



A NATIONAL and INTERNATIONAL Research PROGRAM to Define KIDNEY RISK in YOUTH with DIABETES MELLITUS

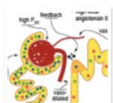
Adolescent Type I Diabetes Cardio-Renal Intervention Trial (AddIT)

BACKGROUND

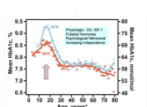
The teen years are a **critical period** in the lives of youth living with Diabetes, where future diabetes-related problems of the **kidney and heart** may begin and progress as a result of **poor sugar control** and other changes.



Hormonal changes; Puberty & Growth Hormone
Increased Insulin Resistance & Cholesterol/ Lipids
Rapid renal growth



Development of renal *hyperfiltration*, a risk factor for future diabetes kidney disease



Also a period of *inadequate diabetes control*, teenagers patients have highest HbA1c across the lifespan

This led to the global study of teens with diabetes, the **Adolescent Diabetes Cardiorenal Intervention Trial (AddIT)** which looked at **early identification** of those at risk and **early prevention** using medicines: **AddIT**, and now its follow-up.



TERTILE/RISK ASSIGNMENT: Algorithm used by ADDIT to identify patients at high risk for progression of *microalbuminuria*, a protein found in the urine as a potential marker of diabetes kidney disease



International, Multi-centered Clinical Study; United Kingdom, Canada, Australia, 2011-2016
Randomized Control Trial – in patients identified as high risk, Observational Study in medium and low risk participants



Randomized, double blind, placebo controlled trial evaluating Statins (Atorvastatin) and ACE-I (Quinapril) alone or in Combination vs. Placebo over 2-4 years



RESEARCH QUESTIONS

- ▶ Can we predict who is at high risk of future long term diabetes kidney and heart problems?
- ▶ Can we **prevent** future long term diabetes kidney and heart problems?



PROJECT GOALS

- ▶ Identify who is at risk of developing kidney problems using the gold standard for measuring how the kidney works, **measured glomerular filtration rate or mGFR**. Look at important **biological markers** to see if they can predict the development of kidney problems



POPULATION AND LOCATION

- ▶ 300 patients with Type 1 Diabetes, who were originally enrolled in the AddIT study are participating in this research study.
- ▶ This research is located at The Hospital for Sick Children, in Toronto, Canada.



WHO BENEFITS

- ▶ Patients identified to be at high risk may benefit, especially when novel therapies are also identified and aimed at early prevention

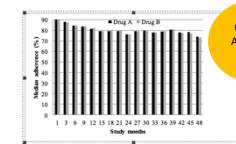
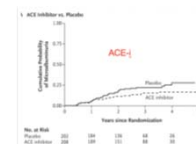


DEFINITIONS, RESULTS, OTHER

- ▶ Diabetes, Kidney and Heart Disease, Prevention.
- ▶ Potential interaction between **Social and Biological** determinants of health in diabetes.
- ▶ Biological samples stored and linked to clinical database.

EARLY RESULTS & RESEARCH PLANS

AddIT Published: Results Published in New England Journal of Medicine 2017; ACE-I or Statins used in the trial were not effective in reducing overall albumin excretion, a marker of kidney disease. However the study did show a 43% reduction in progression of *microalbuminuria*, a clinically important outcome, and achieved remarkable levels of engagement from this population of teens.



Over 75% Adherence rate



Our work continues in AddIT Follow-Up to look at which biological markers are able to better predict kidney and heart complications, using more sensitive tests to measure how the kidneys work.



Accurate Tracking of ACR to identify patients at higher risk of MA onset and Progression in young adulthood



Consideration of the "whole" person, including their physical, mental, and emotional health, while taking social factors into account



Evaluation of Inflammation Measures and Novel Biomarkers including: Serum/ Urine Inflammatory Markers, Urinary Microparticles, Proteomics, Metabolomics, RAAS Makers

Patient Partner Engagement: allows caregivers and patients a voice to include the outcomes that are important to them with aim of improving kidney and heart health in diabetes.

AddIT/ CanSOLVE Investigators; Farid Mahmud, Etienne Sochett, James Scholey and Yesmino Elia (Senior Manager)
Patient Partners: Lynne McArthur, Meaghan Murchie, Adelaide Burgess

CURRENT STATE
KIDNEY/ HEART COMPLICATIONS

TRANSFORMATION PROCESS

FUTURE STATE
PREVENT

Measurement of Kidney and Heart Coupled with Biological Marker Analysis

PROJECT TIMELINE

