Introduction to modeling infectious disease risk

Alan Neaigus, Ph.D.

Lecture delivered at Department of Epidemiology, Joseph L. Mailman School of Public Health, Columbia University, January 30th 2003

Why create models of infectious diseases:

- to predict the future
- to understand complex patterns
- to predict and/or understand the course of an infection through a human (or other animal) population

Two Main Approaches

1. **Single source, common vehicle.**

   The pathogen is spread by water, food, air or innoculation, e.g. salmonellosis is spread through water, food or beverage.

2. **Communicable diseases**.

   Diseases that can be spread from one infected person to another, directly or indirectly, e.g., HIV, syphilis.

1. Single Source, common vehicle

Incubation period:

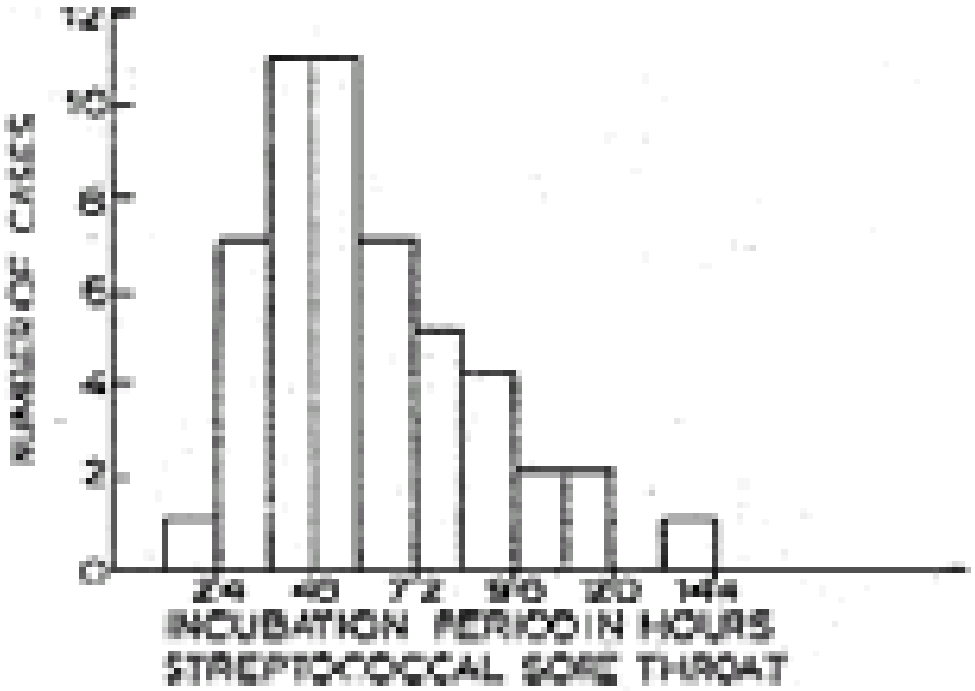
The interval from exposure to an infectious agent and the onset of illness

Epidemic curve:

The distribution of the time of onset of a disease (cases) from initial exposure to an infectious agent, i.e. , the distribution of incubation periods.

Slide adapted from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”

In a single source, common vehicle epidemic, the epidemic curve represents the distribution of incubation periods .



- The distribution of the incubation period for an infectious disease is log normal.

- In a point source epidemic (origins in a common event) , the log normal distribution of cases reflects the incubation period.

Slide adapted from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”

