NETWORK MODELING OF PNEUMOCOCCAL SPREAD

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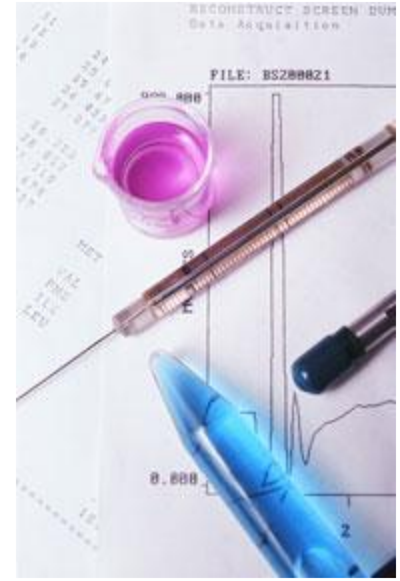
OUTLINE



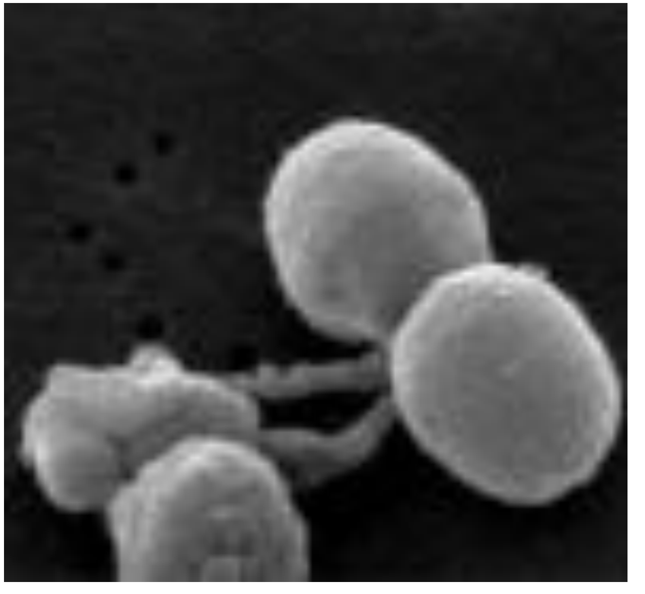
- Background
  - *Streptococcus pneumoniae*
  - Contact network models in infectious diseases epidemiology
- Network models
  - Evaluation of interventions for controlling transmission of pneumococci
  - Examination of consequences of pc-consumption on pneumococcal spread

STREPTOCOCCUS PNEUMONIAE

- Strictly human pathogen
- Major contributor to morbidity and mortality (1-2 millions death annually)
- Causes otitis media, pneumonia, meningitis, septicemia, etc.
- Strikes all age groups
- Risk groups: infants, elderly, and immune-suppressed individuals

CHARACTERISTICS OF *S. PNEUMONIAE*

- Gram-positive diplococcus
- Polysaccharide capsule
  - Most important virulence factor
  - 91 capsular serotypes
  - 23 usually cause of infections
- Naturally competent
  - Serotype-switching
  - Antibiotic resistance



TRANSMISSION

- Many people carries the bacterium in upper respiratory system asymptomatically
- Spread from person to person by inhalation of respiratory droplets
- Requires close contact between individuals
- Prevalence in Sweden:
  - 3% of the adults
  - 15-50% of the children

TREATMENT

- **Antibiotics**: penicillin, erythromycin
- Treatment failures
  - Rapid infection progress
  - Underlying debility of the patient
  - Cell lysis enhances inflammation process
- Worldwide increasing resistance
  - Correlation between antibiotic use and resistance rates
  - 25-35 % of isolates show decreased pc-susceptibility

VACCINES

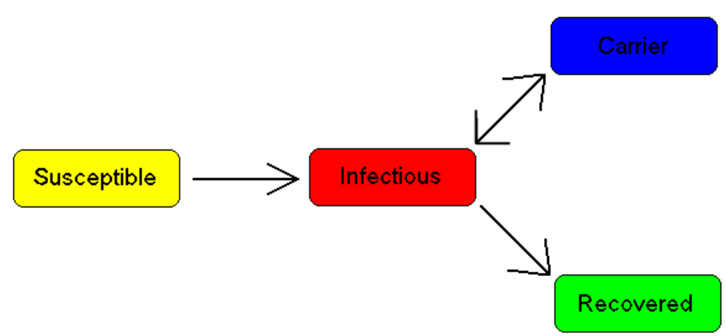
- Polysaccharide vaccine
  - 23-valent
  - Less immunogenic
- Conjugate vaccine
  - 7-13-valent
- Selective pressure
  - Increasing prevalence of NVT
  - Less effective for prevention
- Current efforts on protein-based sub-unit vaccines using surface proteins (e.g., pneumolysin)

