KIDNEY DISEASE EXPANDING DEFINITIONS AND CLASSIFICATIONS TO IMPROVE OUTCOMES

Adeera Levin MD FRCPC FCAHS CM

University of British Columbia

Vancouver Canada

DISCLOSURES AND PERSPECTIVES

- Research Funding
  - Canadian Institute of Health Research
  - Kidney Foundation of Canada
  - Michael Smith Health Research Foundation
  - AstraZeneca
  - Boulenger Ingelheim
  - Janssen
  - Otsuka
  - Reata

- DSMB / Scientific/ Steering Advisory
  - NIH NIDDK (KPMP, others)
  - The George Institute (ASPIRE, RESOLVE)
  - Oxford Clinical Trials (SHARP, EMPA Kidney)

KIDNEY DISEASE: EXPANDING DEFINITIONS AND CLASSIFICATIONS TO IMPROVE OUTCOMES

- Rationale

- Definition vs Classifications

- Diagnosis and Management

- Evidence informed care

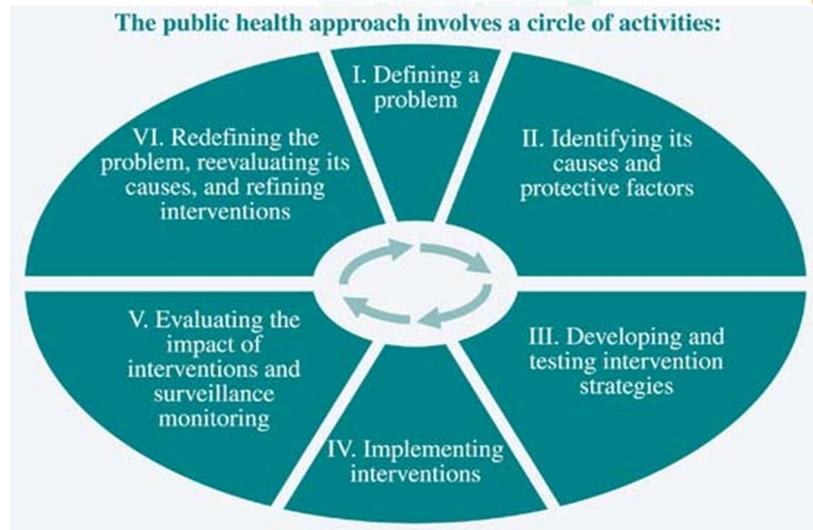# PUBLIC HEALTH STRATEGIES TO PROMOTE KIDNEY HEALTH

- Awareness
- Burden of disease

- Generate solutions

- Define the problem
- Identify causes and risk factors

- Develop and test interventions
- Implement interventions

- Evaluate in practice
- Redefine problem and re-evaluate

The public health approach involves a circle of activities:

I. Defining a problem
II. Identifying its causes and protective factors
III. Developing and testing intervention strategies
IV. Implementing interventions
V. Evaluating the impact of interventions and surveillance monitoring
VI. Redefining the problem, reevaluating its causes, and refining interventions

THE FUTURE OF NEPHROLOGY...BETTER UNDERSTANDING OF

Complexity of Kidney Disease(s)

- Multiple profiles
- Multiple environments
- Different time points
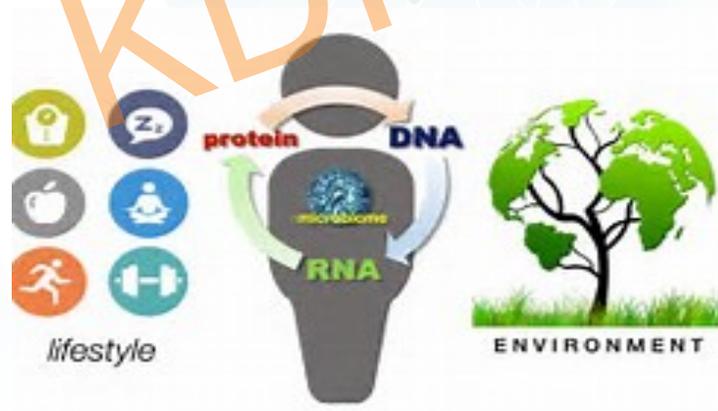
Interactions of lifestyles, genes and
environments differ around the world

