Equitable Access: Ethics in Research with Children

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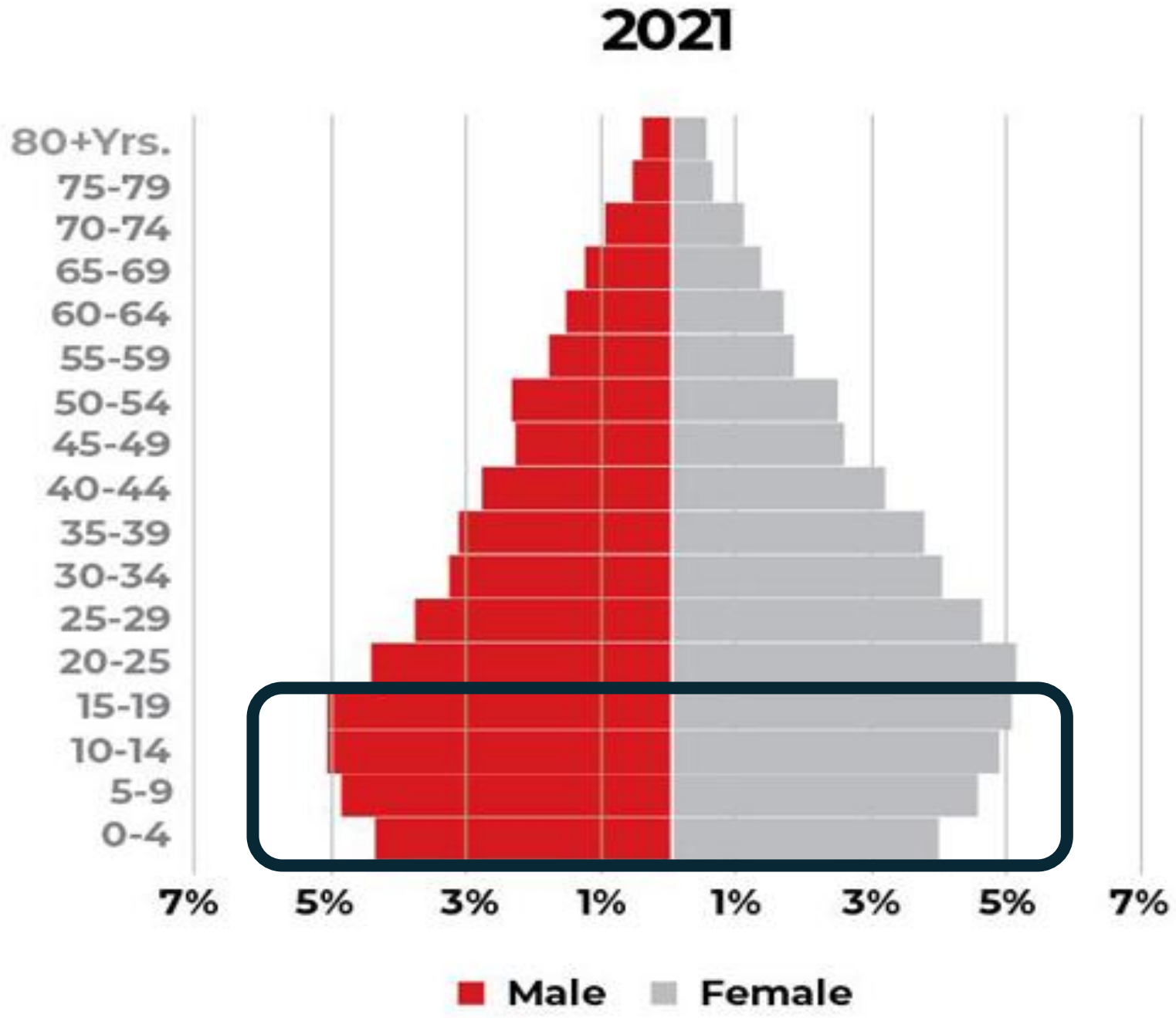
Disclosures

- My husband works for Eli Lilly & Company, Inc. They conduct clinical trials with children and adolescents.

