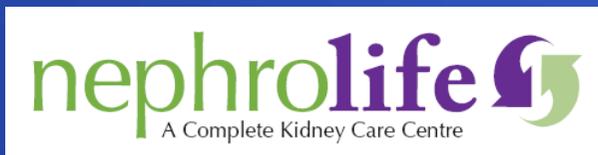


Budapest Nephrology School
August 29, 2008

Predialysis Care

Challenges and opportunities

David C Mendelssohn



Road map

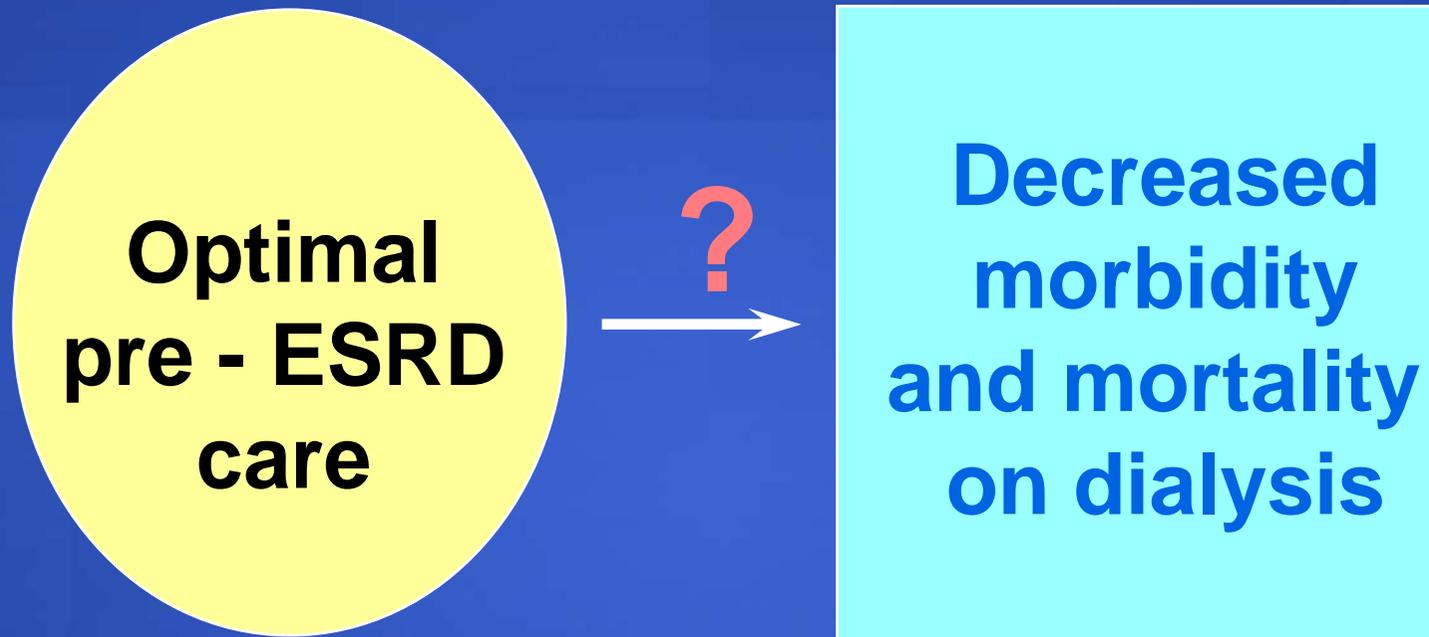
- **Care in the Community**
 - Non referral and late referral
- **Care after referral**
 - Solo nephrology care
 - Multidisciplinary team based care
- **Initiation of Dialysis**
 - Suboptimal starts
- **Optimizing Care**
 - Challenges and opportunities

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**



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.