CURRENT STATE OF NEPHROLOGY: EMERGING

- Biomarkers

- Genetics

- Value of biopsies for
  - diagnosis and prognosis
  - therapeutic targets (molecular dx)
- Novel study design for complex interventions and
  - Adaptive design
    - Responders and non-Responders
  - Platform trials
  - Cluster randomization

- New therapeutic strategies

More clinical trials

More opportunities

More targets

Need to ensure best designs and methods

EPIDEMIOLOGY AND CARE: PRINCIPLES OF MODELS OF CARE

- Define kidney populations in a consistent manner

- Consider development of care models specific to
  - stage(s)
  - severity
  - unique conditions (transplant, GN, PCKD, DM, other)

- Recognize the complexity of KD care and need for integration and specialization

IMPROVING PATIENT OUTCOMES

- Identification of the condition

- Scientific understanding of disease

- Effective evidence-based treatment strategies

- Knowledge dissemination

- Ongoing research

  - Who

  - What

  - When

DEFINITION OF DISEASE

- A disease is a particular, abnormal condition that negatively affects the structure or function of all or part of an organism, and that is not due to any immediate external injury.

- Diseases are often known to be medical conditions that are associated with specific symptoms and signs. A disease may be caused by external factors such as pathogens or by internal dysfunctions.

Classifying Diseases

- A disease is the modification of the structure and function where it affects the body from working normally in the body's system.

- The characteristics of a disease can be shown from particular signs and symptoms.

- These diseases are classified into different types.

CLASSIFICATION SYSTEMS OF DISEASE

The most widely used classifications of disease are

(1) topographic, by bodily region or system,

(2) anatomic, by organ or tissue,

(3) physiological, by function or effect,

(4) pathological, by the nature of the disease process,

(5) etiologic (causal),

(6) juristic, by speed of advent of death,

(7) epidemiological, and

(8) statistical.

Any single disease may fall within several of these classifications

KIDNEY DISEASE: EXPANDING THE DEFINITION AND CLASSIFICATION TO IMPROVE EVALUATION AND MANAGEMENT

There is a need to have an expanded definition of kidney disease that encompasses abnormalities of structure or function **over all time spans and in all situations so as to improve understanding and care**

Currently AKI occurs within 7 days and focuses on urine output and rises in serum creatinine only, thus ignoring other abnormalities like pyuria, hematuria, stone episodes, obstruction, acute GNs, etc.

AKD is a term that expands the current classification to include all abnormalities of structure and function of duration less than 3 months

AKD addresses functional and structural abnormalities and avoids issue of severity

Etiology (CAUSE) remains an important element in improved understanding

EVALUATION AND MANAGEMENT OF AKD CONSIDERATIONS:

- Improve diagnostic accuracy of the condition
  - Does AKD exist
  - What are the potential etiologies?

- The potential role for kidney biopsy?

- General management
  - Awareness
  - drug dosing/selection
  - Initiation of disease modifying drugs

- Future research may help to identify specific therapeutic options and alteration in outcomes

Acute Kidney Disease and AKI

- Definition of AKD

  - Any abnormality of structure or function of kidneys with duration of less than 3 months

  - AKI has specific criteria related only to serum creatinine and urine output and short duration

  - AKD thus encompasses AKI, but is inclusive of events which

    - may not meet criteria for AKI (rise in creatinine not fast or high enough, or urine output not known)

