Chronic Disease Innovation Centre

POWERED BY SEVEN OAKS GENERAL HOSPITAL

Surveillance, Risk Prediction and Preventing Progression in Chronic Kidney Disease

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SEVEN OAKS General Hospital

kidneyhealth.ca
Manitoba Renal Program

Conflict of Interest

Advisory Boards: Otsuka, Alexion, NxStage

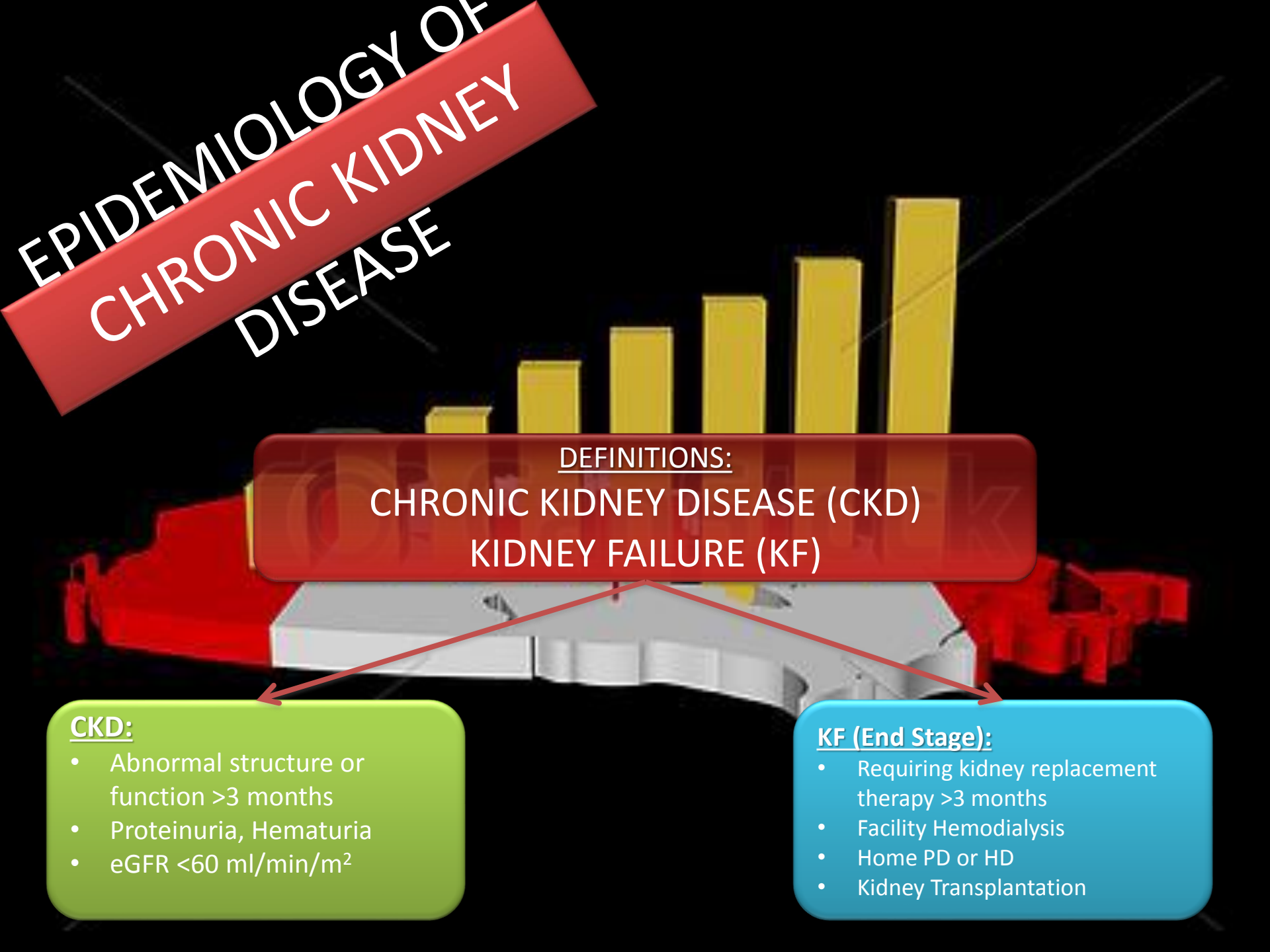
Grants: CIHR, Baxter, Health Canada

No direct conflicts on anything discussed today

Overview

- Discuss the epidemiology of chronic kidney disease in Manitoba
- To understand the science of risk prediction in CKD: aligning treatment and resource allocation
- Discuss ongoing initiatives in Manitoba to reach vulnerable First Nations at high risk of kidney failure
- Propose a model for comprehensive CKD surveillance

EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE



DEFINITIONS:

CHRONIC KIDNEY DISEASE (CKD)
KIDNEY FAILURE (KF)

CKD:

- Abnormal structure or function >3 months
- Proteinuria, Hematuria
- eGFR <60 ml/min/m^2

KF (End Stage):

- Requiring kidney replacement therapy >3 months
- Facility Hemodialysis
- Home PD or HD
- Kidney Transplantation

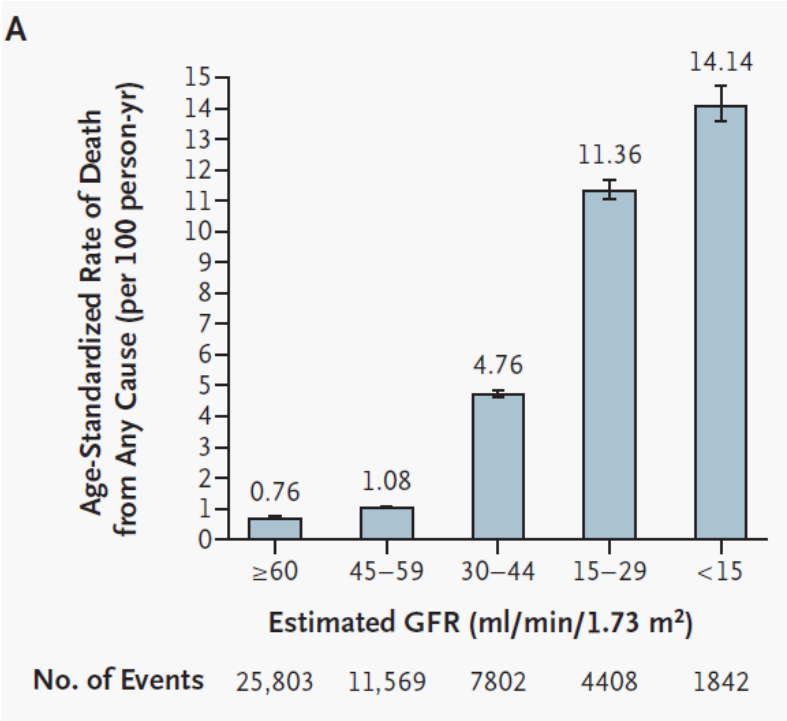
The NEW ENGLAND JOURNAL of MEDICINE

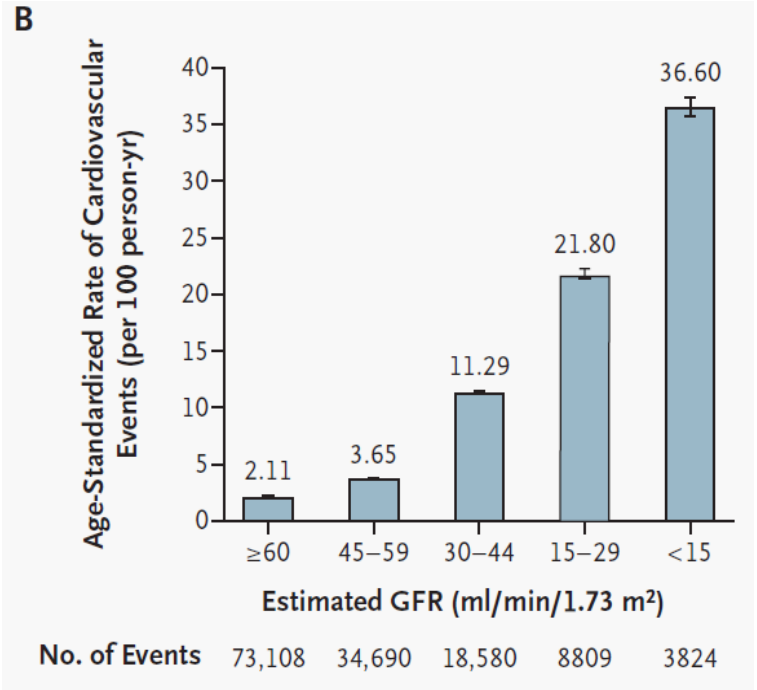
ORIGINAL ARTICLE

Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

Alan S. Go, M.D., Glenn M. Chertow, M.D., M.P.H., Dongjie Fan, M.S.P.H., Charles E. McCulloch, Ph.D., and Chi-yuan Hsu, M.D.

