Vitamin D Requirements and Setting Recommendations

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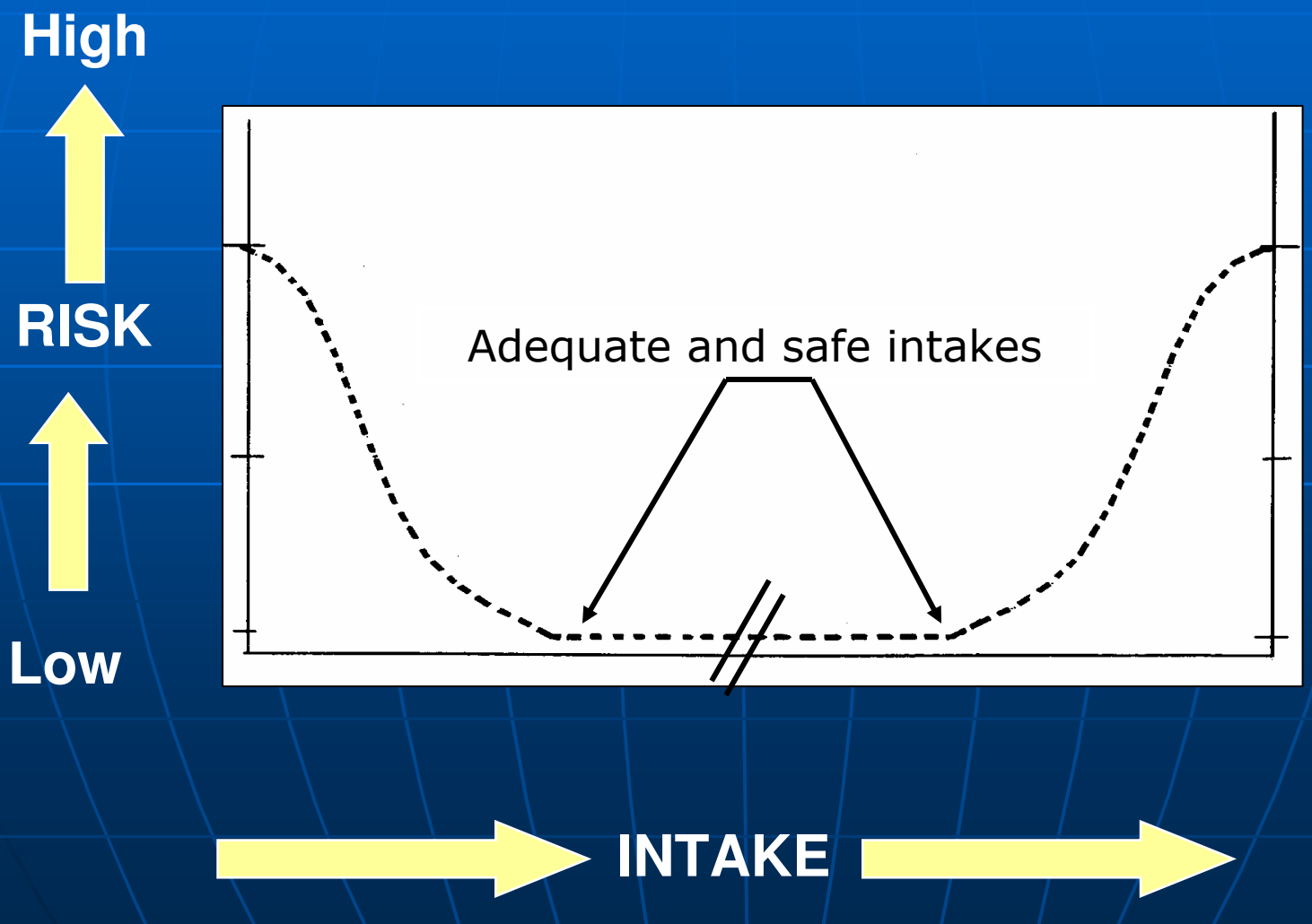