    - include abnormalities of urine sediment, imaging and acute GN's for example
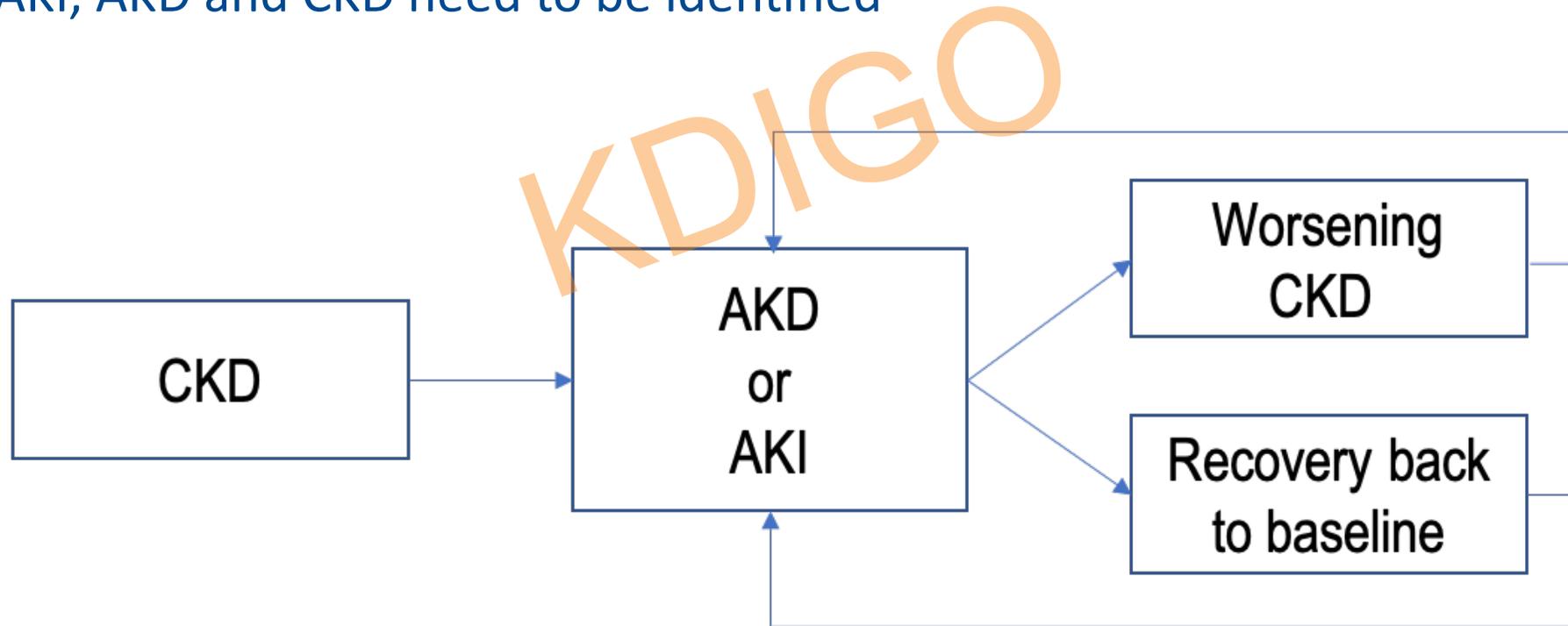
Assumes AKI is always part of AKD
Patients with no KD can develop AKI or AKD

