
Risk Assessment and Management Under Uncertainty: Lessons from Swine Flu and HIV in Blood Products

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Why Swine Flu and HIV and Blood Products?

- ◆ Biological products (vaccine, whole blood, plasma products) subject to PHS oversight
 - interplay between CDC and FDA
- ◆ Tradeoffs between
 - product risks
 - public health benefits
- ◆ Uncertainty in estimating
 - product risks
 - public health risks
 - benefits from prevention

Outline of presentation

- ◆ Swine Flu
 - decision to implement national immunization program
 - (adverse effects of the flu vaccine)
- ◆ HIV and blood products
 - screening donated blood and plasma
 - treatment with possibly infected products
 - (process to inactivate virus in plasma products)
- ◆ The Precautionary Principle
- ◆ Implications for the IOM Immunization Safety Review Committee

Swine flu outbreak

- ◆ 13 flu cases at Fort Dix, NJ in February, 1976
 - one death
 - in “healthy” soldiers
- ◆ Antibody test suggests similarity to 1918 flu virus
 - very few were naturally immune
- ◆ Kilborne’s theory re 11-year pandemic cycle
 - NY Times op-ed
 - last pandemic in 1968, so “almost due”
- ◆ Possibility of up to a million deaths in US 1977

Swine flu decisionmaking

- ◆ Feb. 14 meeting called by CDC Director Sorenson
 - included FDA, NIAID, Army, NJ DPH, Kilborne
- ◆ Decisions
 - special surveillance for swine flu
 - » Army at Fort Dix, including blood samples
 - » surrounding area by NJ DPH
 - » nationwide by NIAID
 - prepare antibodies for use in laboratory tests
 - start preparing a vaccine
 - » Kilborne to develop special virus strains
 - » FDA to send to manufacturers when ready

Swine flu decisionmaking

- ◆ Feb. 19 press conference to “inform the public”
 - NY Times: “... the virus that caused the greatest world epidemic of influenza in modern history ... may have returned.”
- ◆ Feb. 20 meeting at Bureau of Biologics
 - including Kilborne and Albert Sabin
 - no new Swine flu cases in NJ, US, rest of the world
 - new strains in the past always turned to pandemics
 - » could be due to return of warm weather
 - mood changed from “What if ...” to “Well, here it is”

Swine flu decisionmaking

- ◆ Options (as seen at March 10 ACIP meeting)
 - Do nothing
 - » not possible if public knew that policy makers knew of risk
 - Implement national immunization campaign
 - » Pro: possibility of major outbreak could not be dismissed, so an extraordinary federal response was required
 - » Pro: time needed to manufacture sufficient vaccine and immunize entire nation before the flu season
 - » Con: epidemic may not materialize, but will divert resources from programs
 - » Con: will look foolish if no epidemic materializes

Swine flu decisionmaking

◆ Conclusion

– Stallones:

» evidence of a new strain with man-to-man transmission

» new strains “always” lead to pandemics

» for the first time, there was both knowledge and time for mass immunization

– Kilborne: Better to vaccinate without an epidemic than an epidemic without a vaccine”

– Kolata: Predictable, given mission of public health to protect the public and prevent disease

Swine flu decisionmaking

- ◆ Presentation to Secretary of HEW and President Ford de-emphasizes uncertainty
 - necessary to “sell” the program to policymakers and the public
 - Focus on possible consequences (vivid metaphor: 1918 flu) rather than level of risk (hard to grasp)
 - HEW Secretary David Matthews asked about the probability of an epidemic and was told “unknown”
 - » Sensor’s “strong possibility” translated by Matthews to “no”
 - » estimates of the ACIP members ranged from 2 to 20 percent, but were never discussed
 - Agreement of Jonas Salk and Sabin of course of action

Lesson: Probe assumptions and explore uncertainty

- ◆ Alexander's question (Neustadt and May):
 - What information would make the group change its mind about the need to immunize the nation against swine flu?
 - » Every case was mild?
 - » No one but the soldiers at Fort Dix got swine flu?
 - » Timing or location of outbreaks?
 - Pursuing this would flush out deeper questions
 - » tradeoffs between side effects and flu
 - » distinguishing between severity and spread
 - » programming and scheduled review
 - » stockpiling

Lesson: Consider intermediate options

- ◆ Alexander's option: Manufacture vaccine, wait and see if needed (Neustadt and Fineberg)
 - Pro: vaccine ready if surveillance indicates need
 - Pro: immunization risk minimized
 - Con: may not be enough time to get everyone immunized after an outbreak was detected
 - Con: not ACIP's role to design administrative machinery
 - Con: manufacturing but not using vaccine would make the government appear foolish