Mortality and Cardiovascular Events Are STRONGLY related to eGFR





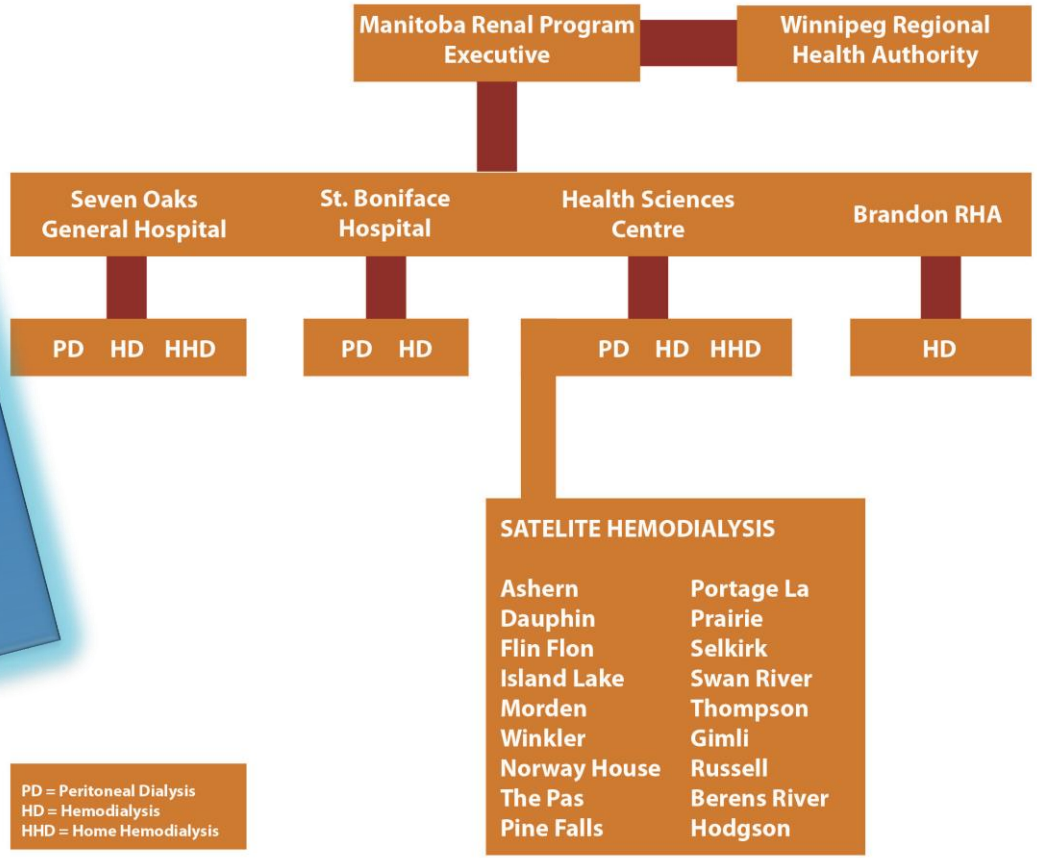
KAISER PERMANENTE®

1.2 million outpatients with eGFR over 3 years

Manitoba Renal Program: Quick Stats

MRP FACTS

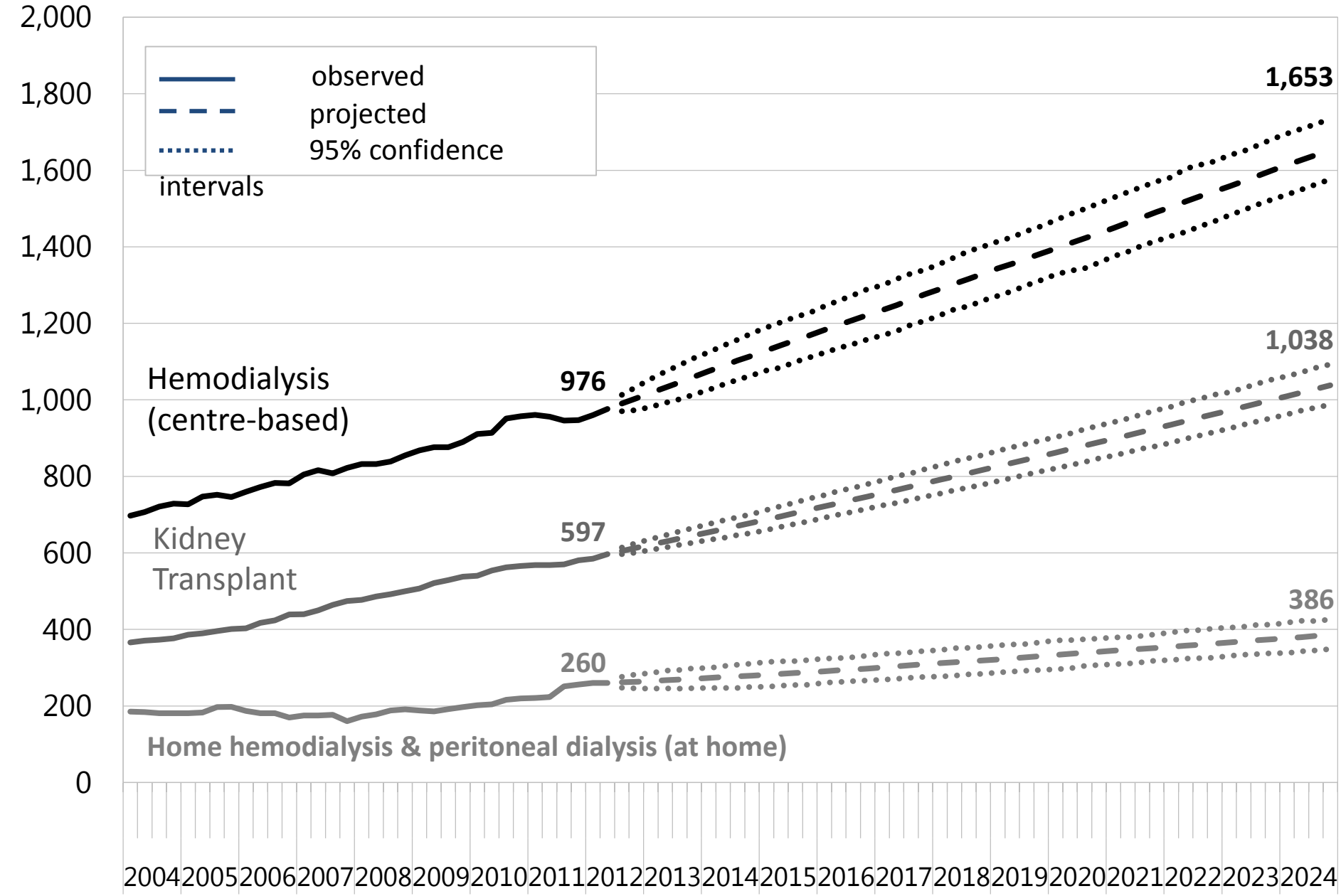
- 4 primary sites
- Budget: >80 million/year
- 26 Nephrologists
- >400 nurses and health care aids
- 22 Dialysis Centers
- >1500 Dialysis Patients
- >4000 CKD patients
- 24/7 consult services for the entire Province of MB