INTERVENTIONAL ACTIONS

- Primarily directed to reduce resistant pneumococci
  - Appropriate antibiotic prescription (Iceland)
  - Introduction of conjugate vaccine programs (the U.S)
  - Restrictive DCC attendance and reduced antimicrobial use for children <6 years (Sweden)

MODELING IN INFECTIOUS DISEASE EPIDEMILOGY

- Long-term effects of interventional actions aiming to limit spread of infectious agents are hard to assess
- Impractical and unethical to conduct such real life experiments
- Mathematical/computational models are invaluable tools



NETWORK MODELS

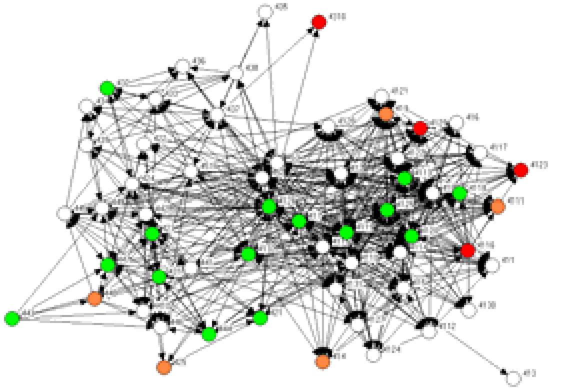
- High degree of realism for infectious disease modeling compared with other approaches
- Captures real diversity in contact patterns
- Allows embedding demographic data
- Individual-based – heterogeneous population
- Probabilistic – takes chance to account
- Different probabilities for different transmission routes

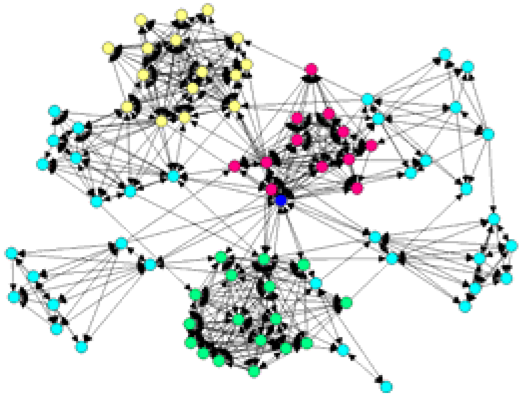
SOCIAL CONTACT NETWORKS

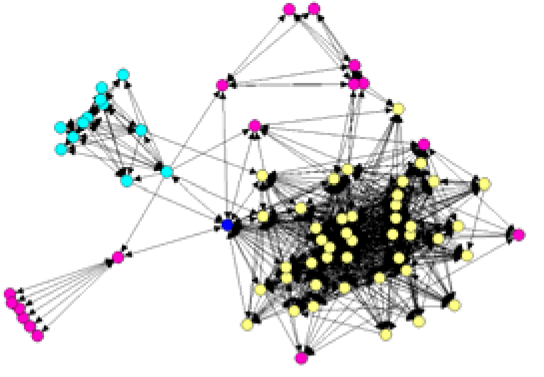
- Network models for spread of infectious diseases constructed from social networks in community
- Contact network characterizes contacts occurring between individuals that potentially may transmit the disease
- Contacts take place within households, DCCs, schools, workplaces, hospitals, etc