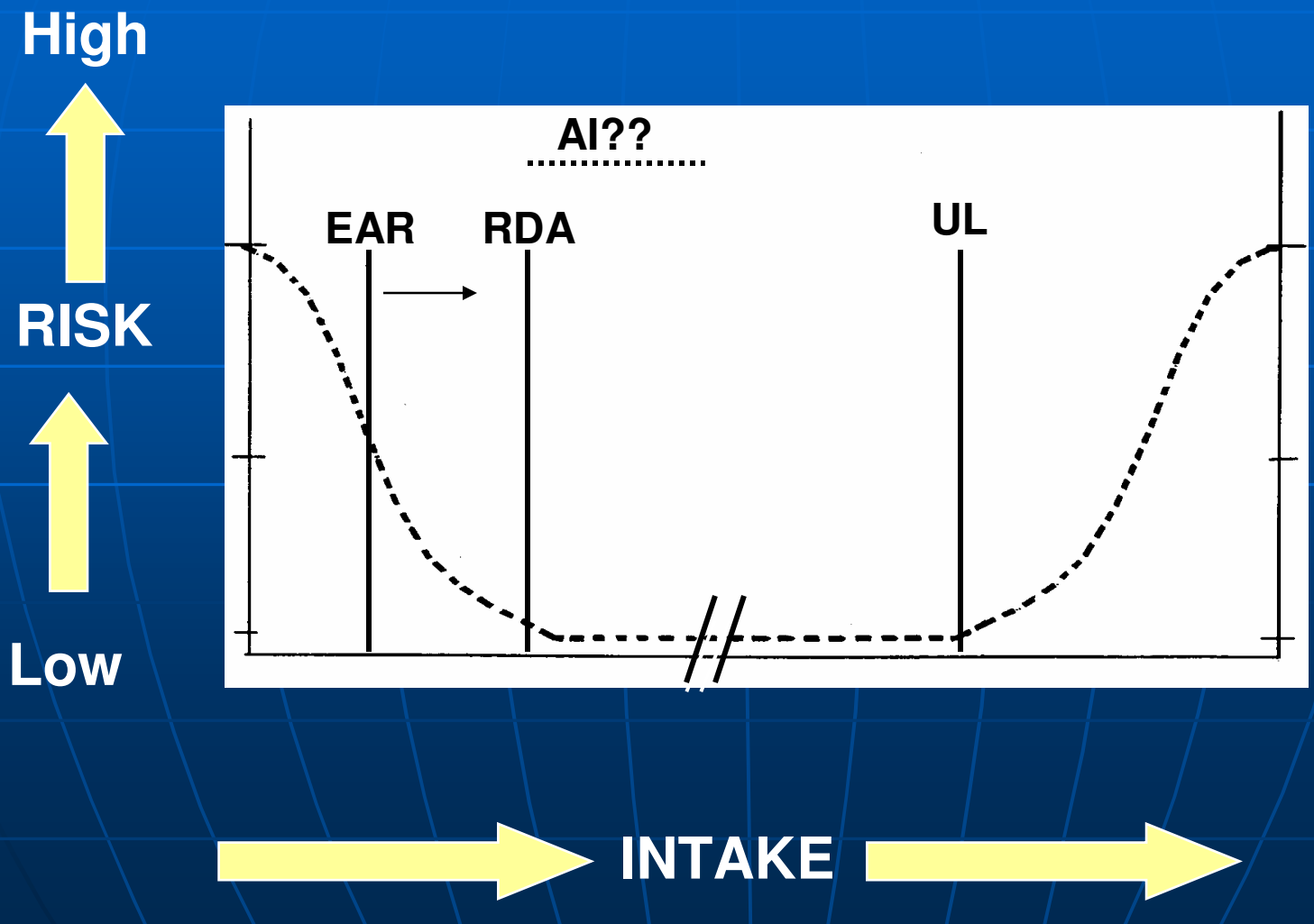
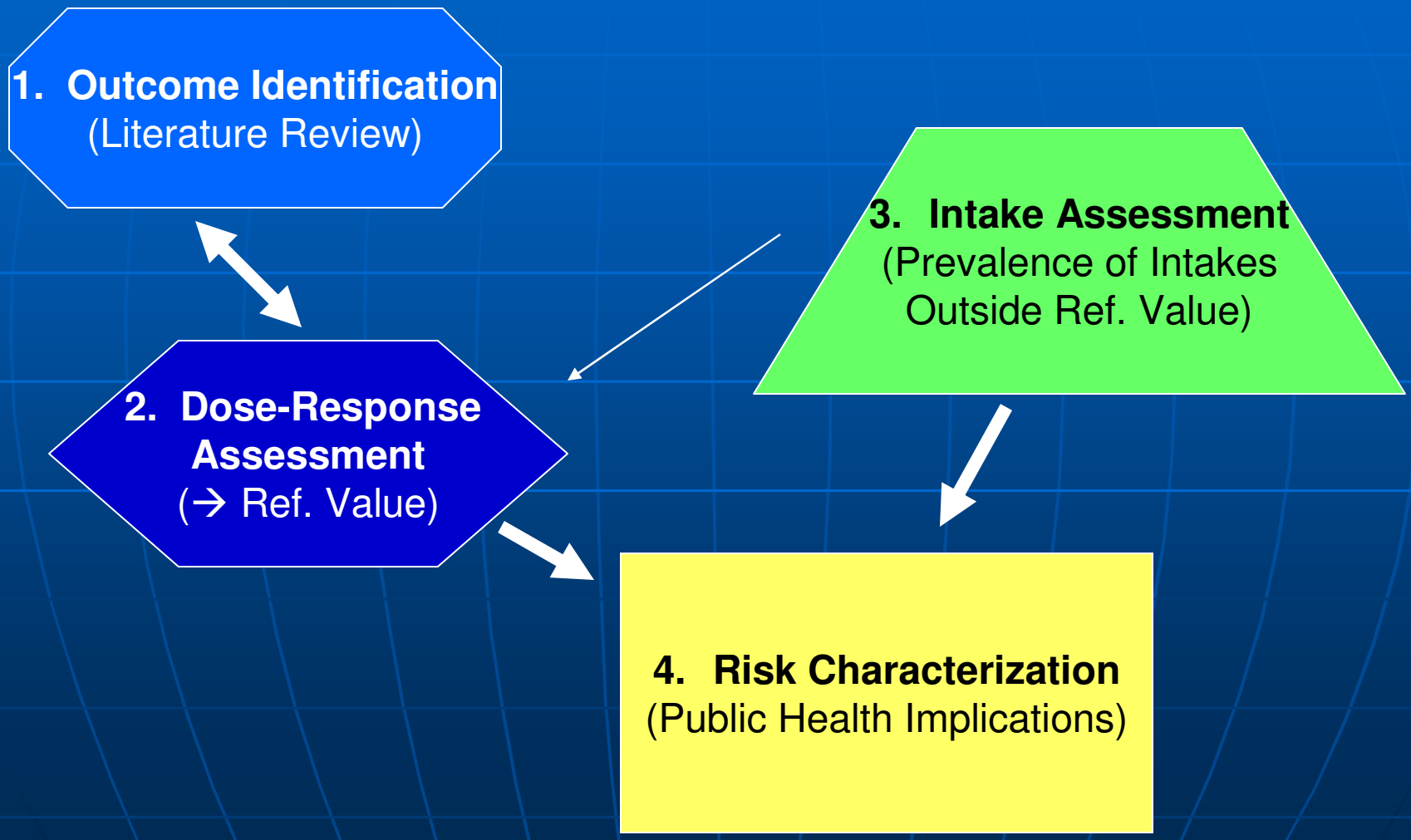
Nature of Nutritional Risk