KIDNEY HEALTH CARE innovating for tomorrow

2012 MANITOBA RENAL PROGRAM CONFERENCE SEPTEMBER 23 2012

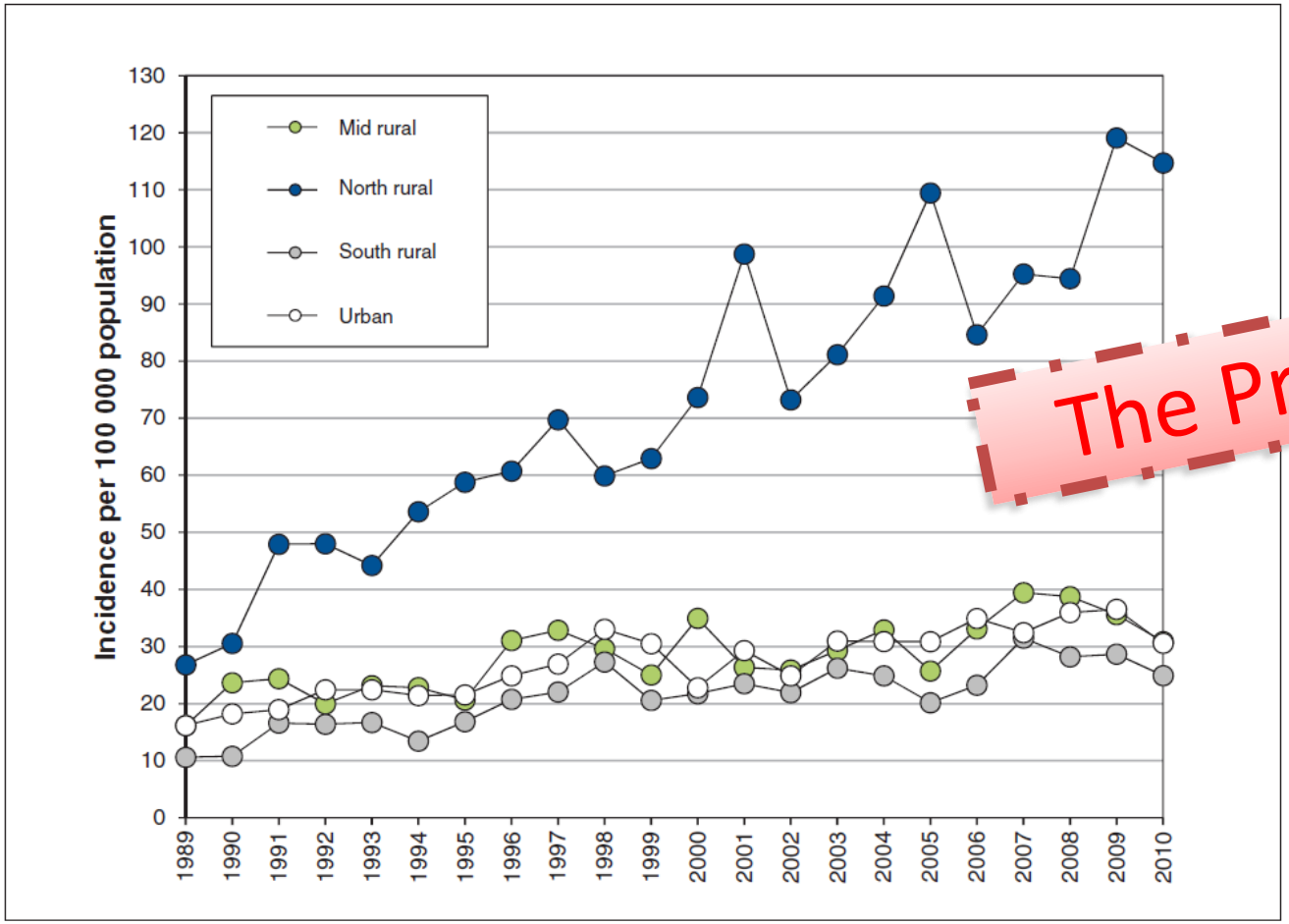
Projected Number of Manitobans with ESKD to 2024



Secular trends in end-stage renal disease requiring dialysis in Manitoba, Canada: a population-based study

Paul Komenda MD MHA, Nancy Yu PhD, Stella Leung MSc, Keevin Bernstein MD, James Blanchard PhD, Manish Sood MD, Claudio Rigatto MD MSc, Navdeep Tangri MD PhD

