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Important quantities, endemicity and structured populations

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The basic reproduction number R_0

Recall: R_0 = expected number individuals an infected person infects when everyone is susceptible

R_0 depends both on disease (infectious agent) and on community!!

$R_0 < 1$ or $R_0 > 1$ makes a very big difference!

Next page: R_0 for some diseases (and communities and time periods), Andersson and May, 1991

R_0 for some diseases, communities and time periods (Andersson & May, 1991)

Table 4.1 Estimated values of the basic reproductive rate, R_0, for various infections (data from Anderson (1982*b*), Anderson and May (1982*d*, 1985*c*, 1988), Anderson *et al.* (1988), Nokes and Anderson (1988)).

Infection	Geographical location	Time period	R_0
Measles	Cirencester, England	1947–50	13–14
	England and Wales	1950–68	16–18
	Kansas, USA	1918–21	5–6
	Ontario, Canada	1912–13	11–12
	Willesden, England	1912–13	11–12
	Ghana	1960–8	14–15
	Eastern Nigeria	1960–8	16–17
Pertussis	England and Wales	1944–78	16–18
	Maryland, USA	1943	16–17
	Ontario, Canada	1912–13	10–11
Chicken pox	Maryland, USA	1913–17	7–8
	New Jersey, USA	1912–21	7–8
	Baltimore, USA	1943	10–11
	England and Wales	1944–68	10–12
Diphtheria	New York, USA	1918–19	4–5
	Maryland, USA	1908–17	4–5
Scarlet fever	Maryland, USA	1908–17	7–8
	New York, USA	1918–19	5–6
	Pennsylvania, USA	1910–16	6–7
Mumps	Baltimore, USA	1943	7–8
	England and Wales	1960–80	11–14
	Netherlands	1970–80	11–14
Rubella	England and Wales	1960–70	6–7
	West Germany	1970–7	6–7
	Czechoslovakia	1970–7	8–9
	Poland	1970–7	11–12
	Gambia	1976	15–16
Poliomyelitis	USA	1955	5–6
	Netherlands	1960	6–7
Human Immunodeficiency Virus (Type I)	England and Wales (male homosexuals)	1981–5	2–5
	Nairobi, Kenya	1981–5	11–12

Exercise 6: Why is $R_0 > 1$ for all diseases above?

Initial growth rate ρ

Exponential growth rate due to "branching" behavior

$I(t) \approx e^{\rho t}$

ρ depends more on specific model assumptions (contact rate, latency period, infectious period, ...)

R_0 and ρ (unfortunately) not too related

R_0 more important

ρ easier to estimate *during* an outbreak

Exercise 7: Suppose the exponential growth rate ρ equals $\rho = 2.8$ (per week) and that there is one index case week 0. Compute the expected incidence ($\approx I(t)$) after 1, 2 and 3 weeks.

Generation interval

Model quantities: infection time, latent period, removal

Observable quantities: onset of symptoms, hospitalization, death, stop of symptoms

Latent period= time between infection and becoming infectious

Incubation period = time between infection and show of symptoms

Very rarely is infection time known. If show of symptoms leads to "isolation" this is approximately the same as "removal"

Latent period can in some controlled experiment be estimated

For determining the growth rate ρ the *mean* of the latency period is most important, but also its *variation*.

The mean infectious period and its randomness is also important

Modelling vaccination

Why is modelling of disease spread important?

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Why is modelling of disease spread important?

