# A Trial of Care for CKD: Can-Prevent

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**The Canadian Collaborative Group for the Prevention of Renal and Vascular Endpoints Trial (CANPREVENT) New Emerging Team is sponsored by:**

CIHR-Institute of  Nutrition, Metabolism and Diabetes

CIHR-Institute of Circulatory and Respiratory Health

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Canadian Diabetes Association

Kidney Foundation of Canada

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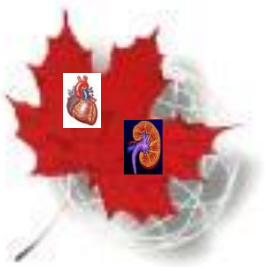


# Background

- CKD is common
- Increases risk for ESRD and CVD events
- There are evidence based therapies
- They are not optimally applies in routine care
- New models of care need to be tested

# CAN-PREVENT

- RCT of care for CKD as a chronic illness
- Nurse coordinated team v. usual care
- Protocols for evidence based therapies
- Aim to reduce kidney & CV outcomes

# Trial Design

- Randomized
- Multi-centre
- Parallel, 2 group trial
- Usual care v. “Intervention Clinic”
- Blinded assessment of end-points

# Inclusion Criteria

- Age 40-75, CrCl 25-60
- Stratum 1 : diabetic
- Stratum 2 : proteinuria ≥ 1g/L
- Stratum 3 : No DM or proteinuria

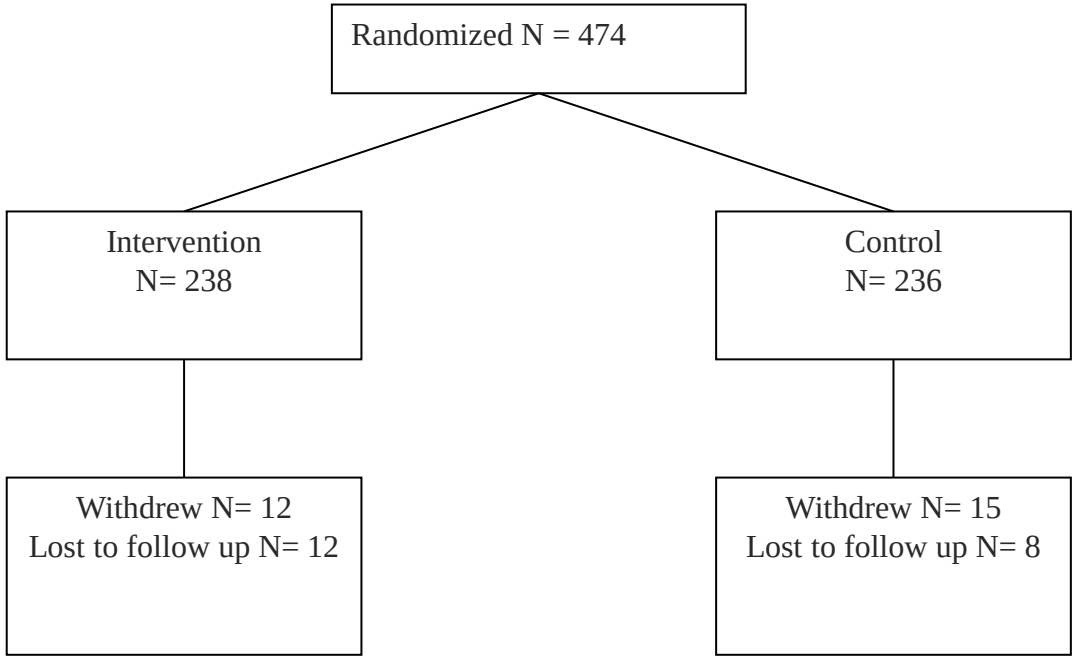
# Exclusion Criteria

- No consent
- Likely to die < 6 months
- Current malignancy, advanced CVD, transplant
- CKD currently treated by immunotherapy
- ESRD likely in < 6 months
- Current care for CKD or CVD by DM program
- Currently in another interventional trial
- Not able to attend for follow-up

# Recruitment

- Used a lab based case finding strategy:
  - Electronic search for those with SCr in range
  - Contact with doctor via lab
  - Doctor refers patients to study
- Mostly (93%) not already referred to nephrology (to minimize contamination)
- 474 randomized and followed - mean 704 days

# We Did Find & Follow Patients



# Intervention

- Nurse co-ordinated
- Protocol guided
- Nephrologist supervised
- Clinic based
- Interventions target CV & kidney disease
- These reflect current state of knowledge
- Modifed as evidence emerged