A Framework

Care in the community

- A) Primary care
- B) No care

 Non Referral

Nephrology Care

- A) Nephrologist alone
- B) Multi-disciplinary predialysis team

Early

Late

ESRD Care

- A) Conservative
- B) Dialysis
- C) Transplant

Referral

Preparation

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**

Nephrology care

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

Early referral



Completion of tasks



**Planned start
Elective
Outpatient
AVF**

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

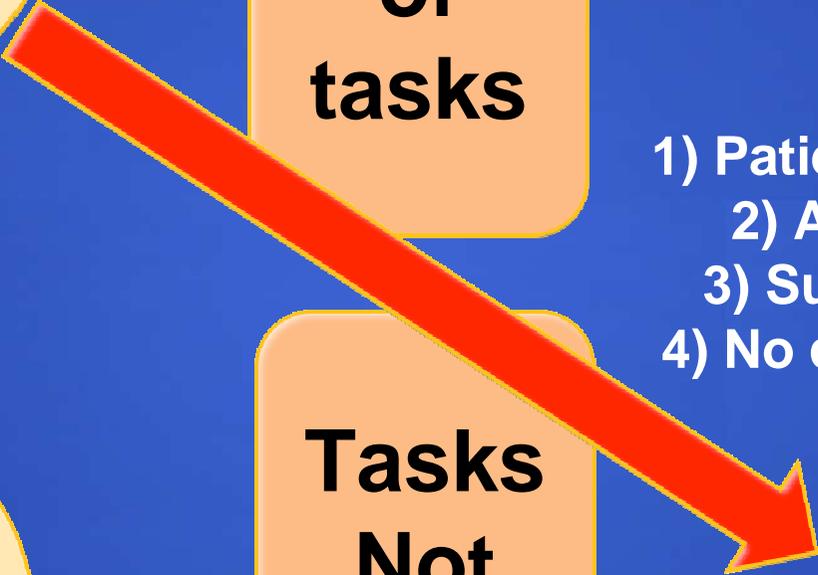
Late Referral



Tasks Not Completed

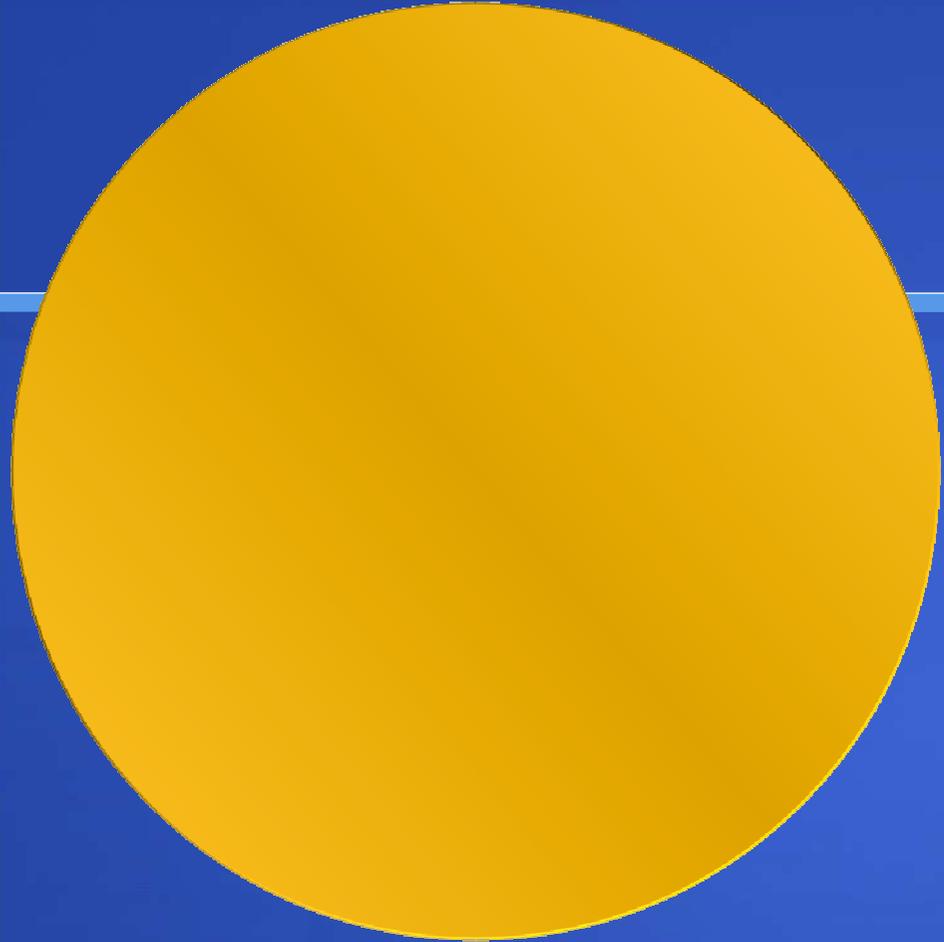


**Unplanned start
Emergent
Inpatient
CVC**



Suboptimal starts

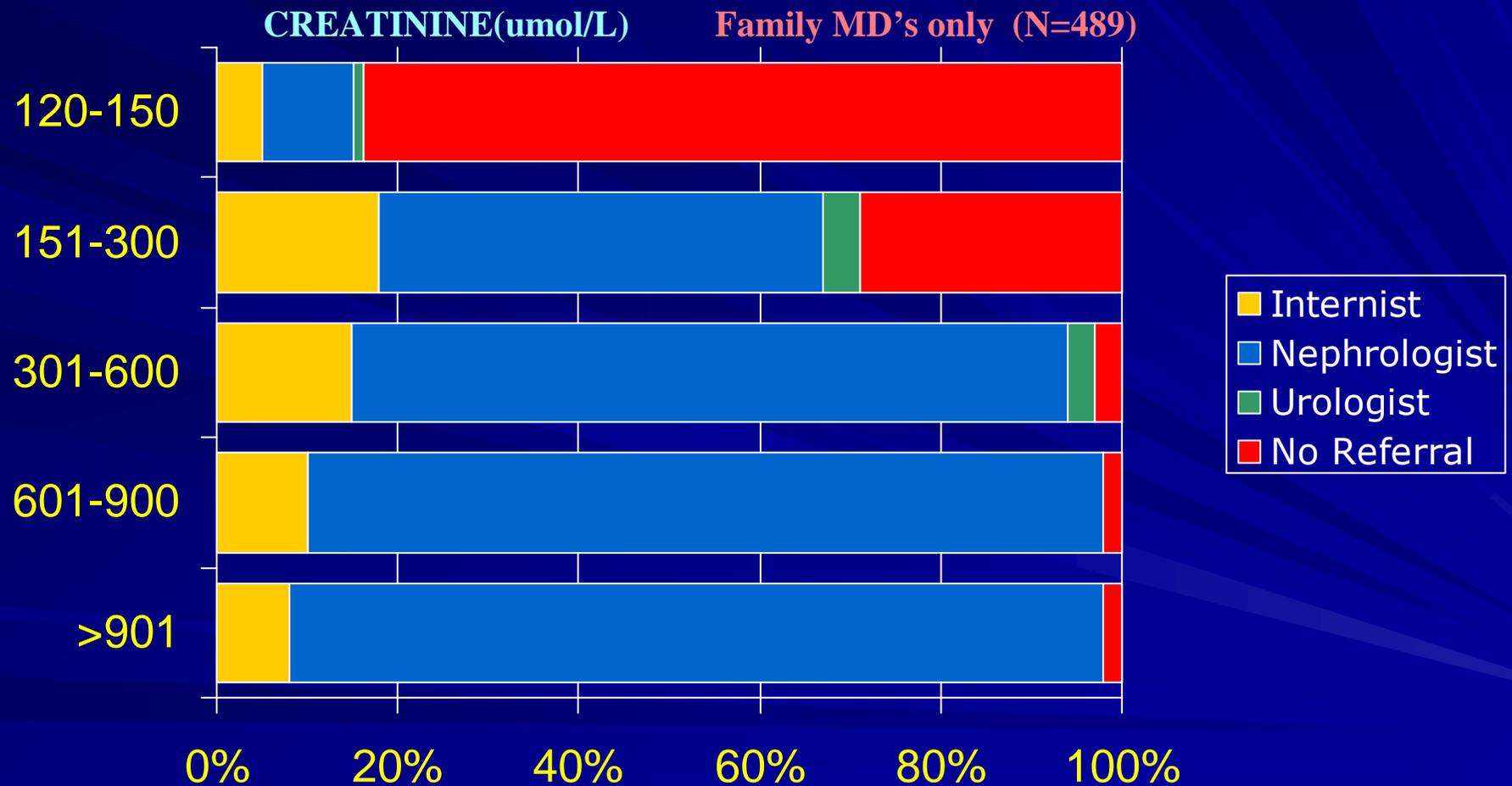




**Care in the
community**

Referral Thresholds

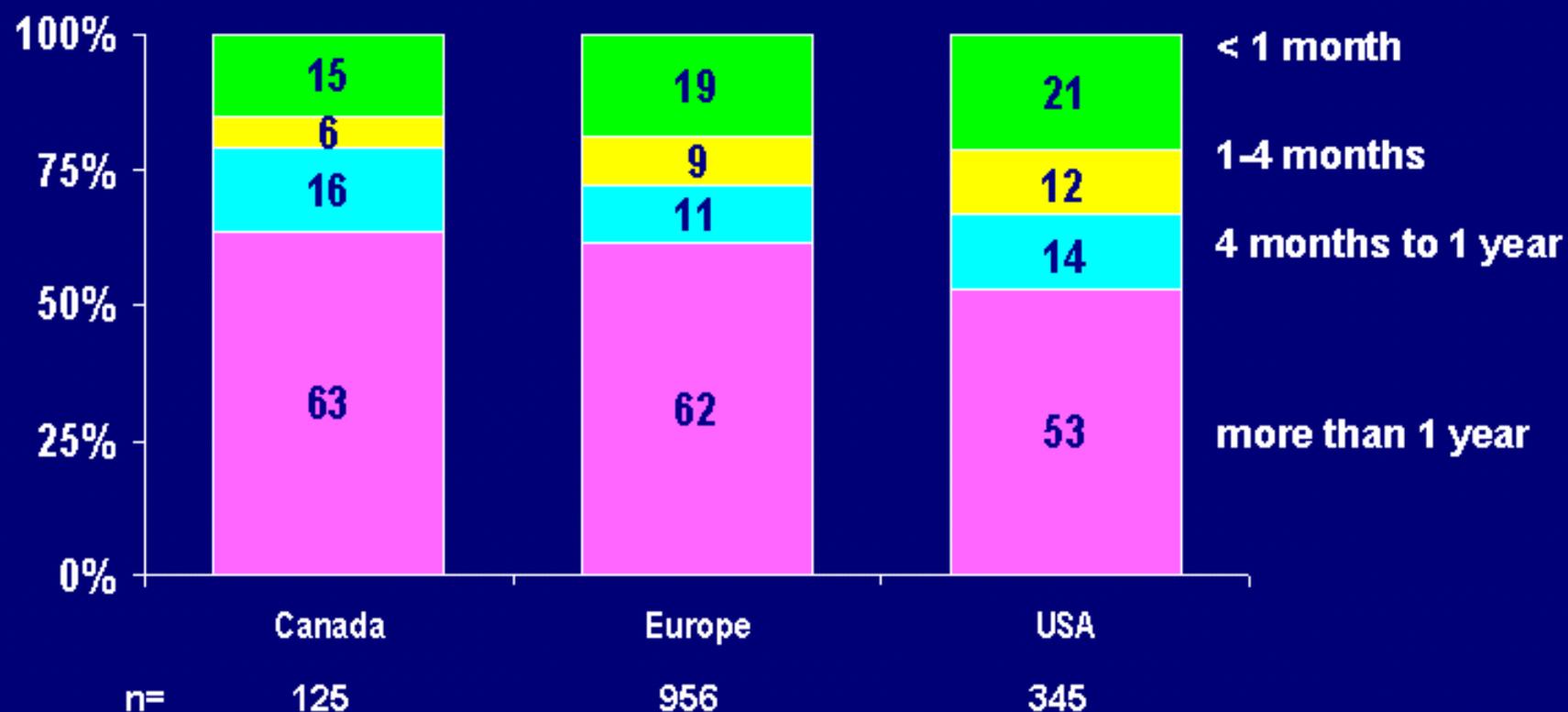
“Consider how you would respond to the following abnormal lab tests”



Mendelssohn, DC et al. Arch Int Med 155; 2473-2478: 1995.

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

% of patients



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.

Hypertension Management

SBP	150
DBP	80
ACEI or ARB	44%
Diuretic	50%
# of BP agents	1.9

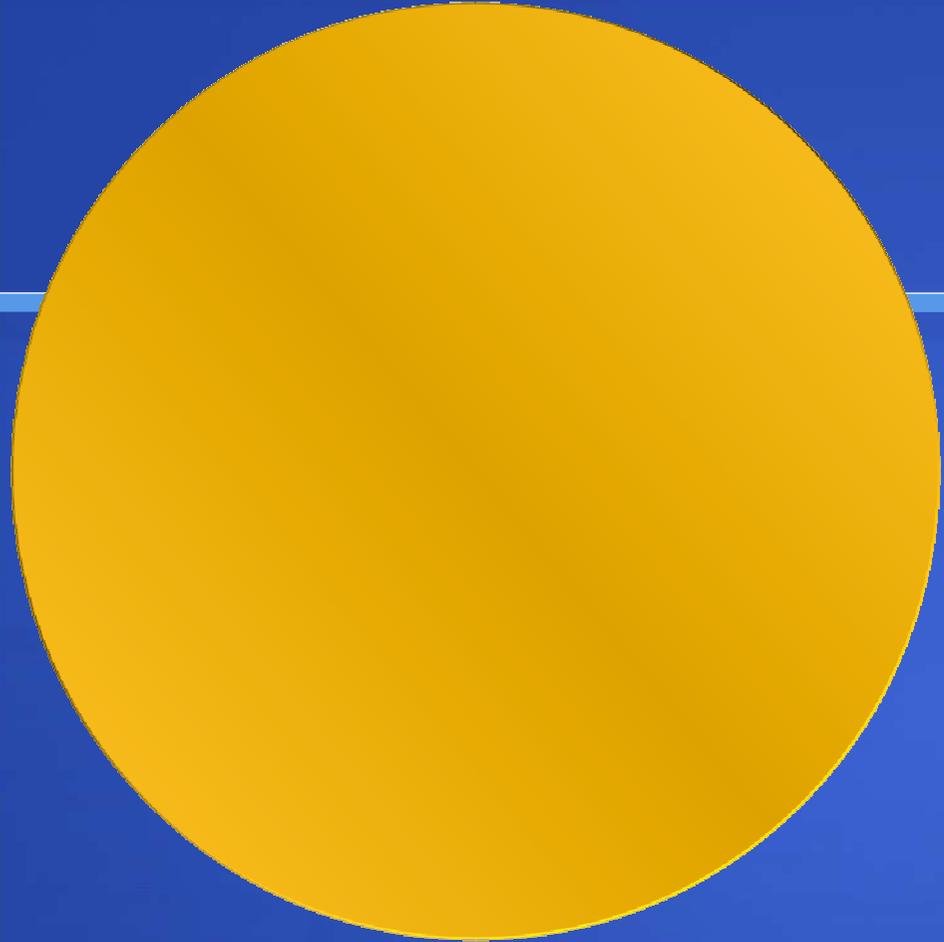
Cleveland DR et al. *AJKD* 40; 30-36: 2002

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**

Cardio/renal protection

Diagnosis
Reversible factors

```
graph LR; A[Diagnosis Reversible factors] --> B[Treat CV risk factors, associated conditions and slow rate of progression towards ESRD]; B --> C[Prepare For ESRD];
```

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

**Prepare
For
ESRD**

Time

Preparation for ESRD

1) Patient education

2) Modality choice

- include no dialysis & trial of dialysis options

3) Transplant consideration

- Is preemptive possible?

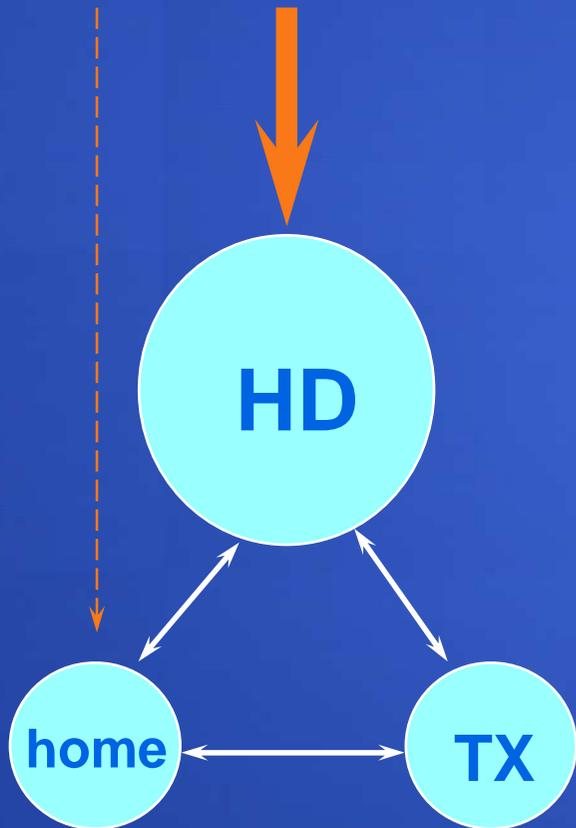
4) Dialysis access creation

5) Smooth entry into ESRD

program

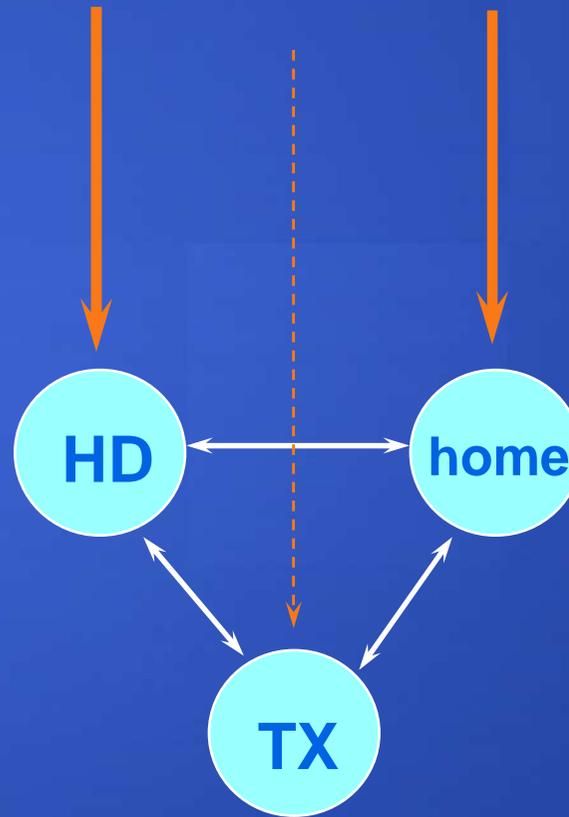
All this takes time, especially vascular access