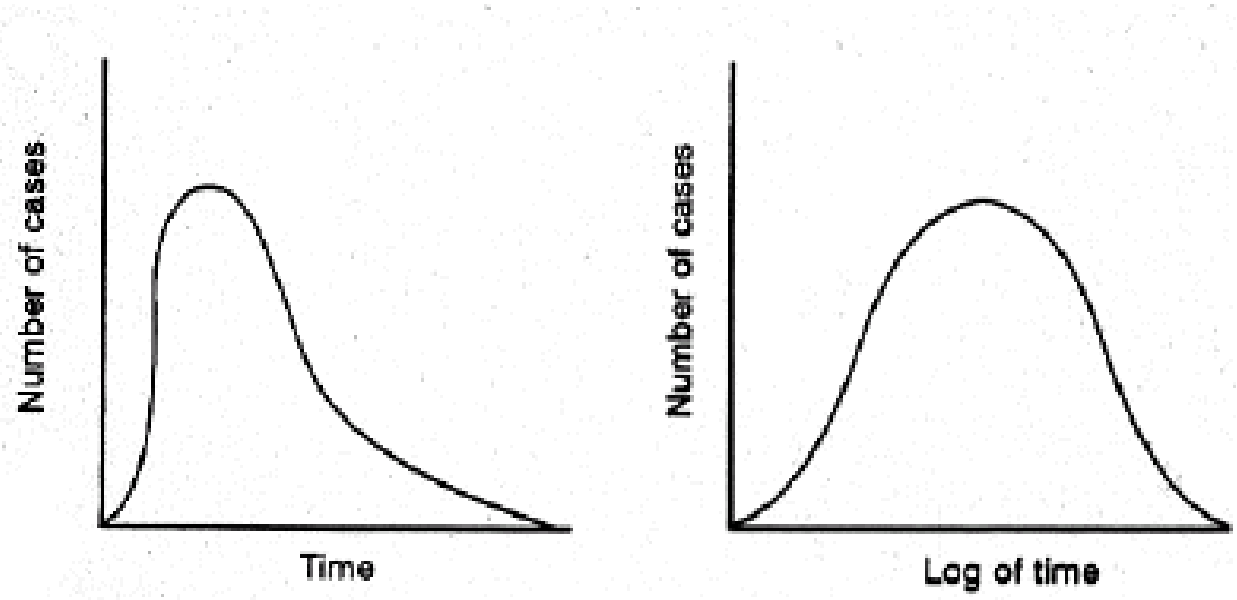
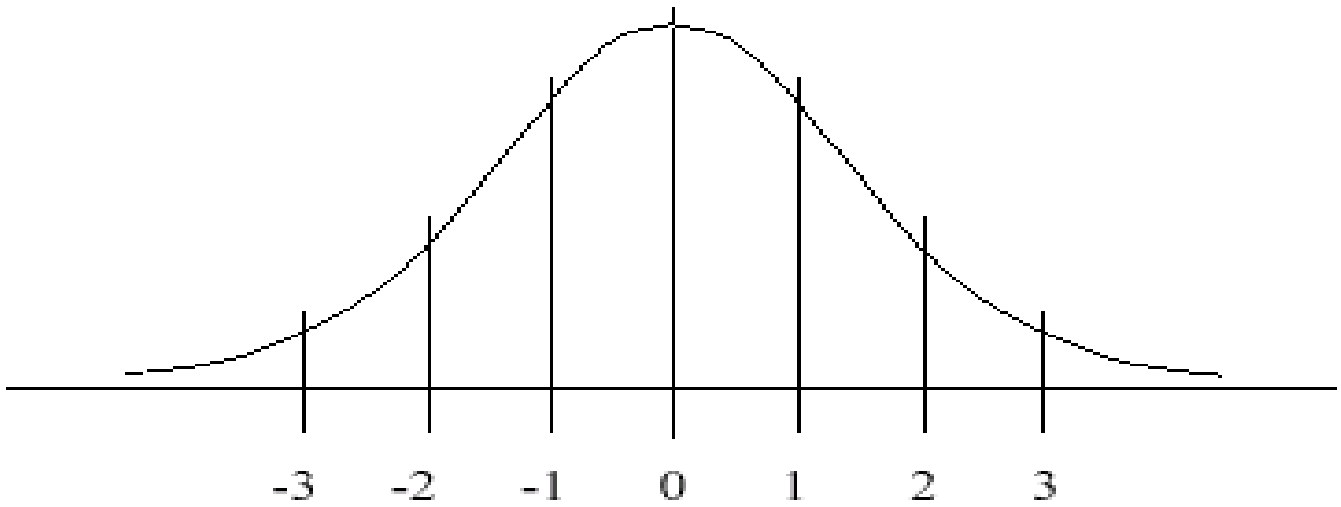


Figure 2–10. Number of cases plotted against time and against the logarithm of time.

Slide adapted from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”

Alan Neaigus, Ph.D. "Intro. Modelling Inf Dis.", Jan 30th, 2003

Normal Curve: Corresponding Z Scores



68% of cases are within 1 standard deviation of the mean

Slide adapted from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”
Alan Neaigus, Ph.D. "Intro. Modelling Inf Dis.", Jan 30th, 2003

Implications for modeling:

1. If we know the incubation period (use the median of the distribution) then we can know the time (when) of exposure.

2. If we know the time of exposure then can investigate what events occurred around that time to determine the cause of the epidemic.

3. If we assume that the epidemic curve is a log normal distribution, then we can estimate the percentage of the exposed population that will become infected at different incubation times on the curve.

2. Communicable Diseases

Epidemics propagated by person-to-person transmission

Ro = ßcD

Ro = Reproductive Rate

(# secondary infections/infected case)

ß= average probability susceptible partner will be infected over duration of relationship

c = average rate of acquiring new partners

D = average duration of infectiousness

-Anderson & May, 1988

Ro > 1 epidemic

Ro = 1 endemic

Ro <1 declining epidemic

To Sustain an Epidemic:

Ro > 1

This requires:

ß > 0: (transmission must be possible)

c > 0: (new susceptibles)

D >0: (maintain infectiousness)

Slide adapted from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”

What are the parameters for the HIV epidemic?

