



An Objective and BCA-Compliant Definition of 'Adverse Effect'

Richard B. Belzer, PhD
Regulatory Checkbook
Mount Vernon, VA

Society for Benefit-Cost Analysis
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**EXISTING DEFINITIONS ARE
INCOMPATIBLE WITH BCA**

An objective benefit assessment...



Benefit assessment

...rests on the shoulders of a well-defined risk objectively estimated.



Benefit assessment

Risk assessment

Dose-response

Adverse effect

...rests on the shoulders of a well-defined risk objectively estimated.



Benefit assessment

Risk assessment

Dose-response

Adverse effect

Risk assessments depend on subjectively defined adverse effects



*Adverse effect
ambiguously
defined and
subjectively
estimated*



**PURPORTEDLY SCIENTIFIC
DEFINITIONS
OF ADVERSE EFFECTS**

Toxicology & pharmacology

Casarett & Doull (6th) 2001

- 1,200+ pages [242]
- Circularity: ‘adverse effects’ are effects determined to be adverse
- Ambiguity: ‘adverse effects’ are bad
- Flashes of transparency:
 - ‘Adversity’ is defined by policy, not science
 - Typically, scientists make policy by deeming effects ‘adverse’

General NRC reports without objective definitions

- 1983 *Risk Assessment in the Fed'l Gov't*
- 1989 *Improving Risk Communication*
- 1993 *Issues in Risk Assessment*
- 1994 *Science & Judgment*
- 1996 *Understanding Risk*
- 2008 *Science & Decisions*
- 2014 *Review of EPA's Integrated Risk Information System (IRIS) Process*



**STATUTORY AND
REGULATORY DEFINITIONS**

Statutory & regulatory

- Stansell & Marvelli 2005
 - Statute: > 300 times
 - Regulation: > 2,000 times
 - Rampant circularity and ambiguity
- Co-located terms also are undefined
 - '[in]Significant'
 - 'Potential'
 - '[un]Reasonable'

Regulatory

- EPA
 - 'A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge.'
- FDA
 - **Serious, adverse health consequences** - any significant adverse experience, including those which may be either life-threatening or involve permanent or long term injuries, but excluding injuries that are nonlife-threatening and that are temporary and reasonably reversible.

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**PRACTICAL DEFINITIONS:
AIR POLLUTION**

Air pollution

- NAAQS
 - Primary standard: ‘requisite to protect the public health’ ‘allowing an adequate margin of safety’ [CAA 109(b)(1)]
 - Secondary standard: ‘requisite to protect the public welfare from any known or anticipated adverse effects’ [CAA 109(b)(2)]


Adverse effects from air pollution

ATS 1985

- 
- Odors
 - Eye, nose & throat irritation that may interfere with normal activity
 - Acute upper respiratory tract infections that do not interfere with normal activity
 - Increased incidence of cough/phlegm production requiring medical attention
 - Increased prevalence or incidence of chest tightness
 - Increased prevalence of wheezing apart from colds, or of wheezing most days or nights
 - Small but sig reduction in population mean FEV1 or FEV75
 - Chronic reduction in FEV1 or FVC associated with clinical symptoms
 - Increased exacerbations of disease in persons with chronic cardiopulmonary or other disease
 - Increased incidence, prevalence or frequency of lower respiratory tract infection, symptomatic asthmatic attacks, cancer or mortality

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CANCER RISK ASSESSMENT

Cancer risk assessment

- EPA 2005
 - Adversity inferred by analogy: ‘animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity’ (EPA 2005, p. 1-11)
 - Adversity inferred by precursor: ‘A *key event* is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element’ (EPA 2005, p. 1-10)



SAFETY ASSESSMENT



Safety assessment

- Reference Dose: An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

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° **A BONA FIDE SCIENTIFIC
DEFINITION OF
'ADVERSE EFFECT'**





A scientific definition of 'adverse effect'

- Requirements

- Positive, not normative.
- Testable.
- Transparent and reproducible.
- Unaffected by the values of the risk assessor.
- Unaffected by the interests of the risk assessor's employer or funder.

A scientific definition of 'adverse effect': WTP

- 'Adversity' objectively defined
 - An 'adverse effect' is anything a person is willing to pay to avoid.
- 'Severity' objectively defined
 - The severity of an 'adverse effect' is the amount a person is willing to pay to avoid it.