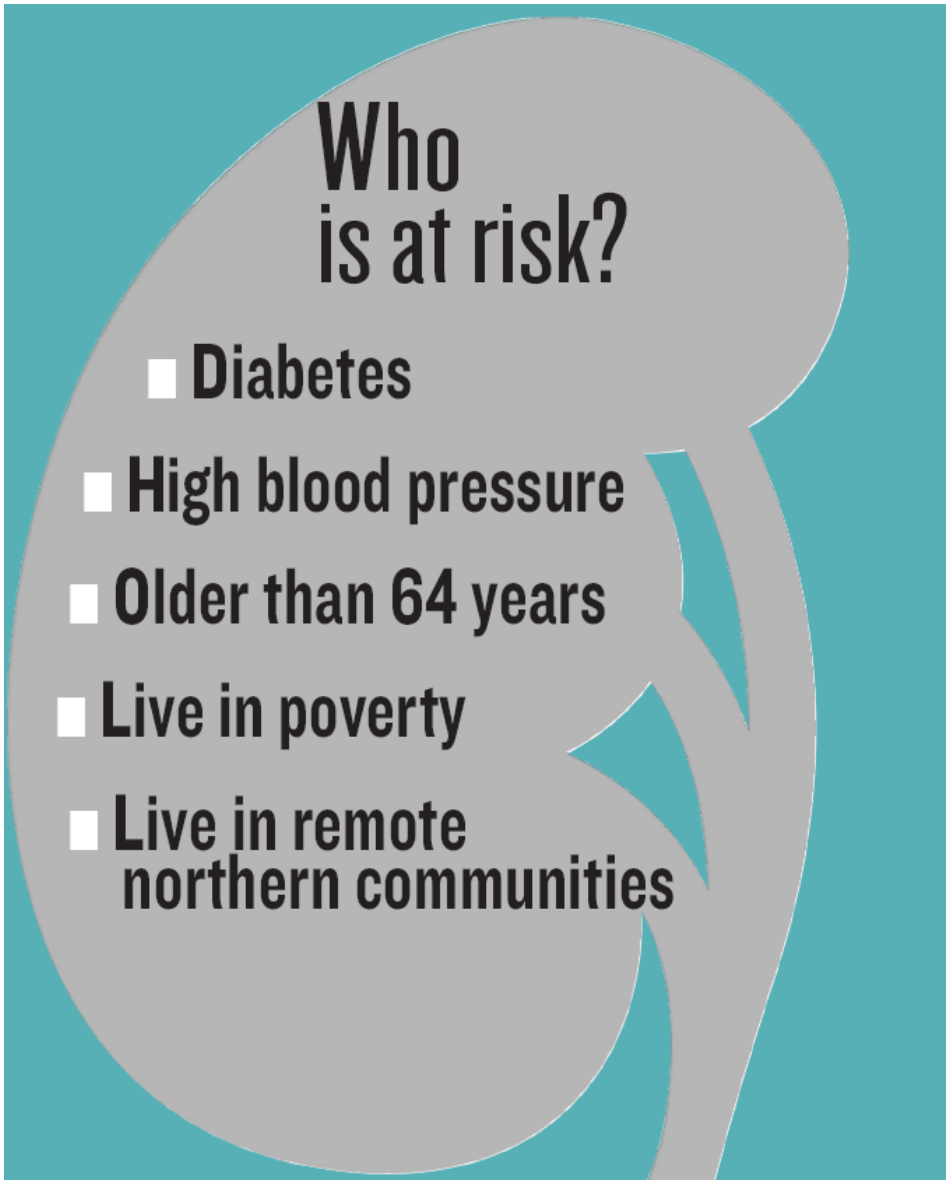
CMAJ OPEN
Research



The Problem

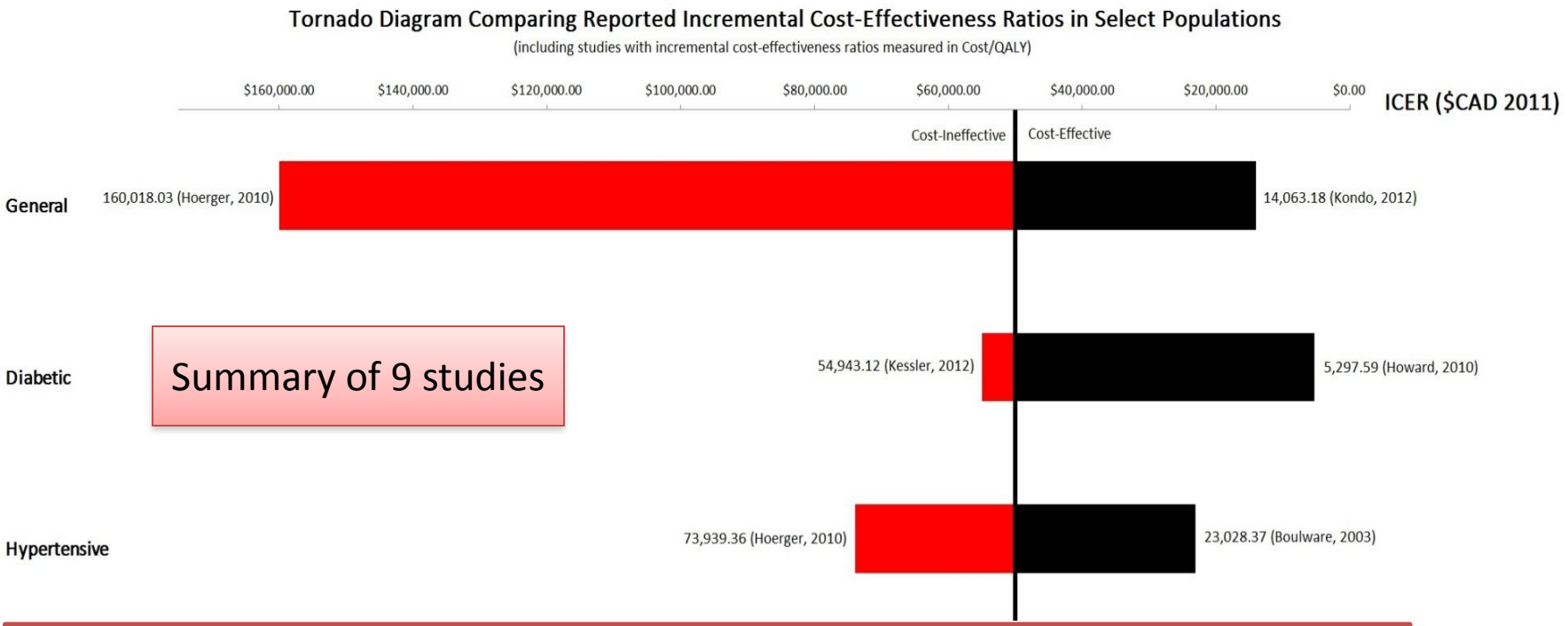
Figure 3: Age-standardized incidence of end-stage renal disease in Manitoba per 100 000 population, by region, 1989–2010.

Manitoba Risk Factors



CKD Deliverable
MCHP

The Cost Effectiveness of Primary Screening for Chronic Kidney Disease: A Systematic Review *(Under Review, AJKD 2013)*

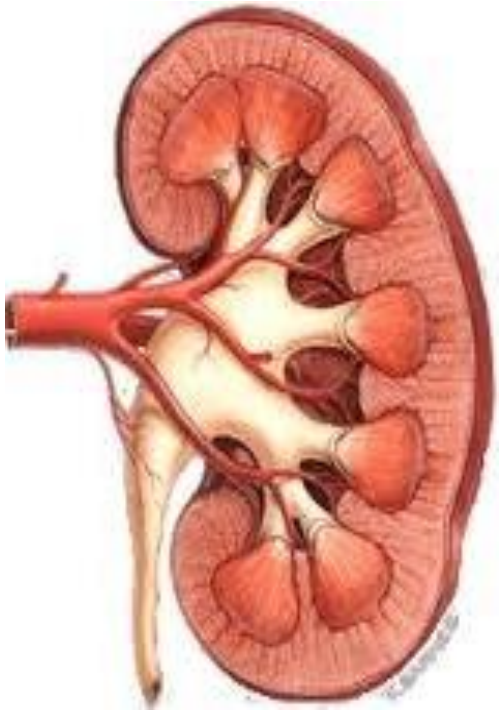


Summary of 9 studies

- **A screening strategy targeting high risk individuals, in diabetic or hypertensive populations, is a cost-effective intervention under all assumptions.**
- CKD screening in the general population may be cost-effective if a higher prevalence of CKD is present, rapid progressors can be identified and aggressive treatment with RAAS inhibitors reduces the risk of non-renal events.

Ferguson T, Komenda P, Tangri N, Rigatto C, et al.

Chronic Kidney Disease



Kidney Failure

Glomerular Filtration Rate (ml/min)

90

60

30

15

0

Stage 1

Normal kidney function with risk factors (measured by GFR*, blood & urine tests)

Stage 2

Declining GFR to 60ml/min/1.73m² (mild kidney damage)

Stage 3

GFR: 30 – 60 ml/ min/1.73m² (moderate kidney damage)

Stage 4

GFR below 30 ml/ min/1.73m² (severe kidney damage)

Stage 5

GFR below 15 ml/ min/1.73m² (kidney failure)

