Review of block 2: Analyses of seroprevalence data and their application to modelling control strategies

Solutions to exercises

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Introduction to Infectious Disease Modelling and its Applications
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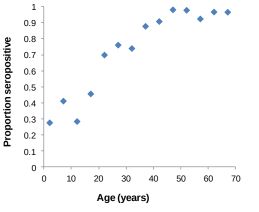
Q1. The following table and figure show data on the age-specific proportion of individuals who were seropositive for hepatitis A in country Z. The life expectancy in the population was about 70 years and the age distribution was rectangular.

Age mid point	Proportion positive	Age mid point	Proportion positive
2	0.278	37	0.879
7	0.413	42	0.909
12	0.286	47	0.982
17	0.458	52	0.979
22	0.7	57	0.925
27	0.762	62	0.968
32	0.741	67	0.967



Which of the following statements is incorrect?

a) The force of infection was probably age-dependent.

b) The force of infection was probably not age-dependent.

c) The average force of infection was about 20%/year.

d) Assuming that individuals mix randomly, 20-30% of the population was probably susceptible.

e) Assuming that individuals mix randomly, we would need to attain a vaccination coverage of at least 70-80% in the population to control transmission

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Which of the following statements is correct?

a) The force of infection was probably age-dependent.
b) The force of infection was probably not age-dependent.

Approach

1. Calculate -ln(observed proportion seronegative)
2. Plot -ln(observed proportion seronegative) against the age mid-point
3. If all the points fall on a straight line then the force of infection is probably not age-dependent; otherwise, it is probably age-dependent

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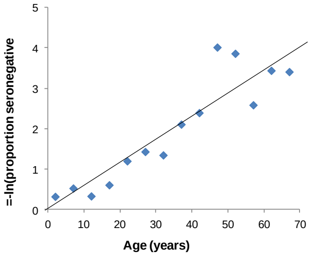
Calculating -ln(observed proportion seronegative) (1)

Age mid point	Proportion positive (p_a)	negative ($1-p_a$)	-LN(propn sero - negative) ($-\ln(1-p_a)$)	Age mid point	Proportion positive (p_a)	Negative ($1-p_a$)	-LN(propn sero-negative) ($-\ln(1-p_a)$)
2	0.278	0.722		37	0.879	0.121	
7	0.413	0.587		42	0.909	0.091	
12	0.286	0.714		47	0.982	0.018	
17	0.458	0.542		52	0.979	0.021	
22	0.7	0.3		57	0.925	0.075	
27	0.762	0.238		62	0.968	0.032	
32	0.741	0.259		67	0.967	0.033	

Calculating -ln(observed proportion seronegative) (2)

Age mid point	Proportion positive (p_a)	negative ($1-p_a$)	-LN(propn sero - negative) ($-\ln(1-p_a)$)	Age mid point	Proportion positive (p_a)	Negative ($1-p_a$)	-LN(propn sero-negative) ($-\ln(1-p_a)$)
2	0.278	0.722	0.32573	37	0.879	0.121	2.111965
7	0.413	0.587	0.53273	42	0.909	0.091	2.396896
12	0.286	0.714	0.336872	47	0.982	0.018	4.017384
17	0.458	0.542	0.612489	52	0.979	0.021	3.863233
22	0.7	0.3	1.203973	57	0.925	0.075	2.590267
27	0.762	0.238	1.435485	62	0.968	0.032	3.442019
32	0.741	0.259	1.350927	67	0.967	0.033	3.411248

Plot of -ln(observed proportion seronegative) for hepatitis in country Z)



Which of the following statements is correct?

a) The force of infection was probably age-dependent.
b) The force of infection was probably not age-dependent.

Is the following statement correct?

c) The average force of infection was about 20%/year.

Answer (APPROACH 1)
The force of infection is approximately equal to the gradient of the line passing through the points of -ln(observed proportion seronegative)

The gradient of the line ≈2/35 , i.e. the line has gone up by 2 units by age 35 years
∴ The force of infection ≈2/35 ≈0.057 or 5.7%/year

Therefore, statement c) is incorrect

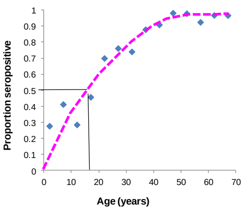
Is the following statement correct?

c) The average force of infection was about 20%/year.

