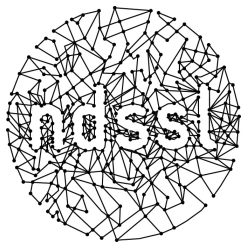
Modeling and Biological Risk Assessments

Stephen Eubank



Network Dynamics and Simulation Sciences Laboratory (NDSSL)
of the Virginia Bioinformatics Institute
and Department of Population Health Sciences
of the Virginia-Maryland Regional College of Veterinary Medicine
at Virginia Tech

National Science Advisory Board for Biosecurity panel discussion
Biological Risk Assessments: Their Strengths and Limitations
Bethesda

How does x change the world?

e.g. x = performing a gain-of-function experiment
"change the world" = affect morbidity and mortality

- What is the change in conditional probability of morbidity & mortality with and without x?
  How it affects decisions is beyond the scope of modeling.
- Hope we don't need to know distributions separately, just their difference.
  Notwithstanding Kahneman ...
- Difference is due to things that can only happen if x obtains.

What can only happen if x?

- Bad Things: costs
  - Worst case: "... and then an asteroid hits the earth"
  - Maximum reasonably foreseeable event, prudent person rule
  - Breach of containment
    bad actor, accident, poor procedures, natural disaster, publication
- Good Things: benefits
  - Less morbidity and mortality doesn't happen by itself
  - Better models for situation assessment and forecasts
    - prepare / plan
    - target surveillance
    - adapt to current situation

Modeling emerging infectious disease

- Output
  - morbidity & mortality (quantifying both risks and benefits)
  - impact of control measures
  - sensitivity analyses
- Input
  - reservoir / vector / ecology (species, prevalence)
  - population susceptibility profile (by demography)
  - route of exposure (droplet, fomite, airborne, fluids)
  - transmission rate (by demography, interaction)
  - case ascertainment (healthcare-seeking, test sensitivity/specificity)
  - serial interval, inter-generation time
  - ID50, LD50
  - risk of severe illness (by demography)
  - social response to outbreak & control measures

Assessing costs – NEIDL example

- Output

NEIDL summary for Ebola

one or more transmissions of EBOV following a needlestick event would be expected to occur **between once in 550 years and once in 18,000 years**, ... frequency category B or C. ... 10 or more public infections would be expected to occur between once in 1,900 years and once in 76,000 years. ... 100 or more ... much less likely than smaller outbreaks, ... once in 110,000 years to less than once in 10 million years.

- Input
  - literature + expert opinion gave credible parameter ranges
  - $p(consequences) = \sum_{threats} p(consequences|threat)p(threat)$ scenario construction gave credible probabilities for threats

Assessing benefits

- How would x improve models?
  - planning: emerging disease can't be parameterized, but results could concentrate credible ranges
  - better estimates of $p(threat)$ as a function of time and place permit targeted surveillance *vs* e.g. shotgun sequencing
  - adapt to current situation: improve therapeutic / vaccine escape modeling
- Could benefits be realized without x?
  Not all benefits accrue only from doing this experiment – there may be alternative, lower-cost solutions.

Catch 22 in the precautionary principle

The Precautionary Principle

First, do no harm:

In the absence of scientific consensus that an action is not harmful, the burden of proof that it is not harmful falls on those taking an action.

The catch:

- inaction can lead to similar harm
- action is prerequisite for scientific consensus

Using models to address the catch

- NRC advice to the NEIDL review:

  qualitative analyses ... [should] be prepared first.
  Quantitative analysis should ... supplement the qualitative approach *for pathogens and release scenarios for which there appear to be potentially significant risk and* **where there are sufficient data** *to support the analyses.*

- Compare lab escape rate to similar gain-of-function evolution rate
- Model possible benefit

Concluding remarks

- Modeling can help estimate costs and benefits of decisions.
  - Risk assessment is not cheap.
  - Lessons learned:
    - Risk assessment should be performed by a disinterested party.
    - The cost of risk assessment should be factored into the research, not be left as an externality.
- If gain-of-function experiments proceed,
  - prioritize those that best inform risk models
  - monitor risk estimates
  - be prepared to stop early