ß= average probability susceptible partner will be infected over duration of relationship

- Biology of viral transmission
  - Viral load
  - HIV clade variant
  - Other biological factors
- The route of administration, i.e. the “delivery vehicle”

Biology

HIV Incubation period to AIDS

• Infectiousness can occur with or without AIDS onset

• Permanently arrested through treatment with antiretroviral drugs ?

• Infectiousness is not dependent on the incubation period, since it can be both shorter or longer.

HIV generation time (period of maximum infectivity)

This may be **multimodal**.

• Soon after infection, i.e. primary infection.

• Prior to the development of AIDS through opportunistic infections.

Routes of administration for person-to-person transmission

Parenteral transmission has been the main route of transmission for injecting drug users (IDUs).

Sexual transmission has been the main route of transmission for Men-who-have-sex-with-Men (MSMs) and non-IDU women.

Vertical transmission: mother-to-child

Any social category may be infected by both routes, e.g. IDUs who are infected sexually, especially young female IDUs, or MSM/IDUs.

Example: Vlahov “The Alive Study” (1994)

Correlates of prevalent HIV infection

Black race/ethnicity

•Needle sharing

•Use of shooting galleries

•Receptive anal intercourse among males

Other:

History of syphilis

•Injection of cocaine

Predictors of incident HIV infection

Female gender

Direct Behavioral Risk Factors

Parenteral (Injecting) Risk

Injecting with contaminated syringes and other injecting equipment:

- syringe/needle sharing
- indirect syringe sharing
- high frequency drug injection
- cocaine/Speedball injection

Sex risk

Engaging in penetrative sex with an HIV infected partner:

- Engaging in unprotected vaginal sex;
- Engaging in unprotected anal sex
- Engaging in male-to-male sex
- The frequency of penetrative sex

How efficient are the routes of transmission?

Parenteral transmission

HIV

- Direct receptive syringe sharing (similar to a blood transfusion) is very efficient
- Indirect syringe sharing, e.g., syringe-mediated drug sharing, may be less efficient (Jose et al. 1993).

HCV/HBV

- Sharing contaminated drug preparation equipment may be highly efficient (Hagan et al. 2000).

Sexual transmission.

HIV

Receptive anal sex is highly efficient, while receptive vaginal sex may be less efficient, and oral sex even less so. But STI cofactors may increase efficiency.

HCV

Low sexual transmission rate, but this is not well understood.

HBV

Efficiently transmitted through sex.

D = duration of Infection

(Prevalence Models)

(Bell et al. 2002)

"The mean amount of time that an infected person remains in the population, or, that any susceptible person is in a transmission facilitating relationship with an infected person"

• Prevalence models are based on assumptions regarding the distribution of disease across population groups (socially, behaviorally, or geographically defined).

• The distribution of HIV is socially and geographically heterogeneous.

Among IDUs in the USA, HIV prevalence is heavily structured by race/ethnicity

Adult/Adolescent AIDS cases among IDUs or cases associated with IDUs by race/ethnicity through June 2001, United States (CDC HIV/AIDS Surveillance Report)

	White, not Hispanic % of all cases (N = 335,470)	Black, not Hispanic % of all cases (N = 296,501)	Hispanic % of all cases (N = 143,169)
Injecting drug use	12%	35%	36%
MSM and injecting drug use	8%	6%	6%
Heterosexual sex partners	2%	6%	5%
<u>Total</u> IDU Assoc.	21%	49%	48%

C = average rate of acquiring new partners

Sociological/Network models (Bell et al. 2002).

This approach focuses on the characteristics of infected and susceptible individuals and their contact patterns.

Among the factors it examines are:

- Number of new partners;
- Type of new partners;
- The structure of the connections among partners, e.g. serial monogamy vs. concurrent sexual partnerships (Morris and Kretzschmar);
- Mixing between infected and susceptible persons ;
- The rate of partner turnover;
- Behaviors performed in the relationships with different types of partners.

Concepts for the Sociological/Network Models

HIV is an infectious pathogen, which is spread largely through close personal contact.

The transmission of HIV therefore requires:

a) close contact between infectious and susceptible individuals, and

b) behaviors between such individuals that allow for HIV transmission.

NETWORK CONCEPTS

1. RISK NETWORKS

“Those people with whom HIV risk behaviors occur.”

Neaigus et al. 1994

Risk networks can act as <u>conduits of infection</u>

2. SOCIAL NETWORKS

Social networks are:

“those people with whom there are social interactions in which members are mutually oriented to one another and may influence each others’ behavior.”