Learning Objectives

1. Use a theoretical framework to assess child vulnerability and appropriate access to research.
2. Apply empiric data on child decision-making capacity to research consent, assent, and permission

Nepal Populatior Pyramid



Drugs used “Off Label” in Children

40%

Objective 1: Theoretical Approach to Vulnerability & Equitable Access

Photo : Dhilung Kirat, https://commons.wikimedia.org/wiki/File:Sakela_Ubhauli_2009,_Tundikhel_Nepal_%283588521516%29.jpg

Inclusion of Children in Research

- Exclusion is NOT protection

- CIOMS - Guideline 17

  “Children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion.”

Theoretical - Vulnerability Paradigm Shift

Group membership
(e.g. child, pregnant person)

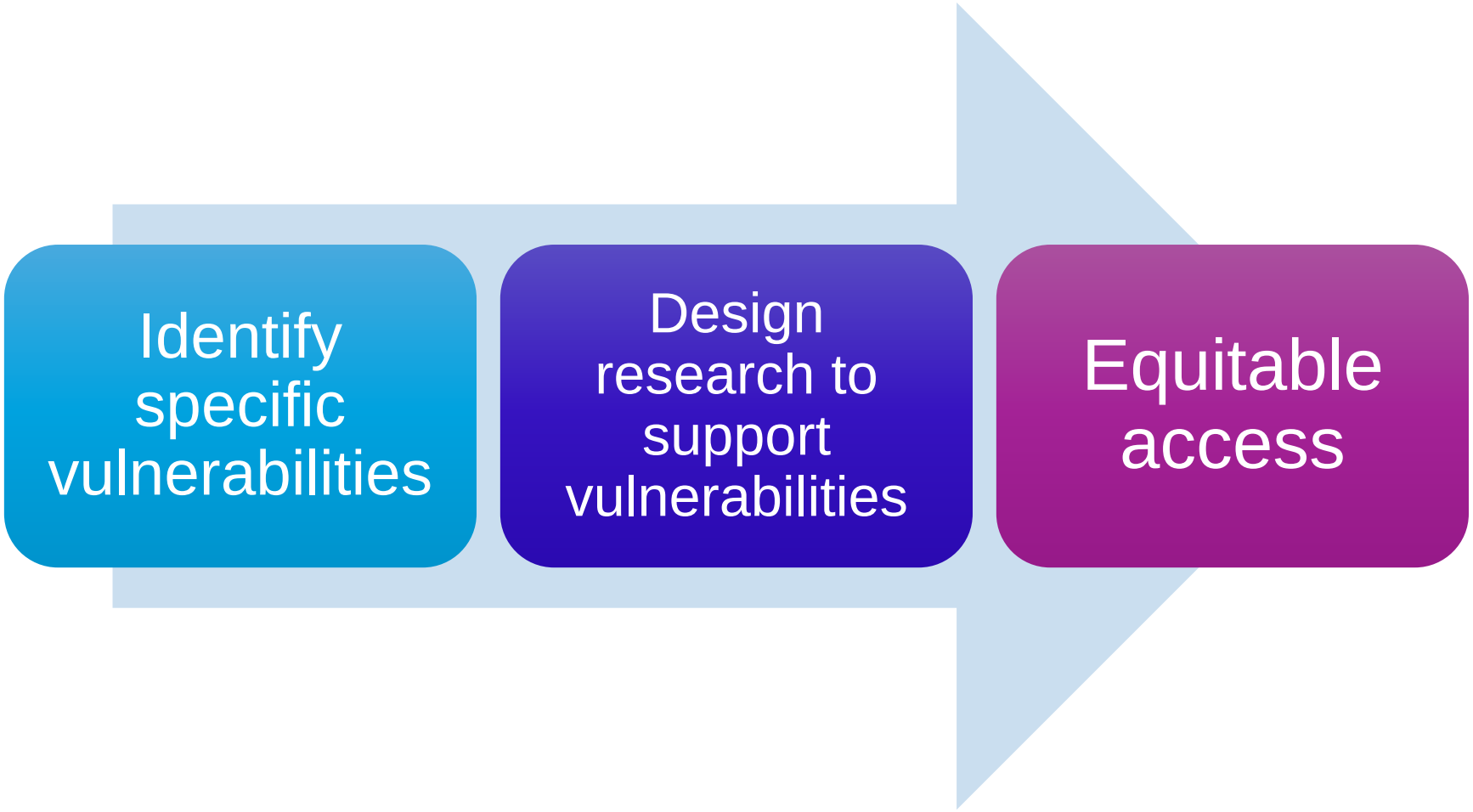
Individual characteristics & contexts that confer vulnerability