Causes of AKI, AKD and CKD need to be identified
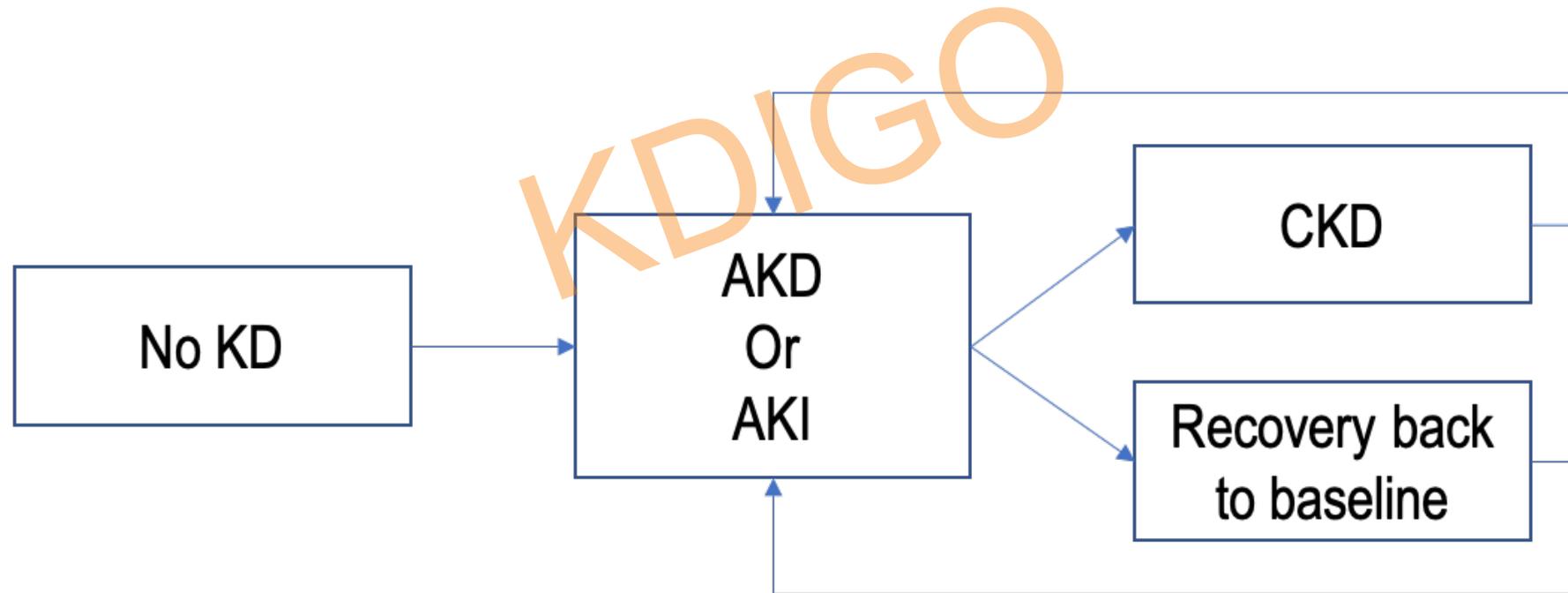
Assumes AKI is always part of AKD

Patients with CKD can develop AKI

Patients with CKD can develop AKD (no meeting criteria of AKI)

All CKD must have once been AKD but not necessarily AKI

Causes of AKI, AKD and CKD need to be identified

Acute and Chronic Kidney Diseases are terms describing abnormalities of structure and/or function
In all cases, seek **Cause** of kidney disease(s)

	AKI	AKD	CKD	NKD*
Duration	Within 7 days	<3 months	>3 months	
Functional Criteria	Increase in Scr by $\geq$50% within 7 days, OR Increase in SCr by $\geq$0.3mg/dL (26.5µmol/L) within 2 days, OR Oliguria for $\geq$4 hours	AKI, OR GFR<60 mL/min/1.73m^2, OR Decrease in GFR by $\geq$35% times baseline, OR Increase in SCr by $\geq$50% times baseline	GFR <60 ml/min/1.73m^2	GFR $\geq$60 ml/min/1.73m^2
AND/OR	OR	OR	OR	AND
Structural Criteria	Not defined	Marker of kidney damage (albuminuria, hematuria, or pyuria are most common)	Marker of kidney damage (albuminuria is most common)	No marker of kidney damage

AKI, acute kidney injury; AKD, acute kidney diseases and disorders; CKD, chronic kidney disease; NKD, no kidney disease. *NKD implies no functional or structural criteria according to the definitions for AKI, AKD, or CKD. Clinical judgment required for individual patient decision making.

IF WE CONSISTENTLY IDENTIFY AKD AND SEEK THE WHY (CAUSE) WE WILL:

- Learn more

- Be able to potentially identify therapeutic targets

- Design clinical trials to test strategies

- In the short term, facilitate patient management
  - Avoidance of medications
  - Increase awareness of risks
  - Time therapeutic interventions appropriately

TIPPING THE BALANCE: BETTER NOMENCLATURE TO BETTER CARE

Towards more evidence base

Epidemiology to inform care

Acknowledging diversity and the continuum of disease and care......