Answer (APPROACH 2)
The force of infection is approximately equal to 1/(average age at infection)

The median age at infection is approximately 17 years

- to see this read off the age by which 50% are seropositive, drawing a curve (if necessary) through the observed seropositive to guide your estimate



∴ The force of infection ≈1/17 ≈0.06 or 6%/year

Therefore, statement c) is incorrect

BUT…this estimate is approximate since the median age at infection is an approximation to the "average" statistic that we need; it is slightly less accurate than the estimate from approach 1

Is the following statement correct?

d) Assuming that individuals mix randomly, 20-30% of the population was probably susceptible.

Answer
The force of infection is about 5.7%/year (depending on rounding)

⇒average age at infection ≈ 1/(force of infection)
≈ 1/0.057 ≈ 17.5 years

Assuming that the population has a rectangular age distribution and life expectancy of 70 years, means that the average proportion susceptible ≈ A/L ≈ 17.5/70 ≈ 0.25 or 25%

Therefore, statement d) is correct

Note: using A≈17 years (from approach 2) would have resulted in average proportion susceptible ≈ A/L ≈ 17/70 ≈ 0.24 or 24%

Is the following statement correct?

e) Assuming that individuals mix randomly, we would need to immunize at least 70-80% of the population to control transmission

Answer
To control transmission, we could need a vaccination coverage of above the herd immunity threshold = $1-1/R_0$

R_0 can be calculated from the equation R_0=1/average proportion susceptible

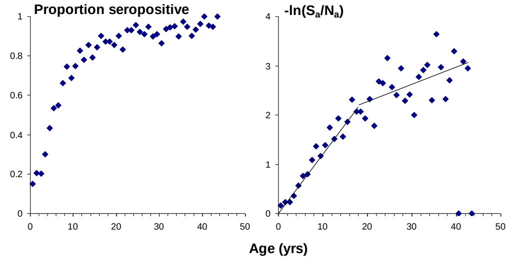
∴ $R_0 \approx 1/0.25 = 4$
∴ The herd immunity threshold $=1-1/4 \approx 0.75$ or 75%

Therefore, statement e) is correct

Which of the following statements is incorrect?

	True statement?	Correct answer
a) The force of infection was probably age-dependent.	✗	✓
b) The force of infection was probably not age-dependent.	✓	✗
c) The average force of infection was about 20%/year.	✗	✓
d) Assuming that individuals mix randomly, 20-30% of the population was probably susceptible.	✓	✗
e) Assuming that individuals mix randomly, we would need to immunize at least 70-80% of the population to control transmission	✓	✗

Exercise: What do the following figures suggest about the dependency of the force of infection on age?



Q2. Country Z has recently introduced rubella vaccination among very young children. If we assume that individuals mix randomly and that the vaccination coverage is below the herd immunity threshold, which of the following statements is likely to be true?

a) The average age at rubella infection is likely to increase.

b) The average age at rubella infection is likely to remain unchanged.

c) The overall proportion of the population that is susceptible may remain unchanged

d) The overall proportion of the population that is susceptible will decrease

e) The overall proportion of the population that is susceptible will increase

Q2. Country Z has recently introduced rubella vaccination among very young children. If we assume that individuals mix randomly and that the vaccination coverage is below the herd immunity threshold, which of the following statements is likely to be true?

a) The average age at rubella infection is likely to increase.

b) The average age at rubella infection is likely to remain unchanged.