**Late referral
No patient choice**



NB: more CVC's

**Early referral
Informed patient choice**



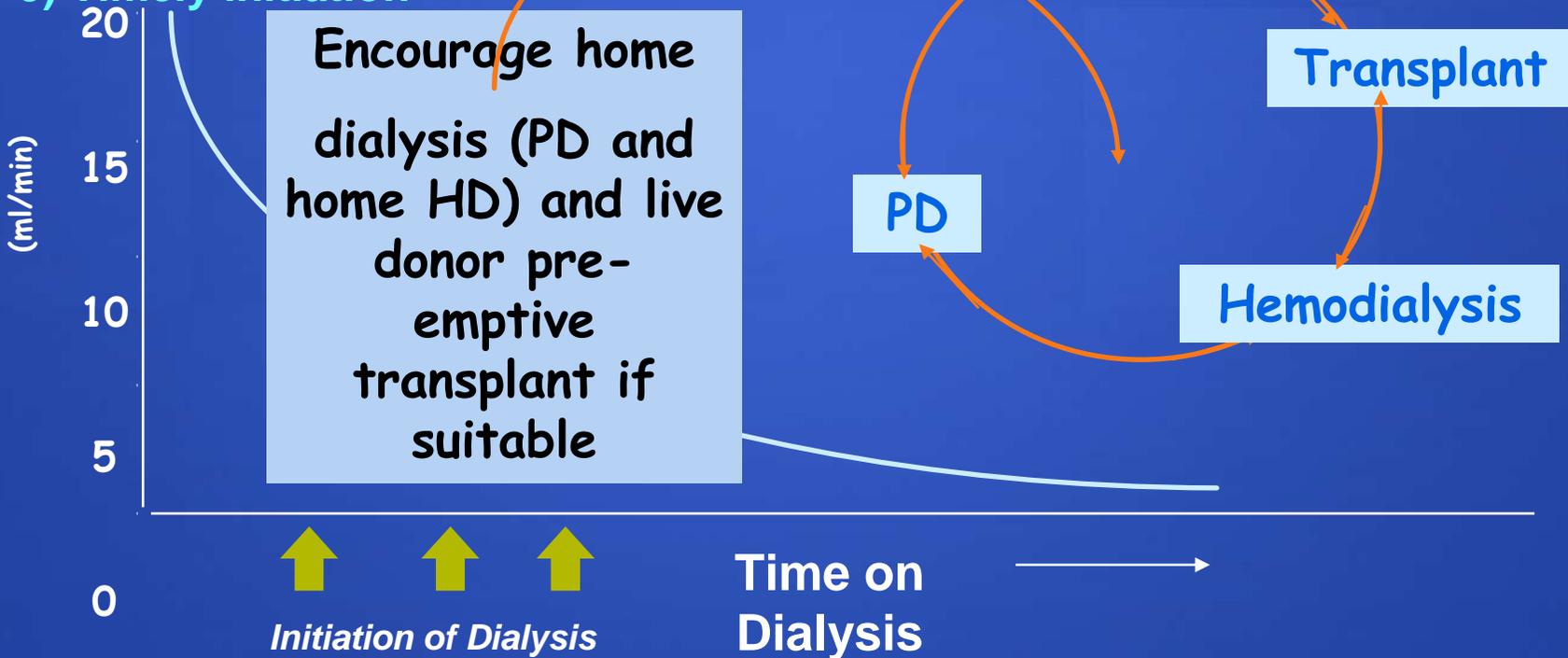
NB: more AVF's

Integrated ESRD Care

The HRRH view

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

Creatinine Clearance
(ml/min)



Mendelssohn DC and Pierratos A. PDI 22; 5-8: 2002

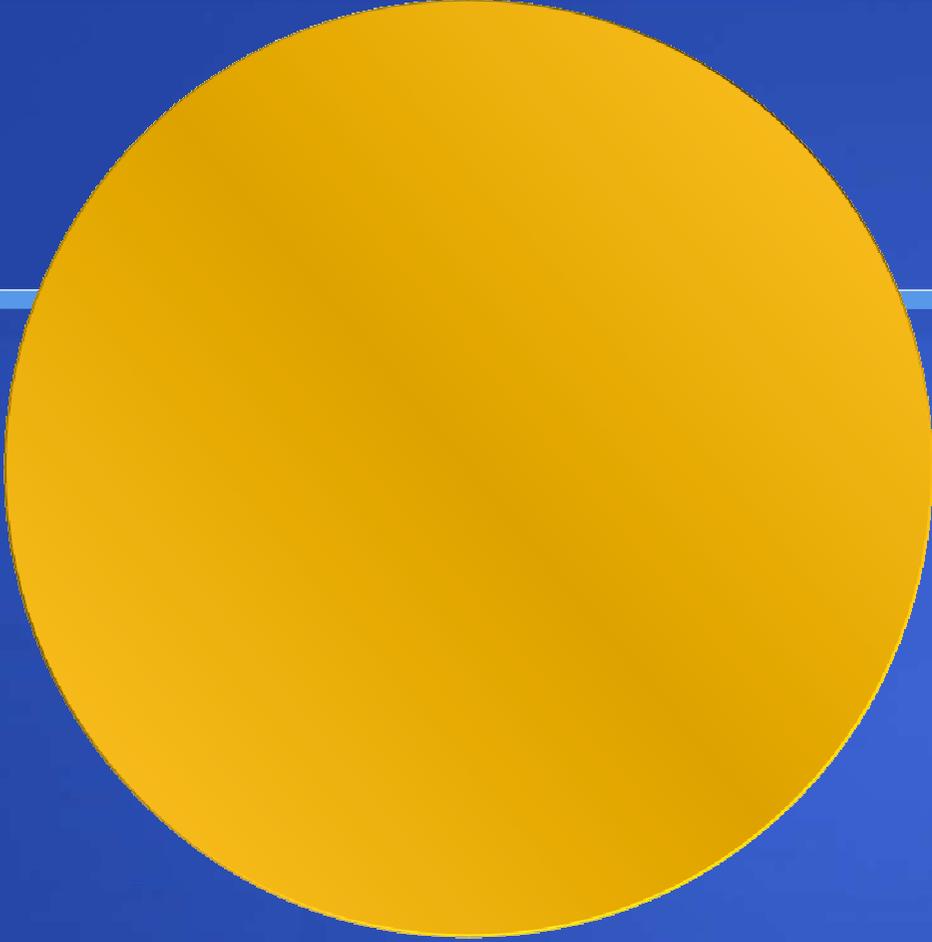
Canadian 8 Centre CKD Study (Levin LVH study)

- 446 consecutive patients
- 8 academic centres
- 1994 – 1997
- 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
- Tonelli et al. *AJKD* 37; 484-489: 2001.
Tonelli et al. *NDT* 17; 1426-1422: 2002.



**What do we know
about
multidisciplinary
team based CKD
care (MDC) ?**

Multidisciplinary vs standard care

	PRDC	No PRDC	P
N	42	21	
Temp access	52.4%	95.2%	<0.01
Fistula	45.2%	4.8%	<0.01
Graft	2.4%	0	NS

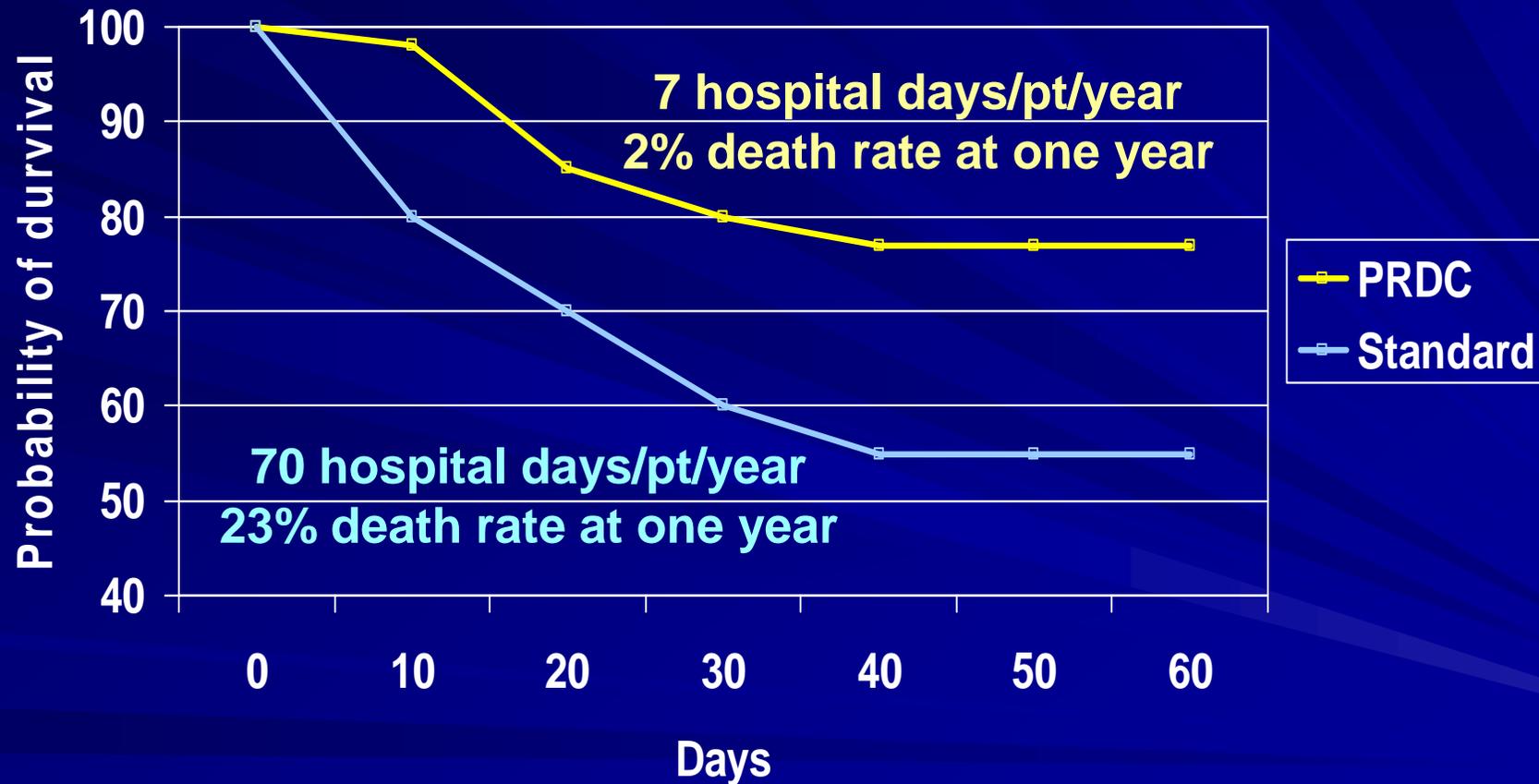
Goldstein MB et al, AJKD 44; 706-714: 2004

Multidisciplinary vs standard care

	PRDC	No PRDC	P
ACEI	46%	15%	<0.01
Iron	74%	50%	0.03
Albumin	36	33	<0.01
Ca	2.22	2.05	0.03