# Protocols Include (Tier 1)

- BP and proteinuria control
- RAAS blockade
- Lipid therapy
- Use of ASA
- Beta-blockade post MI & in CHF

# Protocols Include (Tier 2)

- Anemia Management
- Mineral and parathyroid management
- Acidosis control
- Diabetes control
- Smoking cessation

# Baseline Characteristics

| | Intervention % | Control % |
|---|---|---|
| Diabetes | 31.4 | 32.9 |
| Hx MI | 16.7 | 14.3 |
| Hx CABG | 10.7 | 8.2 |
| HX PTCA | 11.2 | 8.7 |
| Hx CHF | 5.6 | 3.9 |

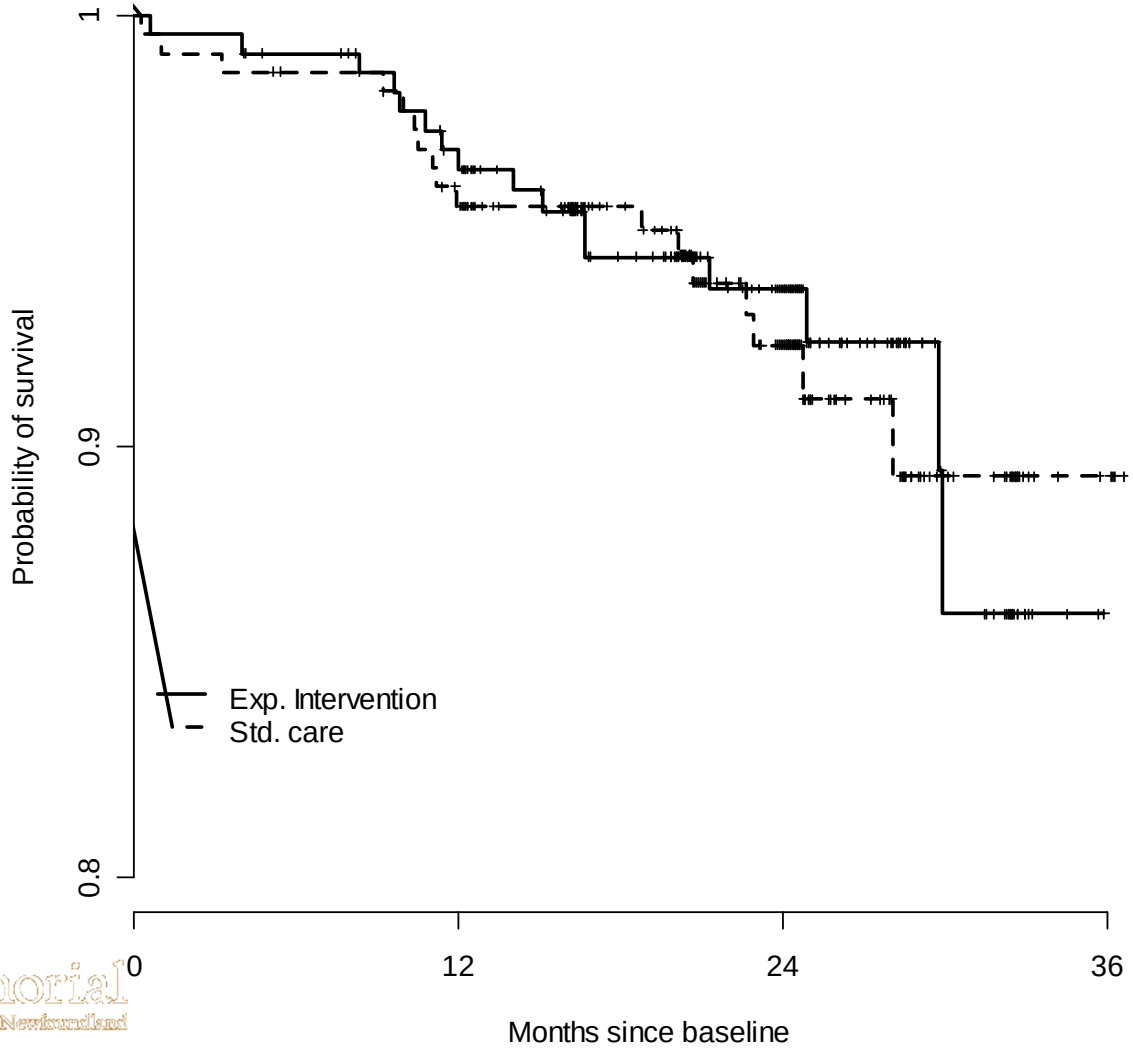
# Baseline Characteristics 2

| Median [IQR] | Intervention | Control |
|---|---|---|
| eGFR | 42.5 [38-46] | 42.3 [37-46] |
| 24 hr urine protein | 0.11 [0.07-0.2] | 0.12 [0.08-0.22] |
| BP | 128/74 [116/66-140/80] | 132/74 [120/68-144/81] |
| Hba1c in diabetics | 7% [6.4-7.9] | 7.1 [6.3-7.6] |
| LDL | 2.6 [2.1-3.3] | 2.7 [2.1-3.5] |

