Predialysis Care
Challenges and opportunities
David C Mendelssohn
Road map

- Care in the Community
  - Non referral and late referral
- Care after referral
  - Solo nephrology care
  - Multidisciplinary team based care
- Initiation of Dialysis
  - Suboptimal starts
- Optimizing Care
  - Challenges and opportunities
## Lets focus on Canadian data

1. It is of interest to look at places other than the USA
2. I know Canada best
3. Unfortunately, there is not much data from eastern Europe
4. Lessons learned are generalizable to other places
Why the Interest in Pre-ESRD Care?

- Death rates and sickness on dialysis remains unacceptably high.
- Attention to dialysis prescription and other dialysis related risk factors has only changed this to a small degree.
- Many problems leading to sickness and death on dialysis begin well before ESRD, and may be modifiable.
- Pre-ESRD care is often less than ideal, and dialysis may be started in a suboptimal manner.
Optimal pre-ESRD care

Decreased morbidity and mortality on dialysis

Clearly, there is an association between mortality on dialysis and suboptimal pre-ESRD care. It seems plausible that better pre-ESRD care will lead to better outcomes.
Care in the Community

- Recognition of CKD
- Workup of CKD
- Control of BP, utilization of renal protective strategies, management of CV risk factors, avoidance of nephrotoxins
- Timing of referral to a nephrologist
Suboptimal starts
Late Referrals/Unplanned starts

Consequences
- Anemia
- Metabolic acidosis
- Hyperphosphatemia
- Hypoalbuminemia
- HTN, volume overload
- Low prevalence of AVF as initial dialysis access
- Low rate of initiation of home dialysis
- Delayed referral to transplant
- Increased hospitalization rate
- Higher cost of dialysis initiation
- Increased 1 yr mortality

Kessler et al 2003; Metcalfe et al 2000; Lorenzo et al 2004
Nephrology care

- Approach to diagnosis
- Specific therapy
- Non specific therapy
  - Renal protection
  - CV protection
- Education
- Modality selection
- Referral for AV access surgery
Early referral

Comp-letion of tasks

Planned start
Elective
Outpatient AVF

1) Patient related delay
2) Acute on CKD
3) Suboptimal care
4) No chronic HD spot

Unplanned start
Emergent
Inpatient CVC

Tasks Not Comp-leted

Late Referral
Suboptimal starts
“Consider how you would respond to the following abnormal lab tests”

Percent of Incident Patients Seeing a Nephrologist at Times Prior to ESRD: Canada, Europe, and USA

% of patients

- Canada: 15% seen < 1 month, 6% seen 1-4 months, 16% seen 4 months to 1 year, 63% seen more than 1 year (n=125)
- Europe: 19% seen < 1 month, 9% seen 1-4 months, 11% seen 4 months to 1 year, 62% seen more than 1 year (n=956)
- USA: 21% seen < 1 month, 12% seen 1-4 months, 14% seen 4 months to 1 year, 53% seen more than 1 year (n=345)

Quality of Prereferral Care in Patients with CKD

- Chart review, consecutive new patients in 1998 and 1999 at QEII HSC, Halifax
- GFR < 60 ml/min
- 411 patients met entry criteria
- Mean CrCl = 31, 18% < 15 ml/min
- 54% referred with CrCl < 30 ml/min

Cleveland DR et al. AJKD 40; 30-36: 2002.
<table>
<thead>
<tr>
<th>Hypertension Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SBP</strong></td>
</tr>
<tr>
<td><strong>DBP</strong></td>
</tr>
<tr>
<td><strong>ACEI or ARB</strong></td>
</tr>
<tr>
<td><strong>Diuretic</strong></td>
</tr>
<tr>
<td><strong># of BP agents</strong></td>
</tr>
</tbody>
</table>

Cleveland DR et al. AJKD 40; 30-36: 2002
Other Issues

- Hb < 10 present in 21%
- Anemia workup in 35%
- NSAID’s used in 10%

In all areas (BP, anemia, metabolic, diabetes, timing of referral), quality of prereferral care was found to be suboptimal.

Cleveland DR et al. AJKD 40; 30-36: 2002
Care After Referral
Early Tasks

- Establish diagnosis
  - Consider biopsy
- Rule out reversible component
  - Review medications
- Consider specific therapy
- Implement non-specific therapies
Prepare For ESRD

Cardio/renal protection

Diagnosis
Reversible factors

Treat CV risk factors, associated conditions and slow rate of progression towards ESRD

Time
Preparation for ESRD

1) Patient education
2) Modality choice
   - include no dialysis & trial of dialysis options
3) Transplant consideration
   - Is preemptive possible?
4) Dialysis access creation
5) Smooth entry into ESRD program

All this takes time, especially vascular access
Late referral
No patient choice

Early referral
Informed patient choice

NB: more CVC’s

NB: more AVF’s
Encourage home dialysis (PD and home HD) and live donor preemptive transplant if suitable.