Neaigus et al. 1994

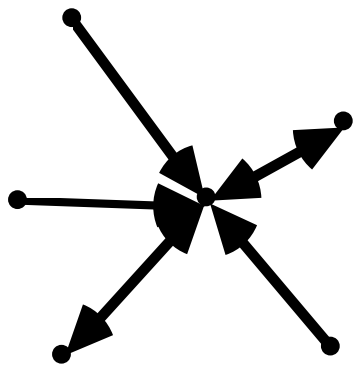
Social networks can act as <u>conduits of influence.</u>

Network methods can be used to study the flow of HIV and influence within:

1. Dyads.

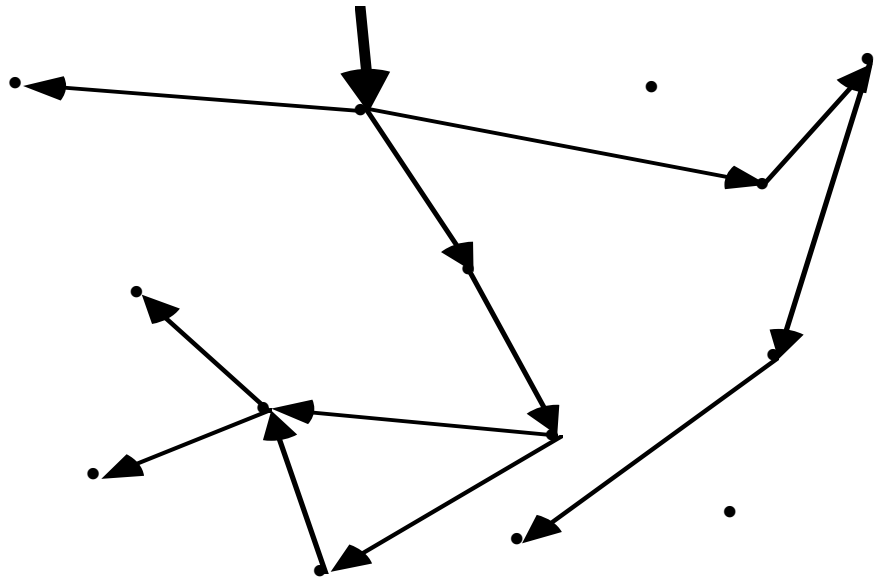
Relationships between 2 people.

2. Egocentric (personal networks).
The direct relationships of an index individual (ego) with other individuals, e.g. injecting partners.



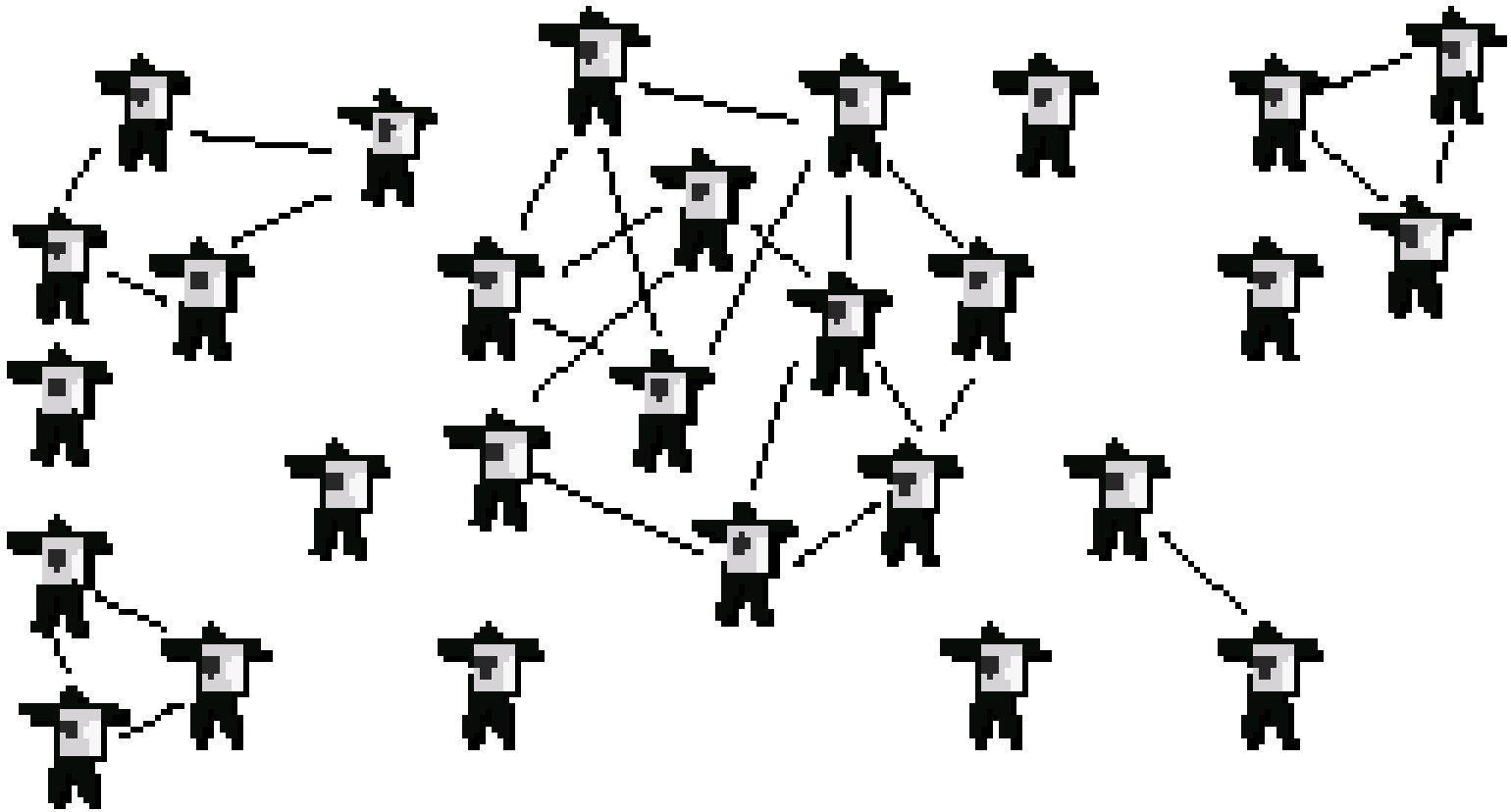
3. Sociocentric (sociometric) networks.