HIV and the blood supply

- ◆ Identification of AIDS and a blood-borne disease
 - June 1981: first cases in homosexual men
 - June 1982: first cases identified in IV drug users
 - July 1982: first cases in hemophiliac patients
 - December 1982: first case in transfused infant
 - Similarity to transmission of hepatitis B
- ◆ By January 1983 epidemiological evidence strongly suggested that blood and blood products transmitted AIDS (IOM)

HIV and the blood supply

- ◆ CDC calls a public meeting on January 4, 1983 to identify opportunities to prevent AIDS
 - included PHS representatives, especially FDA, plus people from the blood services industry
- ◆ Suggestions for immediate action
 - blood banks should question donors directly about their sexual behavior
 - run blood donations through a series of surrogate marker tests, including hepatitis B core antibody
- ◆ Heat treatment to inactivate virus in development

Questioning of blood donors

- ◆ CDC: blood banks should question donors directly about their sexual behavior and defer
 - seen as discriminatory by gay activists and “inappropriate” by blood banks
 - » might drive donors away
 - plasma industry recommends donor education and self-deferral programs for high-risk groups
- ◆ PHS recommendations (March, 1983)
 - members of groups at increased risk for AIDS should not donate plasma and/or blood products

Surrogate marker tests

- ◆ CDC: run blood donations through surrogate marker tests, including hepatitis B core antibody
 - 88% “correlation” with AIDS
 - plasma industry regards recommends against surrogate testing until its feasibility is assessed
- ◆ PHS recommendations (March, 1983)
 - conduct studies to evaluate screening procedures including lab tests and physical exams

Attempts to reformulate policies

- ◆ Plasma industry (June, 1983)
 - risk appears to be 1 per million patients transfused
 - direct donation programs will not increase safety but will seriously disrupt that nation's blood supply
- ◆ Contaminated plasma lots (July, 1983 BPAC)
 - withdraw lots of AHF concentrate on case-by-case basis, only if good evidence that plasma from donor with AIDS present
 - based on concern about supply of AHF concentrate and skepticism that blood products transmitted AIDS
- ◆ Surrogate marker tests (December, 1983 BPAC)
 - would eliminate non-infected donors and threaten blood supply
 - cannot differentiate high-risk from donors from other MSMs
 - would defer too many Asians and others with high prevalence

Advice for hemophiliacs

- ◆ National Hemophilia Foundation (January 1983)
 - use cryoprecipitate rather than AHF concentrate in infants, newly diagnosed patients, and mild cases
 - insufficient evidence to develop specific recommendations about blood product use in the treatment of severe hemophilia
 - advice to physicians rather than patients
 - no advice regarding prophylactic use of AHF concentrate or safe sex
- ◆ Driven by
 - value of AHF concentrate for a devastating disease
 - skepticism AIDS transmitted through blood products

Lesson: Probe assumptions and explore uncertainty

◆ Consider

- strength of evidence that AIDS is a blood-borne disease
- estimates of the risk per transfusion or use of blood product
- performance of potential screening methods
- impact of screening on amount of blood and blood products available
- availability of alternatives for blood and blood products

Lesson: Consider intermediate options

◆ Consider

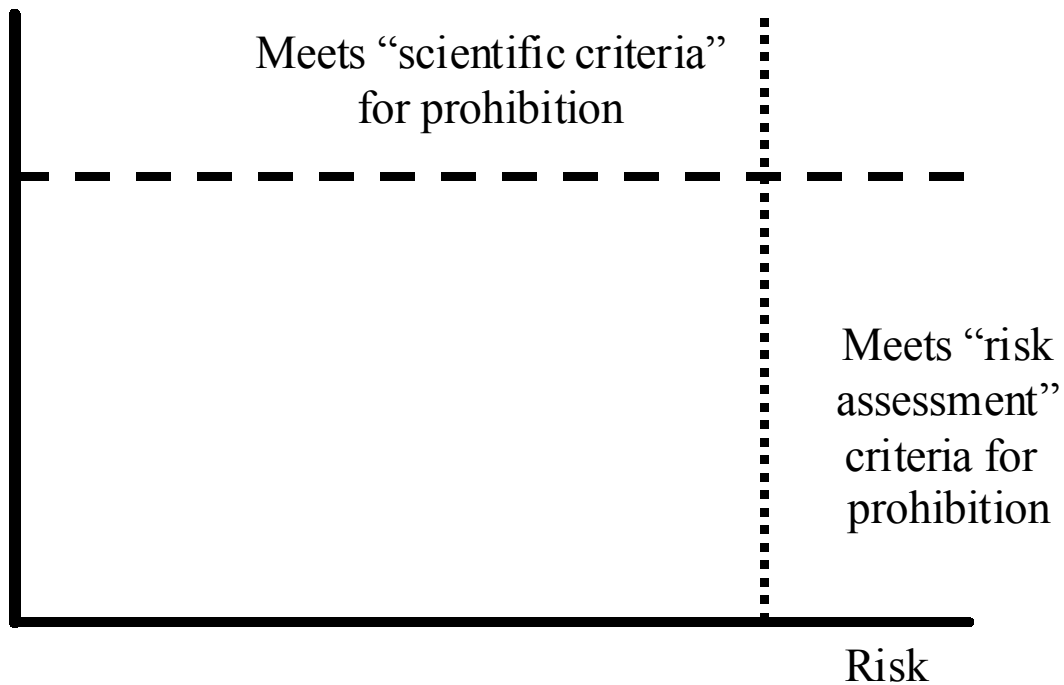
- implementing self-deferral and studying impact on blood supply
- warning hemophiliacs of risks to themselves and sexual partners
- involve patients in decisionmaking about their own care and behavior
- stopping prophylactic use of AHF concentrate