Increase understanding and *prevention* (e.g. **vaccination**)

Suppose that a fraction v are vaccinated prior to outbreak

Assume first a perfect vaccine (100% immunity)

$\Longrightarrow$ a fraction v are initially immune (discussed in previous lecture)

R_v is the reproduction number after a fraction v has been vaccinated

$\Longrightarrow R_v = R_0(1-v)$

$R_v < 1$ equivalent to $R_0(1-v) < 1$ equivalent to $v > 1 - 1/R_0$

Modelling vaccination cont'd

So, if $v > 1 - 1/R_0$ there will be no major outbreak: "Herd immunity"

$v_c = 1 - 1/R_0$ is called the *critical vaccination coverage*

Exercise 8: Compute v_c for a disease having $R_0 = 1.5$, 3 and 6

On next page are estimates of v_c for some diseases

v_c for some diseases (Andersson & May, 1991)

Fig. 5.1. The dependence of the critical level of vaccination coverage required to halt transmission, p_c, on the basic reproductive rate R_0, or, equivalently, on the average age at infection, A (see eqns (5.2) and (5.3)).

Table 5.1 Approximate estimates of the vaccination coverage (the degree of herd immunity) required to eradicate a variety of viral, bacterial, and protozoan infections in developed and developing countries (eqn (5.2) in the main text)

Infectious disease	Critical proportions (p_c) of the population to be immunized for eradication
Malaria (*P. falciparum* in a hyperendemic region)	99%
Measles	90–95%
Whooping cough (pertussis)	90–95%
Fifths disease (human parvovirus infection)	90–95%
Chicken pox	85–90%
Mumps	85–90%
Rubella	82–87%
Poliomyelitis	82–87%
Diphtheria	82–87%
Scarlet fever	82–87%
Smallpox	70–80%

Modelling vaccination cont'd

If vaccine is not perfect but relative risk of getting infected from an infectious contact for vaccinees is $1 - E$ (E for "efficacy", $0 < E \leq 1$), then

$$v_c = \frac{1}{E}\left(1 - \frac{1}{R_0}\right)$$

For a highly infectious disease (R_0 large) and a not so effective vaccine (E not too close to 1) v_c might exceed 1. This means vaccination alone cannot prevent an outbreak!

Endemic diseases

When interest is on long-term situation (as opposed to short term outbreaks) the assumption of a fixed population must be relaxed

Consider an SIR disease in a population where individuals die and new are born. Assume:

- SIR disease (life long immunity)
- population at "equilibrium" (in terms of size and incidence)
- disease endemic (constantly present, no big fluctuations)
- $\hat{s}$, $\hat{i}$ and $\hat{r}$ denote the average fractions susceptible, infectious and removed
- R_0 = average number of infections caused by one individual – if everyone was susceptible!

Think of childhood diseases (e.g. chicken-pox)

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Endemic diseases, expression for $\hat{s}$

When disease is in endemic equilibrium each infected individual on average infects exactly 1 new person!

Given R_0 and $\hat{s}$ an infected individual infects on average $R_0\hat{s}$ new individuals

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Endemic diseases, expression for $\hat{s}$

When disease is in endemic equilibrium each infected individual on average infects exactly 1 new person!

Given R_0 and $\hat{s}$ an infected individual infects on average $R_0\hat{s}$ new individuals

$\Longrightarrow R_0\hat{s} = 1$!!

$\hat{s} = \frac{1}{R_0}$

$\hat{s}$ = average fraction susceptible $= \frac{\text{average age at infection}}{\text{average life-length}}$

Exercise 9 Suppose $R_0 = 1.5$, 3 and 6 respectively, compute $\hat{s}$.

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Endemic diseases, expression for $\hat{i}$

If ι is the average length of infectious period and ℓ average life-length, then ι/ℓ is the average time of the life an individual is infectious

Since population/disease in equilibrium this is also the population fraction of infectives

$$\hat{i} = \frac{\iota}{\ell}$$

Exercises

Exercise 10 Consider an endemic disease with one week infectious period and a population with 75 years expected life-length. Compute the average fraction infective $\hat{i}$.

Exercise 11 Consider the disease in the previous exercise and consider the Icelandic population ($n = 250\ 000$). What is the average *number* of infectives? How about England ($n = 60\ 000\ 000$)?

Exercise 12 What do you think will happen with the disease in the two countries (remember that if the number of infectives drops to 0 the disease goes extinct - until it is "re-imported")?