# Adjudicated Clinical Outcomes

| | Intervention N (%) | Control N (%) |
|---|---|---|
| **Cardiovascular death** | 2 (0.8) | 2 (0.8) |
| **Other death** | 5 (2.1) | 0 (0.0) |
| **Myocardial infarct** | 5 (2.1) | 4 (1.7) |
| **ACS** | 1 (0.4) | 2 (0.8) |
| **Heart failure** | 5 (2.1) | 8 (3.4) |
| **Stroke** | 1 (0.4) | 1 (0.4) |
| **Amputation of leg** | 2 (0.8) | 2 (0.8) |
| **Dialysis** | 2 (0.8) | 1 (0.4) |
| **Doubled SCr** | 1 (0.4) | 4 (1.7) |

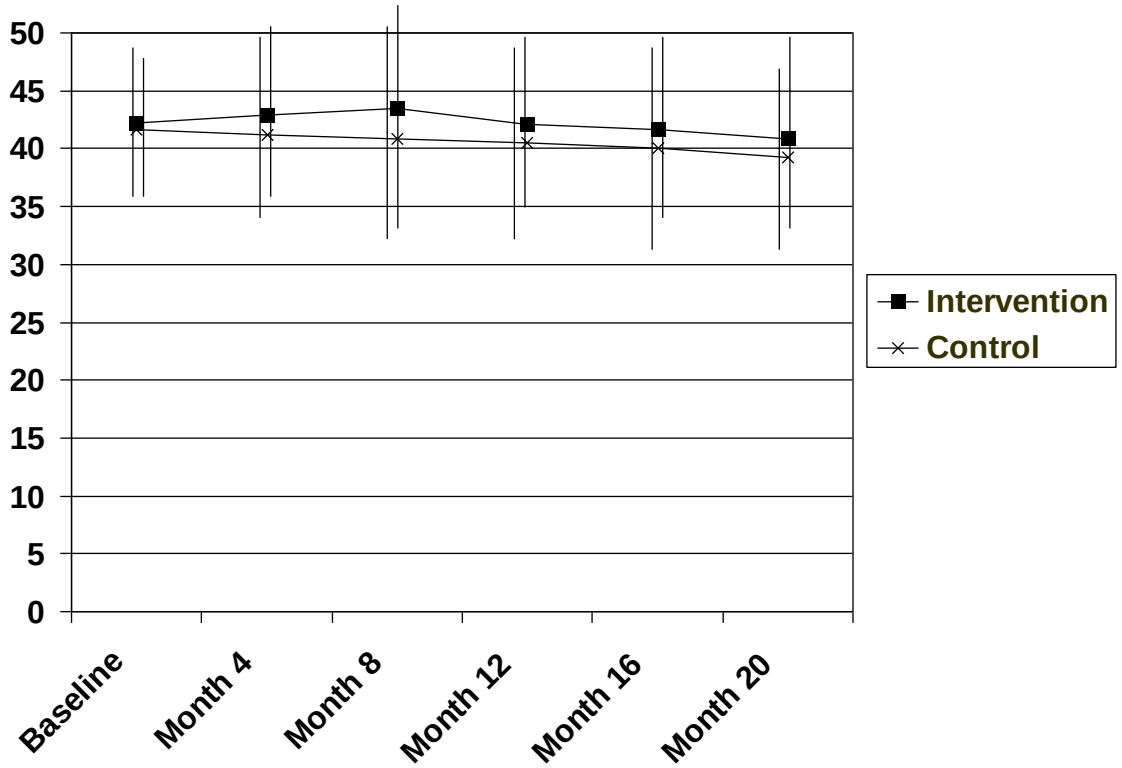
# Time To First Clinical Event



# Rate of Clinical Outcomes

- 48 endpoints
- Two events each in 5 cases
- Three events each in 2 cases
- Annual incidence of events:
  - 5.2% (CI 3.8-6.7%)