1) Timely referral
2) Slow rate of progression
3) Manage CV risks and comorbidities
4) Timely preparation
5) Timely initiation

Mendelssohn DC and Pierratos A. PDI 22; 5-8: 2002
Canadian 8 Centre CKD Study (Levin LVH study)

- 446 consecutive patients
- 8 academic centres
- CrCl 25 – 75 ml/min
- SBP 143.6, DBP 84.6
- 43.1% had BP > 150/100 during F/U (unpublished)
- Use of ACEI 52%

Levin A et al. AJKD 34; 125-134: 1999.
More recent Canadian studies

- Prospective observational study
- 4 centres (Halifax, London, Saskatoon, Vancouver)
- Consecutive patients over 4 weeks in 1999
- CrCl <75 ml/min
- 42% achieved BP targets (130/80 or 125/75)
- 35.5% were not on ACEI/ARB
- Of those with CVD, 33.9% were on BB, 27.3% were on ASA, and 18.4% were on statins

What do we know about multidisciplinary team based CKD care (MDC)?
# Multidisciplinary vs standard care

<table>
<thead>
<tr>
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<th>PRDC</th>
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<tbody>
<tr>
<td>N</td>
<td>42</td>
<td>21</td>
<td></td>
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<tr>
<td>Temp access</td>
<td>52.4%</td>
<td>95.2%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fistula</td>
<td>45.2%</td>
<td>4.8%</td>
<td>&lt;0.01</td>
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<tr>
<td>Graft</td>
<td>2.4%</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>

Goldstein MB et al, AJKD 44; 706-714: 2004
## Multidisciplinary vs standard care

<table>
<thead>
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<th></th>
<th>PRDC</th>
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<tr>
<td>ACEI</td>
<td>46%</td>
<td>15%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Iron</td>
<td>74%</td>
<td>50%</td>
<td>0.03</td>
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<tr>
<td>Albumin</td>
<td>36</td>
<td>33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ca</td>
<td>2.22</td>
<td>2.05</td>
<td>0.03</td>
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</table>

Goldstein MB et al, AJKD 44; 706-714: 2004
Multidisciplinary vs Standard Care
Survival after starting dialysis

Goldstein MB et al, AJKD 44; 706-714: 2004
## Multidisciplinary vs Standard Care at initiation of dialysis

<table>
<thead>
<tr>
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<th>Standard</th>
<th>MDC</th>
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<tr>
<td>GFR</td>
<td>7.0</td>
<td>8.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Hb</td>
<td>90</td>
<td>102</td>
<td>&lt;0.0001</td>
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<tr>
<td>Albumin</td>
<td>34.8</td>
<td>37.0</td>
<td>0.002</td>
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<tr>
<td>Ca</td>
<td>2.16</td>
<td>2.29</td>
<td>&lt;0.0001</td>
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<tr>
<td>PO4</td>
<td>1.73</td>
<td>1.73</td>
<td>NS</td>
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Multidisciplinary vs Standard Care
Survival after starting dialysis

So, it seems that MDC is better than standard care, but exactly how good is MDC? Let's look again!
MDC care is good but not great

- Hb only 102 starting HD in Vancouver/Italian cohort
- 52% of SMH PRDC patients started with temporary access
  - Remember that all were followed > 3 months
Attitudes of Canadian nephrologists towards multidisciplinary predialysis care

Mendelssohn DC et al. AJKD 47: 277-284; 2006
<table>
<thead>
<tr>
<th>Service</th>
<th>Cost</th>
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<tr>
<td>Overhead</td>
<td>11.4%</td>
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<tr>
<td>Level 1 HD</td>
<td>$21311</td>
</tr>
<tr>
<td>Level 2 HD</td>
<td>$31122</td>
</tr>
<tr>
<td>CAPD</td>
<td>$26725</td>
</tr>
<tr>
<td>APD</td>
<td>$30774</td>
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<tr>
<td>Pre-ESRD clinic</td>
<td>$240.85</td>
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</table>

NB: facility fee, does not include MD fee
The challenge

- Canadians have shown the world that management of patients by nephrologists with a multidisciplinary predialysis team is superior to care provided by a nephrologist alone.

- Despite these contributions and a good tool kit, even multidisciplinary team based care is imperfect and must be improved.