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

VOLUME 3 | ISSUE 1 | JANUARY 2013
http://www.kidney-international.org

NEW STAGING SYSTEM

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

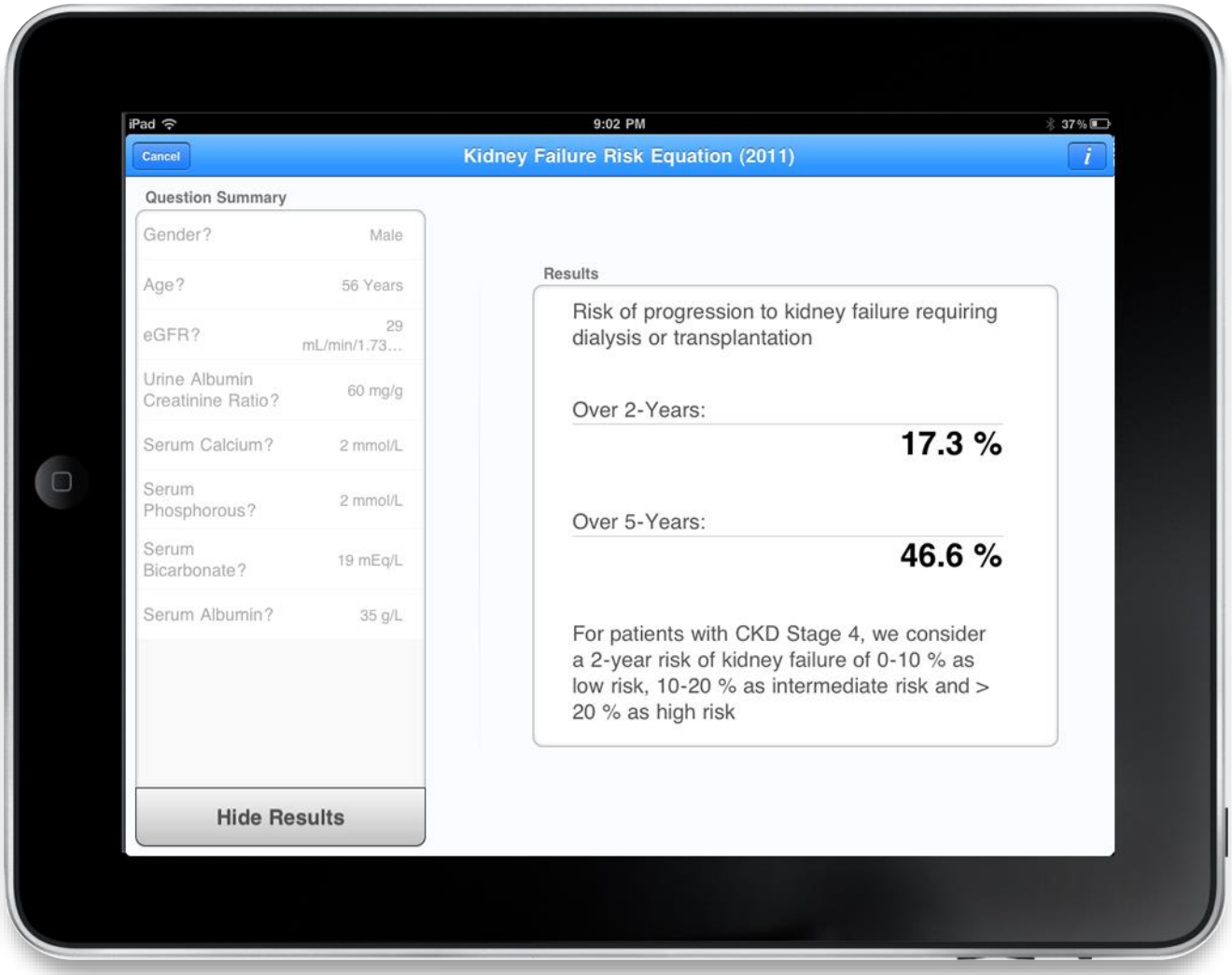
GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Kidney Failure Risk Equation

JAMA®
The Journal of the American Medical Association

Tangri et al. 2011



Available on the App Store

Available on the Android Market

Get it at BlackBerry App World

Risk-Based Teams Approach

Low Risk Patients

Team:

- Primary care provider

Focus:

- Lifestyle
- blood pressure

Medium Risk Patients

Team:

- Primary Care providers
- Kidney specialist

Focus:

- Diagnosis
- Lifestyle
- Blood pressure
- Protein leak reduction

High Risk Patients

Team: Multidisciplinary Kidney Health Clinic

- Primary care provider*
- Kidney specialist
- Kidney Nurse
- Kidney Dietitian
- Kidney Pharmacist
- Kidney Social worker

Focus:

- Healthy Lifestyle
- Reduction of blood pressure
- Reduction of protein leak in the urine
- Treat consequences of low kidney function
- Treat related heart and diabetic diseases

Resource allocation aligned with RISK

ODDS RATIO OF KDIGO CKD STAGE

(FINISHED vs. General Population Derived from NHANES cohort)

			Persistent Albuminruia			
			A1		A2	A3
			Optimal to high-normal		High	Very high to nephrotic
			<10	10-29	30-299	>300
GFR	G1a	>105	0.94	3.58	5.31	8.59
	G1b	90-104	0.50	1.36	2.69	6.54
	G2a	75-89	0.42	1.24	1.25	3.68
	G2b	60-74	0.42	0.75	1.57	4.50
	G3a	45-59	0.45	1.06	0.70	1.23
	G3b	30-44	0.41	1.64	1.36	4.91
	G4	15-29	N/A	N/A	N/A	3.27
	G5	<15	N/A	N/A	N/A	N/A

RESEARCH ARTICLE

An Economic Assessment Model of Rural and Remote Satellite Hemodialysis Units

Thomas W. Ferguson[2], James Zacharias[1,2], Simon R. Walker[1], David Collister[1], Claudio Rigatto[1], Navdeep Tangri[1,2], Paul Komenda[1]*

Table 3. Cost Model–Average Annual Per-Patient Cost in Communities Accessible by Air.

	Facility HD	Unit O	Unit H	Unit C	Unit I	Unit F	Unit K
Dialysis Machinery Costs	$1,551	$2,909	$4,296	$3,878	$4,654	$4,072	$4,654
Consumables and Peripherals Expenses	$5,982	$6,582	$6,582	$6,582	$6,582	$6,582	$6,582
Human Resource Expenses—Salaries and Wages	$13,380	$33,208	$34,352	$49,671	$30,667	$63,719	$43,266
Human Resource Expenses—Benefits	Included	$4,492	$4,647	$6,719	$4,148	$8,619	$5,853
Medical Equipment Costs	$423	$772	$1,598	$1,155	$1,426	$2,964	$1,006
Renal Medication Expenses	$7,938	$7,938	$7,938	$7,938	$7,938	$7,938	$7,938
Dialysis-Related Laboratory Expenses	$1,163	$1,163	$1,163	$1,163	$1,163	$1,163	$1,163
Facility Costs	$11,534	$11,534	$11,534	$11,534	$11,534	$11,534	$11,534
Capital Costs	N/A	$3,790	$19,604	$5,669	$17,502	$36,364	$8,231
Dialysis Transportation Expenses	$1,751	$1,751	$1,751	$1,751	$1,751	$1,751	$65,910
Return to Tertiary Care Centre Expenses	N/A	$19,090	$4,827	$23,470	$45,130	$35,293	$37,365
Costs of Using Dialysis Facility in Tertiary Care Centre	N/A	$2,018	$477	$2,918	$7,995	$8,987	$6,689
Hospitalization-Related Expenses	$4,917	$4,917	$4,917	$4,917	$4,917	$4,917	$4,917
Nephrologist and Physician Costs	$7,792	$11,778	$11,778	$11,778	$11,778	$11,778	$11,778
Total Annual, Per-Patient Cost	$56,431	$111,941	$115,463	$139,143	$157,185	$205,681	$216,885

