Modeling of Exposure to Influenza A Virus

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Exposure Routes

Possible routes of person-to-person influenza transmission are:

- **inhalation**
- **droplet spray**
- **surface-to-hand (body-to-hand) contact and touching target membranes on the face**

Cough Particles

- Several hundred particles (primarily saliva) are emitted in a cough.
- They have initial d_a values ranging from less than 1 μm to greater than 1,000 μm.
- Emitted particles quickly lose water by evaporation and shrink to about ½ their initial diameter values.

Cough Particles

- **Respirable cough particles (d_a < 10 μm) are termed "droplet nuclei." They reach and deposit in the alveolar region, but the majority deposit in the upper respiratory tract.**
- **Inspirable cough particles (10 μm < d_a < 100 μm) cannot reach the alveolar region. All deposit in the upper respiratory tract.**

Cough Particles

- Cough particles with initial $d_a \leq 20\ \mu m$ become droplet nuclei.

- Cough particles with initial $d_a \leq 200\ \mu m$ (but > 20 μm) become inspirable particles (droplets).

- Over 99% of the particle volume is in noninspirable particles (droplets) with initial $d_a > 200\ \mu m$.

Inhalation Exposure

- Droplet nuclei remain airborne for a sufficient time to disperse in a room.
- Larger inspirable droplets settle quickly and do not disperse widely. If one is near a coughing patient, they can be inhaled.
- Being near a cough <u>maximizes</u> inhalation exposure to droplet nuclei and inspirable droplets.

Droplet Spray Exposure

- Droplet spray exposure requires “close contact” (e.g., being within 1 m of the coughing patient).
- Epidemiologic analysis has shown that influenza infection risk is associated with proximity to the source case. This observation is used to argue for droplet spray as the primary transmission route.

Droplet Spray Exposure

- But, close contact permits droplet spray exposure <u>and</u> maximizes inhalation exposure to droplet nuclei and inspirable droplets.

- Ergo, the association of possible droplet spray exposure (strictly, close contact) with infection incidence is confounded by inhalation exposure.

Droplet Spray Exposure

- **There are no published data on the number of cough particles that strike the conjunctivae and membranes of the nares and lips of a person located close to a cough.**

- **A first pass estimate of the likelihood of exposure to droplet spray is offered.**

Droplet Spray Infection

- Assume noninspirable particles (d_a > 100 μm) travel at least 0.6 m after emission in a cough.
- There are 80 noninspirable particles per cough, and these contain >99% of the fluid volume (and virus) in the cough.
- Assume cough particles spread in a conical fashion at a 60^o angle.

Droplet Spray Infection

- **Assume a person's face is 0.6 m from the point of cough release.**
- **At 0.6 m, the receptor's face is within a circle of particle spread with area 3,800 cm^2.**
- **The projected area of the conjunctivae and membranes of the nares and lips is 15 cm^2.**

Droplet Spray Infection

- The probability that a cough particle strikes a target membrane in the circle of spread is:

$$\frac{15\ \text{cm}^2}{3{,}800\ \text{cm}^2} = 0.0039$$

- The expected number of noninspirable droplets that strike a target membrane is:

$$80 \times 0.0039 = 0.31$$

Droplet Spray Infection

- Although few cough particles should strike target membranes, these particles can carry hundreds or thousands of virus depending on the concentration in the saliva.
- We also need to consider the likelihood of being face-to-face with a patient when a cough occurs. Droplet spray exposure might be a low probability/high impact event.

Hand Contact

- **Touching fingers to a surface contaminated with virus can transfer virus to the fingers.**
- **The number of virus transferred depends on:**

- the rate of contact (touches per unit time)

- the surface area contacted (cm^2 per touch)

- the number of virus on surfaces (# per cm^2)

- the transfer efficiency (fraction, 0 to 1)

- exposure duration (time)

Hand Contact

- **Touching contaminated fingers to the face can transfer virus to target membranes.**

- **The number of virus transferred depends on:**

- the rate of contact (touches per unit time)

- contact area of the fingers (cm^2 per touch)

- the number of virus on fingers (# per cm^2)

- transfer efficiency (fraction 0 to 1)

- exposure duration (time)

Hand Contact

- **Need to consider the inactivation or die-off rate of virus on surfaces (and in the air). The rate of inactivation likely vares with the type of surface (textiles, wood, metal, skin).**

- **The rates of *de novo* contamination of different surfaces with infective virus needs to be integrated with the rates of virus inactivation on these same surfaces.**