NETWORK STRUCTURE

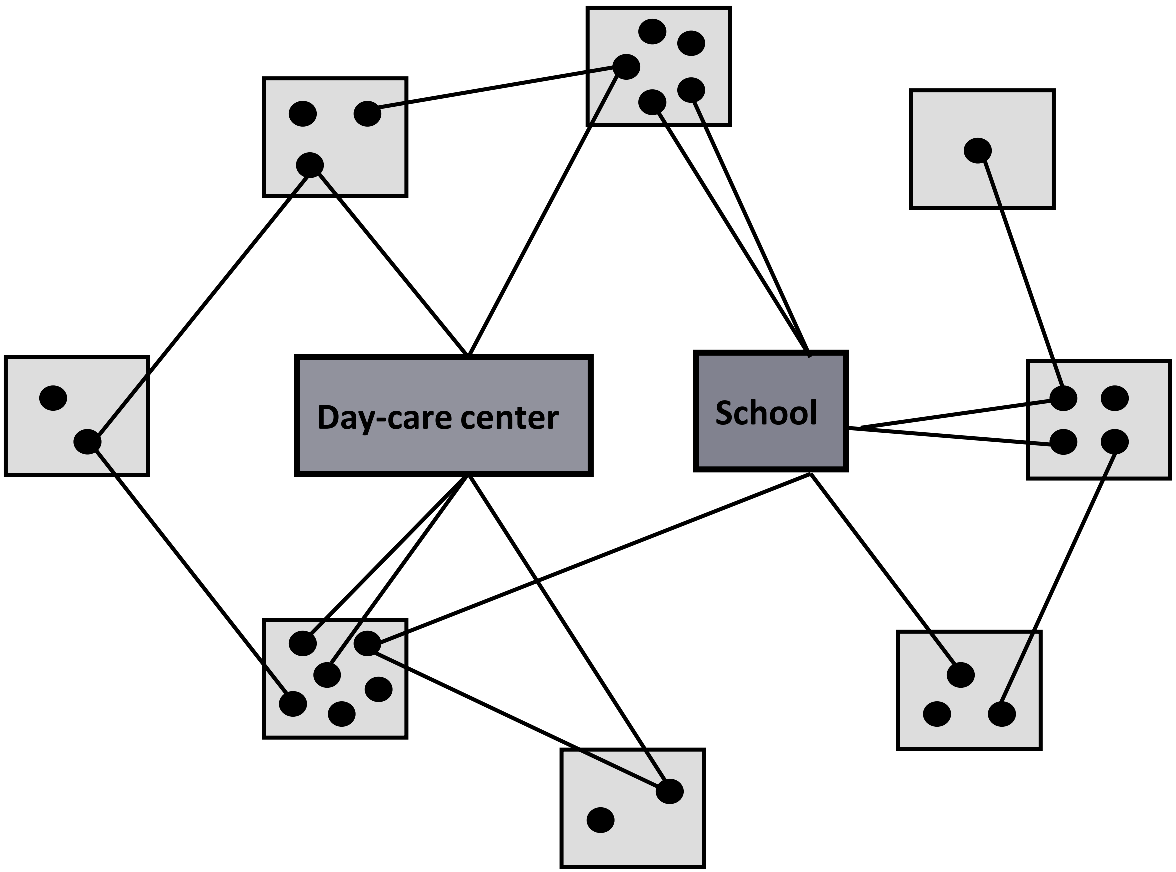
- Provide features that influence spread of contagious diseases
- Differs between different infectious agents – different transmission routes, etc.