U.S. Dietary Reference Intakes
Institute of Medicine

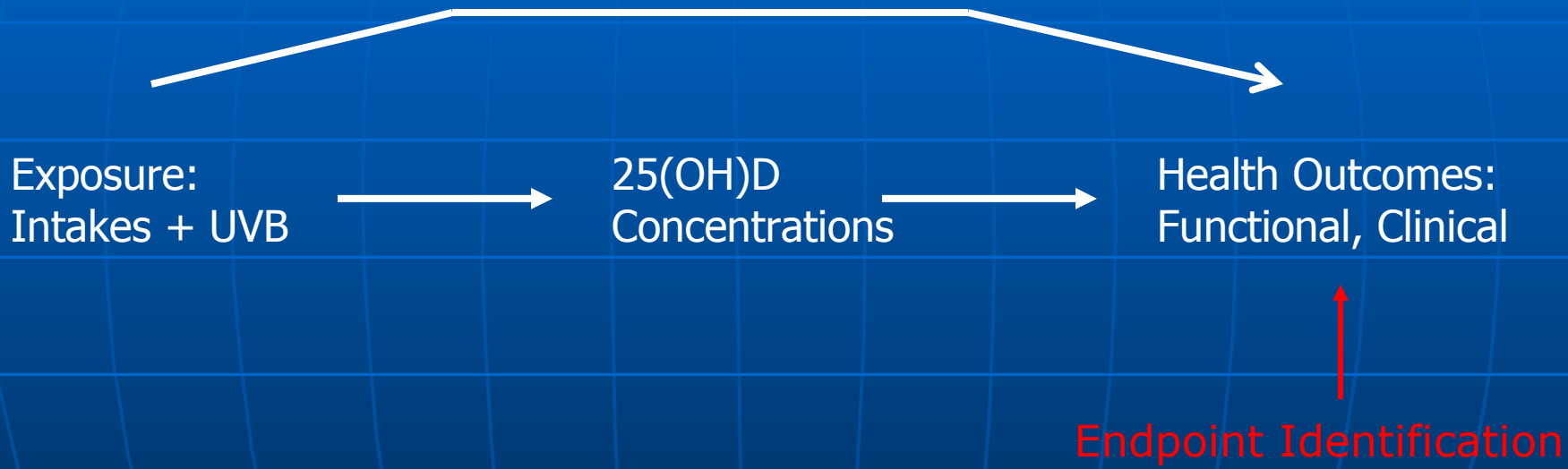


Decision-Making Steps*: A Systematic Approach



*Based on nutrient risk assessment models (WHO, 2006)

Step 1: Outcome (Endpoint) Identification



Health Outcome Identification -- Ideal

- **Evidence:** Causal relationship
  - Nutrient intake → outcome
- **Most protective of public health:**
  - Is:
    - Adequacy: Endpoint with a relatively high intake level
    - Safety: Endpoint with a relatively low intake level
  - May Not Be:
    - Severity of adverse effect
    - Endpoint with the strongest evidence
- **May differ by life stage group**

Possible Outcomes of Adequacy for Consideration 2008-2010

- Growth
- Cardiovascular health
- Cancer
- Immunological outcomes
- Pregnancy-related outcomes
- Bone health
- Hypertension and blood pressure
- Obesity

"Indicators" Used for 1997 DRIs – Real World

- Adequacy
  - Infants:
    - Human milk levels, serum 25(OH)D, linear growth, bone mass
  - Children and adults ≤ 50 y:
    - Serum 25(OH)D <27.5 nmol/L (11ng/ml)
  - Adults > 50 y:
    - Serum 25(OH)D <27.5 nmol/L (11ng/ml)
    - Bone loss