Goldstein MB et al, AJKD 44; 706-714: 2004

Multidisciplinary vs Standard Care Survival after starting dialysis



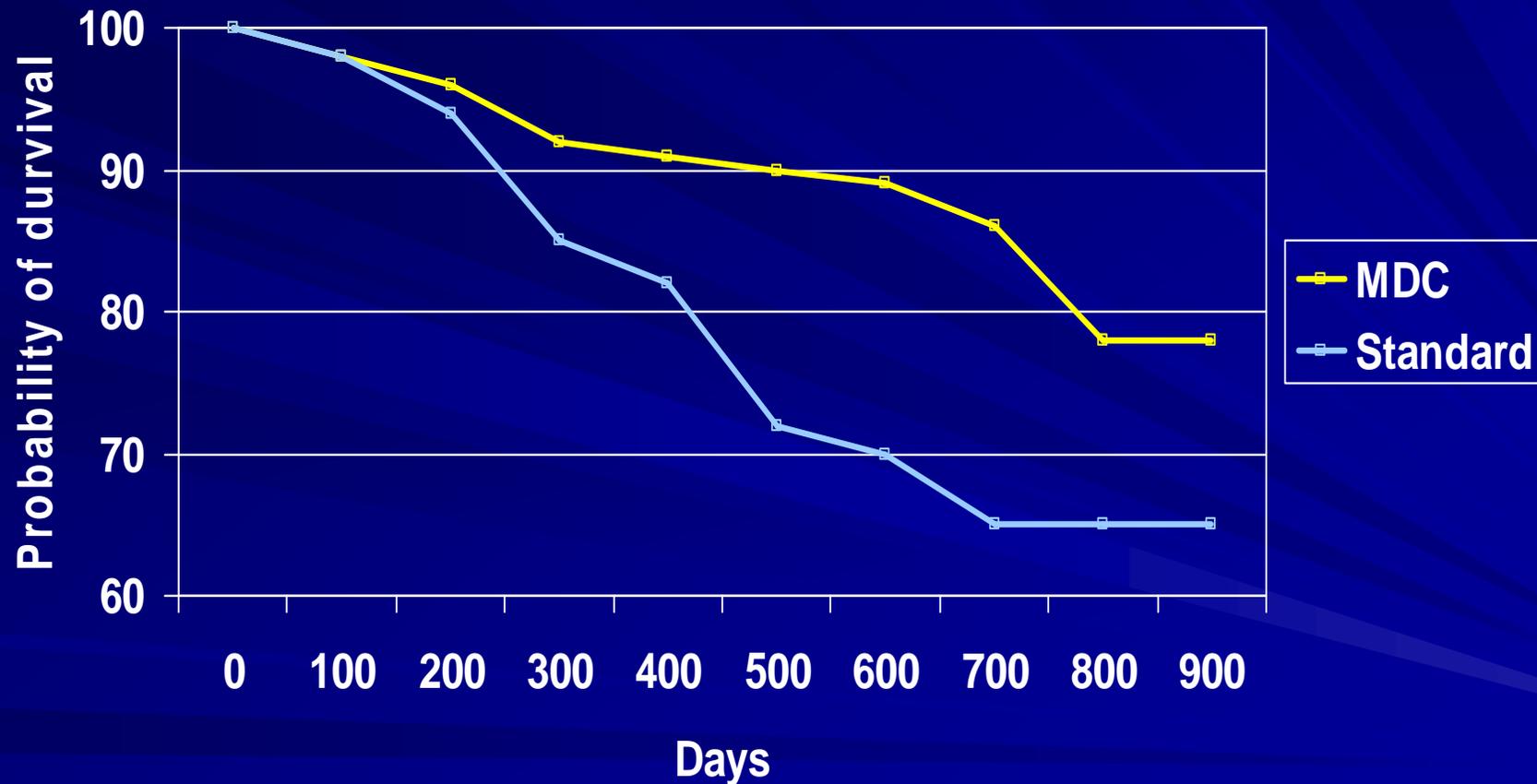
Goldstein MB et al, AJKD 44; 706-714: 2004

Multidisciplinary vs Standard Care at initiation of dialysis

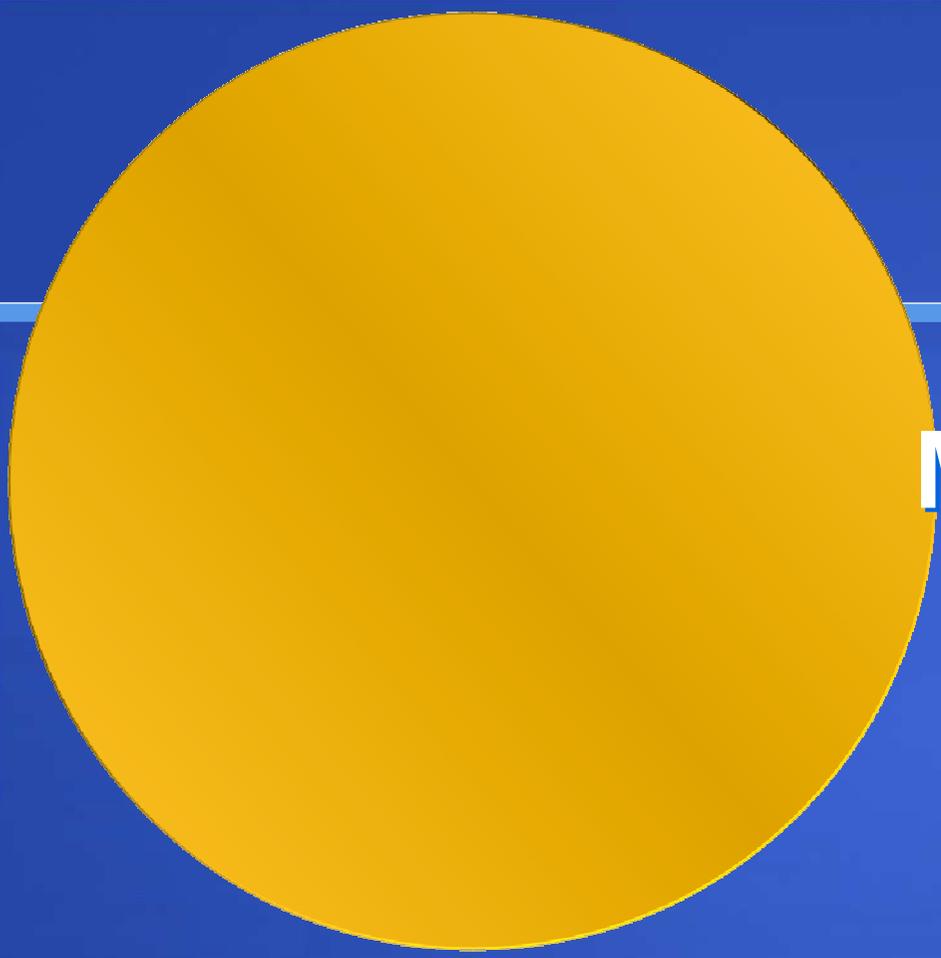
	Standard	MDC	P
GFR	7.0	8.4	0.001
Hb	90	102	<0.0001
Albumin	34.8	37.0	0.002
Ca	2.16	2.29	<0.0001
PO4	1.73	1.73	NS

Curtis BM et al. NDT 20; 147-154: 2005.

Multidisciplinary vs Standard Care Survival after starting dialysis



Curtis BM et al. NDT 20; 147-154: 2005.



**So, it seems that
MDC is better than
standard care,**

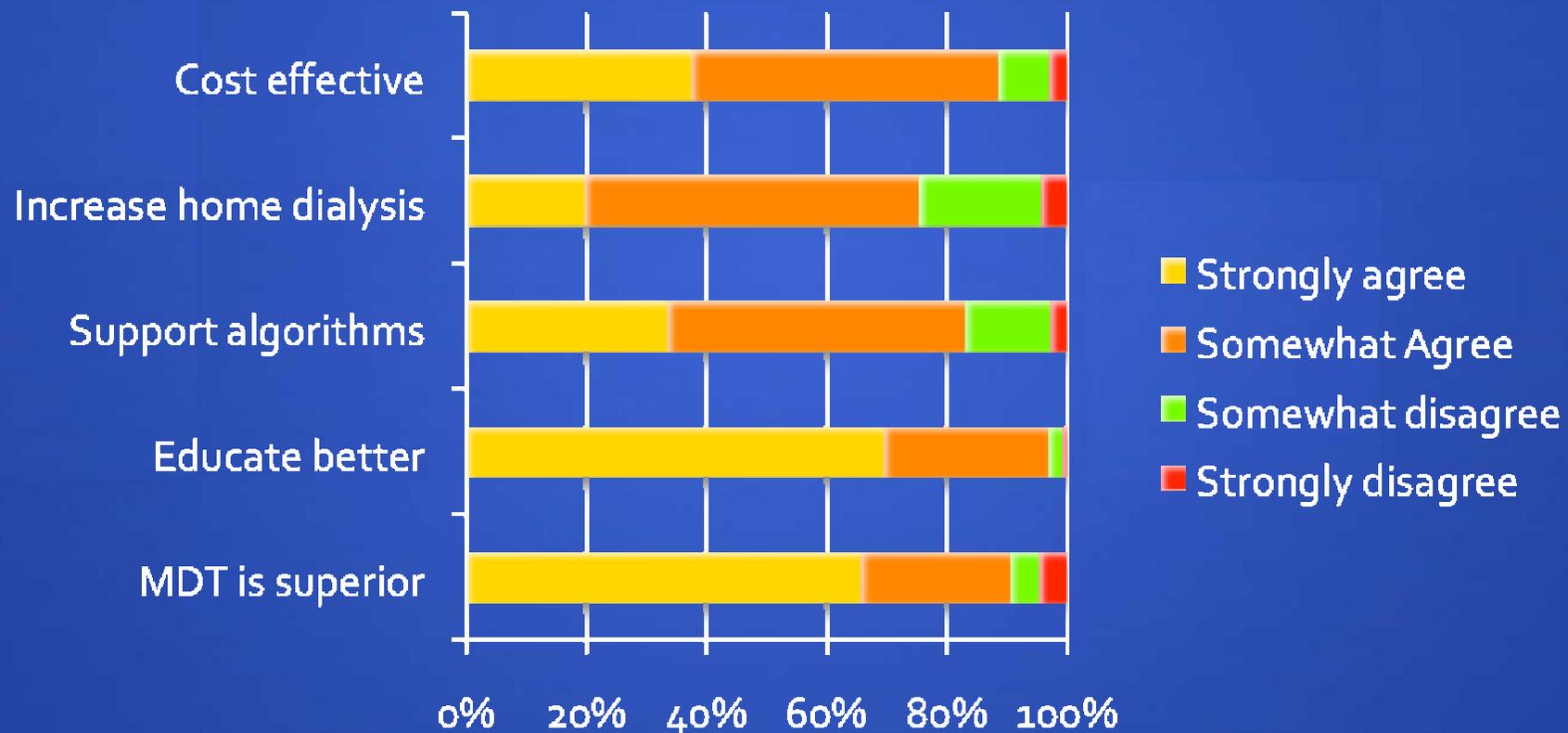
**but exactly how
good is MDC?**

Lets 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

Ontario Funding Formulas

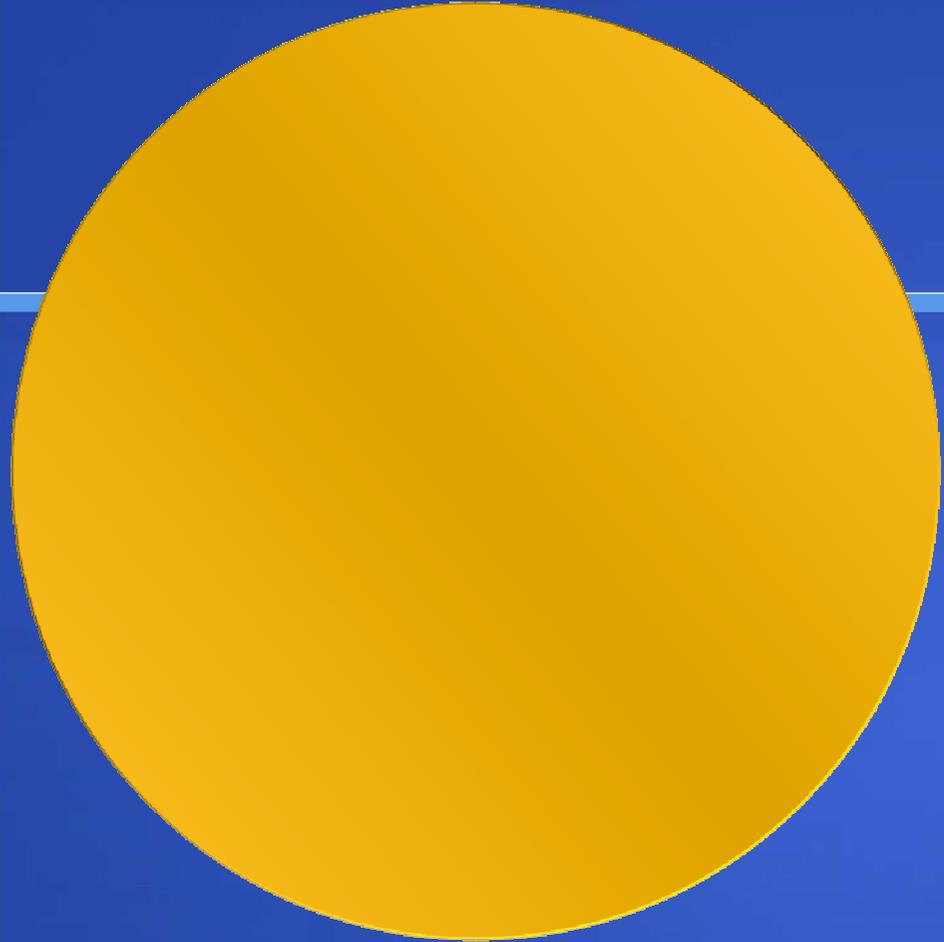
JPPC 1998

Overhead	11.4%
Level 1 HD	\$21311
Level 2 HD	\$31122
CAPD	\$26725
APD	\$30774
Pre-ESRD clinic	\$240.85

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

Curtis BM et al. Clin Neph 58; 282-288: 2002.

