

CARSK

Canadian-Australasian Randomized Trial of Screening Kidney Transplant Candidates for Coronary Artery Disease

Seattle Investigators' Meeting
June 2, 2018



Hypothesis

- After screening for wait list entry, non use of cardiac screening tests is non-inferior versus the current standard care, which is screening all asymptomatic wait-listed patients for coronary artery disease (CAD) at regular intervals
- We will also compare the benefits and costs of screening and subsequent treatment versus not screening from a health system perspective

Inclusion Criteria:
At least 18 years of Age
No symptoms of active cardiac disease
Actively Wait-listed For Kidney Only Transplant
No previous extra-renal transplant
Anticipated date of transplantation > 12 months from date of enrollment
Anticipated to require cardiac screening before transplantation*

Informed Consent

Randomization

Regular Screening
During Wait-listing

No Screening after
Wait-listing

Note patients in both groups may be investigated for symptoms

Annual from date
of last test
-Diabetes
Angiographic
CAD not
revascularized
-PTCA
Incomplete CABG
CABG > 3 yrs ago

Every 24 months
for all others

Management of a positive non-invasive test irrespective of whether it was done for screening or symptoms will be managed as per center protocol

CARSK FUNDING HISTORY

- Canadian Pilot: Feasibility n =144, 2 years follow up
 - John Gill, Greg Knoll, PJ Devereux
 - Sites: Vancouver (Gill), Ottawa (Knoll), Hamilton, Toronto (Joe Kim), Montreal (Cantarovich)
- Australia/ Zealand- Funded for definitive trial
 - Chadban/ Pilmore
 - N=1100 4 years follow up
- CARSK Funded in Canada March 2018
 - Jag Gill, Scott Klarenbach, Joe Kim
 - John Gill, Greg Knoll, PJ Devereaux – Awarded Foundation Grants
 - John Gill Foundation Grant – supporting pilot and pilot patient continuation in CARSK
 - N= 2200 5 years follow up

CARSK TEAM

- Project Lead: Gillian Hughes
- Steering Committee: Jag Gill, Scott Klarenbach, Joe Kim, John Gill, Greg Knoll, Steve Chadban, Tracey Ying, Charles Herzog, Angela Webster
- Advisory Committee: Tim Ramsay, PJ Devereaux, Rachel Morton, Krish Ramanathan, Cello Tonelli, Patrick Kelly, Ben Chow

CARSK Canadian Sites

- Vancouver SPH – Gill/Gill
- Vancouver VGH – Olwyn Johnston
- Edmonton – Scott Klarenbach
- Winnipeg – David Rush
- Ottawa – Greg Knoll
- Toronto/ UHN – Joe Kim
- Toronto/ SMH – Ramesh Prasad
- Hamilton – Christine Ribic
- U of M / Hôpital Maisonneuve-Rosemont - Duy Tran
- McGill – Marcelo Cantarovich
- Halifax – Amanda Vinson

CARSK Australian/ NZ Sites

- Royal Alfred – Chadban/Ying
- Westmead – Webster/Chapman
- Canberra Hospital
- Monash Medical Center – John Kanellis
- Austin Health Center – Peter Mount
- Prince of Wales Hospital- Grant Luxton
- Sir Charles Gardiner Hospital – Wai Lim
- St George Hospital – Sunil Badve
- Liverpool Hospital
- Auckland City Hospital – Pilmore
- Wellington – Murray Lekkis
- Christchurch – Nick Cross

Clinical Events Committee

- Chair – Charles Herzog

DSMB

- Andreas Laupacis - Chair
- Andrew Day - Statistician/Queens
- Brenda Hemmelgarn – Nephrologist/Calgary
- Matthew Jose – Nephrologist/Tasmania
- Anushka Patel – Cardiologist Sydney/Royal Alfred

- Independent Statistician – Stephanie Clark

CEC and DSMB Status

- DSMB Charter – will be finalized July
- CEC Procedure Manual – finalized July
 - First CEC Adjudication October, 2018
 - CEC will likely meet quarterly