Cost Effectiveness

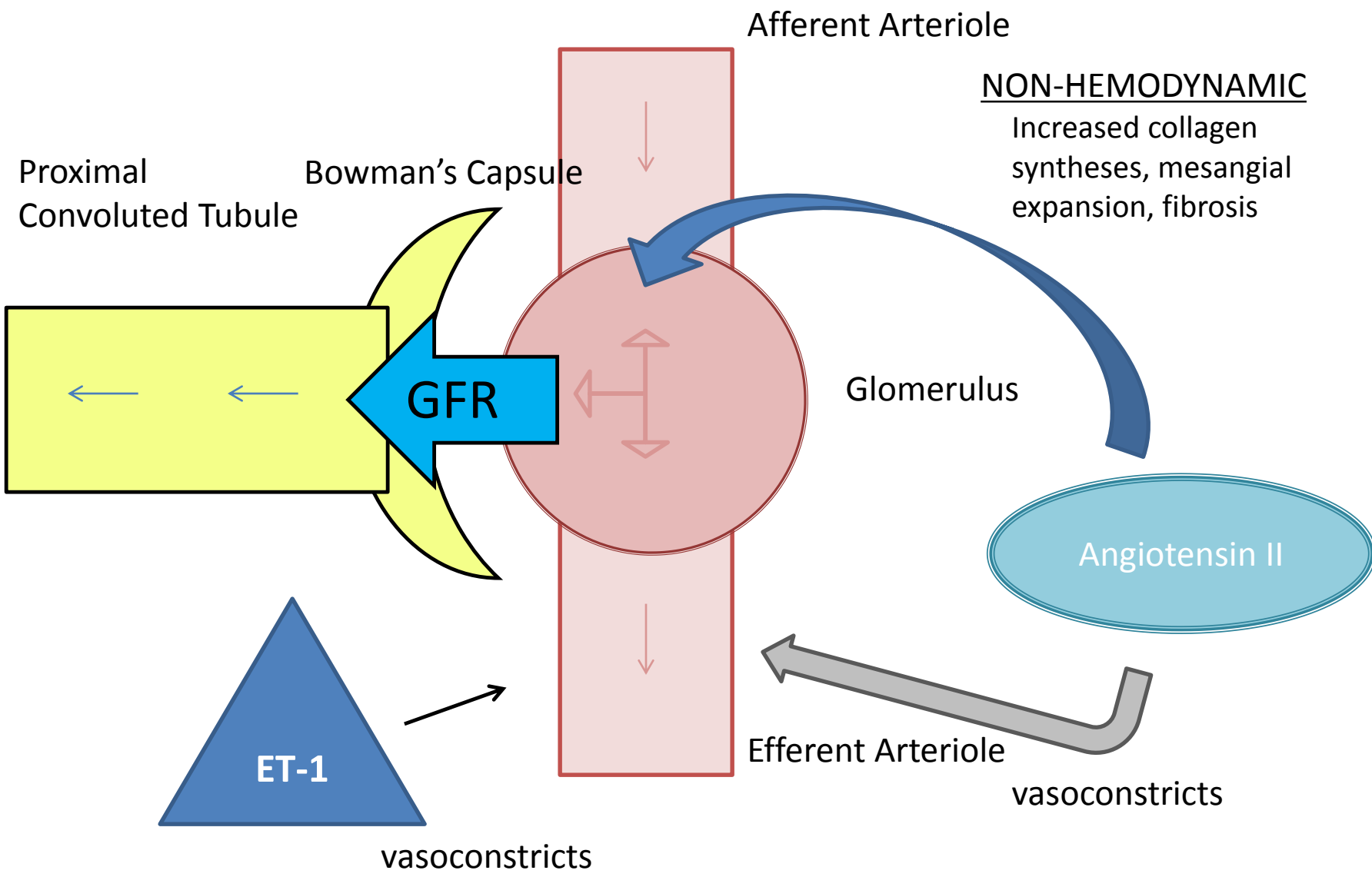
Variable	Incremental Cost ($C)	Incremental QALYs	Cost/QALY
Baseline	850	0.0254	**33,500**
Threshold for relative risk reduction afford by treatment extended to patients with microalbuminuria (urine ACR > 30 m/g) (Baseline urine ACR threshold of > 300 mg/g)			
All communities	176	0.0657	2,680
Road access	-360	0.0903	***Dominant***
Air access	556	0.0469	11,870
Increase in home modality uptake			
Increased PD and HHD use by 25%	349	0.0254	13,760
Increased PD and HHD use by 50%	-218	0.0254	***Dominant***
Increased PD and HHD use by 100%	-1170	0.0254	***Dominant***

Convention: New interventions funded at $50,000/QALY (or 2-3x GDP)

Medical Therapy for DN

- *Metabolic Control (glucose and lipids)*
- *Blood Pressure Control*
- *Anti-albuminuric agents (RAAS blockade)*
- **Novel Agents:**
  - **Endothelin receptor antagonists**
  - **Sodium glucose transporter 2 inhibitors**
  - **Mineralocorticoid receptor antagonists**

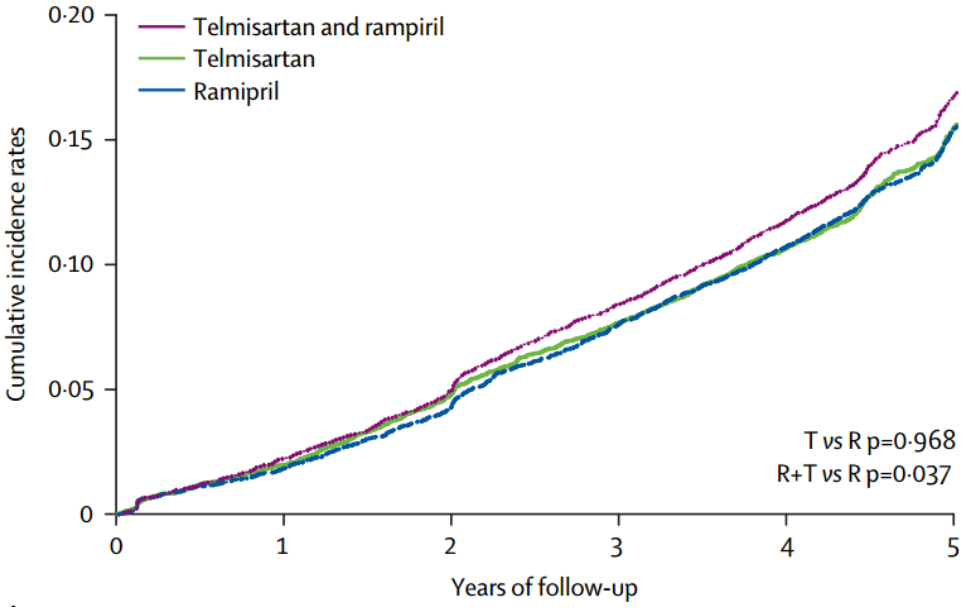
AngII and ET-1 Glomerular Hemodynamics



ONTARGET – Renal Outcomes

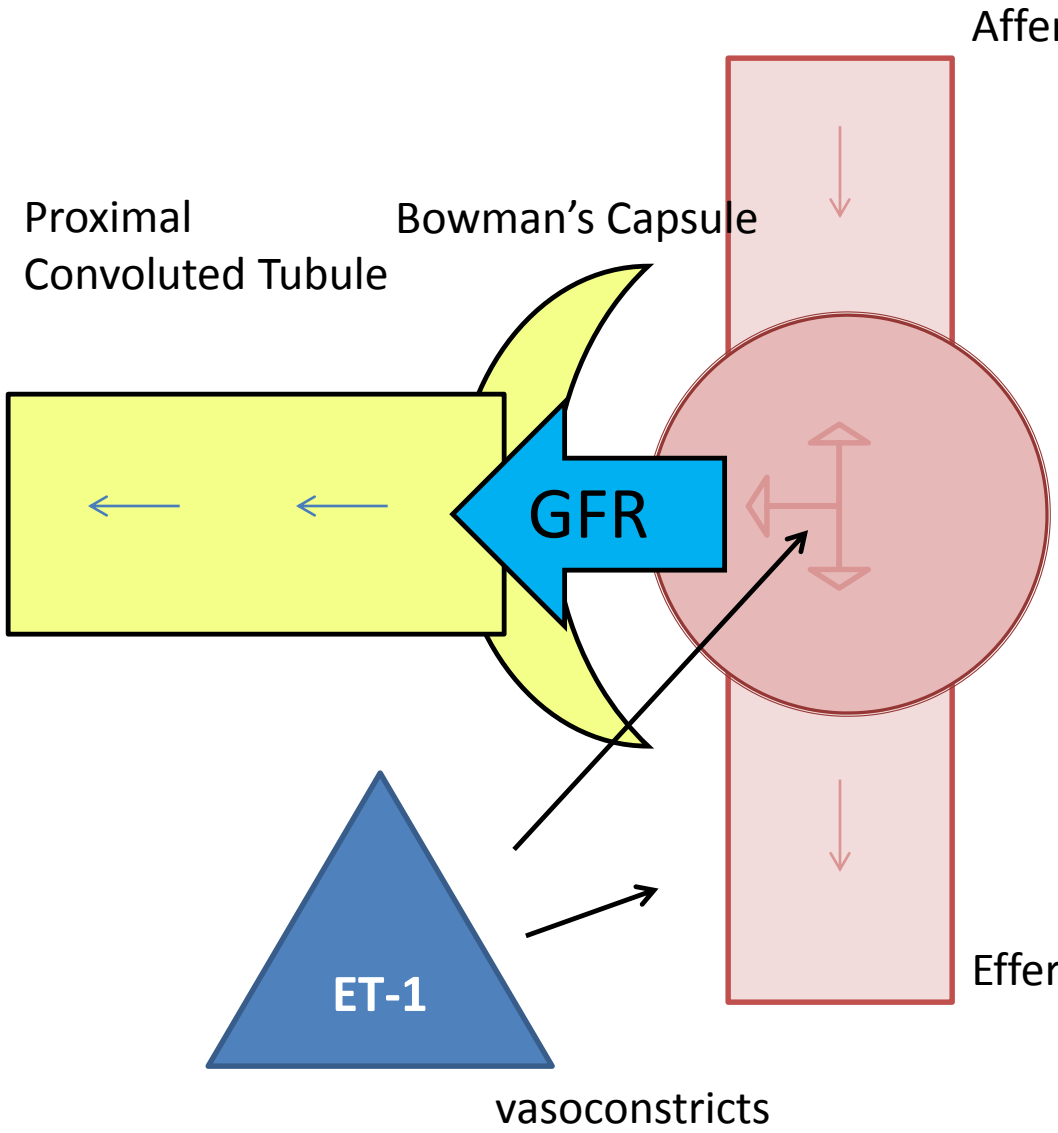
- Primary Outcome:
  - dialysis, doubling of serum creatinine, and death
  - Pre-specified analysis