- Defining targets (guidelines or CPR’s) for MDT care to drive CQI is not easy.

- Defining which elements of expensive MDT care are cost effective and which are not is required.
Initiation of ESRD Care
Is this how dialysis should start?
Canadian Survey of Clinical Status at Dialysis Initiation 1998-99

- Multicentre prospective study
- 15 centres
- 1 month per centre consecutive patients

# Canadian prospective study

**Known = 3 months**

<table>
<thead>
<tr>
<th></th>
<th>All (n=238)</th>
<th>Known (n=164)</th>
<th>Unknown (n=84)</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>59</td>
<td>58</td>
<td>63</td>
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<tr>
<td><strong>GFR (MDRD)</strong></td>
<td>8.0</td>
<td>8.1</td>
<td>7.7</td>
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<tr>
<td><strong>Sx</strong></td>
<td>3</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Albumin (g/L)</strong></td>
<td>32.7</td>
<td>33.7</td>
<td>30.6</td>
</tr>
<tr>
<td><strong>Hb (g/L)</strong></td>
<td>92.6</td>
<td>94.3</td>
<td>89.5</td>
</tr>
</tbody>
</table>

**Canadian prospective study**

<table>
<thead>
<tr>
<th></th>
<th>All (n=238)</th>
<th>Known (n=164)</th>
<th>Unknown (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial modality (%HD)</strong></td>
<td>66.7</td>
<td>67.5</td>
<td>65.1</td>
</tr>
<tr>
<td><strong>Permanent access (%)</strong></td>
<td>52.6</td>
<td>65.6</td>
<td>28.6</td>
</tr>
<tr>
<td><strong>Temporary line (%)</strong></td>
<td>53.2</td>
<td>41.2</td>
<td>75.0</td>
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</table>

*Curtis BM et al. Clin Neph 58; 282-288: 2002*
<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>Epo Use Prior to ESRD (% of pts)</th>
<th>At Start of Dialysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean Hgb (g/dl)</td>
</tr>
<tr>
<td>Sweden (SW)</td>
<td>168</td>
<td>65</td>
<td>10.7</td>
</tr>
<tr>
<td>United States (US)</td>
<td>458</td>
<td>27</td>
<td>10.4</td>
</tr>
<tr>
<td>Spain (SP)</td>
<td>170</td>
<td>56</td>
<td>10.6</td>
</tr>
<tr>
<td>Belgium (BE)</td>
<td>213</td>
<td>33</td>
<td>10.3</td>
</tr>
<tr>
<td>Canada (CA)</td>
<td>150</td>
<td>43</td>
<td>10.1</td>
</tr>
<tr>
<td>Australia/New Zealand (ANZ)</td>
<td>108</td>
<td>50</td>
<td>10.1</td>
</tr>
<tr>
<td>Germany (GE)</td>
<td>142</td>
<td>46</td>
<td>10.5</td>
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<tr>
<td>Italy (IT)</td>
<td>167</td>
<td>59</td>
<td>10.2</td>
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<tr>
<td>United Kingdom (UK)</td>
<td>93</td>
<td>44</td>
<td>10.2</td>
</tr>
<tr>
<td>France (FR)</td>
<td>86</td>
<td>43</td>
<td>10.1</td>
</tr>
<tr>
<td>Japan (JA)</td>
<td>131</td>
<td>62</td>
<td>8.3</td>
</tr>
</tbody>
</table>

*Includes patients who were new to ESRD and entered DOPPS within seven days of first-ever chronic dialysis treatment. Patients receiving Epo prior to ESRD had a 0.35 g/dl higher Hgb at time of starting dialysis compared to patients not receiving Epo during pre ESRD period (p<0.001).

Pisoni RL et al. AJKD 44(1):94-111, 2004
Vascular Access Use, Among Incident HD Patients: Canada, Europe, and USA

Incident patients entering DOPPS within 5 days of first-ever chronic dialysis; n= # of patients

Vascular Access Trends in Canada

Mortality rate amongst those who start in hospital:
Overall 27%, CRRT 51%, HD 20%, PD 10%
Status at 90 Days Based on Initial Dialysis Treatment Modality

- CRRT
- HD
- PD

RECOVERED
ON DIALYSIS
DEAD

ICES Institute for Clinical Evaluative Sciences
Optimizing Care
Opportunities and challenges
Optimizing CKD Care