Canadian prospective study

known n = 3 months

	All (n=238)	Known (n=164)	Unknown (n=84)
Age	59	58	63
GFR (MDRD)	8.0	8.1	7.7
Sx	3	3	3.5
Albumin (g/L)	32.7	33.7	30.6
Hb (g/L)	92.6	94.3	89.5

Curtis BM et al. Clin Neph 58; 282-288: 2002

Canadian prospective study

	All (n=238)	Known (n=164)	Unknown (n=84)
Initial modality (%HD)	66.7	67.5	65.1
Permanent access (%)	52.6	65.6	28.6
Temporary line (%)	53.2	41.2	75.0

Curtis BM et al. Clin Neph 58; 282-288: 2002

Patients New to ESRD: Mean Hgb and Pre-ESRD Epo Use

Country	n	Epo Use Prior to ESRD (% of pts)	At Start of Dialysis*	
			Mean Hgb (g/dl)	Hgb<11 g/dl (% of pts)
Sweden (SW)	168	65	10.7	55
United States (US)	458	27	10.4	65
Spain (SP)	170	56	10.6	61
Belgium (BE)	213	33	10.3	66
Canada (CA)	150	43	10.1	70
Australia/New Zealand (ANZ)	108	50	10.1	70
Germany (GE)	142	46	10.5	61
Italy (IT)	167	59	10.2	68
United Kingdom (UK)	93	44	10.2	67
France (FR)	86	43	10.1	65
Japan (JA)	131	62	8.3	95

*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

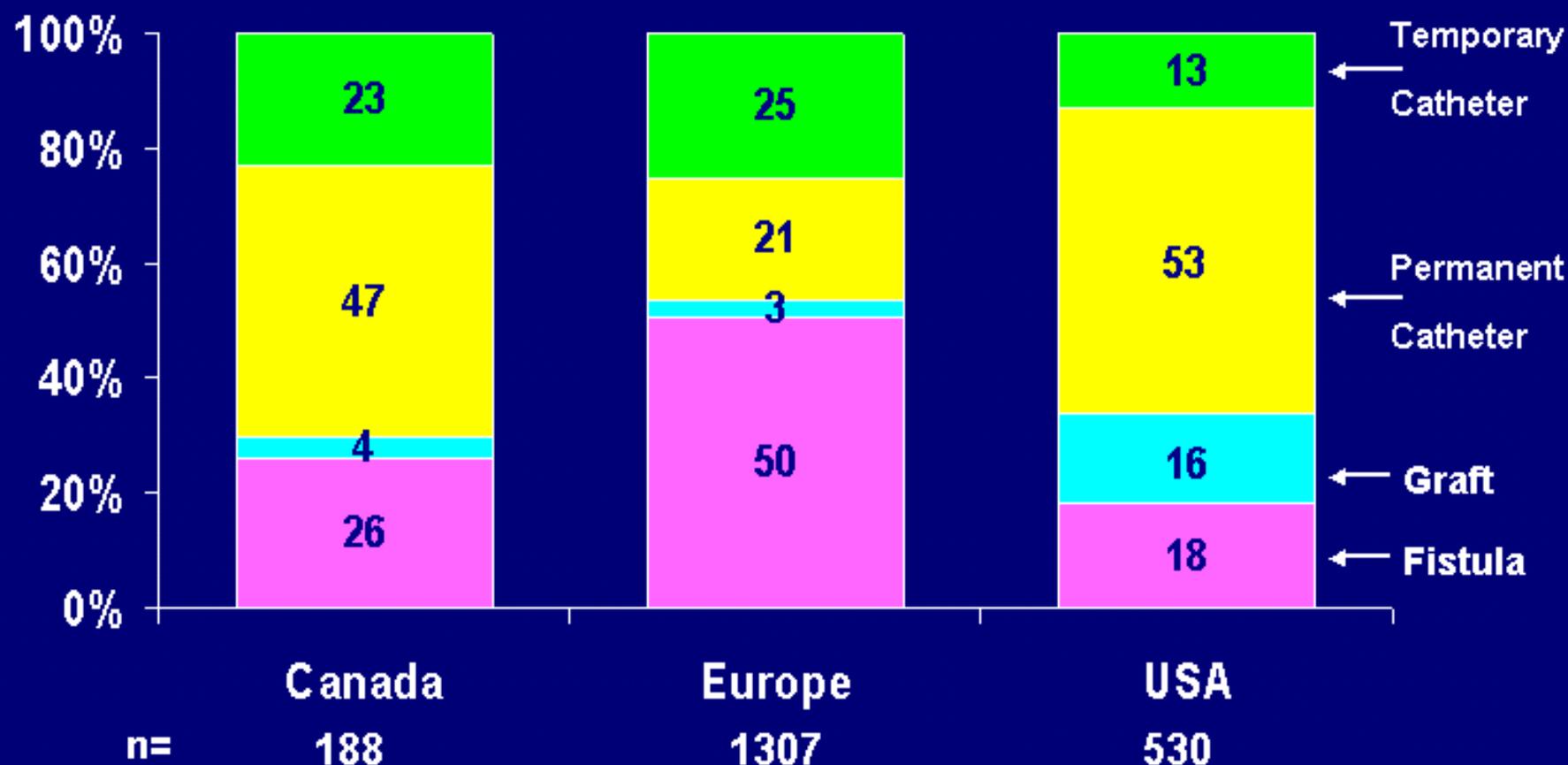


to patients not receiving Epo during pre ESRD period (p<0.001).

Pisoni RL et al. AJKD 44(1):94-111, 2004

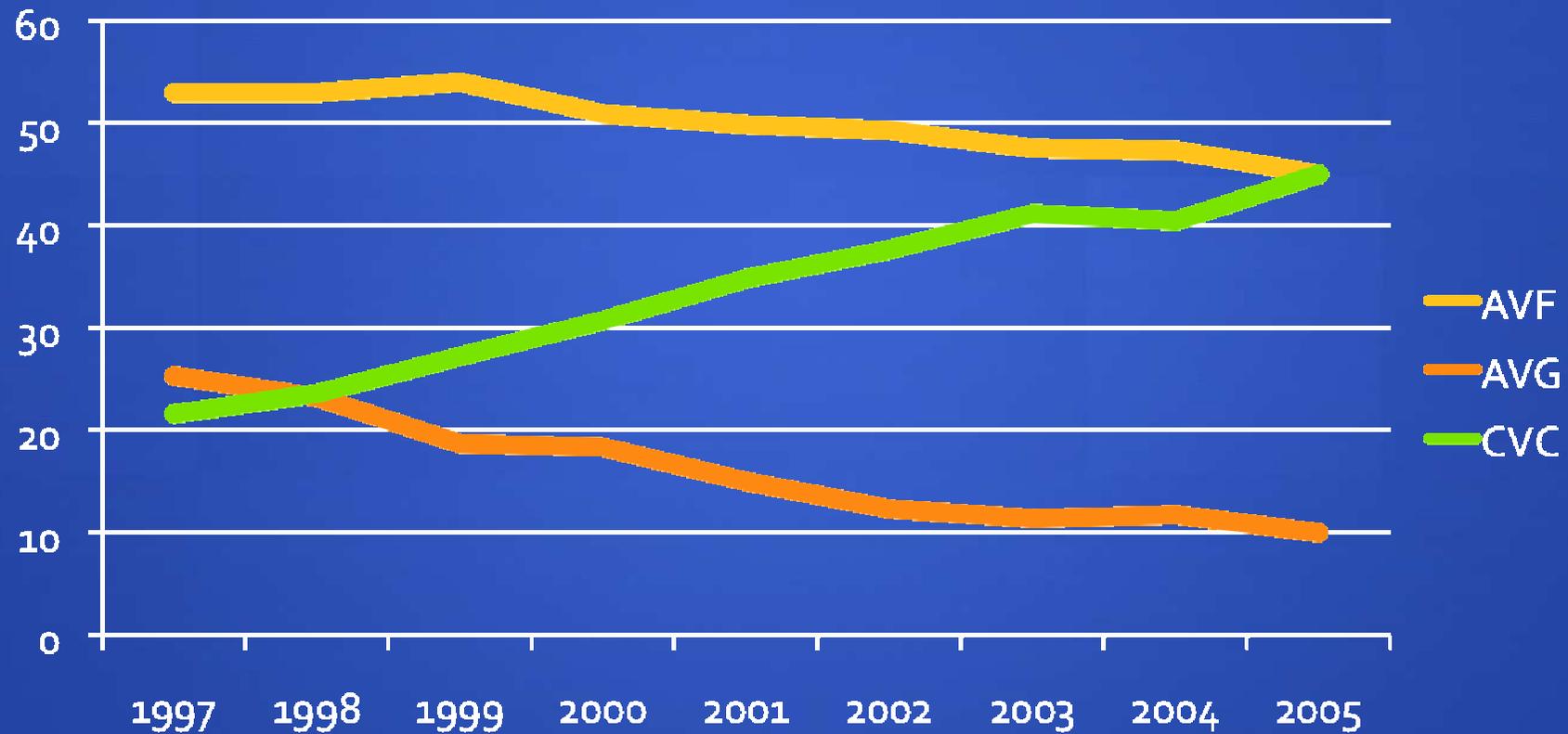
Vascular Access Use, Among Incident HD Patients: Canada, Europe, and USA