1. Dependent on others (legal, financial)
2. Extreme poverty, lack of resources
3. Capacity, education
4. Medical illness
5. Social group whose rights devalued
6. Power differential (age, gender, ethnic)
7. Deferential behavior

Developmental Moving Targets

Source: https://english.onlinekhabar.com/covid-19-outbreak-and-fear-of-increasing-school-dropout-rate-in-nepal.html

Equitable (Appropriate) Access



Objective 2: Empiric Approach to Consent, Assent & Permission

Photo : Dhilung Kirat, https://commons.wikimedia.org/wiki/File:Sakela_Ubhauli_2009,_Tundikhel_Nepal_%283588521516%29.jpg

Regulations Affecting Consent, Assent & Permission

- NHRC: “Research involving children should be carried out only after taking informed consent from their parents or LAR.”

- CIOMS: Before undertaking research involving children and adolescents, the researcher and the REC must ensure that:
  - Parent/LAR has given permission; AND
  - Agreement (assent) of child obtained in keeping with their capacity
  - Information tailored to the child’s maturity.

Assent

- Child’s affirmative agreement to research procedures
- Typically recommended for ages 7 and above
  - Language appropriate to child’s age
  - Oral script, Separate assent document, Informed consent with added signature lines
- NHRC:
  - 7-11 years - Verbal assent
  - 12-17 years - Written assent
  - 18+ years – Written informed consent

Decision-Making Capacity

- Capacity – the ability to appreciate the risks and benefits of clinical situation and to make reasoned choices
- Elements:
  - Understanding
  - Appreciation of their own situation, and how it will be affected by research
  - Reason among different options
  - Voluntary choice
- Evolves across adolescence and into adulthood

Child Capacity to Consent-NCD Research

- Dutch capacity study
  - 200 children 6-18 years old
  - Multiple different diagnoses, research protocols
  - Standardized capacity assessment tool (MacCAT-CR – adapted)
- Adequate capacity by 12 years of age

- Source: Hein et al. Accuracy of the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) for Measuring Children's Competence to Consent to Clinical Research. JAMA Pedaitr. 2014;168(12):1147-1153

Capacity to Consent to an RCT

MacCAT-CR Subscales	Range	12-21 yo Mean (±SD)	Healthy Adults (range)
Understanding	0 - 26	21.0 (±3.4)	20.2 - 25.8
Appreciation	0 - 6	5.5 (±0.9)	4.2 – 5.9
Reasoning	0 - 8	6.6 (±1.9)	4.4 - 7.1
Choice	0 - 2	2 (±0)	2

Predictors of Capacity to Consent

Predictors	Beta	SE	Std. Beta	T
Age				
12-14 yrs	-2.770	1.143	-0.213	-2.423*
15-17 yrs	-0.686	0.859	-0.063	-0.798
18-21 yrs (ref)	(ref)	(ref)	(ref)	(ref)
Gender (female ref)	-2.276	0.766	-0.201	-2.970**
Family Affluence	0.758	0.219	0.242	3.464***
Health Literacy - REALM	0.518	0.066	0.614	7.889***
Experiences with Health Care Score	-0.043	0.369	-0.008	-0.116
Adjusted R squared=0.648				

