

Risk vs Benefit analysis in children

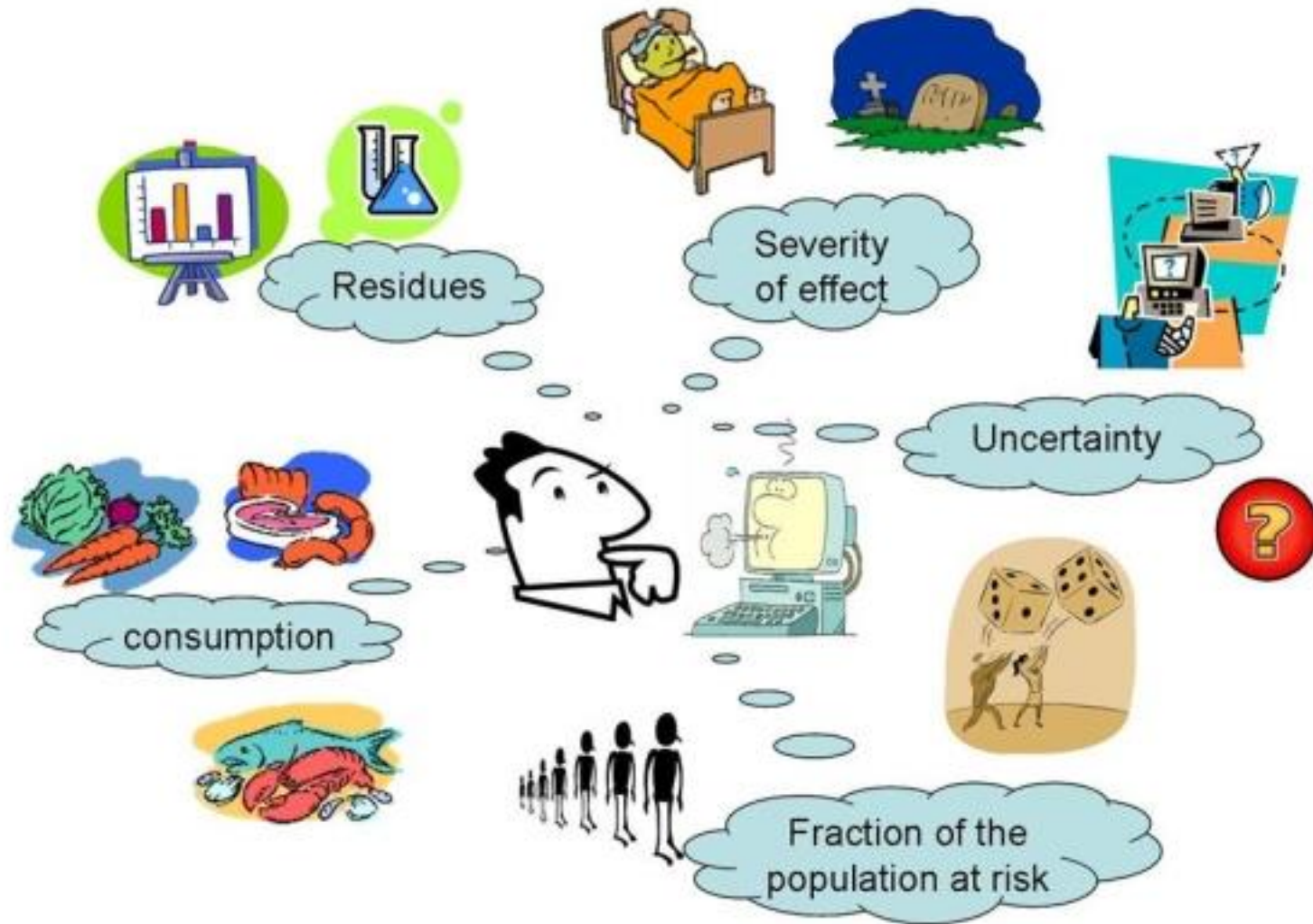
Dr. Jithangi Wanigasinghe

**IS THE BENEFIT
REALLY WORTH
THE RISK?**



Risk Vs Benefit assessment

It is a framework for determining how far it is worth controlling the production, use, storage and disposal of existing substances in order to achieve reductions in the risk to human health and the environment.