SIMPLIFIED ILLUSTRATION OF CONTACT NETWORK CONCEPT



MODEL DEFINITIONS

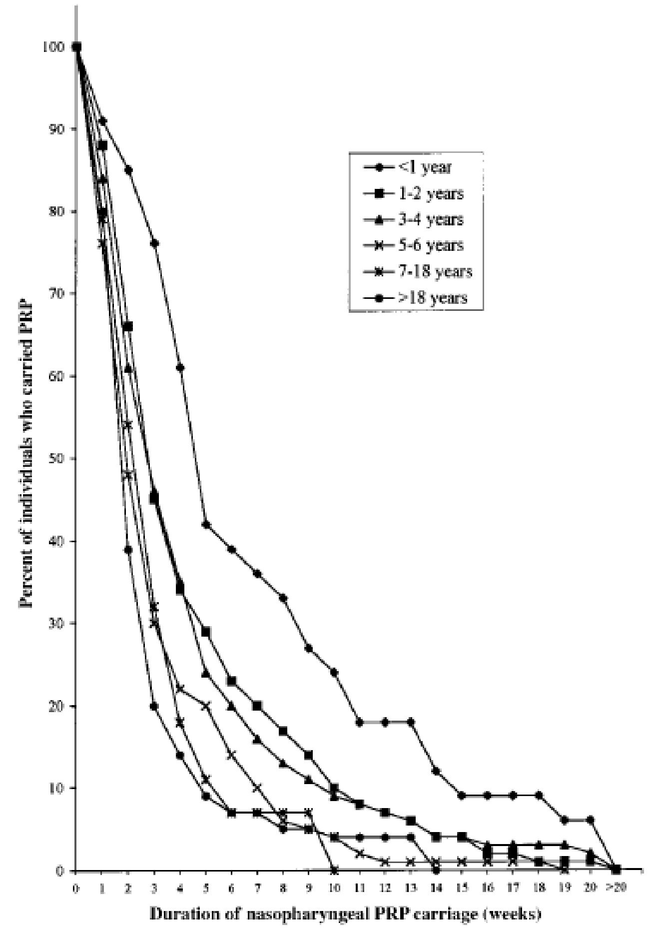
- Population 25 000 individuals
- Probabilistic and individual-based
- Spread of one single, hypothetical clone
- Discrete time-steps (weeks)
- Demographic data of Sweden for year 2006 were embedded in the model
- Asymptomatic carriage

CONTACT SITES

- Sites: households, DCCs, school classes and other close contacts
- Each contact site was represented by an adjacency matrix defining contacts occurring within respective network
- Demographic data were employed (SCB)

DURATION OF CARRIAGE

- Inverse relationship between age and duration of carriage
- Individuals are assigned a carriage duration at the time point for colonization
- Drawn from an exponential distribution with a mean that varied depending on age



Ekdahl et al., 1997 CID

TRANSMISSION PARAMETERS

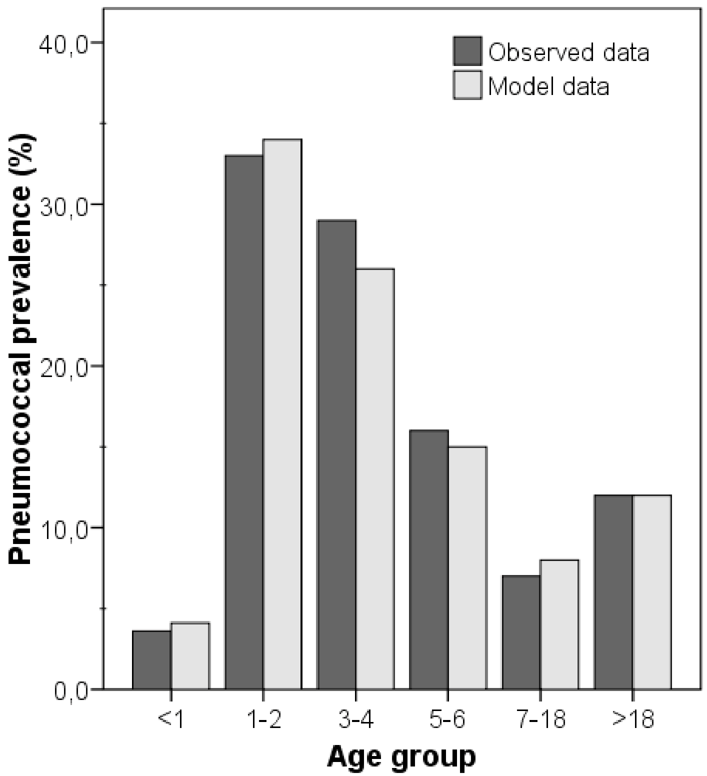
- Probability of pneumococcal transmission varied depending on contact type
- Estimated with respect to average proportion of contacts within a specific site per unit time and the type of contacts (closeness)

AGE-RELATED BIASES

- Age-related biases for susceptibility of pneumococcal colonization reflect the degree of immunity in the population
- Define relative susceptibilities for different age groups