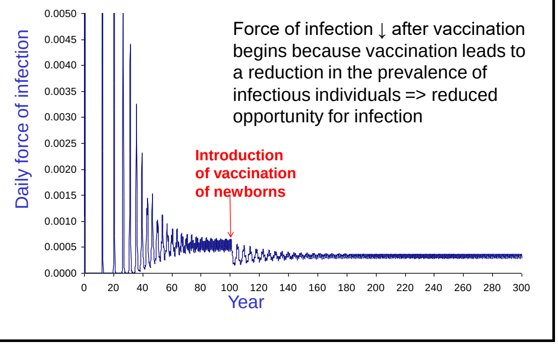
Answer

The force of infection (λ) decreases after the introduction of vaccination

Since $A \approx 1/\lambda$, if λ decreases, A increases

So a) is most likely to be correct

Model predictions of the effect of 40% vaccination coverage among newborns, introduced 100 years after the start of model simulations, on the force of infection in China



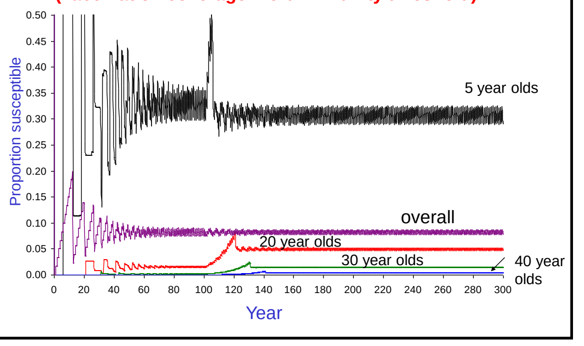
Q2. Country Z has recently introduced rubella vaccination among very young children. If we assume that individuals mix randomly and that the vaccination coverage is below the herd immunity threshold, which of the following statements is likely to be true?

c) The overall proportion of the population that is susceptible may remain unchanged

d) The overall proportion of the population that is susceptible will decrease

e) The overall proportion of the population that is susceptible will increase

Why does the overall proportion of individuals who are susceptible remain unchanged following the introduction of infant vaccination (vaccination coverage<herd immunity threshold)?



Why does the overall proportion of individuals who are susceptible remain unchanged following the introduction of infant vaccination (vaccination coverage<herd immunity threshold)?

Recall net reproduction number (R_n) is related to R_0 and proportion susceptible (s) through the equation:

$$R_n = R_0 s$$

If vaccination coverage < herd immunity threshold, the infection is still endemic, so

$$R_n = 1$$

Since $R_n = R_0 s = 1$, and R_0 is constant, this implies that

$$s = 1/R_0$$

∴ The overall proportion susceptible remains unchanged if the vaccination coverage is below the herd immunity threshold

Q2. Country Z has recently introduced rubella vaccination among very young children. If we assume that individuals mix randomly and that the vaccination coverage is below the herd immunity threshold, which of the following statements is likely to be true?

c) The overall proportion of the population that is susceptible may remain unchanged ✔

d) The overall proportion of the population that is susceptible will decrease ✘

e) The overall proportion of the population that is susceptible will increase ✘

Q2. Country Z has recently introduced rubella vaccination among very young children. If we assume that individuals mix randomly and that the vaccination coverage is below the herd immunity threshold, which of the following statements is likely to be true?

a) The average age at rubella infection is likely to increase. ✔

b) The average age at rubella infection is likely to remain unchanged. ✘

c) The overall proportion of the population that is susceptible may remain unchanged ✔

d) The overall proportion of the population that is susceptible will decrease ✘

e) The overall proportion of the population that is susceptible will increase ✘

Q3. The following WAIFW matrix describes contact between individuals in urban and rural areas. (Note that the letters u and r next to the rows and above the columns reflect urban and rural areas respectively.) Assuming that β_1 is not equal to β_2, which of the statements below is incorrect? (Note that there may be more than one incorrect answer).

$$\begin{array}{cc} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

Assuming that β_1 is not equal to β_2, which of the statements below is incorrect? (Note that there may be more than one incorrect answer).

$$\begin{array}{cc} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

a) Individuals in urban areas effectively contact each other at a different rate from the rate at which they effectively contact individuals in rural areas.

b) The rate at which individuals from rural areas contact each other is different from the rate at which individuals from urban areas contact each other.

c) Individuals from rural areas contact individuals from urban areas at the same rate at which they contact other individuals from rural areas.

d) The rate at which individuals from rural areas contact each other is equal to the rate at which individuals from urban areas contact each other.

e) Individuals from rural areas contact individuals from urban areas at a rate which is different from the rate at which they contact other individuals from rural areas.

$$\begin{array}{cc} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

a) Individuals in urban areas effectively contact each other at a different rate from the rate at which they effectively contact individuals in rural areas.