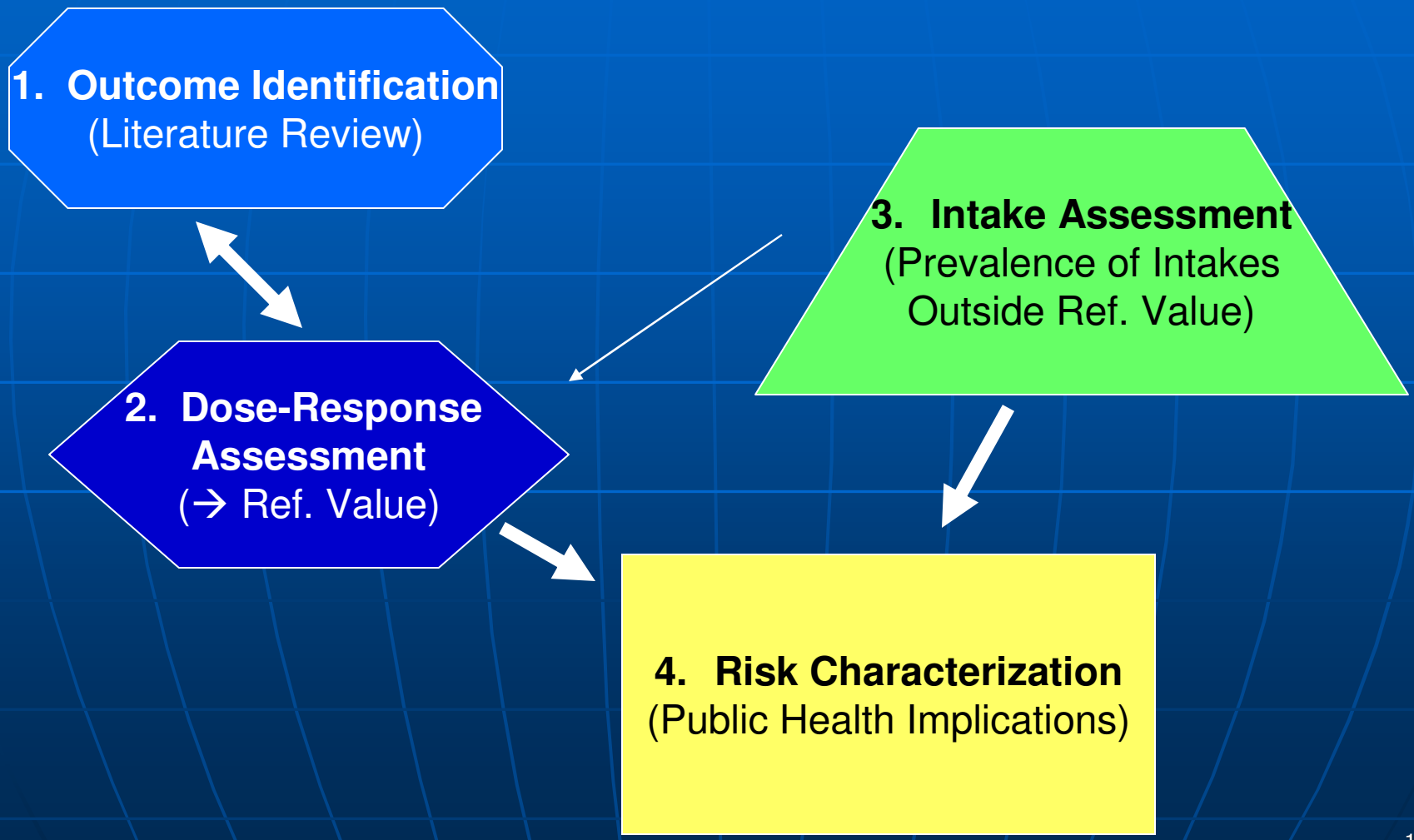
Possible Endpoints of Safety for Consideration 2008-2010

- Hypercalcemia and hypercalciuria
- Renal stones
- ↑ risk of some cancers (e.g., pancreatic cancer)

“Indicators” Used for 1997 DRIs – Real World

- Safety
  - Infants:
    - Retarded linear growth
  - All others:
    - Serum calcium >2.75 nmol/liter (11 mg/dl)

Decision-Making Steps*: A Systematic Approach



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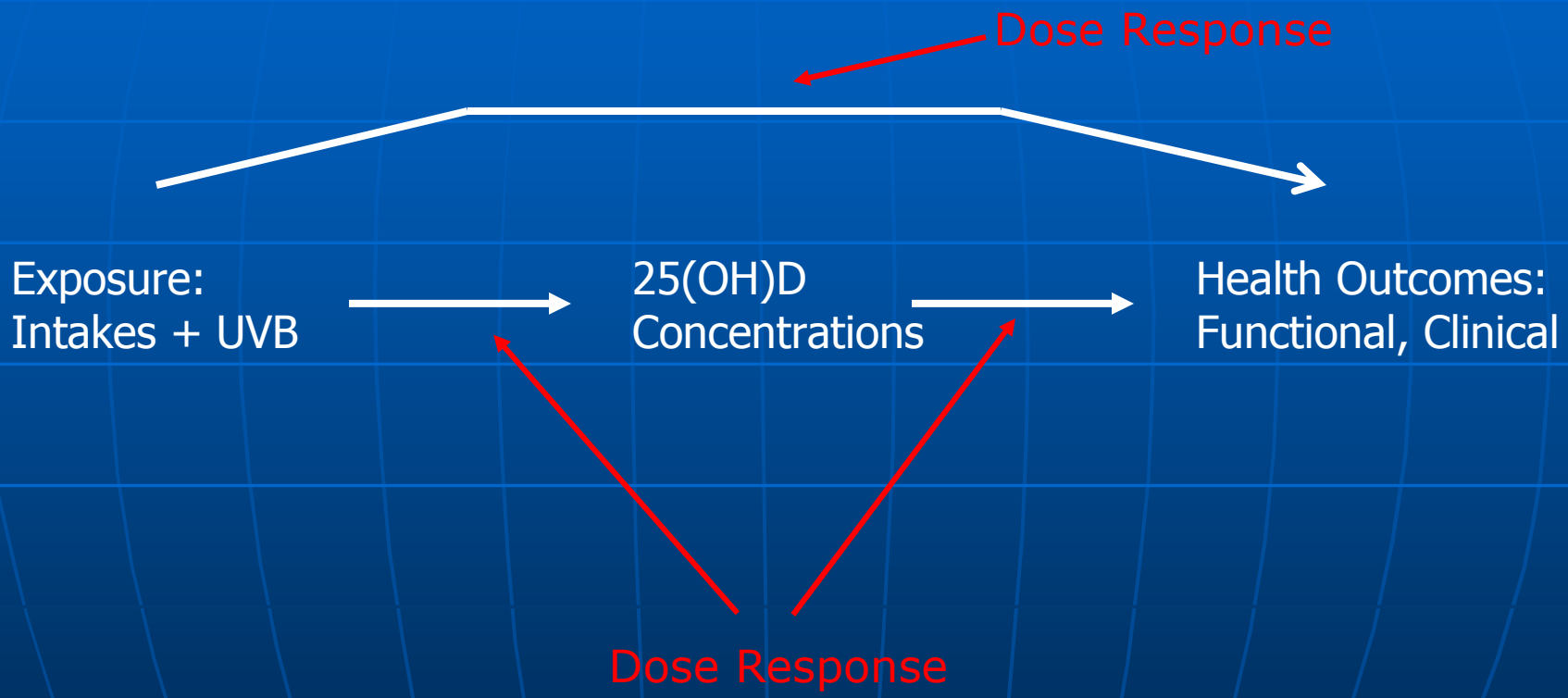
Step 2: Dose-Response Relationships