A scientific definition of 'adverse effect': WTP

- Desirable technical attributes
 - All health endpoints are eligible
 - Minimal constraints on functional form
 - Inflection points are permitted
 - Not zero bounded; negative WTP = benefit
 - Can be estimated using conventional tools



A scientific definition of 'adverse effect': WTP

- Desirable ethical attributes
 - No theological constraints
 - Limits scientists to science, policy officials to policy
 - Policy choices are not embedded in risk assessment or valuation
 - Unequal treatment arises in decision-making

A scientific definition of 'adverse effect': WTP

Desirable political attributes

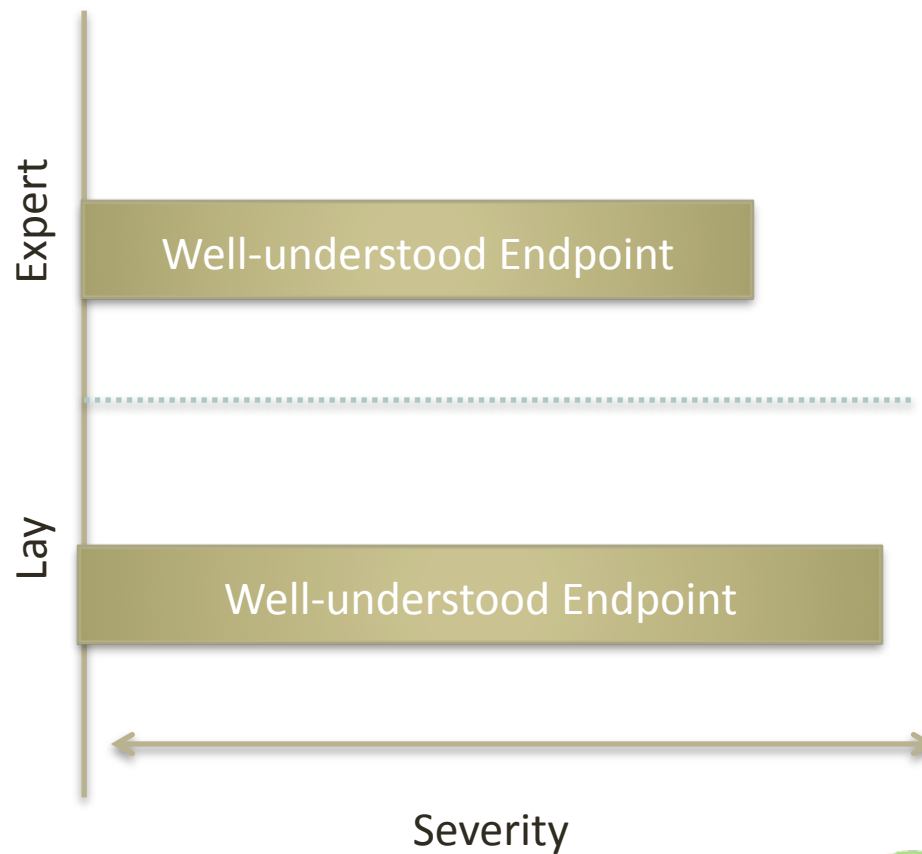
- Consistent with NRC 1983 ('Red Book')
- Compatible with benefit-cost analysis
- Aggregate WTP = Σ individual WTPs
- Makes unequal treatment of individuals transparent
- Makes inefficient decisions transparent



**WHAT ABOUT EFFECTS
UNDERSTOOD ONLY BY
SCIENTISTS?**

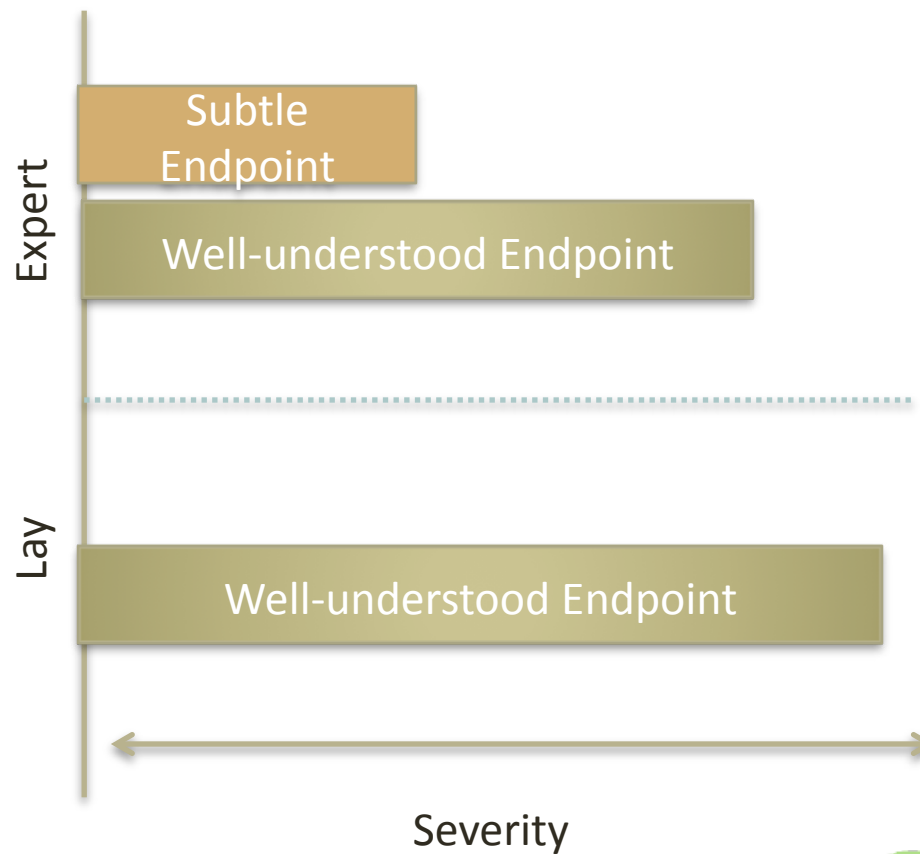
What about effects understood only by scientists?’