- Combination HR 1.09 (1.01-1.18) for primary outcome (graph) despite reduction in proteinuria



Mann et al. Lancet. 2008 Aug 16;372(9638):547-53.

RAAS & ET-1 Renal Pathophysiology



- ET-1 acts on ET_AR and ET_BR.
  - A receptors vasoconstrict
  - B receptors vasodilate
- Endothelin system is upregulated in diabetes
- **ET_AR blockade likely dilates efferent arteriole**, reducing glomerular hypertension, but may also have direct effects on podocyte signalling
- Can block this by ET-converting enzyme inhibitors (ECE inhibitors) or by ERBs specific for A receptors

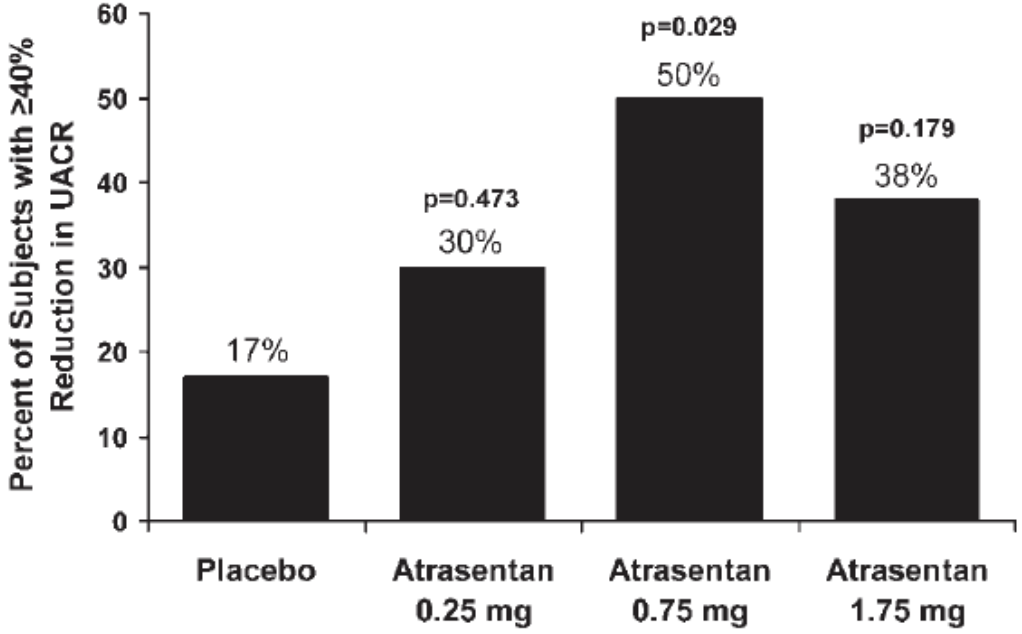
Endothelin Antagonists

- Avosentan – selective ET_AR agonist (50:1)
  - Trial prematurely terminated due to excess fluid retention and CV risk
    - B receptor activation causes vasodilation, Na retention, and fluid overload

- Atrasentan - selective ET_AR antagonist
  - 1800:1 selectivity for ET_AR vs ET_BR

Atrasentan + ACEi/ARB

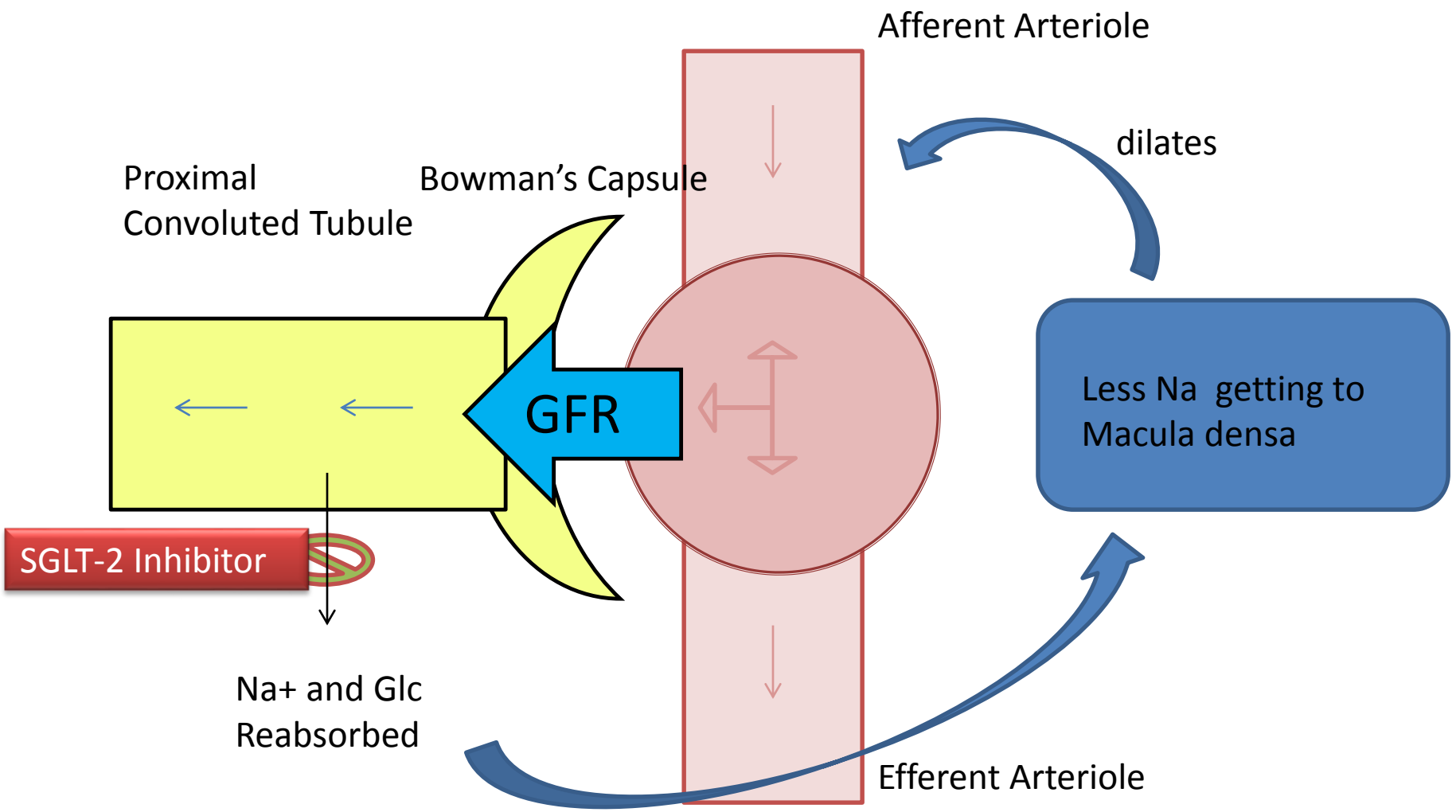
- RCT, double-blind placebo controlled trial in
- N=89 with DN, GFR>20 already on stable dose of ACEi/ARB
- Followed for 8 weeks
- Atra lowered ACR independent of lowered BP
  - ET_AR-mediated vasoconstriction likely contributes to CKD hypertension



SONAR trial will look at GFR.