Challenges: Deriving Dose-Response Relationships

- Measurement challenges:
  - Exposure = sun + diet
  - 25(OH)D varies by assay
  - Studies limited in number of doses used
  - Time to detect many outcomes
- Evidence + Scientific Judgment

Dose-response Relationships: Unstudied Groups

- Limited or no data for some life-stage groups – but need DRIs
  - Use scientific judgment to extrapolate from studied groups
- Examples of 1997 U.S. AI extrapolations:
  - Children 1-8 y -- data from:
    - Slightly older children
    - Different continents
  - Adult males:
    - Data from women
  - Lactation:
    - Data from nonlactating women

Dose-response Relationships: Unstudied Groups

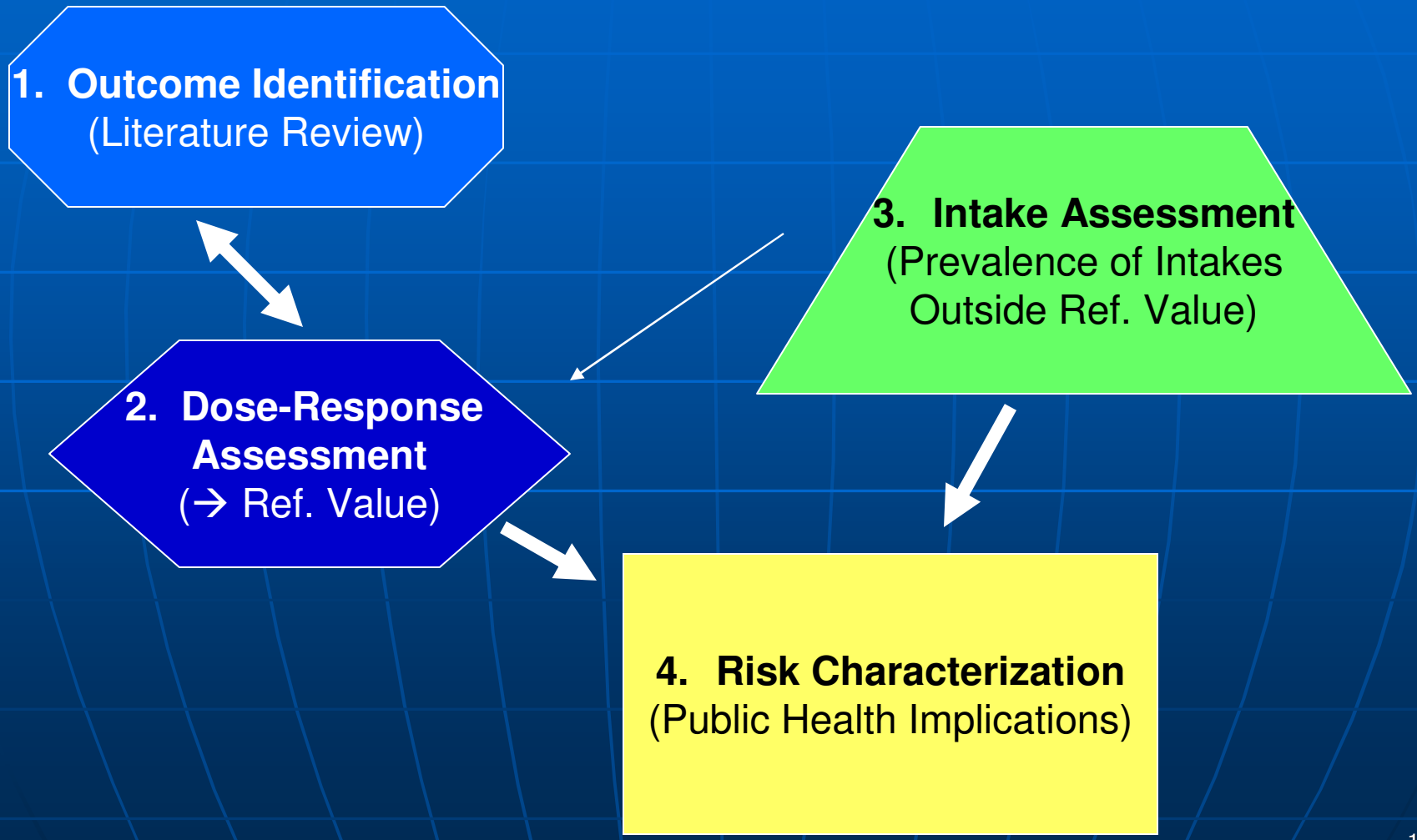
- Examples of 1997 ULs:
  - Children 1-18 yr:
    - Used adult UL
  - Pregnancy and lactation:
    - Used adult UL