Answer:
Correct, because individuals in urban areas effectively contact each other at a rate β_1, which is different from the rate at which they effectively contact others from rural areas. which equals β_2

$$\begin{array}{c c} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

b) The rate at which individuals from rural areas contact each other is different from the rate at which individuals from urban areas contact each other.

Answer:
Correct, because individuals in rural areas effectively contact each other at a rate β_2, which is different from the rate at which individuals in urban areas effectively contact each other. which equals β_1

$$\begin{array}{c c} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

c) Individuals from rural areas contact individuals from urban areas at the same rate at which they contact other individuals from rural areas.

Answer:
Correct, because individuals in rural areas effectively contact urban residents at a rate β_2, which is equal to the rate at which they contact other individuals from rural areas

$$\begin{array}{c c} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

d) The rate at which individuals from rural areas contact each other is equal to the rate at which individuals from urban areas contact each other.

Answer:
Incorrect, because individuals in rural areas effectively contact each other at a rate β_2, which is different from the rate at which individuals in urban areas effectively contact each other, which equals β_1

$$\begin{array}{c c} & \begin{array}{cc} u & r \end{array} \\ \begin{array}{c} u \\ r \end{array} & \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \end{array}$$

e) Individuals from rural areas contact individuals from urban areas at a rate which is different from the rate at which they contact other individuals from rural areas.

Answer:
Incorrect, because individuals in rural areas effectively contact urban residents at a rate β_2, which is equal to the rate at which they contact other individuals from rural areas

Assuming that β_1 is not equal to β_2, which of the statements below is incorrect?

	True statement?	Correct answer?
a) Individuals in urban areas effectively contact each other at a different rate from the rate at which they effectively contact individuals in rural areas.	✓	✗
b) The rate at which individuals from rural areas contact each other is different from the rate at which individuals from urban areas contact each other.	✓	✗
c) Individuals from rural areas contact individuals from urban areas at the same rate at which they contact other individuals from rural areas.	✓	✗
d) The rate at which individuals from rural areas contact each other is equal to the rate at which individuals from urban areas contact each other.	✗	✓
e) Individuals from rural areas contact individuals from urban areas at a rate which is different from the rate at which they contact other individuals from rural areas.	✗	✓

Q4. The following is the Next Generation Matrix relating to an infection that is transmitted between children and adults, in population Y. Children and adults are denoted by the letters c and a respectively. Which of the following statements is correct?

$$\begin{array}{c c} & \begin{array}{cc} c & a \end{array} \\ \begin{array}{c} c \\ a \end{array} & \begin{pmatrix} 2 & 1 \\ 1 & 2 \end{pmatrix} \end{array}$$

a) Each adult leads to fewer infections in adults than they do in children.
b) Each adult leads to more infections in adults than they do in children.
c) The basic reproduction number is 2
d) The basic reproduction number is 1
e) The basic reproduction number 6

$$\begin{array}{c|cc} & c & a \\ \hline c & 2 & 1 \\ a & 1 & 2 \end{array}$$

a) Each adult leads to fewer infections in adults than they do in children.
b) Each adult leads to more infections in adults than they do in children.

Answer
Each adult leads to 1 infection in children and to 2 infections in adults

$\therefore$b) is correct

$$\begin{array}{c|cc} & c & a \\ \hline c & 2 & 1 \\ a & 1 & 2 \end{array}$$

c) The basic reproduction number is 2
d) The basic reproduction number is 1
e) The basic reproduction number 6

Answer
Each adult leads to 1 infection in children and to 2 infections in adults , i.e, 3 infections in total
Each child leads to 2 infections in children and to 1 infection in adults , i.e, 3 infections in total
$\therefore$ $R_0=3$

$\therefore$c), d) and e) are incorrect

Q4. The following is the Next Generation Matrix relating to an infection that is transmitted between children and adults, in population Y. Children and adults are denoted by the letters c and a respectively. Which of the following statements is correct?