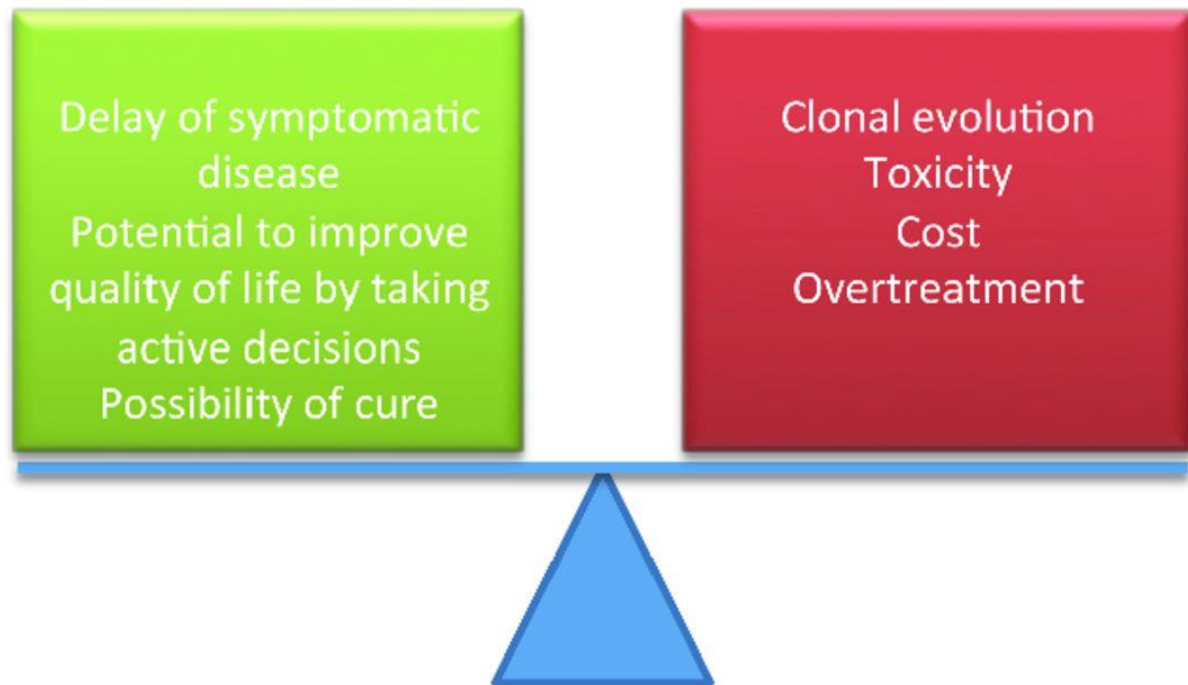


BENEFITS

Delay of symptomatic disease
Potential to improve quality of life by taking active decisions
Possibility of cure

RISKS

Clonal evolution
Toxicity
Cost
Overtreatment



What is special about pediatric research?

- Historically both “understudied” and “overstudied”
- Children may be vulnerable to
 - Not understand the risks and benefits of research
 - Not be able to object to enrollment
- Children may enroll in research
 - Not in their interest
 - Against their wishes
- “Protecting” children in 45 CFR 46
 - Limiting risks
 - Parental Permission
 - Child Assent



Role of ERCs

“Reasonable risk in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.”

Risk analysis

Defining risk

- Combination of the probability and magnitude of some future harm
- Multiple categories of risk is to trigger different requirements
 - “high” or “low”
 - “minimal” or “greater than minimal”
 - “minimal risk”, “minor increase over minimal risk” and “greater than minimal risk”

What is Minimal Risk?