1997 DRIs

Group	***Adequate Intake****
7 mon – 50 y	200 IU (5 µg)
51-70 y	400 IU (10 µg)
>70 y	600 IU (15 µg)
	Upper Limit
All persons ≥ 1 y	2000 IU (50 µg)

*Used AI instead of EAR/RDA because of limited information on sun exposure

Decision-Making Steps*: A Systematic Approach



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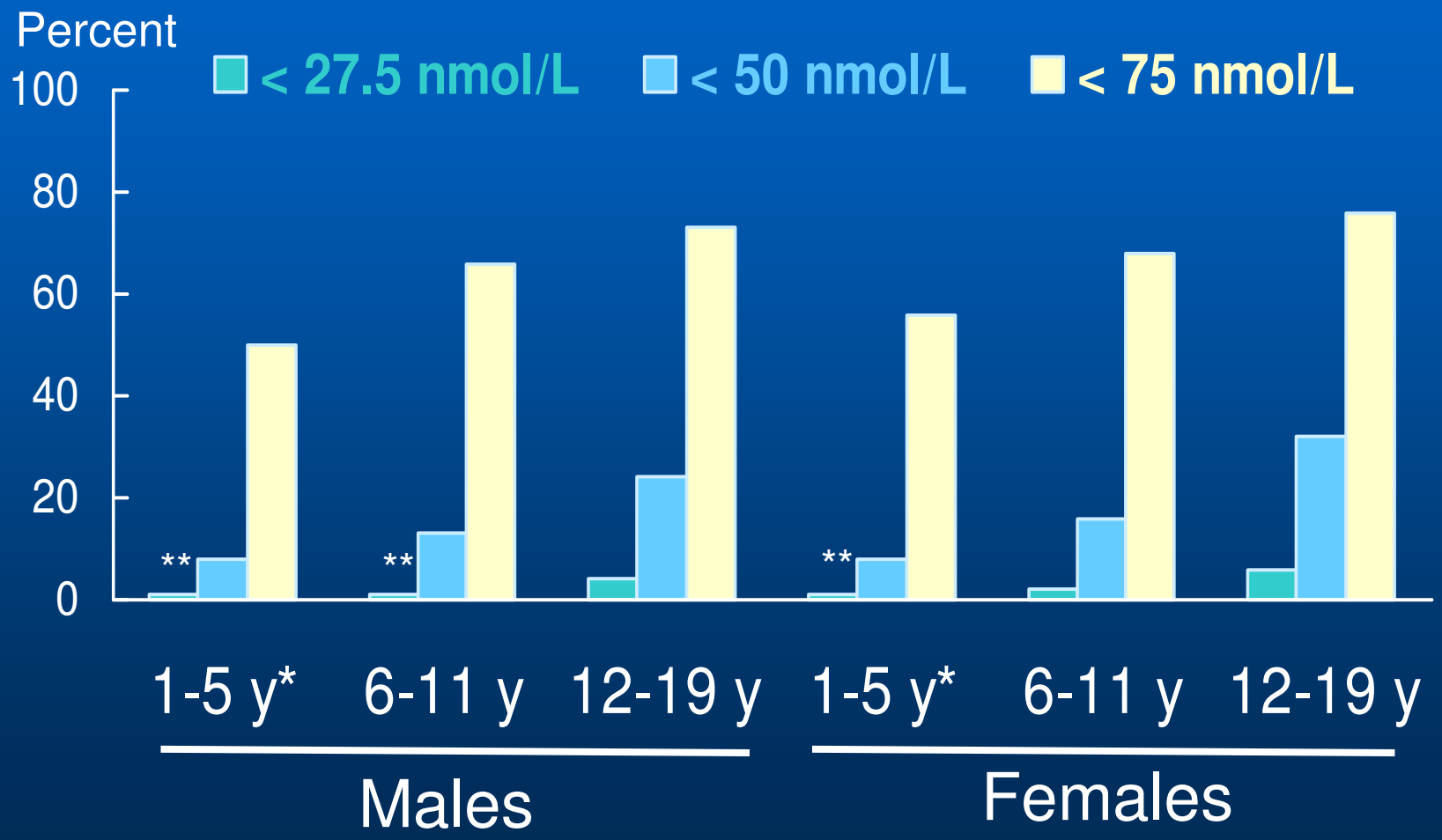
Step 3: Intake and Status Assessments

- Meets user needs – how to use the reference intake values in policy and other applications?
- What is the prevalence of intakes and 25(OH)D concentrations:
  - < DRIs for adequacy?
  - > ULs for safety?
  - By life-stage group?