Worst possible care

Best possible care

FP care
Nephrologist based care

We aren’t there yet

?Multidisciplinary team based care
Can we find the right road?
<table>
<thead>
<tr>
<th>Definitions</th>
<th>Optimal start</th>
<th>Suboptimal start</th>
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</thead>
<tbody>
<tr>
<td></td>
<td><strong>Planned</strong></td>
<td><strong>Unplanned</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Elective</strong></td>
<td><strong>Urgent</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Outpatient</strong></td>
<td><strong>Inpatient</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Early referral</strong></td>
<td><strong>Late referral</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chronic modality of choice</strong></td>
<td><strong>Acute modality</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Permanent access</strong></td>
<td><strong>Usually HD</strong></td>
</tr>
<tr>
<td></td>
<td><strong>AVF/AVG</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>PD catheter</strong></td>
<td><strong>Temporary access</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>CVC</strong></td>
</tr>
</tbody>
</table>
Figure 5: The literature is unclear about what the cut off time between an early referral and a late referral should be. If the cut-off is defined as the minimum amount of time required to adequately (or optimally) prepare a patient for an elective start on either modality, then in my opinion the cut-off should be:

AJKD 47: 277-284; 2006
Early referral

Comp -letion of tasks

Planned start Elective
Outpatient AVF

1) Patient related delay
2) Acute on CKD
3) Suboptimal care
4) No chronic HD spot

Late Referral

Tasks Not Comp -leted

Unplanned start Emergent
Inpatient CVC
Problems and Solutions

- Improve community based care
  - Referral guidelines
  - CKD Management guidelines
- Improve nephrology care
  - Targets for CKD clinics, CQI based on them
  - Advocate for resources
    - Multidisciplinary team based care
    - Chronic dialysis resources
  - Reduce patient related delays
- Improve the initiation of dialysis, especially during the first 90 days
  - Overcome problems related to late referral and/or unplanned starts
    - Right Start Program
CSN Position Paper on Care and Referral of Adult Patients with Reduced Kidney Function

October 2006
www.csnsnscn.ca
Pragmatic Balance

- Identify and refer earlier patients with serious and progressive CKD
- Identify and manage without referral, patients with stable and non-progressive CKD
Referral is recommended when:

1) Acute renal failure
2) Stage 4 (eGFR 16 – 30) and stage 5 imminent ESRD (eGFR < 15)
3) Progressive decline of eGFR
4) Persistent proteinuria > 100 mg/mmol
   NB: 100 mg/mmol = 890 mg/24 hr
5) Inability to achieve treatment targets
Management of CKD (1)

- Most patients with non-progressive CKD can be managed without referral to a nephrologist.
- Consider reversible factors, such as medications, intercurrent illness, or obstruction. An abdominal ultrasound may be indicated when eGFR <60 ml/min/1.73m2
Management of CKD (2)

- Implement measures to slow the rate of progression of CKD.
  a) Target BP is < 130/80 mmHg. Most patients will need 3 or more medications. Diuretics and salt restriction are very useful, and if needed, consider furosemide BID dosing when eGFR < 30 ml/min/1.73m²
  b) Target urine protein/creatinine ratio (mg/mmol) is < 60 (< ~ 500 mg/day) or target urine albumin/creatinine ratio (mg/mmol) is < 40. ACEI and/or ARB are first line therapies in patients with albuminuria or proteinuria.
  c) Control blood sugar in diabetes, target HbA1C < 7%
Management of CKD (3)

- Implement measures to modify CV risk factors (NB: CV risk >> ESRD risk)
  
  a) Follow the Canadian Hypertension Education Program, the Canadian Diabetes Association, and the Canadian Cardiovascular Society guidelines as per groups at highest risk for CV disease.
What we know about initiation of HD?

- Mortality rates within the first 90 days of initiation of hemodialysis are relatively much higher than after that.

- Many factors seem to interact to cause this effect:
  - Patient instability
  - Late referral
  - Inadequate preparation for HD
  - Fragmented and ineffective care provided by medical programs
  - Imbalance of pt at initiation – rapid decline of RRF
  - Vascular access
Early Intervention Improves Mortality and Hospitalization Rates in Incident Hemodialysis Patients: RightStart Program

Rebecca L. Wingard,1 Laza B. Pupim,2 Mahesh Krishnan,3 Ayumi Shintani,1 T. Ali Ikizler,3 and Raymond M. Hakim1

1Renal Care Group, Inc., Nashville, Tennessee; 2Vanderbilt University Medical Center, Nashville, Tennessee

Background and objectives: Annualized mortality rates of chronic hemodialysis (CHD) patients in the first 90 d of treatment range from 20 to 30%. Limited studies show high hospitalization rates. It was hypothesized that a structured quality improvement program (RightStart), focused on medical needs and patient education and support, would improve outcomes for incident CHD patients.