Networks can extend beyond the direct contacts of an individual and include indirect as well as direct ties, e.g. communities, neighborhoods, populations.



Component: a bounded network in which members are directly or indirectly connected to each other

Concurrency, Components, 2-Core



Five examples

Transmission

1. HIV prevalent infection among new IDUs
2. HIV transmission probabilities among non-injecting heroin users.
3. HCV transmission among new IDUs.

Epidemic spread

4. HIV prevalence and sociocentric networks.
5. Vancouver Study: explosive outbreak of HIV among IDUs

1 and 4 from “Social Factors and HIV Risk” (SFHR) study (S. Friedman, PI). Brooklyn, 1990-1993

2 and 3 from “Non-Injecting Heroin Users, New Injectors and HIV Risk (A. Neaigus, PI). East Village/LES 1995-ongoing.

5. Schecter et al. Do needle exchange programmes increase the spread of HIV among injection drug users? An investigation of the Vancouver outbreak”. AIDS 1999

RISK NETWORKS AND HIV INFECTION AMONG INJECTING DRUG USERS

Two studies from the Social Factors and HIV Risk (SFHR) project.

1. Personal risk networks.

Neaigus, Friedman, Jose, et al. "High-Risk Personal Networks and Syringe Sharing as Risk Factors for HIV Infection among New Drug Injectors." Journal of Acquired Immunedeficiency Syndromes and Human Retrovirology. 1996;11:499-509.

2. Sociometric risk networks.

Friedman, Neaigus, Jose, et al. "Sociometric Risk Networks and HIV Risk". American Journal of Public Health 87(1997);8:1289-1296.

METHODS

Design: Cross-sectional;
Structured private interviews;
HIV testing and counseling.

Recruitment: Street-recruited in Brooklyn, New York City, by targeted sampling and chain-referral;
July 1991 - January 1993.

Criteria: ≥ 18 years of age, injected during the 12 months prior to the interview.

Sample: 767 IDUs.

2. Social network questions:

Subjects were asked to describe up to 10 people with whom they had injected drugs, had sex, or had other close social contact during the prior 30 days.

<u>Network member</u> data included:

their socio-demographic background;

how long they had known subjects;

their relationship to subjects;

their drug and sexual behaviors with subjects and with others.

Example 1.

HIV prevalent infection among new IDUs Percent HIV seropositive by subject's syringe sharing and by whether there is a drug injector who injects more than once daily in subject's personal risk network

Table entries are % HIV seropositive (# seropositives/# subjects)

		Subject injects with other injectors' used syringes: Yes	No	OR	p($\chi 2$)*<
Any personal risk network member who injects > one time per day	Yes	40% (16/40)	10% (4/42)	6.33	0.002
	No	11% (4/38)	19% (10/52)	0.49	0.261
	OR	5.67	0.44		
	p($\chi 2$)**<	0.004	0.190		

*** Row comparison, and ** column comparison.**

(Neaigus, Friedman, Jose, et al. 1996).