Patients



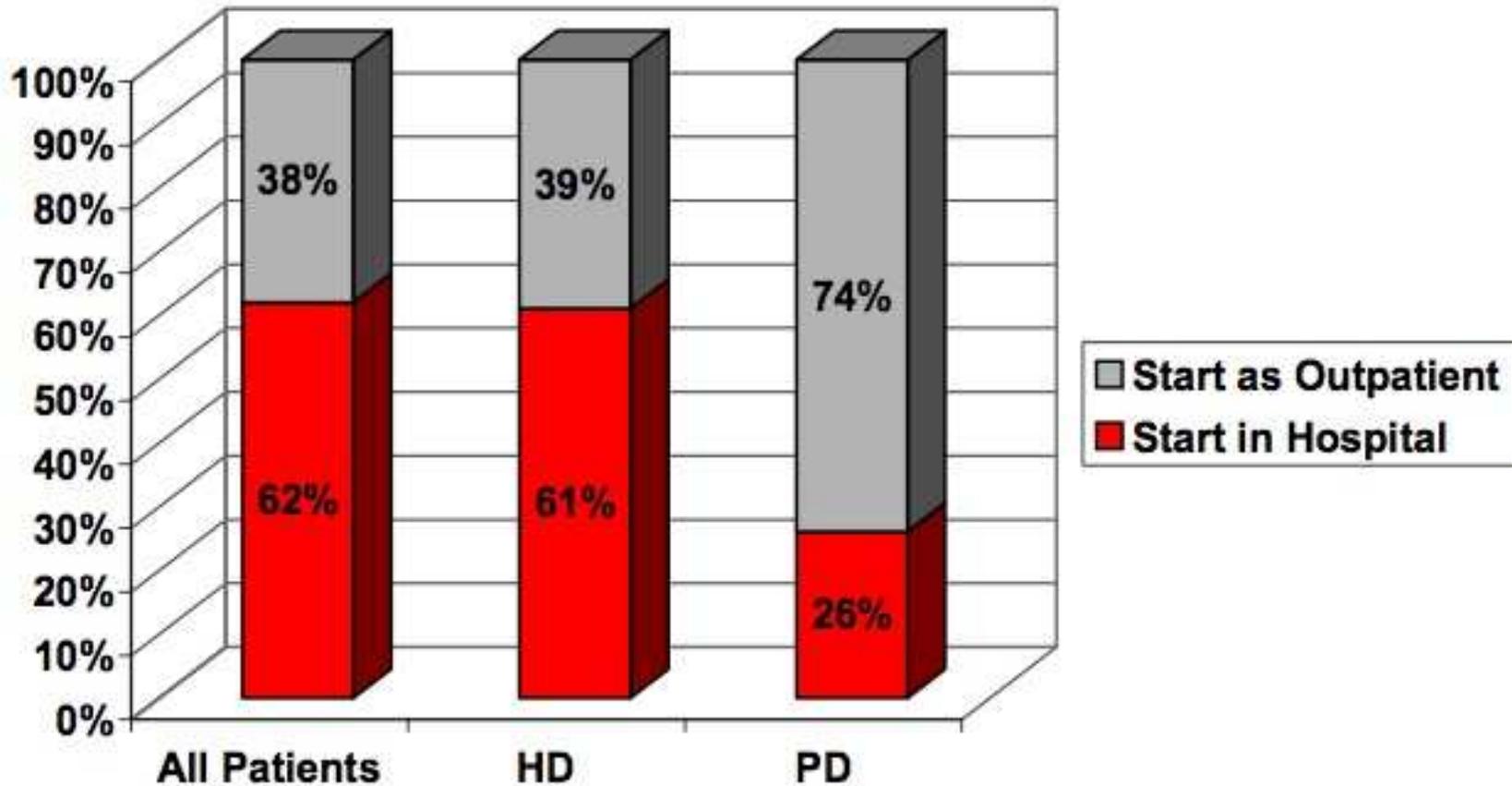
Incident patients entering DOPPS within 5 days of first-ever chronic dialysis; n= # of patients

Vascular Access Trends in Canada



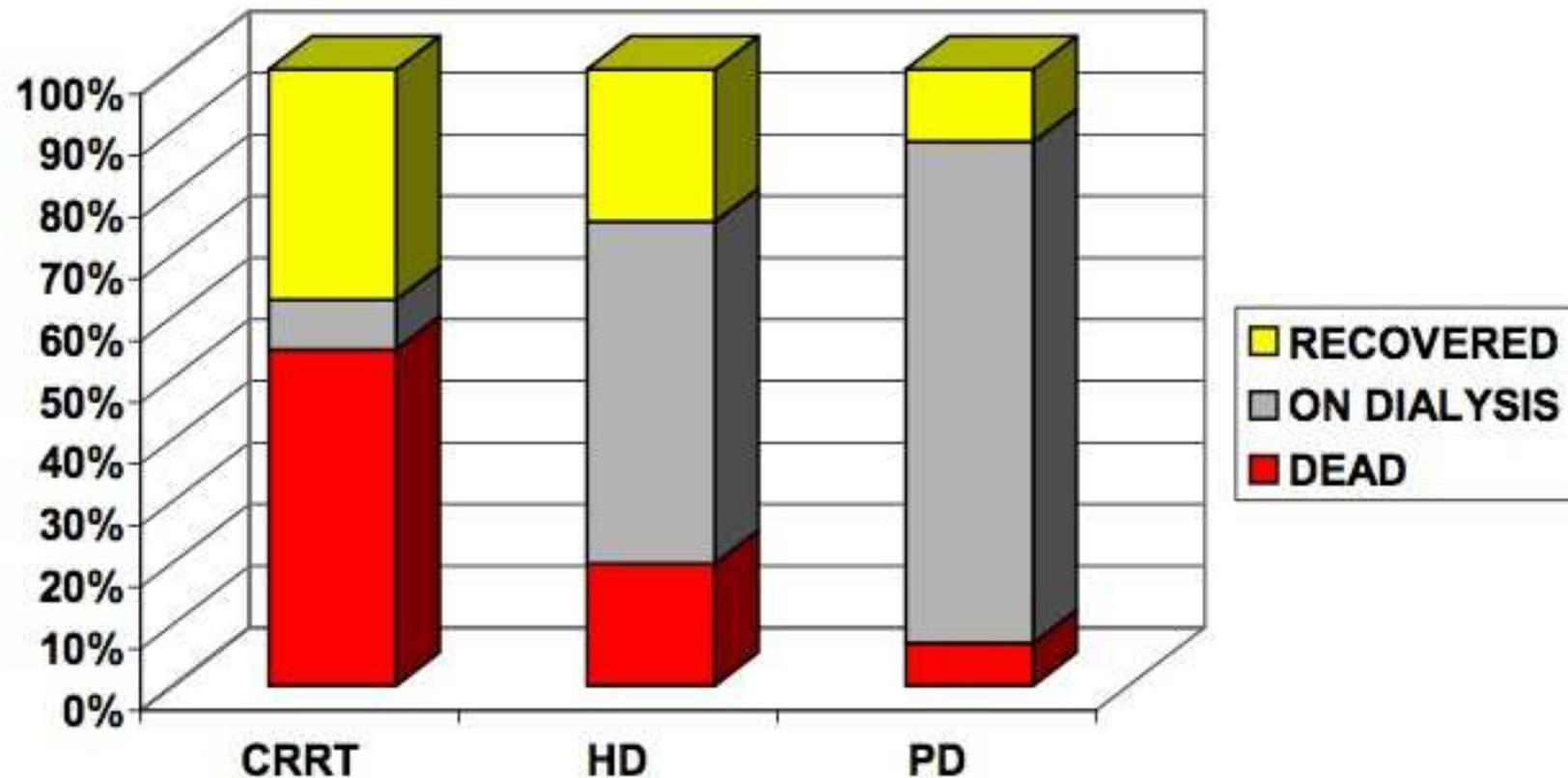
NNI 21:5:69-85, 2007.

Patients Who Start Dialysis as an Inpatient by Modality



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





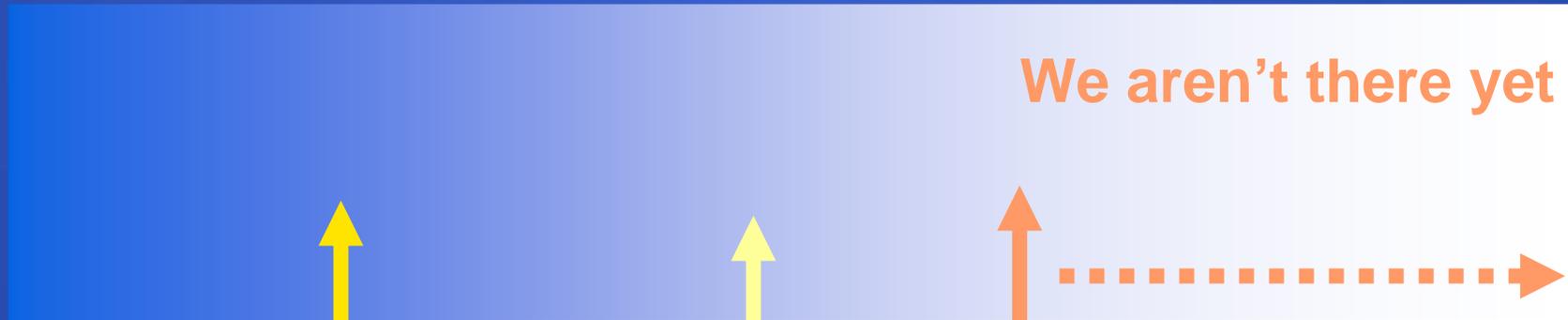
Optimizing Care

Opportunities and challenges

Optimizing CKD Care

Worst possible care

Best possible care



FP care **Nephrologist based care**

?Multidisciplinary team based care

Can we find the right road?



Definitions

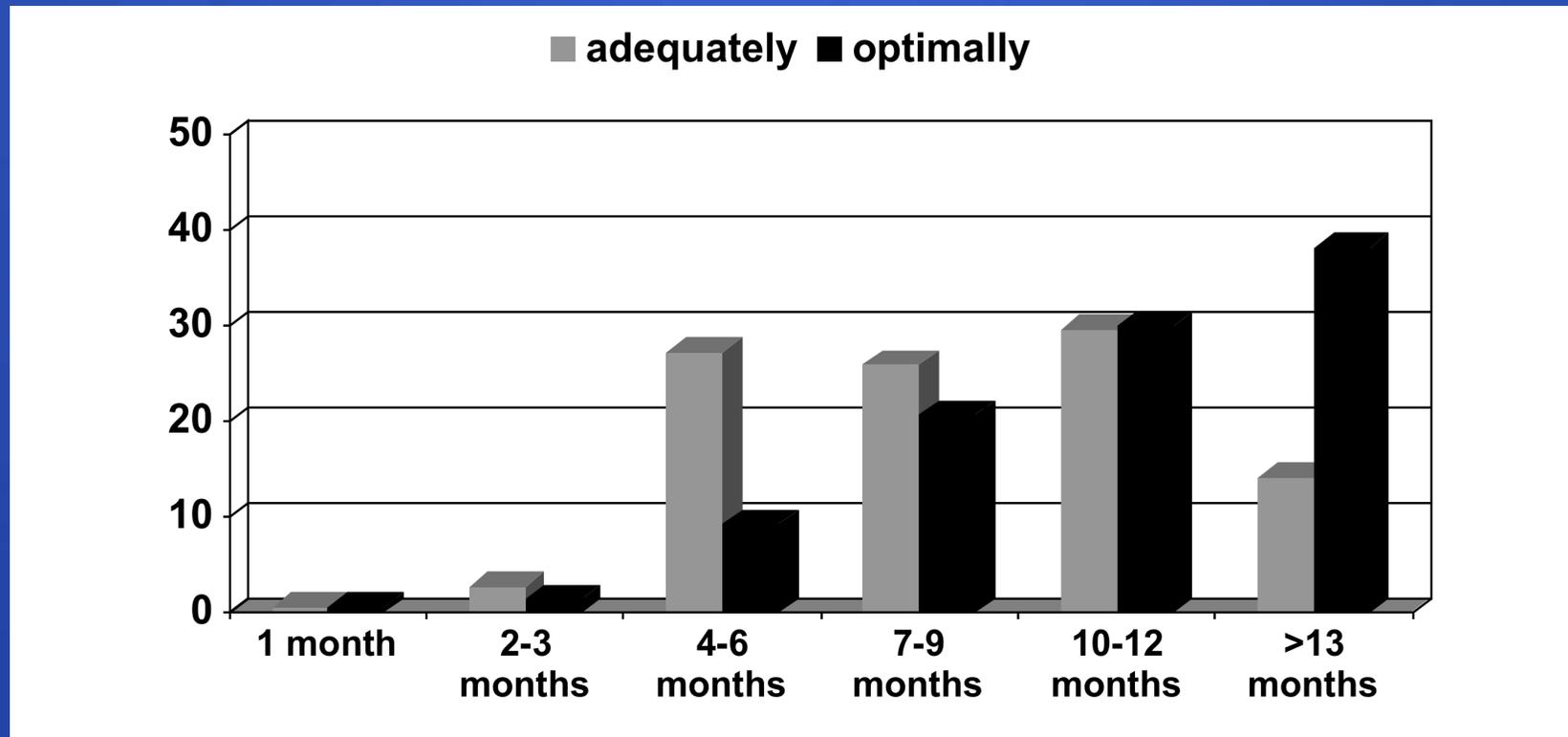
- Optimal start

- Planned
- Elective
- Outpatient
- Early referral
- Chronic modality of choice
- Permanent access
 - AVF/AVG
 - PD catheter