# Impact on Kidney Function



# Blood Pressure Control

- Good overall
- Intervention v Control SBP
  - 129 v 133 @ baseline
  - 124 v 130 @ 12 mos, $p<0.01$
  - 123 v 128 @ 24 mos, p=NS

95% CI for the difference -1.1 to -8.5 mmHg for marginal mean in GLM adjusting for baseline

# Management of SBP > 140

| | Intervention | Control |
|---|---|---|
| % SBP > 140 @ baseline | 25.8 | 34.5 |
| In which # BP meds @ baseline | Av 2.4 | Av 2.3 |
| In which # BP meds @ 12 mo | Av 2.9 | Av 2.5 |
| % BP >140 @ 12 mo | 15.6 | 26.1 |

# % on RAAS Blockers

| | Intervention | Control |
|---|---|---|
| Baseline (DM) | 88 | 91 |
| Baseline (all) | 70 | 66 |
| 12 months all | 75 | 66* |
| 24 months all | 78 | 66* |

Memorial University of Newfoundland

* p<0.05

# Mean LDL Levels

| | Intervention | Control |
|---|---|---|
| Baseline | 2.75 | 2.82 |
| 12 months | 2.56 | 2.65 |
| 24 months | 2.34 | 2.41 |

P<0.0001 for time, NS between groups

# Impact on Lipid Management

- % on statin among those with baseline LDL > 2.5 mmol/L

| | Intervention | Control |
|---|---|---|
| Baseline | 39 | 35 |
| 12 mos | 65 | 42* |
| 24 mos | 84 | 51* |

P<0.001 between groups

# Other Impacts

- ESA use in 1-5 of each group at any time
- Tsat < 0.2 treated in 35% v. 14%
- No difference in hemoglobins
- No difference in phosphate, calcium or PTH levels (≈ 90% of upper normal)
- No difference in phosphate binders (used in 2-5% cases during trial)

# What The Intervenors Did Not Do

| | Intervention Grp by 12 months | Controls by 12 months |
|---|---|---|
| Δ Hba1c in diabetics | -0.49% | -0.52% |
| Mean Hgb if < 110 at baseline | 110 (3 on ESA) | 108 (0 on ESA) |

# What The Intervenors Did Not Do

- Refer more to dietitians (23% v. 25% in the first 12 months)
- Involve diabetes nurse educators (16% v. 18% in the first 12 months)

# Cost-effectiveness

- We monitored all health care resources used
- We measured quality of life by EQ5D
- We constructed a cost-utility analysis

$$\frac{\text{Diff in \$}}{\text{Diff in QALYs}}$$

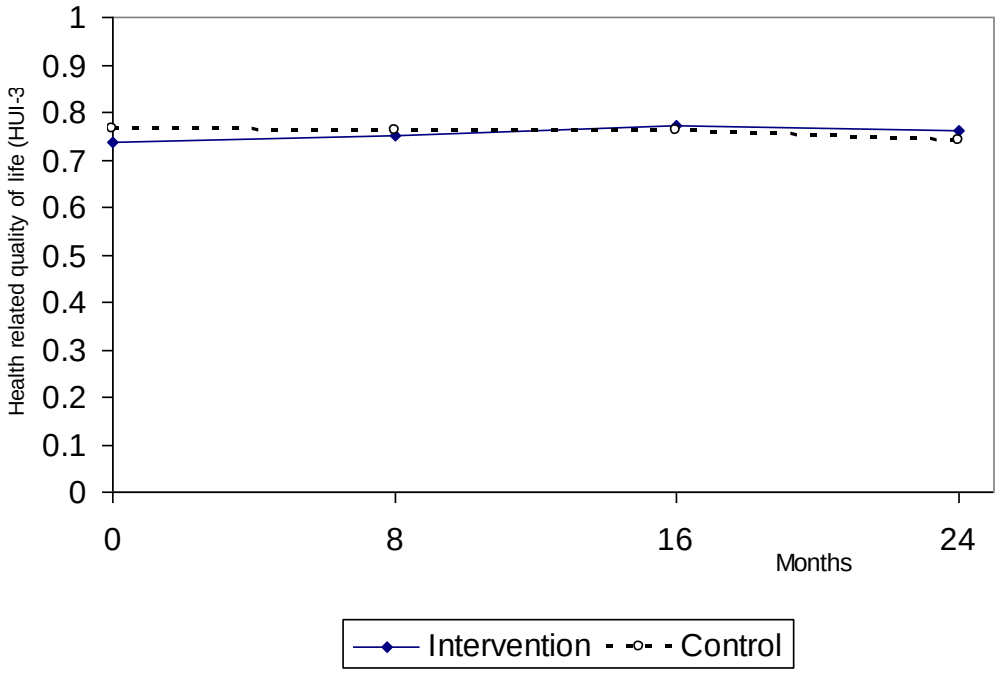
# Costs – 2 year study patients

| | Intervention | Control |
|---|---|---|
| Disease related costs (mean) | $4,631 | $5,741 |
| All costs (mean) | $11,739 | $14,180 |