$$\begin{array}{c|cc} & c & a \\ \hline c & 2 & 1 \\ a & 1 & 2 \end{array}$$

a) Each adult leads to fewer infections in adults than they do in children.
b) Each adult leads to more infections in adults than they do in children.
c) The basic reproduction number is 2
d) The basic reproduction number is 1
e) The basic reproduction number 6

Q5. The following is the Next Generation Matrix for an infection which is transmitted from vectors to humans and from humans to vectors, but cannot be transmitted from humans to humans or from a vector to another vector.

$$\begin{array}{c|cc} & v & h \\ \hline v & 0 & 3 \\ h & 1.5 & 0 \end{array}$$

Which of the following is incorrect?
a) The basic reproduction number is approximately 2.12.

b) One of the following statements is correct:
i) The fraction of the typical infectious "person" that is a vector is approximately 0.59. ii) The basic reproduction number is 4.5.

c) If vaccination is introduced just among humans, with two thirds of humans becoming completely protected against infection, the infection will eventually disappear among humans.

d) If vaccination is introduced just among humans, with one third of humans becoming completely protected against infection, the net reproduction of the infection will be approximately equal to 1.7.

d) If no humans are vaccinated but the vector population is sprayed with a chemical agent, so that all vectors are half as infectious as they were previously, the net reproduction will be approximately equal to 1.5.

Is the following incorrect?
a) The basic reproduction number is approximately 2.12.

$$\begin{array}{c|cc} & v & h \\ \hline v & 0 & 3 \\ h & 1.5 & 0 \end{array}$$

Recall, for the following type of Next Generation Matrix:

$$\begin{array}{c|cc} & \text{Group 1} & \text{Group 2} \\ \hline \text{Group 1} & 0 & R_{12} \\ \text{Group 2} & R_{21} & 0 \end{array}$$

R_0 is given by: $R_0 = \sqrt{R_{12}R_{21}}$

So R_0 is given by: $R_0 = \sqrt{R_{vh}R_{hv}}$

Substituting for R_{vh}=3 and R_{hv}=1.5 gives: $R_0 = \sqrt{3\times1.5} = \sqrt{4.5} \approx 2.12$

a) The basic reproduction number is approximately 2.12.

Is the following incorrect?

b) One of the following statements is correct:
i) The fraction of the typical infectious "person" that is a vector is approximately 0.59. ii) The basic reproduction number is 4.5.

Answer:
ii is incorrect as $R_0 \approx 2.12$

To find out if i is correct, calculate the fraction of the typical infectious person that is a vector, assuming $R_0 \approx 2.12$

Calculating the fraction of a typical infectious "person" (x) that is a vector (1)

Note that the fraction of a typical infectious "person" that is a vector has to satisfy the equation:

$$\begin{pmatrix} 0 & 3 \\ 1.5 & 0 \end{pmatrix}\begin{pmatrix} x \\ 1-x \end{pmatrix} = R_0\begin{pmatrix} x \\ 1-x \end{pmatrix}$$

Writing this equation in full, we obtain the following 2 equations:

$$0.x + 3(1-x) = R_0 x$$
$$1.5x + 0.(1-x) = R_0(1-x)$$

These equations simplify to the following:

$$3(1-x) = R_0 x \qquad Eq1$$
$$1.5x = R_0(1-x) \qquad Eq2$$

Rearranging equation 1, we get: $x = \frac{3}{R_0 + 3}$

Calculating the fraction of a typical infectious "person" (x) that is a vector (2)

Substituting for $R_0 \approx 2.12$ into $x = \frac{3}{R_0 + 3}$, we get:

$$x \approx \frac{3}{2.12 + 3} \approx 0.59$$

Is the following incorrect?

b) One of the following statements is correct:
i) The fraction of the typical infectious "person" that is a vector is approximately 0.59. ii) The basic reproduction number is 4.5.

Answer:
b) Is correct since only statement i) is correct

Which of the following is incorrect?

c) If vaccination is introduced just among humans, with two thirds of humans becoming completely protected against infection, the infection will eventually disappear among humans.

d) If vaccination is introduced just among humans, with one third of humans becoming completely protected against infection, the net reproduction of the infection will be approximately equal to 1.7.

d) If no humans are vaccinated but the vector population is sprayed with a chemical agent, so that all vectors are half as infectious as they were previously, the net reproduction will be approximately equal to 1.5.