Different heterogeneities

In reality individuals behave differently both

- in terms of susceptibility and infectivity given that a "contact" takes place, and
- in terms of whom they have contact with

Previous results assumed individuals have equal susceptibility and infectivity AND that they "mix" uniformly

Question: Does this simplification make results useless?

Qualitative answer: The more infectious a disease is the less "problematic" is this simplification

$\Longrightarrow$ ok for measles (except immunity) but not "valid" for STDs

Individual heterogeneities

In several situations individuals can be grouped into different *types* of individual

Different types may differ in terms of susceptibility + infectivity

Examples: infants – school children – adults, male – females, partially immune (vaccinated) – fully susceptible

Natural extension: **Multitype epidemic model**

- Let π_j = community fraction of type j, $j = 1, \ldots, k$
- Suppose an i-individual infects a given type-j individual at rate β_{ij}/n and recovers at rate $1/\nu$

Exercise 21 How many j-individuals does an i-individual on average infect when everyone is susceptible?

Multitype epidemics

Answer: $n_j \frac{\beta_{ij}}{n} \nu$ (=numbers at risk * infection rate * average length of infectious period) $= \beta_{ij} \nu \pi_j$

The matrix with these elements defines the expected number of new infections of various types caused by individuals of various types:

$M = (m_{ij}) = (\beta_{ij} \nu \pi_j)$

Often referred to as *next generation matrix*

$R_0 =$ largest eigenvalue to this matrix (same interpretations as before)

In general no explicit expression, but if $\beta_{ij} = \alpha_i \gamma_j$ then $R_0 = \sum_i \alpha_i \gamma_i \nu \pi_i$

Multitype epidemics

Exercise 22 Interpret α_i and γ_j

Exercise 23 Compute R_0 for the case: $\pi_1 = \pi_2 = 0.5$, $\nu = 1$ and $\beta_{11} = 1$, $\beta_{12} = \beta_{21} = 2$ and $\beta_{22} = 4$. Is the answer surprising?

Household epidemics

Previous heterogeneity mainly for "individual heterogeneities"

Equally (or more!) important: which individuals people have contact with

For many diseases (influenza, childhood disease, common cold) transmission within *households* is high

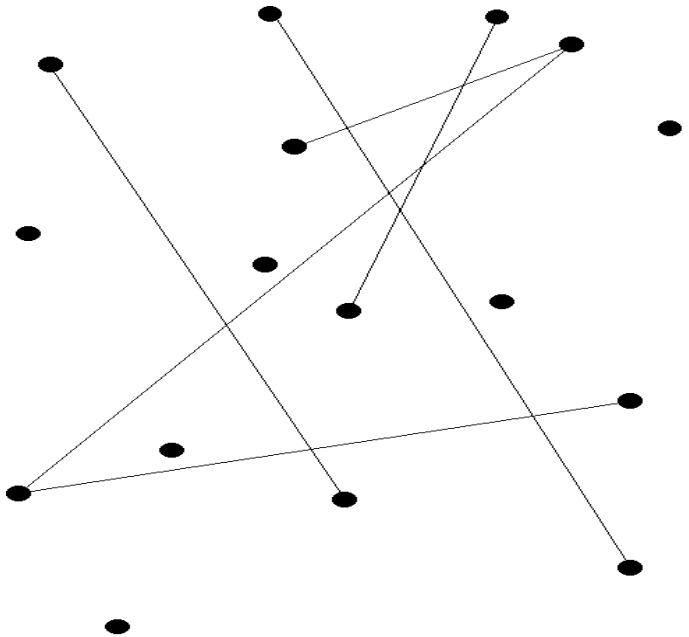
$\Longrightarrow$ Important with models allowing for higher transmission within households

Households are small $\Longrightarrow$ randomness important

Networks

For other diseases (e.g. STDs) individuals are not connected in small sub-units

Common representation of social structure: network/graph **nodes** (individuals) and **edges** ("friendship")



Random networks

Social structure only partly known: modelled using random graph/network **with structure**