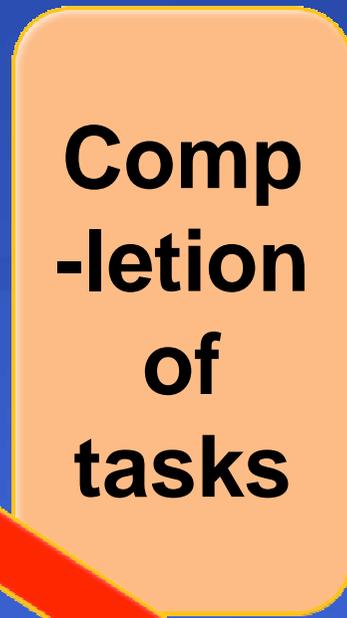
- Suboptimal start

- Unplanned
- Urgent
- Inpatient
- Late referral
- Acute modality
 - Usually HD
- Temporary access
 - CVC

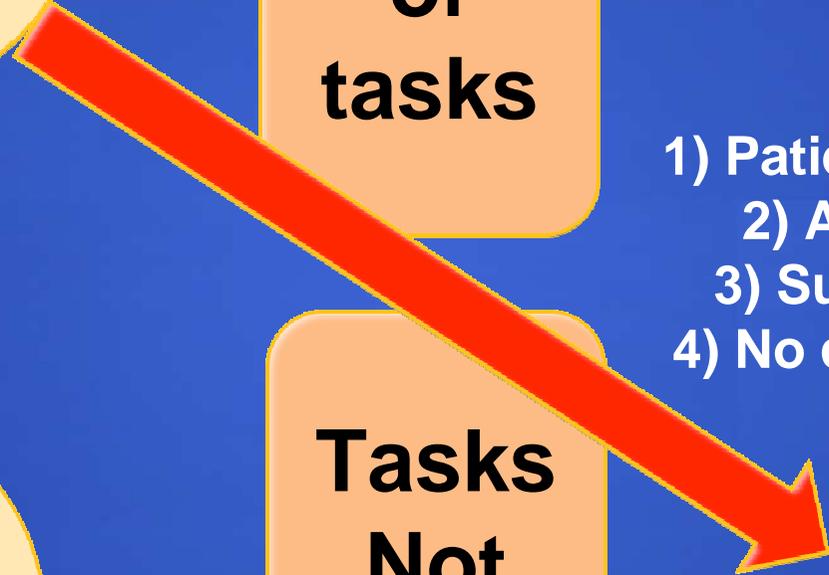
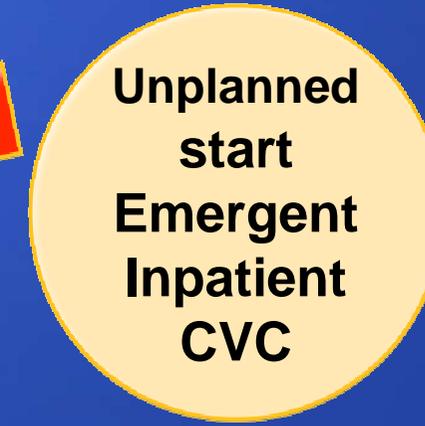
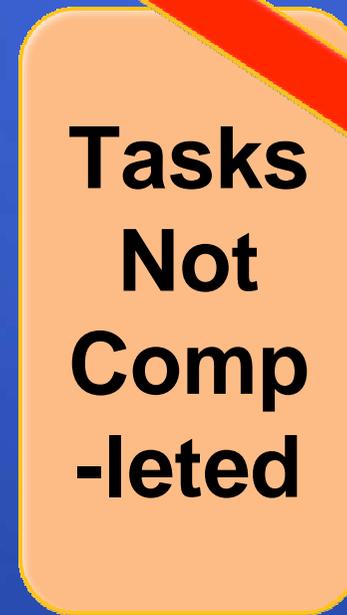
Figure 5: The literature is unclear about what the cut off time between an early referral and a late referral should be. If the cut-off is defined as the minimum amount of time required to adequately (or optimally) prepare a patient for an elective start on either modality, then in my opinion the cut-off should be:

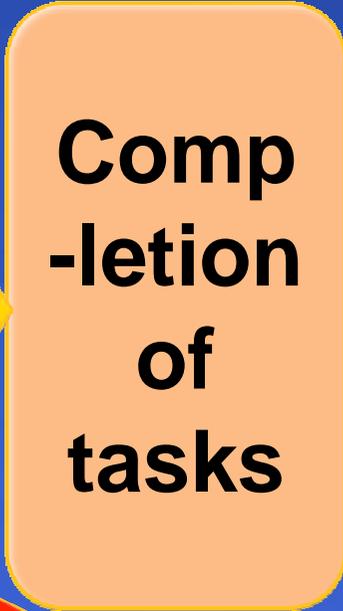


AJKD 47: 277-284; 2006

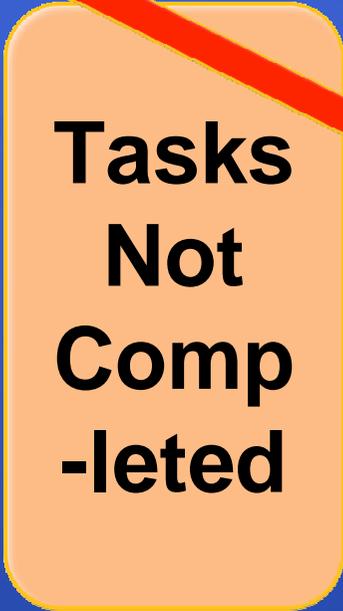


- 1) Patient related delay
- 2) Acute on CKD
- 3) Suboptimal care
- 4) No chronic HD spot





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



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

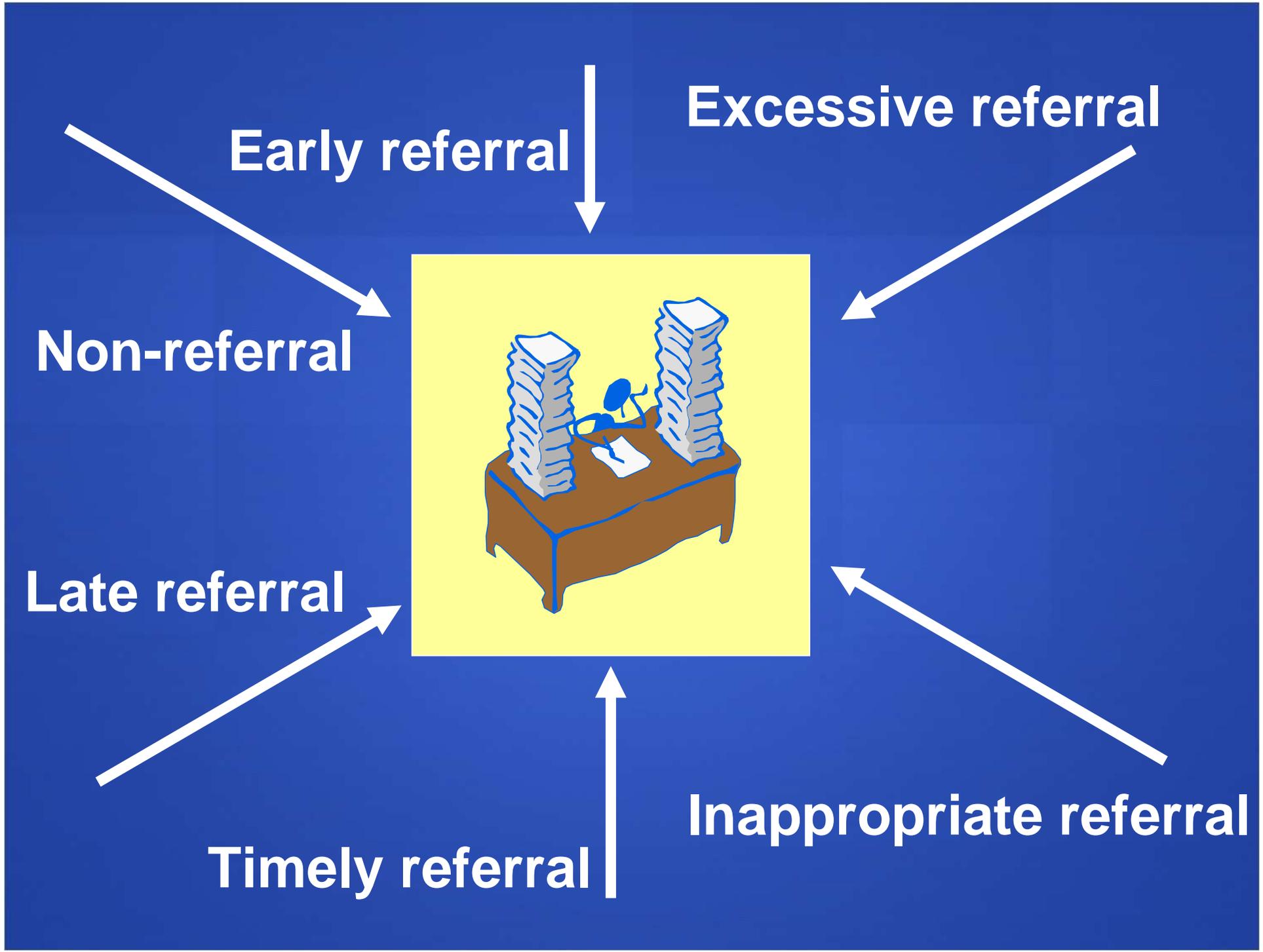


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CSN Position Paper on Care and Referral of Adult Patients with Reduced Kidney Function

October 2006

www.csnsn.ca



Early referral

Excessive referral

Non-referral

Late referral

Timely referral

Inappropriate referral

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



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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



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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 ($< \sim 500$ 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.



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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,* Lara B. Pupim,[†] Mahesh Krishnan,[‡] Ayumi Shintani,[†] T. Alp Ikizler,[†] and Raymond M. Hakim*

*Fresenius Medical Care—North America, Inc., and [†]Division of Nephrology, Vanderbilt University Medical Center, Nashville, Tennessee; and [‡]Amgen, Inc., Thousand Oaks, California

Background and objectives: Annualized mortality rates of chronic hemodialysis (CHD) patients in their first 90 d of treatment range from 24 to 50%. Limited studies also 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 918 CHD incident patients were prospectively enrolled in a multicenter RightStart Program, and compared with a time-concurrent group of 1020 control patients from non-RightStart clinics. RightStart patients received 3 mo of intervention in management of anemia, dosage 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 hematocrit values. Dose of dialysis and permanent access placement were not statistically significantly different from control subjects. Compared with baseline, Mental 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 mo were 20, 18, and 17 for RightStart patients versus 29, 33, and 30 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.