- **The US regulations define minimal risk as:**

“Probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests”

45CFR 46.102(i)

Risk assessment



Red

High risk and requires high level of scrutiny



Amber

Medium risk and requires internal review



Green

Low risk, might not require internal review as long as compliant with school governance procedures

Defining the risk

- There is ongoing debate over the “best definition of risk”
- The risk evaluation may vary depending on the type of subjects
- This is particularly important in the vulnerable populations

Participant vulnerability

- Participant capacity (mental, emotional, cognitive)
- Age
- Wellness or health status
- Institutionalization
- Power relationships
- Gender and gender identity
- Ethnic, racial, or national minority status
- Setting and recruitment
- Dependency
- Socio-economic status

Risk assessment

- Technique used to determine the nature, likelihood, and acceptability of the risks of harm
- National Commission's *Report on Research Involving Children* list following a common-sense estimation of the risk
 - estimation based upon investigators' experience with similar interventions or procedures
 - statistical information
 - situation of the proposed subjects
- Difficult as it may be, careful risk assessment is the key to deciding on the appropriate level of protections

Risk assessment in children

- Certain procedures in children identified as “greater than minimal risk” (Janovsky 1981)

Survey of IRB Chairs (N=188)

	Minimal	Minor increase over Minimal	Greater than Minimal
Blood draw	82%	17%	1%
Sexual activity survey	45%	30%	25%
Allergy skin testing	23%	43 %	27 %
PK Study 1/100,000 chance of death	8%	30%	59%
LP	6%	24%	70%
Drug tested safe in 500 adults	5%	23%	65%

Risk assessment in children- Consent

- Age of consent and assent
 - Under the age of 18, children cant legally give consent
 - Assent involves children in the process of consent
- Interpreting a child's consent
 - Keep an eye open for any indications of refusal, vigilance at all times

Elements of Informed Consent

- Decisional Capacity
 - Ability to understand options
 - Ability to understand consequences of actions
 - Ability to relate consequences to set of personal values
- Disclosure
 - Reasonable practitioner
 - Reasonable patient
 - Particular patient
- Comprehension
 - Context dependent
- Voluntariness
 - Persuasion
 - Coercion

Consent/Assent/Permission

- Parental Permission
 - Not the same as consent
 - More limited scope and authority than consent
- Child Assent
 - Obtaining assent vs respecting “dissent”
 - Assent demands less competence
 - Limited understanding of the research process, its aims, and a wish to participate (Backe-Hanson 2002)

Risk versus benefit analysis

Participant Risks vs. Benefits

Study on STD prevalence and response to therapy in the hotel industry

- ❑ Biologic/Physical
- ❑ Social/Emotional
 - From the product: side effects
 - From HIV/STI testing
 - Partner issues
 - Stigma
- ❑ Improved access to health care
- ❑ Better prevention
 - Risk reduction counseling
 - STD treatment
 - Condoms
- ❑ Other
 - Cash
 - Sense of social contribution

