

The Distinguishing Risk of Progressive Chronic Kidney Disease (DROP CKD) Study

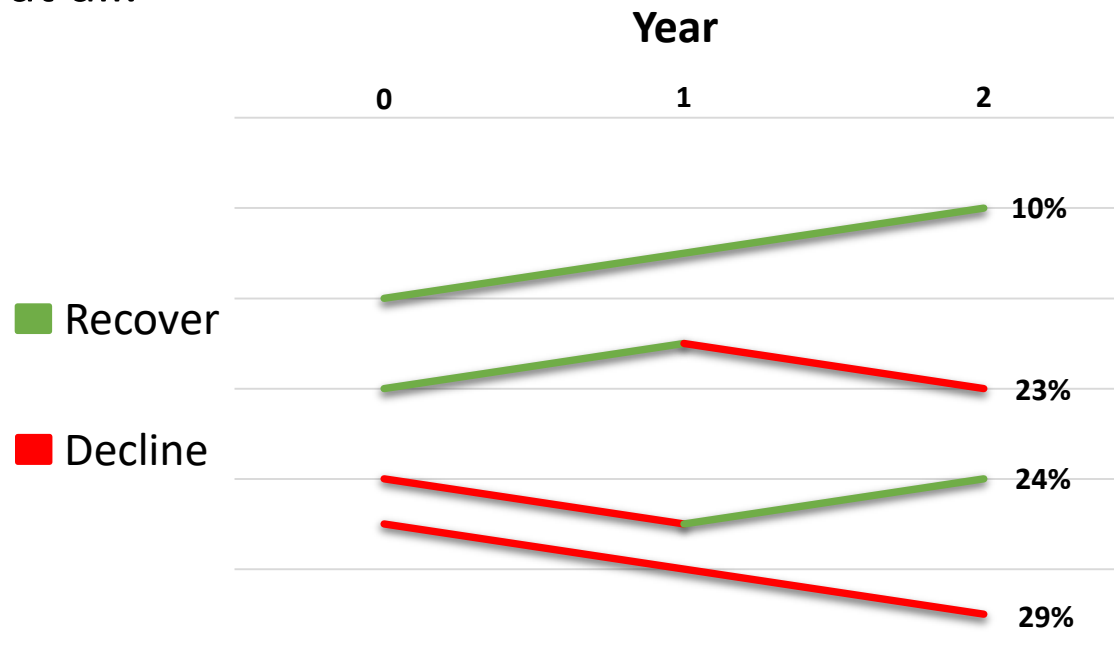
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CKD IS A PROBLEM!

Progressive CKD

- ❖ The continual decline of kidney function to end-stage kidney disease where kidney replacement therapy is needed.
- ❖ Not all patients progress to end-stage kidney disease at the same rate or at all.



Gap in the literature

- ❖ CKD has numerous primary causes. Characterised by inflammation, fibrosis, tissue injury and regeneration, oxidative stress.
- ❖ Biomarkers to differentiate between patients who will progressively lose kidney function in the short term and those who will not, is needed.
- ❖ Progressive CKD cannot accurately be characterised by a single biomarker, a panel of biomarkers is needed to accurately characterise CKD.

DROP CKD Study - Aim

Create a clinical tool, underpinned by a multi-parameter biomarker panel, for use by clinicians and researchers to assess a patient's likelihood of progressively losing kidney function in the following 1-3 years.

DROP CKD Study - Hypotheses

- ❖ Commonly measured biological variables, along with primary diagnosis and present comorbidities, are potential prognostic biomarkers of kidney function.
- ❖ The level of circulating inflammatory and fibrotic cell populations will predict future changes in kidney function.

DROP CKD Study - Hypotheses

- ❖ Circulating and urinary levels of inflammatory, fibrotic, tissue damage, and regeneration cytokines/chemokines and degree of oxidative stress will predict future kidney function.
- ❖ A combination of these biomarkers will have a greater sensitivity and specificity for predicting future kidney function.

DROP CKD Study - Methods

- ❖ Pathology and clinical data from the CKD.QLD Registry.