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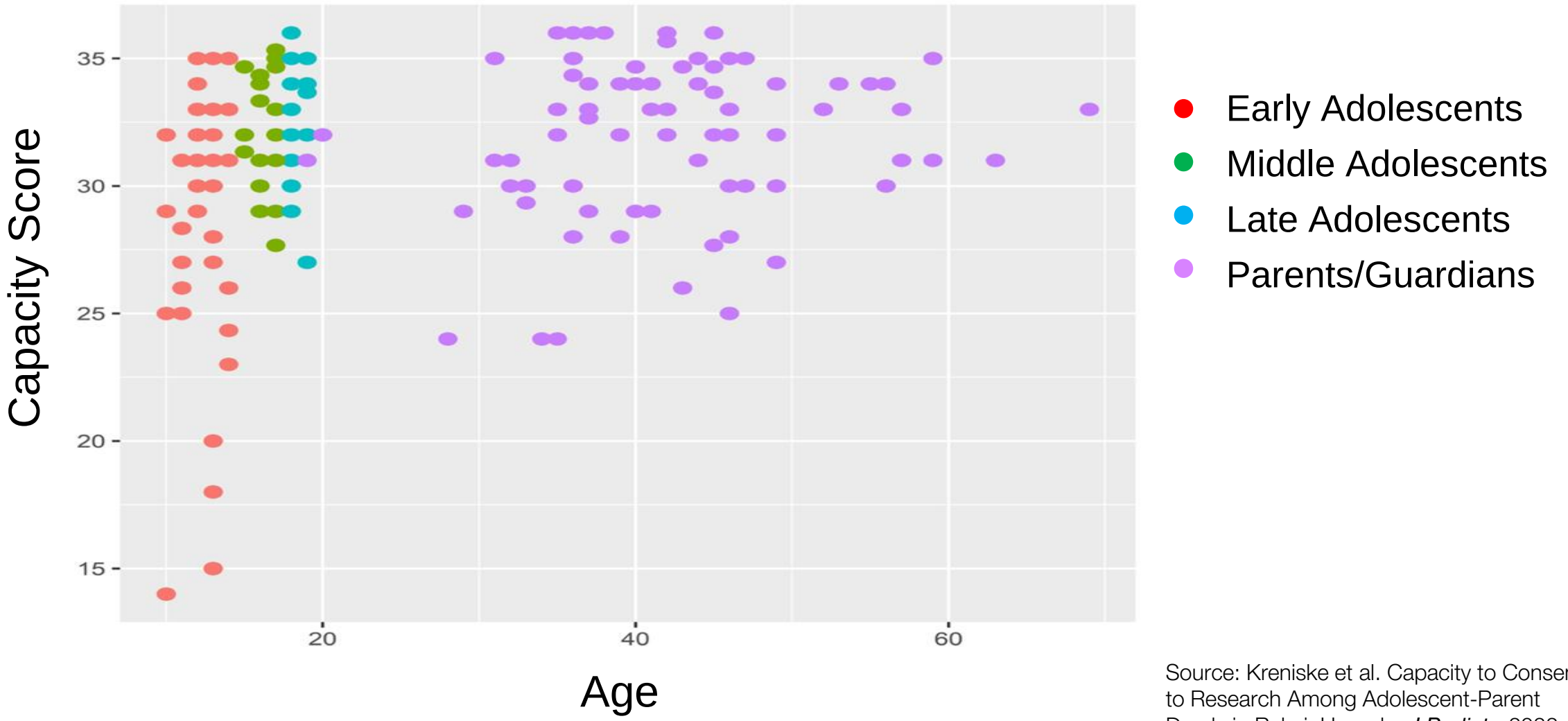
Capacity to Consent to HIV Research by Age Rakai, Uganda



Source: Kreniske et al. Capacity to Consent to Research Among Adolescent-Parent Dyads in Rakai, Uganda. *J Pediatr*. 2022.

What Does the Mean for Child Research in Nepal?

- Consent processes
  - Legal – Assent/Permission
  - Conceptually – “co-consent”
- Waivers of parental permission
- Meaningful engagement of children in research

THANK YOU!
QUESTIONS?