Design, setting, participants, & measurements: A total of 88 CHD incident patients were prospectively enrolled in a multicenter RightStart Program, and compared with a time-matched group of 1023 control patients from non-RightStart clinics. RightStart patients received 2 mo of intervention in management of azotemia, design of dialysis, nutrition, and dialysis access and a comprehensive educational program. Outcomes were tracked for up to 12 mo.

Results: At 3 mo, RightStart patients had higher albumin and hemoglobin values. Some of dialyzers and permanent access placement were not statistically significantly different from control subjects. Compared with baseline, Multimodal Composite Score for RightStart patients improved significantly. Mean hospitalization days per patient year were reduced with RightStart versus control subjects. Mortality rates at 3, 6, and 12 mos were 16, 36, and 57 for RightStart patients versus 56, 72, and 109 deaths per 100 patient-years for control subjects, respectively.

Conclusions: A structured program of prompt medical and educational strategies in incident CHD patients results in improved morbidity and mortality that last up to 1 yr.

Wingard et al (2007) CJASN:2, 1170-75

The RightStart® Program: Reduction of Mortality in Incident ESRD Patients with Early intervention

RL Wingard1, L Pupim2, TA Ikizler2, JE Thomas1, R Hakim1

1Renal Care Group, Inc., Nashville, Tennessee; 2Vanderbilt University Medical Center, Nashville, Tennessee

The RightStart® Program: Reduction of Mortality in Incident ESRD Patients with Early intervention

Wingard et al (2007) CJASN:2, 1170-75
## Co-Morbidities and Risk Factors Associated with Early Mortality

<table>
<thead>
<tr>
<th>Co-Morbidity</th>
<th>Risk Factors</th>
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<tbody>
<tr>
<td>Age</td>
<td>Unplanned start (w/o permanent access)</td>
</tr>
<tr>
<td>Nutritional Status</td>
<td>Short (&lt;4 months) prior nephrological care</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Low residual renal output</td>
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<tr>
<td>Cardiovascular Disease</td>
<td></td>
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<tr>
<td>LVH</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
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</tr>
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</table>

### Reversible Risk Factors
- Anemia
- Low albumin
- High Phosphorus
- High catheter rate
RightStart® Goals
Defined goals for each healthcare team member

**General Goals**
Ongoing individualized Patient Education & Self-Care, Medication Reviews, care plans, recommendation for a liberal diet
Protocol-driven outcomes

**Specific Goals**

Week 2: URR >=70%

Weeks 3-4: Target EDW
Hct >=30%, T. Sat >=20%
Transplant referral & permanent access planning

Weeks 5-6: Stable BP

Weeks 7-8: Hct >=33%
PO4 3.5-5.5 mg/dL
Use Permanent Access

Weeks 9-10: Review Goal Achievement

Weeks 11-12: HgbA1C <=7%
Albumin >=3.7 g/dL
PTH 150-300 (BiPTH 75-150)
Enrollment Process

**RightStart®, N=923**
- Prospective enrollment of ALL new patients within one to three weeks of dialysis initiation
- Exclusions:
  - Seasonal or transient patients
  - Nursing home residents
  - Patients with cognitive dysfunction that precludes ability to learn

**Time-Concurrent Control Group, N=1,047**
- Retrospective data retrieval of all new patients in non-RightStart® clinics in same geographic area for one year concurrent with the RightStart® program
Survival Curve, 1st 90 Days
Adjusted Cox-proportional hazards regression model

Adjusted by age, race, gender, diabetes

P<0.001 by Cox Log-rank, Breslow, and Tarone-Ware tests at 90 day exposure levels.
Survival Curve, 1st 365 Days
Adjusted Cox-proportional hazards regression model

P<0.001 by Cox Log-rank, Breslow, and Tarone-Ware tests at 90, 180, and 365 day exposure levels.

Adjusted by age, race, gender, diabetes
A Prospective Randomized study of Case Managed Initiation of HD

- An Ortho sponsored, investigator driven RCT
- Nurse case manager deliver focused intervention and education
- Control group receives similar philosophy of care, guidelines and targets but applied routinely by clinical staff without a specific case manager
- Randomization by patient or by facility?
Conclusions

- Late referral, unplanned starts, and initiation of HD with a CVC are linked problems, the term I prefer is suboptimal start

- Predialysis care is well organized and well financed in Canada, and is superior to care provided by nephrologists who work without a multidisciplinary clinic team
  - But outcomes are suboptimal and we can do better!

- The Right Start program may be adaptable to the Canadian environment

- Retrospective and prospective studies are under way

- We will find the right road!!