Example 2

Expected Population Probabilities and Observed Percentages of HIV Infected NIUs Engaging in Unprotected Vaginal or Anal Sex and Having "Lower Risk" Sex Partners, by Injection History

HIV positive Never IDUs (N = 28)				
	N (%)	Expected probability	(95% CI)	Observed %
Any unprotected vaginal or anal sex	8 (28.6)			
Any "lower-risk" partners	15 (53.6)			
Both engaging in unprotected vaginal and/or anal sex *and* having any "lower-risk" sex partners		15.3	(2.0%, 28.6%)	28.6*

Example 3

Injecting partnerships among the HCV infected			
Total number of partners	Partners are not known to be HCV infected	DES in partnerships with those not known to be infected	HCV transmission probability in the partnerships
83	67 (80.7%)	21(31.3)	25.3%

Injecting partnerships among the HCV uninfected			
Total number of partners	Partners are known to be HCV infected	RES in partnerships with those who are known to be infected	HCV transmission probability in the partnerships
163	21 (12.9%)	12 (57%)	7.4%

Example 3 cont.

HCV transmission probability in all injecting partnerships

(1) Total number of partnerships	(2) HCV discordant partnerships	(3) Transmission behavior	(4) Probability of HCV transmission (2) x (3)
246	88 (35.7% of 246)	33 (37.5% of 88)	13.4%

Example 3 cont.

HCV seroconversion rates in recent studies

Sample	Location and time	Rate per 100 PYAR
Non-injecting heroin users who started to inject	New York City, 1996-1998	19.4
Young injectors, 18-29 years old	Baltimore, 1994-96	16.0
Young injectors, 18-30 years old, injecting 1 year or less	Chicago, 1997-99	10.0 (estimated)

Example 3 cont.

HCV transmission probability in injecting partnerships assuming a 50% reduction in parameter probabilities

(1) Total number of partnerships	(2) HCV discordant partnerships	(3) Transmission behavior	(4) Probability of HCV transmission (2) x (3)
246	35.7%	37.5%	13.4%
246	35.7%	**18.75%**	**6.7%**
246	**17.85%**	37.5%	**6.7%**
246	**17.85%**	**18.75%**	**3.3%**

Modeling Infectious Disease Spread

What are the possible ways in which infectious diseases spread through a population?

- Concurrency
- Sociocentric networks
- Microstructures

HIV can spread rapidly among IDUs

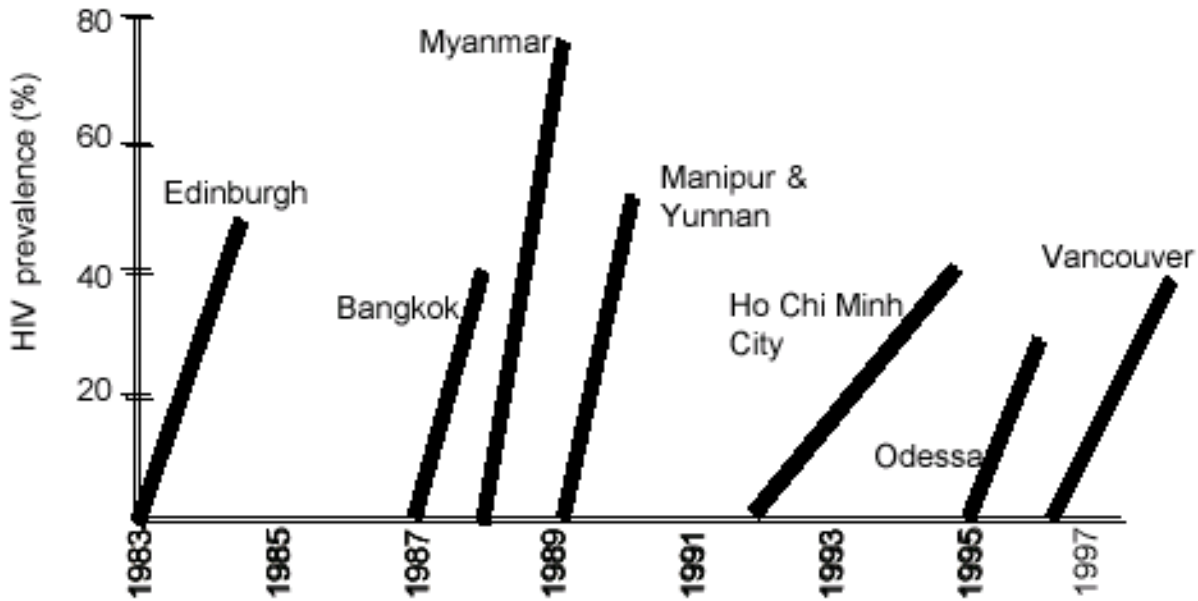
Prevalence increased rapidly to 40% or more in several areas:

- Edinburgh
- Bangkok
- Myanmar
- Manipur
- Yunnan
- Ho Chi Minh City
- Odessa

(Friedman, Des Jarlais, Neaigus, 1992)

Explosive HIV spread among IDUs

prevalence quickly rising to 40% or more



Slide from D. Vlahov , Ph.D. “Concepts in Infectious Disease Epidemiology: Models and Predictions”

Alan Neaigus, Ph.D. "Intro.
Modelling Inf Dis.", Jan 30th, 2003

Concurrency
(Morris and Kretzschmar, 1997)

It's not just the number of partners, but how they are connected.

Having two or more injecting or sex partners within the same time frame compared to serial single partner relationships, increases the potential for connections among large numbers of injectors and sex partners.

Infectious pathogens have many more paths through which they can be transmitted.

The rate of propagation is high.

Population level measure of concurrency

K= the average number of concurrent partnerships per partnership in the population

Can use the degree distribution (number of contacts of ego) for egocentric networks.
$K= \sigma^2 / \mu + \mu - 1$

0 = sequential monogamy

1 = every partnership is concurrent to every other partnership on average

Assumptions of model

The rate of new partnership formation depends on the number of partnerships already present.

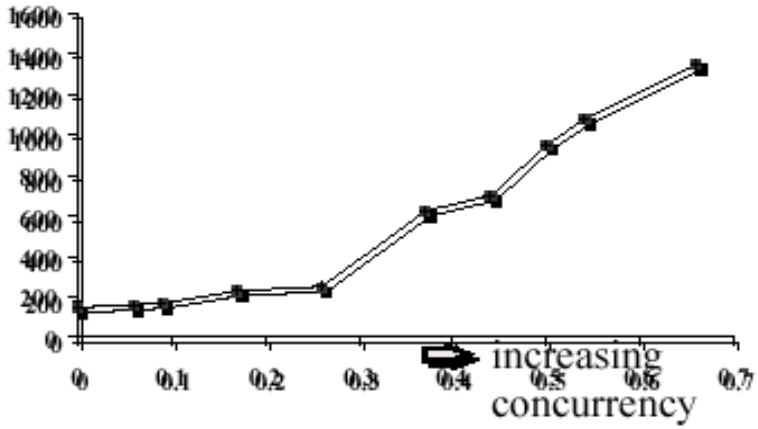
Existing partnerships separate at a constant rate.

The number of partnerships fluctuate around a constant average.

Random mixing of low- and high-frequency partnerships.

Partnerships (typical) last 6-7 months.

Concurrency Simulations



Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS 1997; 11:641-8.

Concurrency increase the size and the rate of increase of HIV epidemics (or other communicable infectious diseases).

e.g., when κ = .26 the average size of the epidemic is 3 x the average size under sequential monogamy at the end of 5 years.

Concurrency increases the size of the largest connected component.

Components are networks in which every member is directly or indirectly linked to every other network member.

Example 4

Sociocentric (sociometric) Networks and Exposure to HIV

Friedman, Neaigus, Jose, et al., 1997.

In an analysis of the links of 761 injectors, 230 were connected directly or indirectly with one another in a large component.

Among these, 105 injectors were more highly connected to one another (they were a 2-core, i.e. they were all connected to 2 or more other IDUs).

The 105 (2-core) were more likely to be HIV positive.

Example 4 cont.

HIV seroprevalence by sociometric category

	Large component		Small	Unlinked with risk	Unlinked w/out risk	p**
	2-Core	Periphery	comps.	partner	partner	
% HIV+	57%	35%	37%	39%	36%	.026
% HBV CAb+	84%	74%	71%	71%	68%	.036

Example 5

Explosive Epidemic of HIV among Vancouver IDUs (Schechter et al. 1999)

Prospective cohort study of 694 IDUs, HIV negative, recruited in downtown Vancouver, 1996-1998.

64 seroconverted for HIV, 8.3/per 100 PYAR.

Frequent needle exchange program (NEP) attenders were more likely to seroconvert.
(47 of 405, 11.6% vs. 17 of 289, 5.9%, RR = 1.9)

Was frequent NEP attendance a risk factor for HIV seroconversion?

If not, what might explain the rapid spread of HIV ?

Example 5 cont.

Empirical model

Predicted seroconversions, excluding NEP attendance, using Cox proportional hazard model.