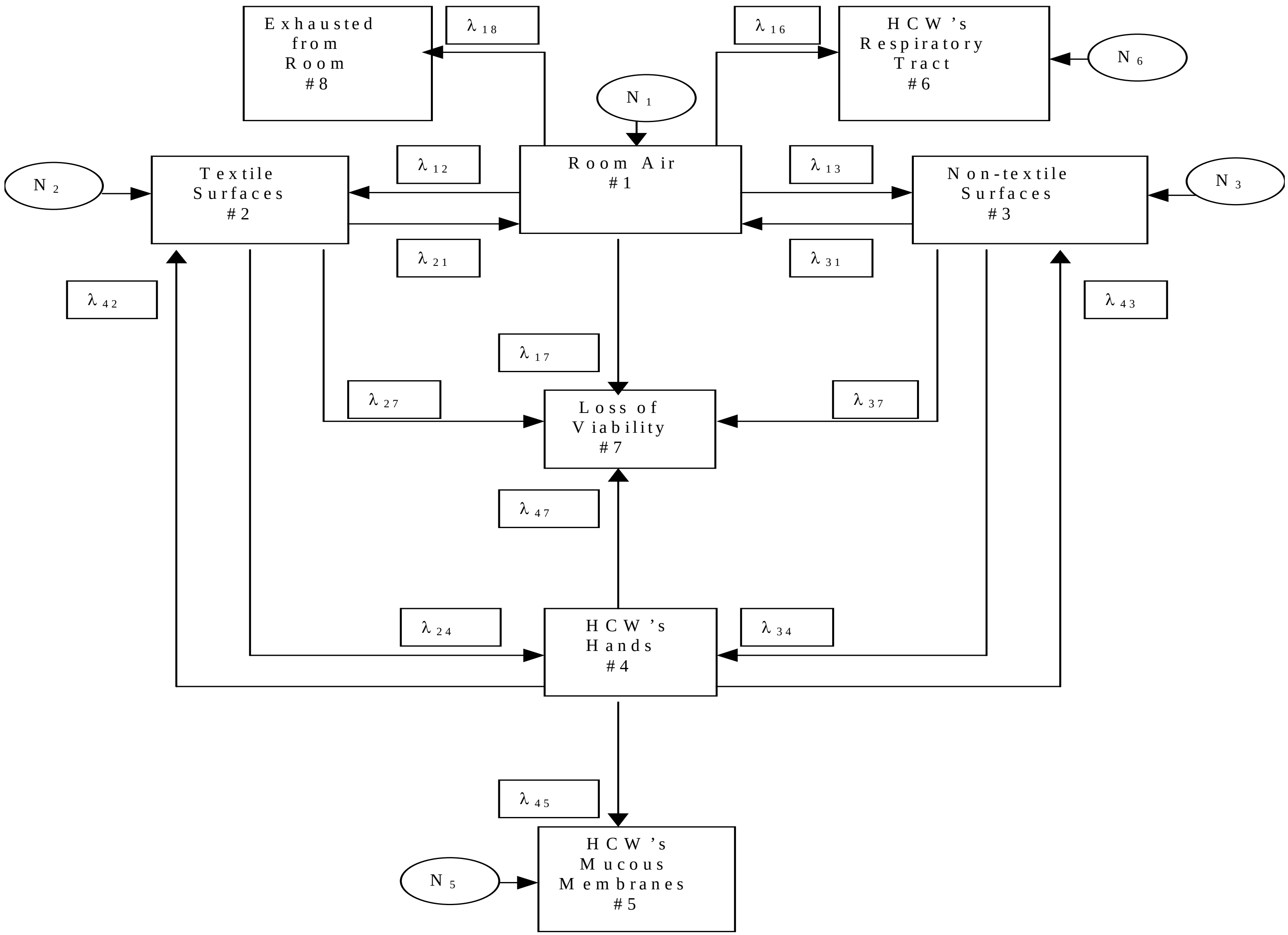
Interaction Across Exposure Routes

- Virus in coughs settles onto room surfaces.
- Virus in nasal discharge and saliva can be directly seeded onto room surfaces.
- Virus is transferred between room surfaces via hand contact.
- Virus on surfaces might be resuspended into room air.

An Integrative ProbabilityModel

- We created a generic model that considers the three exposure pathways (Nicas and Sun, Risk Analysis, Vol. 26, pp 1085-1096).

- Inputs include the cough rate, the number of virus settling on diferent surfaces, the rates of hand contact with different surfaces and with target membranes, the rate of virus inactiva-tion on different surfaces, and the likelihood of close contact when coughing occurs (drop-let spray and inspirable droplet exposure).


Exhausted from Room #8
λ 18
λ 16
HCW's Respiratory Tract #6
N 6
N 1
Room Air #1
Textile Surfaces #2
N 2
λ 12
λ 13
Non-textile Surfaces #3
N 3
λ 21
λ 31
λ 42
λ 43
λ 17
λ 27
Loss of Viability #7
λ 37
λ 47
λ 24
HCW's Hands #4
λ 34
λ 45
HCW's Mucous Membranes #5
N 5

An Integrative ProbabilityModel

- The output is the infective virus dose to the upper and lower respiratory tract (due to inhalation) and to target membranes on the face (due to droplet spray and hand contact).

- Given estimates for virus infectivity at each target site (eg, probability of infection per virus particle), the model permits estimating overall infection risk <u>and</u> permits apportioning risk among the three exposure pathways.

Research Questions

- For a given influenza A strain, what is virus infectivity at each target site?
- In fact, are the conjunctivae, lips and nares target membranes for influenza A?
- If so, how much fluid volume in a cough strikes target membranes on the face given close contact?
- If so, what are the rates of hand contact with room surfaces and with target membranes on the face?

Research Questions

- What is the infective virus concentration in saliva and nasal fluid?
- Can we obtain more accurate data on the number and szie distribution of cough particles emitted by influenza A patients?
- Can we obtain more accurate data on the inactivation rates of influenza A virus on different surafaces (textiles, wood, metal, skin) and in the air?