Some (potentially observed) local structures

- $D = \#$ friends of randomly selected individual (*degree distribution*)
- $c = P$(two friends of an individual are friends) (*clustering*)
- $\rho =$ correlation of degrees in a randomly selected friendship (*degree correlation*)

Other features unobserved $\Longrightarrow$ Random network

Stochastic epidemic model "on" network

Also spreading is uncertain $\Longrightarrow$ stochastic epidemic model "on" the (random) network

Simplest model: an infected person infects each susceptible friend independently with prob p and then recovers (one index case)

Effect on graph: thinning – each **edge** is removed with prob $1 - p$

Interpretation: remaining edges reflect "potential spreading"

Graph and its thinned version

Those connected to index case make up final outbreak

The degree distribution and its effect on R_0

Case study: Network epidemic model with arbitrary degree distribution $\{p_k\}$

- Social structure: Individuals have degree distribution $D \sim \{p_k\}$ and "friends" are chosen completely at random
- Epidemic model: each susc. friend is infected with prob p
- 1 randomly selected index case, $n-1$ susceptibles

What is R_0?

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What is R_0?

- $R_0 = pE(D)$?

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- $R_0 = p(E(D)-1)$?

The degree distribution and its effect on R_0

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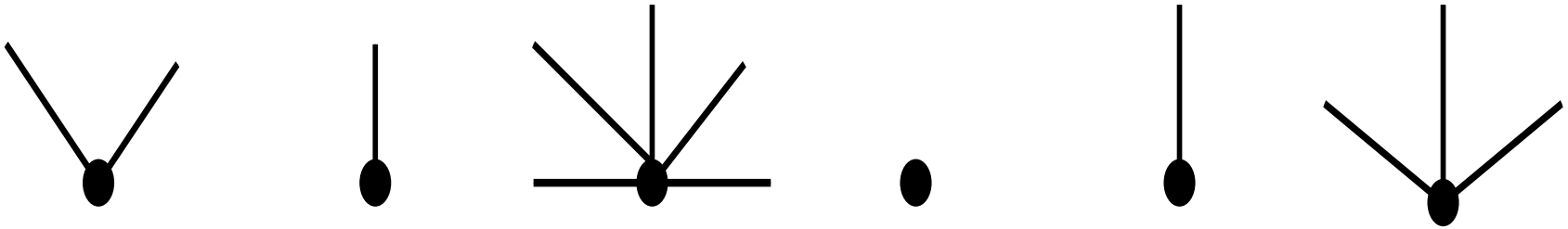
The basic reproduction number

What is the degree distribution of infectives (during early stages)?



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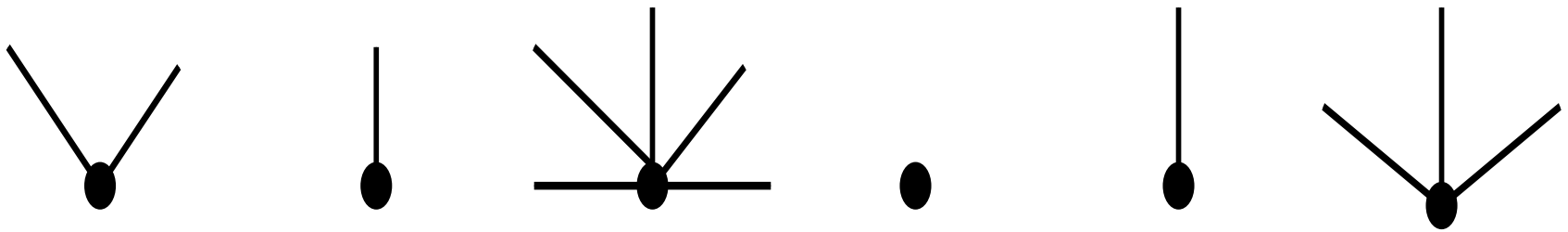