Risk factors included:

- Unstable housing,
- Hotel living,
- Injecting four or more times per day,
- Cocaine injecting 1 or more times a day,
- Downtown eastside as main injecting site,
- Needing assistance injecting

The predicted number of seroconversions was close to the observed number of seroconversions for frequent and infrequent attenders.

NEP attendance was not significant when other covariates were in the model.

Example 5 cont.

Theoretical model

Biology/Behavior, Social/Risk Network, Geography, i.e. ßcD

Biology/Behavior, ß

Primary infections with high viral loads, therefore hosts are more infectious.

Some risk behaviors are more efficient in transmitting HIV

Vancouver: rapid spread oif primary infections over 15 month period frequent injecting, cocaine injecting.

Social Network, c

Concurrency, mixing patterns, interacting clusters that spread the infection (“core groups”), settings that promote cross-network mixing.

Vancouver unstable housing, hotel living, de facto “shooting galleries”, needing assistance injecting

Example 5 cont.

Geography, D

(effective prevalence of infectious population)

The geographic concentration of infections increases area prevalence, which increases the probability of exposure in a given time frame.

Vancouver: downtown eastside,

Change in C

Social Network Dynamics and HIV Transmission

Individual approaches tend to examine changes in HIV risk behaviors and their effect on HIV transmission.

An analoguous network approach is to examine the effect of network change on HIV transmission.

Rothenberg RB, Potterat JJ, Woodhouse DE, Muth SQ, Darrow WW, Klovdahl AS. Social network dynamics and HIV transmission. *AIDS.* 1998;12:1529-1536.

Methods

A longitudinal study of people at risk for HIV (IDUs, sex workers, MSMs) recruited between 1988-1992 in Colorado Springs, Co.

96 individuals interviewed three times at 1 year intervals.

2 cohorts;
Baseline in year 1 of study (n = 44)
Baseline in year 2 of study (n=52)

Networks ascertained in the past 6 months:

Network type:
Sex, social, drug using, needle sharing, any.

30 groups, comprising index and named contacts
(i.e. 2 cohorts x 5 network types x 3 waves).

Measures for:

- ***Network stability***

(B/(A+C-B)) – the proportion of all named contacts who appear in a network at two time points

- ***Behavioral change***

Risk behavior – proportion of available risk in which respondent partakes (# of partners/number of actual connections).

Risk configuration – risky structure within a personal network (# drug or sex risk partners/total relationships)

- ***Structural change***

Macrostructures

- The number and size of connected components.
- Centrality
  - Degree centrality
  - Information centrality

Micro-structures of intense interaction

- The number of cliques of size 3
- The number of 2-cliques of minimum size 3
- The number of k-plexes of size 3 and 4, with k = 2..

Results

- **Network Stability**
  - Sexual and social networks became more stable (t2-t3 vs. t1-t2).
  - Drug using partnerships did not change in their low stability.
  - Needle sharing partnerships became more stable in cohort 2.
- **Risk Behavior and Risk Configuration**
  - Decreasing risk from the first to the third time interval.

•Structural change

Macrostructures

• Declines in intergroup and intragroup interaction [Indicators of structural change] “taken together…suggest a diminution of in group interaction (smaller and fewer components) and a decrease in intragroup interaction (lowered centrality)”

- The number of components increased for multiplex relationships but not uniplex relationships
- The size of the largest component diminished for all relationships
- Mean degree centrality remained constant or declined.
- Information centrality was inconstant

Microstructures

•Cohesion within subgroups declined

Declines in:

- the number of microstructures
- the density of activity within these microstructures

(i.e., declines in the number of cliques, n-cliques, and k-plexes).

HIV-infected individuals (n=7)

They were rarely in the sex or needle-sharing networks nor were they central in these subgroups

Implications for HIV transmission and spread

Even when risk-taking behaviors exist, social network structures may facilitate or impede the transmission as well as the spread of HIV in a population.

The decline of network connectivity and cohesion (or preventing an increase) can contribute to controlling and preventing the spread of HIV in a population.

Synthetic model

(D. Bell et al. 2002.)

- Prevalence (D)
  - Tested
  - Estimated
- Sociological (C)
  - Matrix of transmission probabilities with given partners (n = 1541).
  - Random mixing
- Biological (β)
  - Variation in infectivity
  - 3 models

20 year estimates

Highest relative prevalence (2123%)

- Tested prevalence.
- Biological model 1
- Random mixing

Lowest relative prevalence (60%)

- Estimated prevalence
- Biological model 2
- Structured mixing

End Notes

What are the assumptions behind the model?

Is there a theory of the epidemic guiding the model?

How precise is the model?

How open is the model, since parameters can change?

How valid is the model?

What use is the model-can it be used to intervene to improve the health of individuals and of populations?