Community Burdens and Benefits

— Risks and Burdens

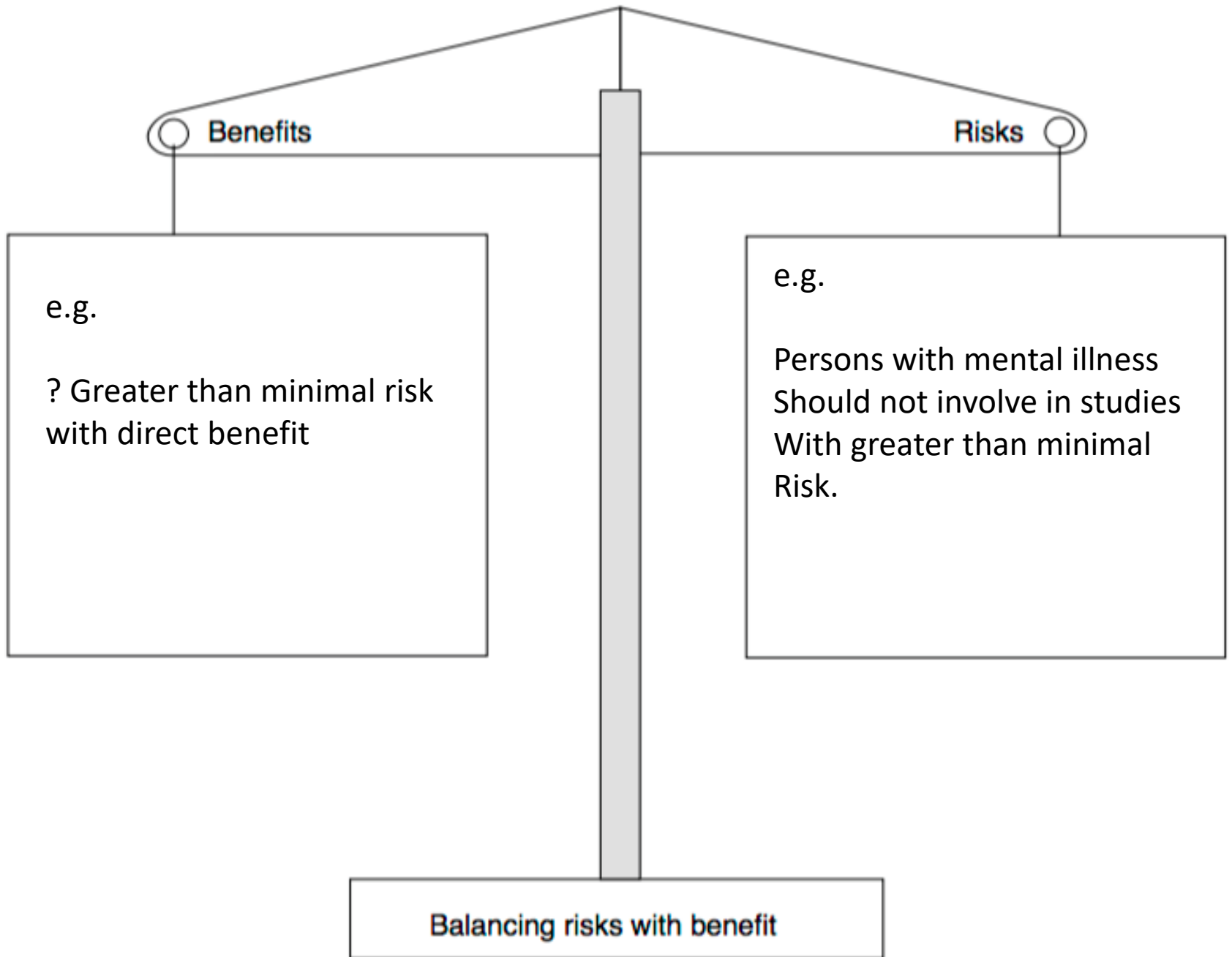
- Possible stigma
- Diversion of local health personnel

— Benefits

- Improved health infrastructure
- Training
- Community education on HIV/research
- Preferential access to product if it proves effective

Defining benefits

- Adult research yield three types of benefits
 - (1) direct medical benefit to subjects
 - (2) indirect benefit to subjects
 - (3) benefit to others



Benefits

Risks

e.g.

? Greater than minimal risk
with direct benefit

e.g.

Persons with mental illness
Should not involve in studies
With greater than minimal
Risk.

Balancing risks with benefit

Limiting pediatric research based on risks and benefits

	Minimal risk	Minor increase over minimal risk	Greater than minor increase over minimal risk
Prospect of direct benefit		Risk is justified by the benefits Risk/benefit is as favorable as alternatives	Risk is justified by the benefits Risk/benefit is as favorable as alternatives
No prospect of direct benefit		Commensurate experiences Vital knowledge about subjects disorder	Address serious problem affecting children

Enhance IRB Education and Decision Making

- Clear understanding on risk analysis – prevents over restriction as well as safe guards children
- Establish certain minimal protections
- Uniformity in categorisation

Summary

- Define risk analysis and benefit assessment
- Discuss how risk benefit balance should be done

1982

Lawson



Late at night, and without permission, Reuben would often enter the nursery and conduct experiments in static electricity.