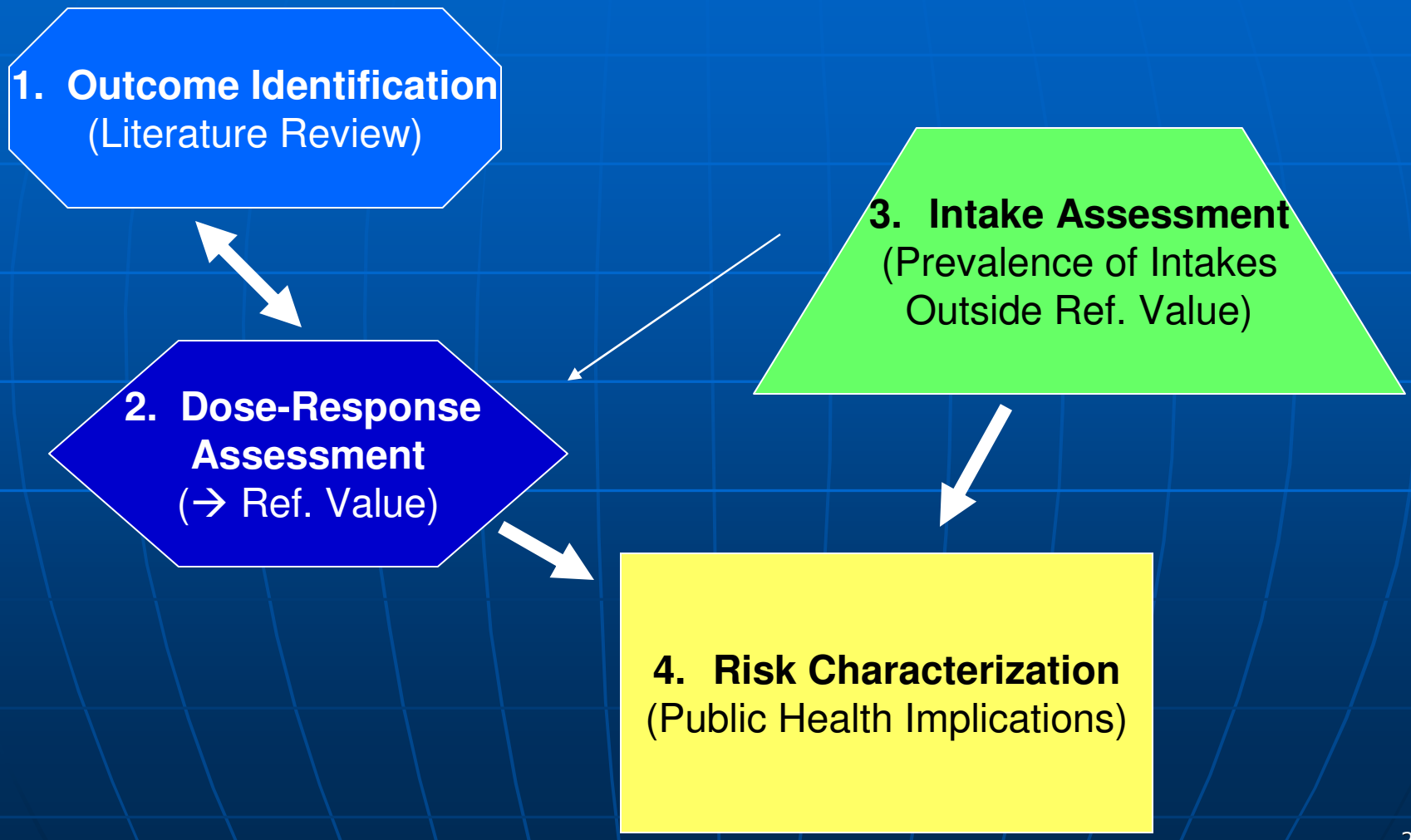
Children with serum 25OHD < selected cutpoints (NH 2000-2004)



**may be statistically unreliable; relative standard error > 30%

*Data for age 1-5 available from NHANES 2003-04 only

Decision-Making Steps*: A Systematic Approach



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Step 4: Risk Characterization

- Taking into account the:
  - Prevalences for low and high intakes and 25(OH)D concentrations, and
  - DRI values for adequate and safe intakes
  - Across all life-stage groups
  - What is the nature of the public health concerns (if any)?
- What other groups warrant special concern?
  - How to apply DRI values for special groups?