Adjudicated Events

- Cardiovascular death
- Non-fatal MI
- Urgent revascularization for symptoms
- Hospitalization for unstable angina
- Death from any cause
- Stroke
- Major bleed / procedural bleed

Enrolment Current Status

- Pilot n = 144 (50 % rolled over into CARSK); expect 125 to be enrolled
- Australasia enrolment n = 350
- Canadian CARSK enrolment to start in Vancouver July

CARSK Enrolment Plan Canada

- Canadian Pilot Sites (Ottawa, Montreal, Toronto, Hamilton, Vancouver) – complete patient rollover Sept 2018
- CARSK Contracts and REB Documents to be sent to all sites June 30
- Anticipate 3-4 month approval for budget and REB with all Canadian Sites enrolling new patients before end of 2018.

Enrolment Targets - Canada

| Site | Anticipated recruitment (N) (<u>estimated</u> annual and monthly recruitment based on 3 year recruitment period)* |
|------------------------------------|---|
| St. Paul's Hospital | 350 (116/yr; 10/month) |
| Vancouver General Hospital | 300 (100/yr; 8/month) |
| University of Alberta | 100 (33/yr; 3/month) |
| Manitoba | 100 (33/yr; 3/month) |
| Toronto General Hospital | 250 (83/yr; 7/month) |
| St. Michael's Hospital | 250 (83/yr; 7/month) |
| Hamilton | 150 (50/yr; 4/month) |
| Ottawa | 200 (66/yr; 5-6/month) |
| <u>Universite de Montreal/CHUM</u> | 150 (50/yr; 4/month) |
| McGill University Hospital | 100 (33/yr; 3/month) |
| Quebec City | 50 (16/yr; 1-2/month) |
| Atlantic Canada | 100 (33/yr; 3/month) |
| TOTAL 12 sites | Total required: 2200 |

Enrolment

- De novo WL Patients
 - In person during de novo WL assessment
 - Patient may not yet be on WL but can be consented and randomized once activated to WL
- Prevalent WL patients
 - During in person transplant center review
 - During local dialysis center treatment
 - Patients living at distance may be enrolled by telephone in most centers
 - Patient is a wait-list candidate and therefore a patient of the transplant center
 - Obviates need for separate ethics/ contracts with dialysis centers

Study Operations

- Screening tests are considered Standard of Care and should be ordered by the transplant center (these are clinical indicated tests)
- Weekly interaction with transplant nursing team responsible for monitoring the medical fitness of wait-listed patients
- Q 6 month patient visits (can be in person or by telephone)
 - If a hospitalization event has occurred
 - Clinical record requested through the transplant program

Website



In development



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WHAT IS CARSK?

CARSK stands for the "Canadian-Australasian Randomized Trial for Screening Kidney Transplant Recipients for Coronary Artery Disease."

Why is this trial important?

Cardiovascular disease is the commonest cause of death while on the kidney transplant waitlist and after transplantation. Current standard care involves screening for coronary artery disease prior to waitlist entry, then every 1-2 years, according to perceived risk, until transplanted. This current screening strategy is not evidence based, has substantial known and potential harms, and is very costly.

Study overview

CARSK is a multicentre, non-inferiority, two-parallel-arm randomized trial. It aims to test the hypothesis that after screening for waitlist entry, no further screening for coronary artery disease (CAD) is not inferior to the current standard care, which is screening all asymptomatic waitlisted patients for CAD at regular intervals.

Additionally, it will compare the benefits and costs of not screening versus regular CAD screening from a health system perspective.

Trial registration

Please visit [ANZCTR](#) for more information.

Publications

- Pilot results – last quarter of 2018
- Protocol – last quarter of 2018

Authorship

- SC/Advisory members will be listed as authors
- All site investigators acknowledged in the manuscript

Future Studies

1. Biomarker collection
2. Ancillary analysis
3. Building on CARSK