Answer: Rewrite the Next Generation Matrix to account for vaccination and changes in infectiousness and calculate R_n

Which of the following is incorrect?

	True statement?	Right answe to question?
a) The basic reproduction number is approximately 2.12.	✓	✗
b) One of the following statements is correct: i) The fraction of the typical infectious "person" that is a vector is approximately 0.59. ii) The basic reproduction number is 4.5.	✓	✗
c) If vaccination is introduced just among humans, with two thirds of humans becoming completely protected against infection, the infection will eventually disappear among humans.	✗	✓
d) If vaccination is introduced just among humans, with one third of humans becoming completely protected against infection, the net reproduction number of the infection will be approximately equal to 1.7.	✓	✗
e) If no humans are vaccinated but the vector population is sprayed with a chemical agent, so that all vectors are half as infectious as they were previously, the net reproduction will be approximately equal to 1.5.	✓	✗

Q5. Which of the following is incorrect?

c) If vaccination is introduced just among humans, with two thirds of humans becoming completely protected against infection, the infection will eventually disappear among humans.

Original Next Generation Matrix:

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5 & 0 \end{pmatrix} \end{array}$$

New Next Generation Matrix – multiply the terms relating to humans by 1/3 (as only 1/3 of humans are not protected)

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5\times\frac{1}{3} & 0 \end{pmatrix} \end{array} = \begin{pmatrix} 0 & 3 \\ 0.5 & 0 \end{pmatrix}$$

Which of the following is incorrect?

c) If vaccination is introduced just among humans, with two thirds of humans becoming completely protected against infection, the infection will eventually disappear among humans.

New Next Generation Matrix

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 0.5 & 0 \end{pmatrix} \end{array}$$

R'_{hv} R_{vh}

Adapting the result that R_0 is related to R_{vh} and R_{hv} through the following equation:

$$R_0 = \sqrt{R_{hv} R_{vh}}$$

we obtain the result:

$$R_n = \sqrt{R'_{hv} R_{vh}} = \sqrt{0.5 \times 3} = \sqrt{1.5} \approx 1.22$$

c) Is incorrect since R_n>1, and so the infection will not eventually disappear (assuming that no other intervention is introduced)

Q5. Which of the following is incorrect?

d) If vaccination is introduced just among humans, with one third of humans becoming completely protected against infection, the net reproduction of the infection will be approximately equal to 1.7.

Original Next Generation Matrix:

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5 & 0 \end{pmatrix} \end{array}$$

New Next Generation Matrix – multiply the terms relating to humans by 2/3 (as only 2/3 of humans are not protected)

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5\times\frac{2}{3} & 0 \end{pmatrix} \end{array} = \begin{pmatrix} 0 & 3 \\ 1.0 & 0 \end{pmatrix}$$

$$R_n = \sqrt{R'_{hv} R_{vh}} = \sqrt{1 \times 3} = \sqrt{3} \approx 1.73$$

d) Is correct

Q5. Which of the following is incorrect?

d) If no humans are vaccinated but the vector population is sprayed with a chemical agent, so that all vectors are half as infectious as they were previously, the net reproduction will be approximately equal to 1.5.

Original Next Generation Matrix:

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5 & 0 \end{pmatrix} \end{array}$$

New Next Generation Matrix – multiply the terms relating to infectious vectors by 0.5 (as vectors are half as infectious as they were previously

$$\begin{array}{cc} & \begin{array}{cc} v & h \end{array} \\ \begin{array}{c} v \\ h \end{array} & \begin{pmatrix} 0 & 3 \\ 1.5\times 0.5 & 0 \end{pmatrix} \end{array} = \begin{pmatrix} 0 & 3 \\ 0.75 & 0 \end{pmatrix}$$

$$R_n = \sqrt{R'_{hv} R_{vh}} = \sqrt{0.75 \times 3} = \sqrt{2.25} = 1.5$$

e) Is correct