Groups Warranting Special Attention in 1997 DRIs

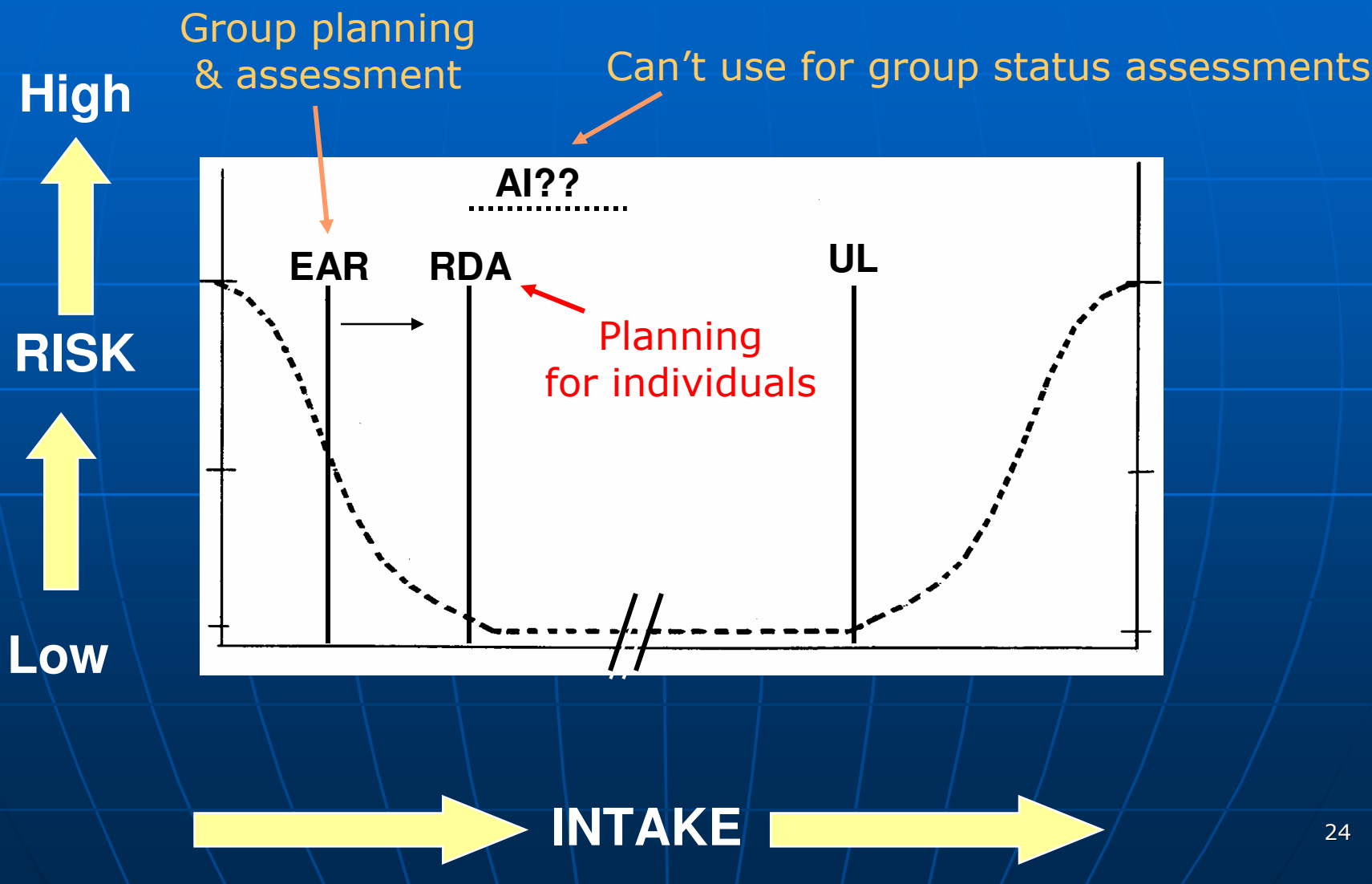
- Persons or conditions that may require intakes > AI:
  - Persons with ↓ skin production of Vit. D_3:
    - Older
    - Limited sun exposure
    - Darker skin pigmentation
    - Use of sunscreens
  - Conditions causing malabsorption
  - Medications that interfere
    - Glucocorticoids
    - Seizure control medications

DRI Applications

	Planning	**Assessment**
Groups	EAR or AI UL	EAR* UL
Individuals	RDA or AI UL	EAR or AI UL

*If AI is reference intake of adequacy, group status assessments can not be made.

Reference Intakes for Nutrients



Next Steps: U.S. DRIs for Vitamin D

- Current Institute of Medicine Committee
  - http://www.iom.edu/en/Activities/Nutrition/DRIVitDCalcium.aspx
- Reviewing Vitamin D and calcium
- Systematic reviews:
  - 2007 -– *Effectiveness and Safety of Vitamin D in Relation to Bone Health* http://www.ahrq.gov/clinic/tp/vitadtp.htm
  - 2009 -- *Vitamin D and Calcium: Systematic Review of Health Outcomes* http://www.ahrq.gov/clinic/tp/vitadcaltp.htm
- Publication date: May 2010

Possible Outcomes: New DRIs

- Confirmation of previous values
  - ± confidence
- Change from AI → EAR/RDA
- Change values based on:
  - New endpoints
  - Better data on Dose-response relationships
  - New data to replace extrapolations for unstudied groups
- Some combination of the above

EXTRA SLIDES

Characteristics of Nutrient Reference Values

- Maintenance of nutritional status
  - Safe and adequate intakes
  - Not: treatment
- Apparently healthy population
  - Not diseased population
- Health promotion and disease risk reduction
  - Primary prevention for disease risk (↓ incidence)
  - Not: ↓ severity without ↓ incidence
- Dose-response relationships
  - Not effect size

Process → Reference Intakes

- Scientific Review:
  - Qualified experts
  - Comprehensive scientific review +
  - Expert scientific judgment
- Free of vested interests:
  - Food industry
  - Government policy-makers
  - Consumer advocacy groups

Process → Reference Intakes

- No reference value: not an option
  - Consensus regarding "essentiality"
  - Uncertainties → "optimal" intakes
  - Adverse public health consequences if no reference value
- Decision-making process:
  - Systematic and transparent
  - Document, document, document

DRI Reference Intake Values of Adequacy: U.S.

- EAR:
  - Estimated Average Requirement
  - Meet requirements of half of healthy persons
- RDA
  - Recommended Daily Allowance
  - Meet requirements of nearly all
  - Derived from EAR
- Adequate Intake
  - Adequate Intake
  - Assumed to be adequate
  - Used when insufficient data for EAR/RDA

DRI Reference Intake Values for Safety: U.S.

- UL:
  - Tolerable Upper Intake Level
  - Highest intake likely to pose no risk