Answer: $\{\tilde{p}_k; k \geq 1\}$, where $\tilde{p}_k = const \cdot kp_k = kp_k/E(D)$

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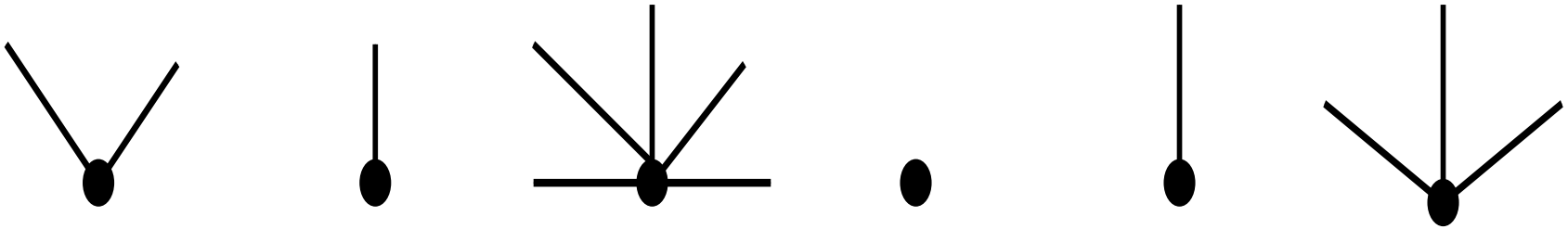

Answer: $\{\tilde{p}_k; k \geq 1\}$, where $\tilde{p}_k = const \cdot kp_k = kp_k/E(D)$

$$\implies R_0 = p(E(\tilde{D}) - 1) = \cdots = p\left(E(D) + \frac{V(D) - E(D)}{E(D)}\right)$$

Empirical networks have heavy-tailed degree distributions ...

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

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Who are vaccinated?

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Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

a) Randomly chosen individuals

$$\Longrightarrow R_v = p(1-v)(E(\tilde{D})-1) = (1-v)R_0$$

$$\Longrightarrow \text{if } v \geq 1 - 1/R_0 \text{ then } R_v \leq 1 \Longrightarrow \text{no outbreak!}$$

- Critical vaccination coverage: $v_c = 1 - 1/R_0$

Vaccination

Suppose a fraction v are vaccinated prior to outbreak

Who are vaccinated?

a) Randomly chosen individuals

$\Longrightarrow R_v = p(1-v)(E(\tilde{D})-1) = (1-v)R_0$

$\Longrightarrow$ if $v \geq 1 - 1/R_0$ then $R_v \leq 1 \Longrightarrow$ no outbreak!

- Critical vaccination coverage: $v_c = 1 - 1/R_0$
- **Problem**: If R_0 large (e.g. due to large $V(D)$), $v_c \approx 1 \quad \Longrightarrow$ impossible!

Vaccination, cont'd

Can we do better than selecting vaccinees randomly?

Vaccination, cont'd

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Yes! Vaccinate social people

But social network usually not observed ...

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b) Acquaintance vaccination strategy

- Choose individuals at random

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- Choose individuals at random
- vaccinate one of their friends

Vaccination, cont'd

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Yes! Vaccinate social people

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b) Acquaintance vaccination strategy

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- vaccinate one of their friends

Vaccinees will have degree distribution $\{\tilde{p}_k\}$ rather than $\{p_k\}$

$\Longrightarrow$ much more efficient

Proportion infected as function of v, $D \sim$ Poisson

$$\left.\begin{array}{l} D \sim Po(6) \\ p = \frac{1}{2} \end{array}\right\} \Rightarrow R_0 = 3$$

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$\Pi(v)$ = final proportion infected