Clin J Am Soc Nephrol 2: 1170–1175, 2007. doi: 10.2215/CJN.04261206

The mortality rate of treated patients with ESRD was 23 deaths per 100 patient-years at risk in 2003, as reported by the US Renal Data System (USRDS) (1). This high mortality rate, as compared with other countries (2), persists despite recent advances in our understanding of the uremic state and improvements in the science and technology of renal replacement therapy. In addition, in 2003, patients with ESRD spent an average of 14 d/yr in the hospital, which comprises more than one third (38%; \$6 billion dollars) of the \$16 billion dollars spent annually to care for patients with ESRD (1).

Although patients with ESRD qualify for Medicare benefits, regardless of age, those who are younger than 65 yr must undergo 90 d of therapy before qualifying for these benefits. To present uniform outcomes data, the USRDS analyzes all data for all patients after 90 d of therapy, regardless of age at initiation of therapy; therefore, the high mortality rate noted may represent an underestimation of the mortality risk for all incident patients, because it does not include mortality data of the first 90 d of dialysis therapy.

A limited number of studies have examined the outcomes of patients in the first 90 d. The earliest data reported were by Held *et al.* in 1990 (3), citing a 12% mortality rate in the initial 90 d of dialysis treatment. This represents an annualized rate of 48 deaths/100 patient-years in patients who start dialysis. These data are confirmed by Khan *et al.* (4), who reported a similar annualized rate of 50 deaths/100 patient-years. Scouie and McClellan (5), using voluntary facility reports, measured a mortality rate of 24 deaths/100 patient-years at risk. Finally, mortality data from Renal Care Group (unpublished data) as tracked for all patients from 1996 until 2006, ranged from 40 to 45 deaths/100 patient-years of annualized mortality ($N > 10,000$ incident patients). No study has systematically examined this issue, especially in terms of interventions to improve this unacceptably high death rate.

The goal of this particular quality improvement program was to implement an intervention strategy focused on improving the clinical outcomes during the initial 90 d of maintenance hemodialysis. We hypothesized that application of a broad and systematic program in the first 90 d may improve the mortality and morbidity rates of this incident CHD population. Specifically, we developed a program that comprises intensive patient education, encouragement, and support coupled with an intervention strategy to implement in a timely manner “best practices” and National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines, which have

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Correspondence: Dr. T. Alp Ikizler, Vanderbilt University Medical Center, 1161 First Avenue South & Garland, Division of Nephrology, S-3223 MCN, Nashville, TN 37232-2372. Phone: 615-343-6104; Fax: 615-343-7156; Email: alpkizler@vanderbilt.edu

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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

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

Co-Morbidities and Risk Factors Associated with Early Mortality

Co-Morbidity

- Age
- Nutritional Status
- Diabetes
- Cardiovascular Disease
- LVH
- Depression

Risk Factors

- **Unplanned start (w/o permanent access)**
- **Short (<4 months) prior nephrological care**
- **Low residual renal output**

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 $\geq 70\%$

Weeks 3-4: Target EDW
Hct $\geq 30\%$, T. Sat $\geq 20\%$

Transplant referral & permanent access planning

Weeks 5-6: Stable BP

Weeks 7-8: Hct $\geq 33\%$
PO₄ 3.5-5.5 mg/dL
Use Permanent Access

Weeks 9-10: Review Goal Achievement

Weeks 11-12: HgbA1C $\leq 7\%$
Albumin ≥ 3.7 g/dL
PTH 150-300 (BiPTH 75-150)

Enrollment Process

RightStart®, N=923

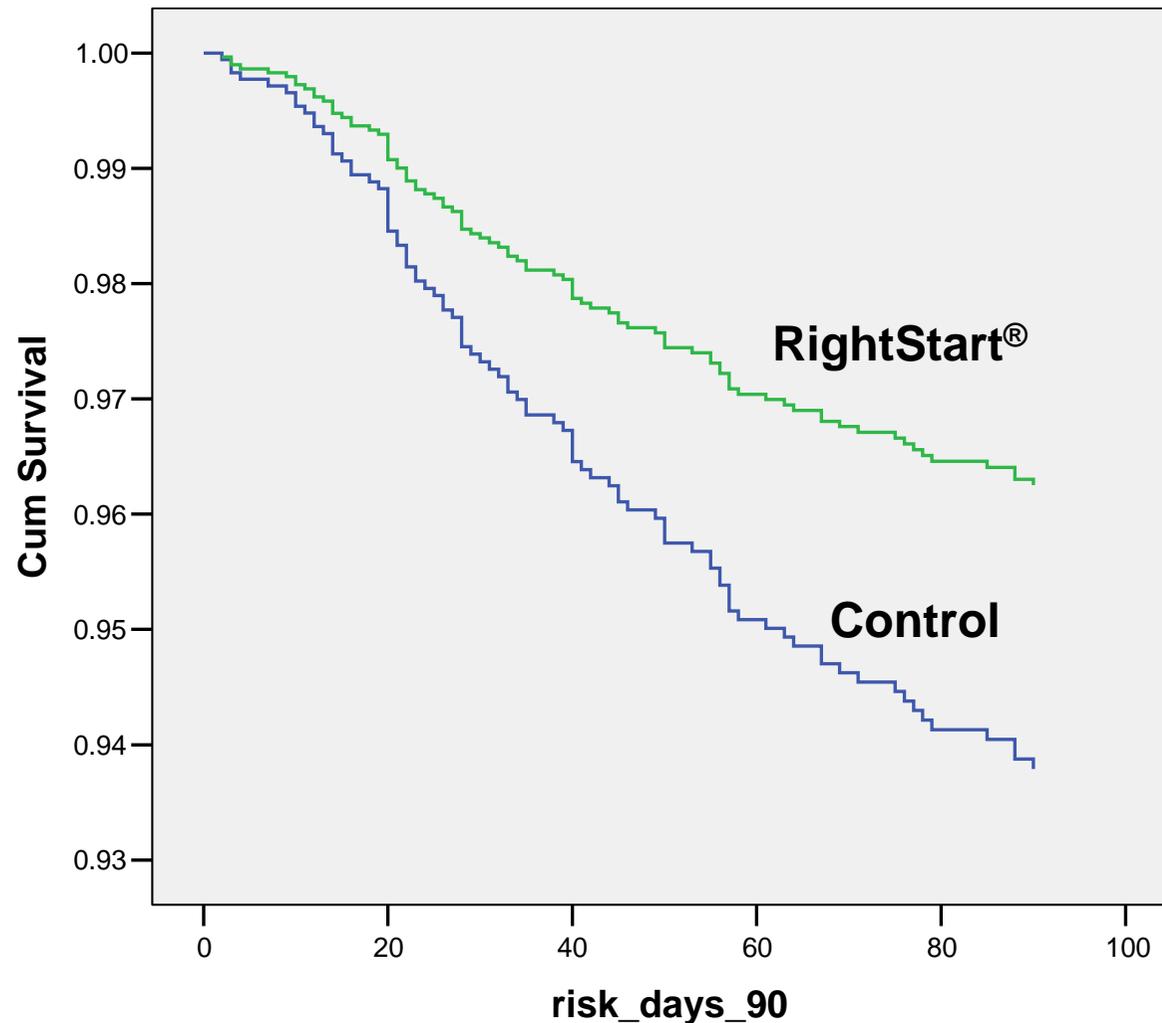
- Prospective enrollment of ALL new patients within one to three weeks of dialysis initiation
- Exclusions:
 - Seasonal or transient patients
 - Nursing home residents
 - Patients with cognitive dysfunction that precludes ability to learn

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

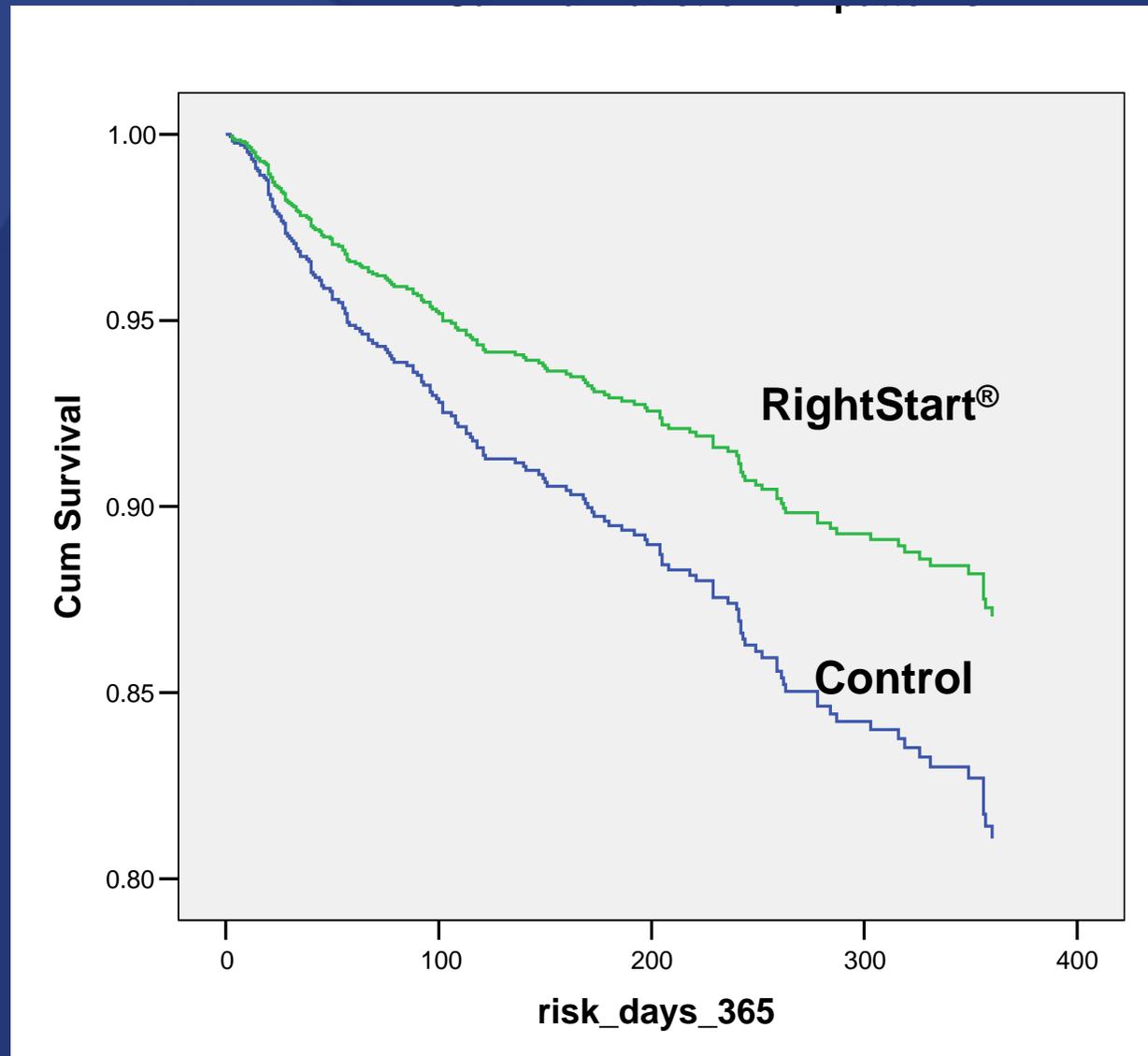


Adjusted by age,
race, gender,
diabetes

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



Adjusted by age,
race, gender,
diabetes

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

A Prospective Randomized study of Cased 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!!

