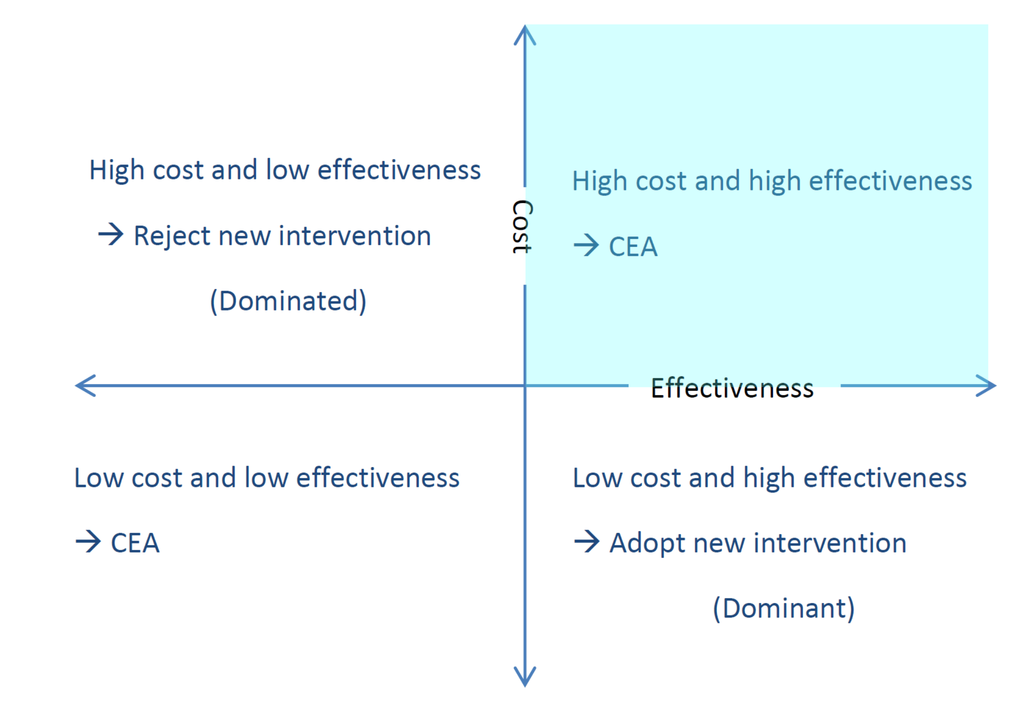
$$ICER = \frac{Cost_{new\ intervention} - Cost_{control}}{Effectiveness_{new\ intervention} - Effectiveness_{control}}$$

Incremental Cost-Effectiveness Ratio

DALY = *100.52 DALYs averted*

Cost of Intervention = *$30,492*

ICER = $303 / DALY averted



Pertussis
Tuberculosis
Fungal Meningitis

Comparative analysis of different interventions

Uniform metric: ICER = $/DALY averted

Prioritization of limited public health resources

Intervention	ICER
Pertussis	$7,468 / DALY averted
Tuberculosis	-$15,461/DALY averted (Cost saving)
Fungal meningitis	$303 / DALY averted

Cost-effectiveness thresholds

Table 15.4 International thresholds for cost-effectiveness

Organization/group	Cost-effectiveness thresholds	Reference
Australia*	Costs per LYG < AU $ 42,000 – 76,000 (costs per LYG < AU $ 42,000: reimbursement likely, costs per LYG > AU $ 76,000 reimbursement unlikely)	George et al. (2001)
The Netherlands	Costs < € 20.000 per QALY or LYG: cost-effective* Costs < € 80.000 per QALY: cost-effective**	Welte et al. (2004c); Raad voor de Volksgezondheid & Zorg (2007)
UK National Institute of Clinical Evidence (NICE)*	Costs per QALY < £ 20,000–30,000: cost-effective Costs per QALY < £ 45,000: cost-effective	Devlin and Parkin (2004); Appleby and Devlin, Parkin (2007)
US Institute of Medicine (IOM)**	Saves money and QALYs: most favorable Costs per QALY < US $ 10,000: more favorable Costs per QALY > US $ 10,000 and < 100.000: favorable Costs per QALY > US $ 100,000: less favorable	Institute of Medicine (2000)
World Health Organization (WHO)**	Costs per DALY < GDP per capita: highly cost-effective Costs per DALY = 1x – 3x GDP per capita: cost-effective Costs per DALY > 3x GDP per capita: not cost-effective	WHO (2008)
International and especially US decision analysts**	Costs per QALY or LYG < US $ 50.000: cost-effective	Grosse (2008)
US and British health economists**	Costs per LYG < US $ 60.000: cost-effective	Newhouse (1998)

* Thresholds derived from past decisions
** Officially stated thresholds
LYG = Life year gained
QALY = Quality-adjusted life year
GDP = Gross domestic product

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- APHA conference
  - Session organizers
  - Participants

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Thank you