# Cost Difference was significant

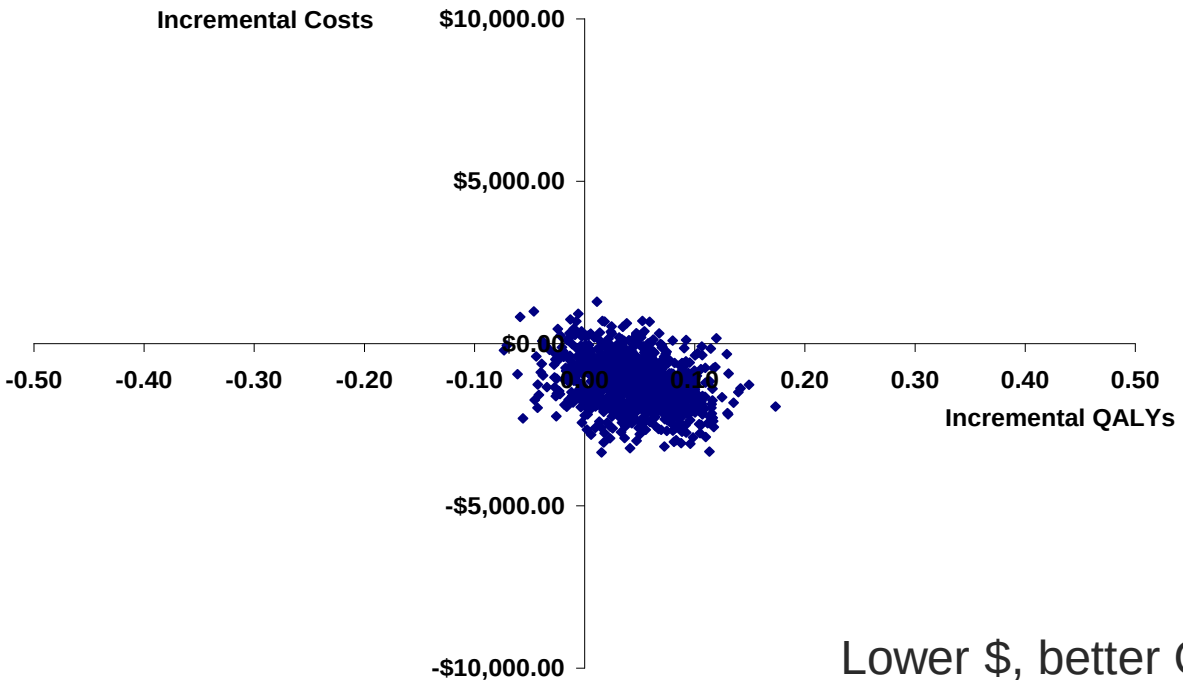
- Trend to higher up front costs in the intervention group (clinic time etc)
- More than offset by less hospitalization and indirect costs in the intervention group

# Difference in Utility (EQ-5D)




Intervention started lower and rose. Area under curve greater for Intervention over 2 years - implies better quality of life

# Overall Cost-Utility




Lower $, better QALYs

With Intervention in this quadrant

# Conclusions

- The largely unreferred population had a low risk of renal progression, but some CV risk
- Trial was too small to detect effect on clinical outcomes
- No impact on QoL
- Intervenors did address BP, RAAS blockade, lipids and iron
- Need for and use of ESAs was low
- Need and use of phosphate binders was low
- Diabetes impact equal to controls

# Conclusions 2

- There is potential for the model of care to impact clinical outcomes beyond usual care
- It was feasible to apply the intervention, but the impact on surrogate outcomes was not consistent
- Intervention was cost-effective
- The trial did not really test impact on those at risk for kidney disease progression
- Further studies may be justified

# The Bottom Line

- There are people out there with CKD who may need care aimed at reducing CV risk, but the nature of the care should be within the competence of many physicians
- Nephrologists are likely to have little specific to offer in many of these cases

# Thanks

- Questions?
- Comments?
- Criticism?