- ❖ Blood and urine samples from the CKD.Biobank:
 - ❖ Unhealthy kidney function
 - ❖ Progressive decline **P**
 - ❖ Stabilised **S**
 - ❖ Recovering **R**
 - ❖ Healthy kidney Function **H**

DROP CKD Study - Methods

- ❖ All participants must be aged ≥ 18 old at consent

“Healthy” Kidney Function

- ❖ No CKD
- ❖ Minimal albuminuria
- ❖ No other major illness.

“Unhealthy” Kidney Function

- ❖ CKD stage 3A \rightarrow 4

DROP CKD Study - Methods

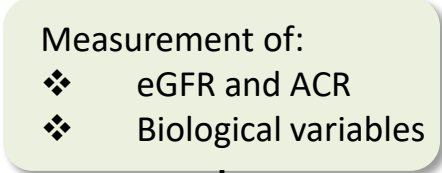
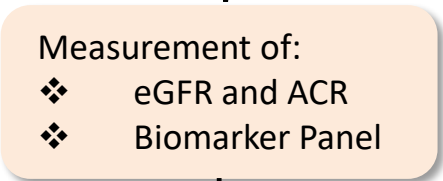
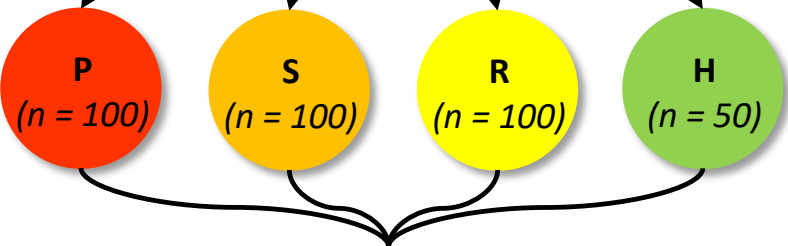
- ❖ “Unhealthy” kidney function will be stratified into three experimental groups:
 - ❖ Progressive → $\geq 25\%$ reduction in eGFR/24 months
 - ❖ Stable → [+15%, -25%] change in eGFR/24 months
 - ❖ Recovering → $\geq 15\%$ increase in eGFR/24 months

DROP CKD Study - Methods

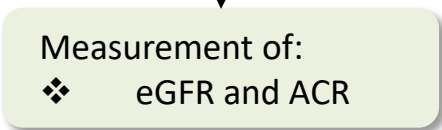
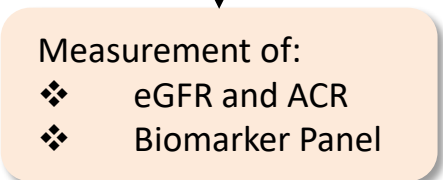
Biomarkers

Established	Novel	
NGAL	Tryptase	Mast Cell Progenitor
FGF-23	Chymase	Fibrotocytes
TNF- α	MCP-1	T _{regs}
IL-6	CRP	Monocytes
	F2-Isoprostane	Protein Carbonyl
	8-oxodG	

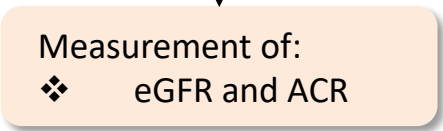
DROP CKD Study - Methods



T₀ Months



T₁₂ Months



T₂₄ Months

DROP CKD Study - Methods

Univariate Analysis

- ❖ ANOVA with appropriate post-hoc testing,
- ❖ Receiver operating characteristic (ROC) analysis.

Multivariate Analysis

- ❖ A forward-step-wise discriminate function analysis (DFA),
- ❖ ROC analysis.

DROP CKD Study - Methods

Chronic Kidney Disease Index (CKDi)

- ❖ The outcome of the DFA will be used to create a clinical tool for indexing a patient's potential for progressing, termed CKDi.

DROP CKD Study – Significance

- ❖ There is clinical and research need for capacity to discriminate between progressive and non-progressive patients.
- ❖ The CKDi will help address this need in a minimally invasive and easy to implement manner.
- ❖ It will allow for the personalisation of a patient's treatment, the appropriate allocation of medical resources, and the recruitment of appropriate CKD populations by researchers.