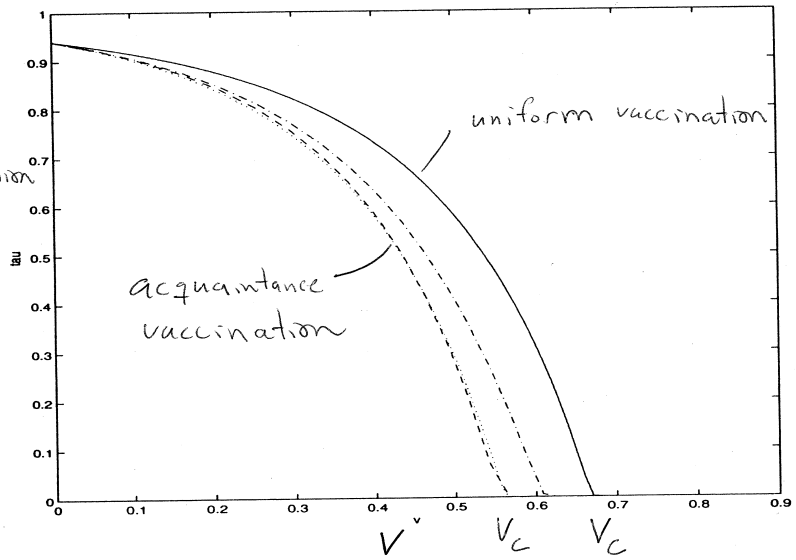

FIGURE 2. Final proportion infected τ as a function of the vaccination coverage v for four vaccination strategies: uni-

Proportion infected as function of v, $D \sim$ heavy-tailed

$D \sim$ Heavy tail $(E(D)=6)$
$p = 0.5$

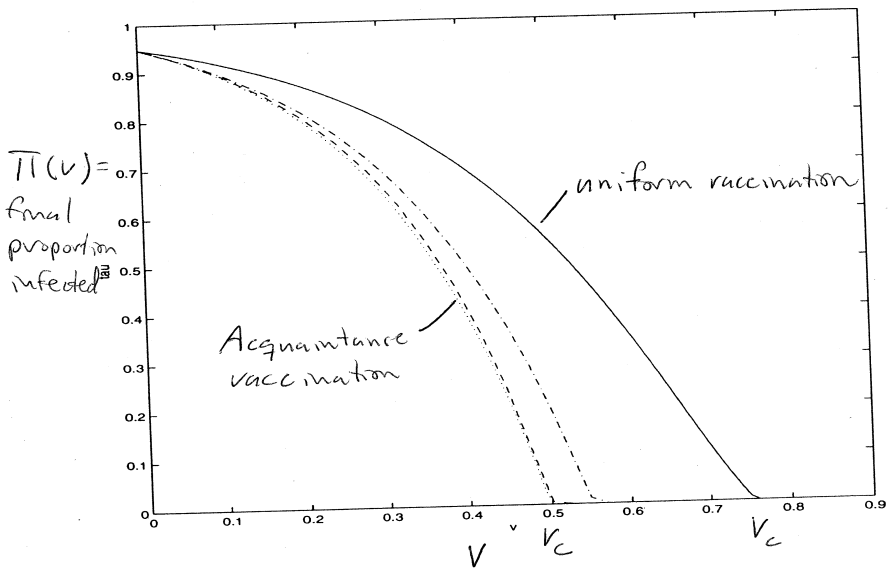

FIGURE 3. Final proportion infected as a function of the vaccination coverage for four vaccination strategies: uniform (—), acquaintance (· · ·), E1 (- - -) and E2 (— · — · —.) The degree distribution is heavy-tailed ($p_d \propto d^{-3.5}$) with mean

Network epidemics: summary and exercise

Main conclusion:

- Not only mean number of partners but also variance important!
- Core-groups play important roll
- Large variance imply large R_0 (but not necessarily large outbreak)

Important extensions: time-dynamic network, clustering, varying/dependent transmission probabilities, degree correlation

Exercise 24. Suppose the mean degree equals $E(D) = 3$ and the transmission probability per relationship equals $p = 0.25$. Compute R_0 and v_c (assuming uniform vaccination) assuming the standard deviation $\sqrt{V(D)}$ of number of partners equal 0, 1, 3, 10.