1. Estimate expert and lay WTPs for a well-understood endpoint



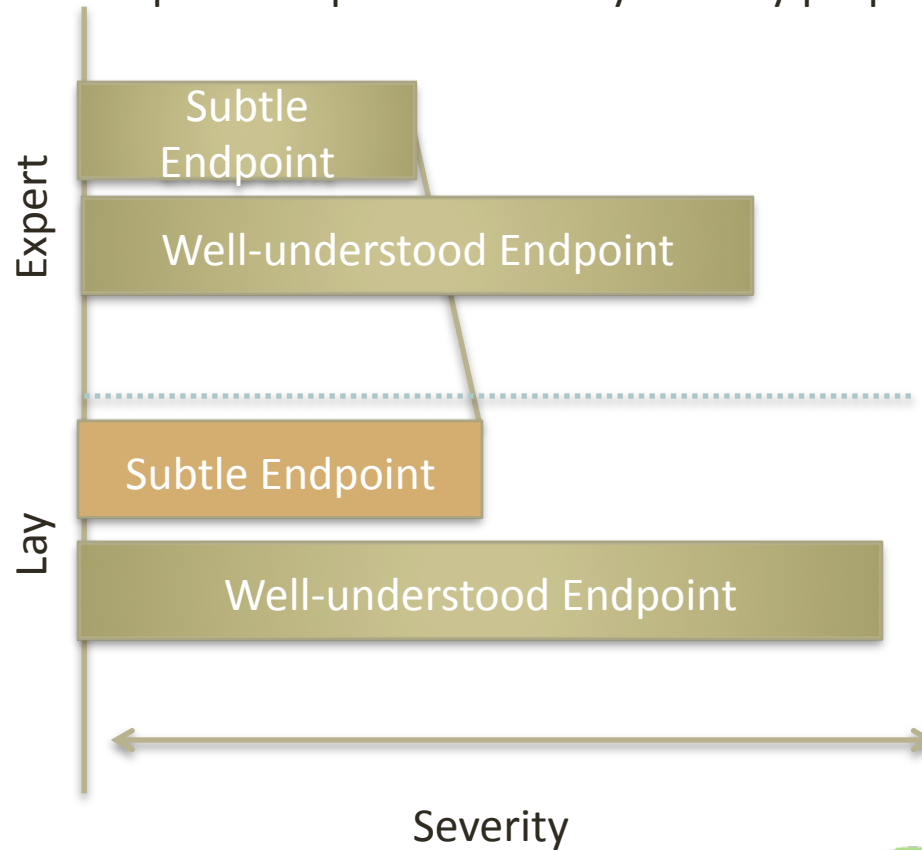
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2. Estimate expert WTP for a subtle endpoint



What about effects understood only by scientists?’

1. Estimate expert and lay WTPs for a well-understood endpoint
2. Estimate expert WTP for a subtle endpoint
3. Extrapolate expert WTP to lay WTP by proportionality





SUMMING UP

Summing up

- Existing definitions of ‘adverse effect’ are nonscientific, lack objectivity, and are incompatible with benefit-cost analysis.
- Decades of risk assessment practice and NRC reports have achieved little.
- Economics provides scientific and BCA-compatible principles and methods determining adversity.
- Toxicologists and other experts have a key role to play, but it’s different than the role they have played to date.

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