(Study Of Diabetic Nephropathy With Atrasentan)

Sodium glucose transporter 2 inhibitors

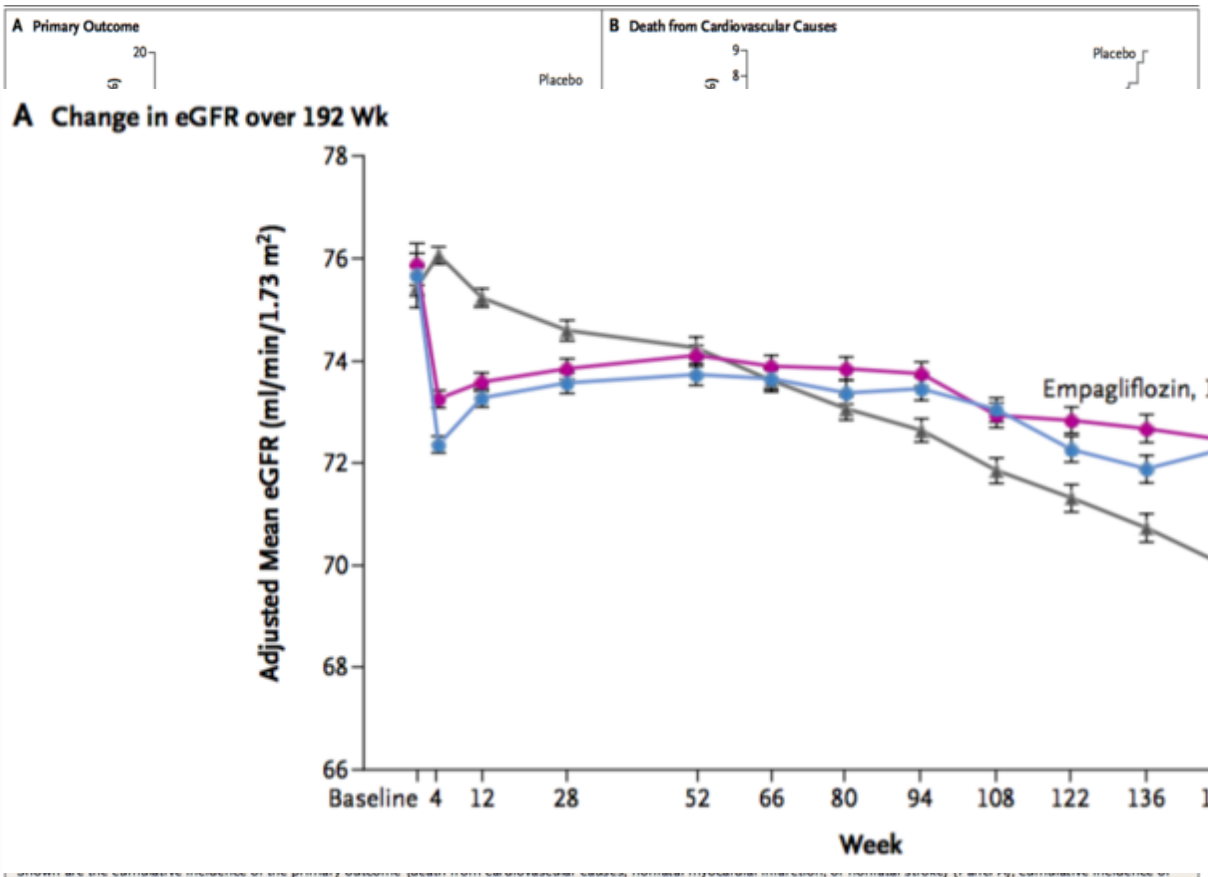


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,



death from cardiovascular causes (Panel B), the Kaplan–Meier estimate for death from any cause (Panel C), and the cumulative incidence of hospitalization for heart failure (Panel D) in the pooled empagliflozin group and the placebo group among patients who received at least one dose of a study drug. Hazard ratios are based on Cox regression analyses.

CKD Surveillance and Detection Unit

DSM Lab Repository

MB Health Repository

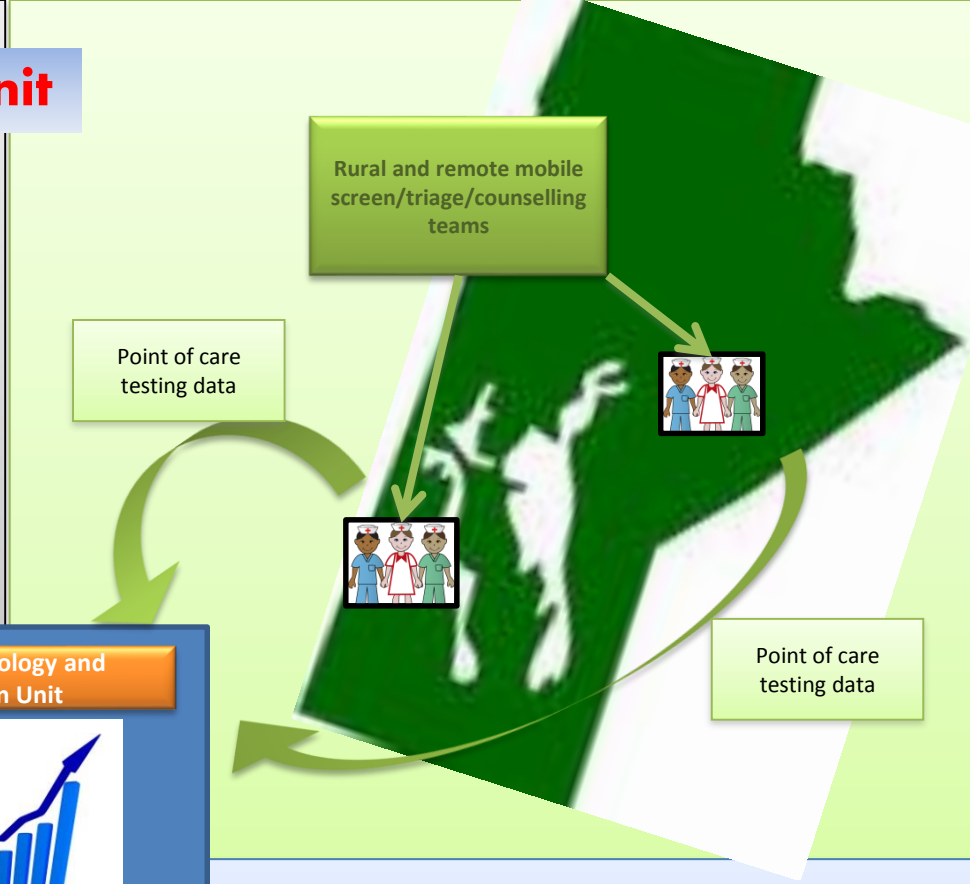
eGFR, UACR, HgbA1C

- Diabetes
- Hypertension
- Nephrology referral?

Rural and remote mobile screen/triage/counselling teams

Point of care testing data

Point of care testing data



CKD Epidemiology and Education Unit

- Patient level risk prediction
- Surveillance Reports
- Communication
- Renal Health Outreach Education Activities

Feedback to primary care practitioners

Treatment of low risk CKD
Appropriate referral to nephrology

Feedback directly to patients

Their individual risk profile
Self management guidelines
Indications for referral

Quarterly surveillance reports

Manitoba Health

kidneyhealth.ca

Conclusions

- Screen with urine ACR and eGFR
- Screen HTN, DM2, CVD, and all First Nations patients
- Additional pathologic processes must be inhibited to slow progress of CKD.

Optimizing Screening and Surveillance remain our best chance at prevention!