Precautionary Principle

- ◆ Many different statements
 - sometimes contradictory
- ◆ General ideas
 - appropriate weight to public health and environmental concerns
 - » counter balance industry
 - consideration of appropriate burden of proof for maintaining status quo and making changes
 - explicit consideration of scientific uncertainty

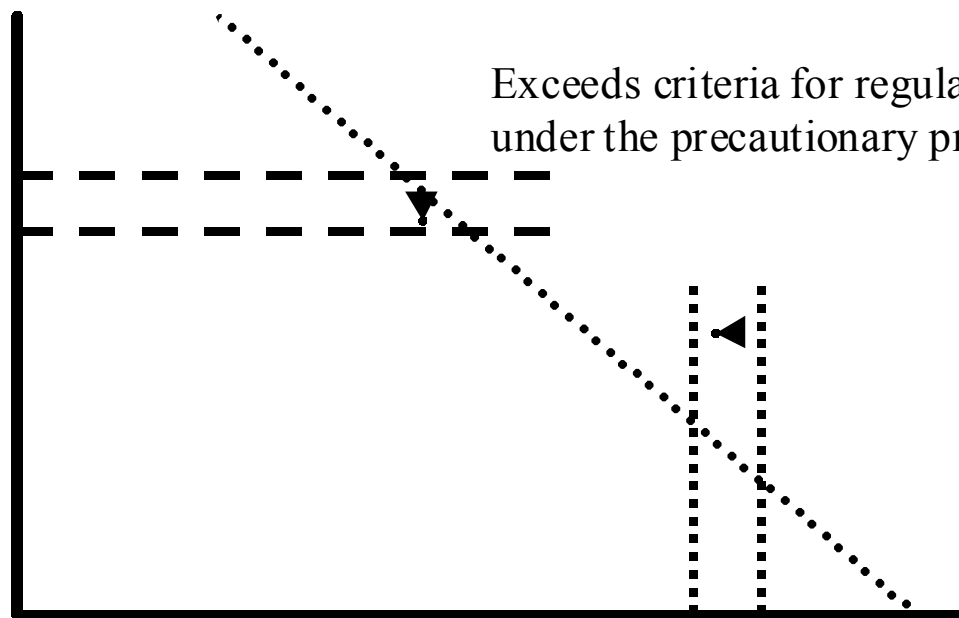
Standard risk management model

Strength of evidence



Precautionary Principle

Strength of evidence



Exceeds criteria for regulation
under the precautionary principle

Risk

EU guidelines for application of the Precautionary Principle

- ◆ **Proportional** to the chosen level of protection
- ◆ **Non-discriminatory**
 - comparable situations treated similarly
- ◆ **Consistent** with similar measures already taken
- ◆ **Based on examination of the potential benefits and costs** of action or lack of action
- ◆ **Subject to review** in the light of new data
- ◆ **Capable of assigning responsibility for producing the scientific evidence** for risk assessment

EU guidelines for application of the Precautionary Principle

- ◆ Proportional to the chosen level of protection
 - zero risk is generally not achievable
 - adopt the least restrictive option that meets public health needs
- ◆ Examples:
 - warning hemophiliacs of risks to themselves and sexual partners
 - involve patients in decisionmaking about their own care and behavior

EU guidelines for application of the Precautionary Principle

- ◆ Based on examination of the potential benefits and costs of action or lack of action
 - including economic C/B analysis where appropriate and feasible
 - also include social concerns such as
 - » distributional effects
 - » ethical obligations
 - » institutional credibility
- ◆ Example:
 - balancing potentially reduced risk of AIDS with availability of blood products

EU guidelines for application of the Precautionary Principle

- ◆ Subject to review in the light of new data
- ◆ Capable of assigning responsibility for producing the scientific evidence for risk assessment
- ◆ Examples:
 - Alexander's option (manufacture vaccine and wait to see if needed) for Swine Flu
 - Reconsideration of
 - » AIDS risks associated with various products and uses
 - » impact of screening alternatives on AIDS risk and availability of blood and blood products