MODEL VALIDATION

A



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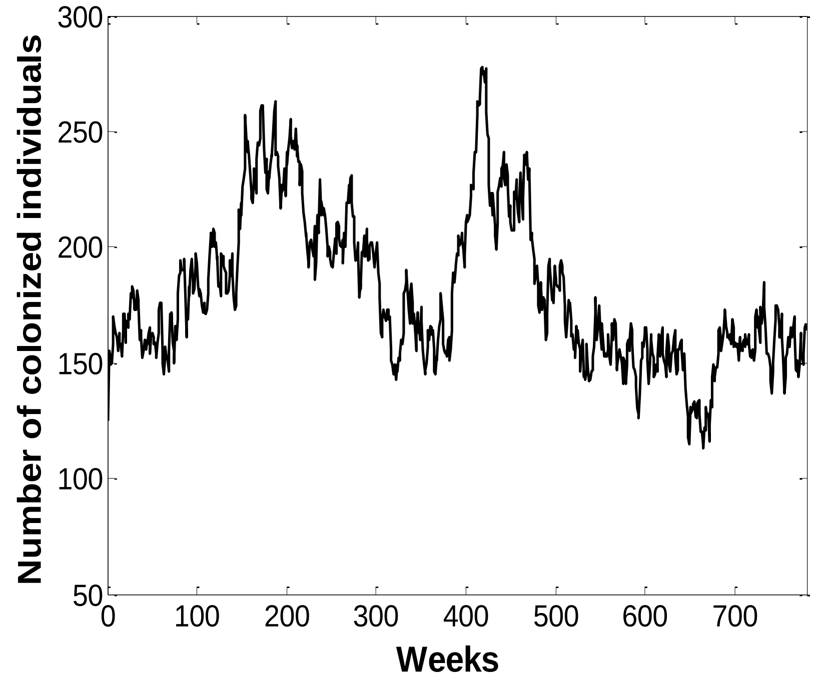

PARAMETER ANALYSIS

- Elucidate key determinants of pneumococcal spread
- Parameters exerting most control
  - Transmission probability within DCCs (improved hygiene routines)
  - Group size in DCCs
  - Age-related biases for children

  of 1-2 yrs age

INTERVENTION SCENARIOS

- Several intervention scenarios were simulated
- Most effective intervention: reduce the sizes of DCC groups
- Reference scenario (2006) 16.7 children/DCC group
  - 1985: 13.4 children/DCC group: **82% reduction**
  - 2003: 17.2 children/DCC group: 20% increase

CONCLUSIONS

- Strategies aiming to control pneumococcal disease and organism transmission should include
  - reducing DCC group size on a community-wide basis
- Vaccination of children of age 1-2 yrs also effective
  - requires serotype independent and protein-based vaccine type for optimal effect

Karlsson *et al*., (2008). An individual-based network model to evaluate interventions for controlling pneumococcal transmission. *BMC Inf Dis*, 8:83.

VACCINE

- 7-valent conjugate vaccine now included in our national vaccine program (January, 2009)
- Effects of vaccine program in other countries:
  - Decreased frequency of invasive pneumococcal infections caused by resistant pneumococci in children
  - 50% reduction of otitis media in children
  - Decreased antibiotic use
  - Decreased resistance rates
  - But also increased prevalence of NVT

RESISTANCE: AN EMERGING GLOBAL PROBLEM

- Resistance rates correspond with frequency antimicrobial use
- Increasing rates of resistant pneumococci are mainly due to spread of strains belonging to a few number of clones
- Biological cost for resistant bacteria

PC-CONSUMPTION VS. PNEUMOCOCCAL SPREAD

- How does pc-consumption in the community affects the spreading pattern of pneumococci?
- Which strategy should be used for reduce the rates of resistant pneumococci?
  - No biological cost
  - Biological cost

MODEL DEFINITIONS

- Individual-based network approach
- Discrete time steps
- Transmission parameters, age-biases, carriage durations as in previous network model
- Pc-consumption according data from STRAMA (Sweden)
- PSP clone resp. PRP clone

METHODS & PRELIMINARY RESULTS

- Simulations performed with
  - One single clone
  - Two clones (S and R) to include competition perspective
- Even a low pc-consumption leads to
  - Decreased carriage rate of susceptible pneumococci
  - Increased carriage rate of resistant pneumococci

INTERVENTIONAL STRATEGIES TO REDUCE RESISTANCE RATES

- Biological cost exists – reduction in penicillin consumption is enough
  - Reduction depends on the cost
  - Time needed depends on the cost
- No biological cost -a combinatorial strategy is required
  - Vaccine targeting major resistant serotypes
  - Diminished penicillin use to prevent (1) NVT aquires resistance; (2) further spread of resistant minor NVT

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