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Declaration of Helsinki – Vulnerable Groups

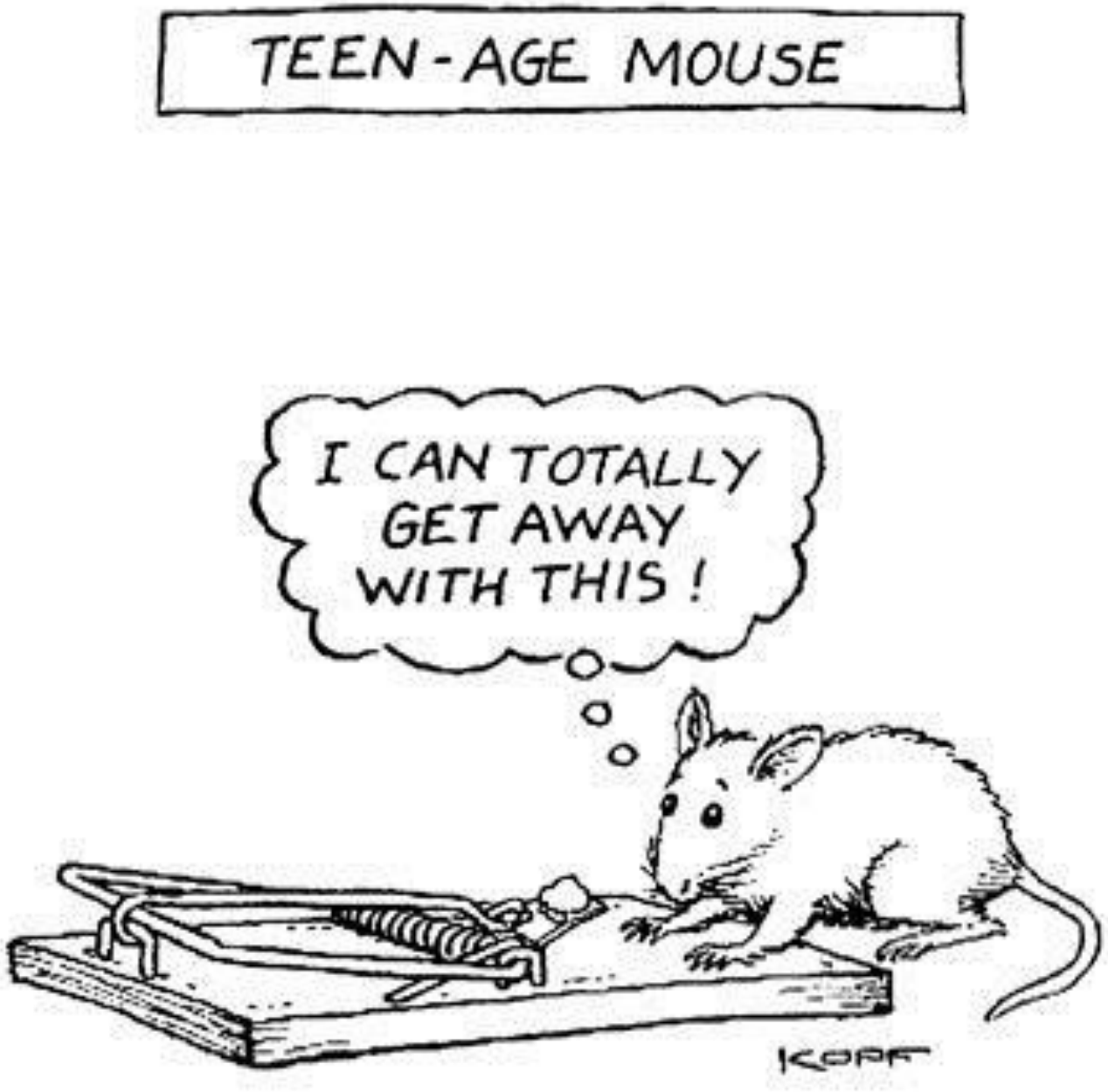
- Medical research with a vulnerable group is only justified if:

1. The research is responsive to the health needs or priorities of this group
2. The research cannot be carried out in a non-vulnerable group
3. The vulnerable group should stand to benefit from the knowledge, practices or interventions that result from the research

National Ethical Guidelines for Health Research in Nepal

1. Diseases only seen in children;
2. Information that cannot be obtained by alternative means;
3. Health issue is significantly different for adults and children;
4. Adverse effects of drugs/vaccines need to be checked or investigated in children;
5. Drug delivery formulations are required to follow precise, safe, and age-appropriate routes of administration.

Different, Not Deficient



Can Risk-Taking be Healthy?