Models of Chronic Kidney Disease Care and Initiation of Dialysis

Dr Paul Stevens
Kent Kidney Care Centre
East Kent Hospitals, UK
Early Crash Landings

Figure 1. R.A. McCance flying off the midship gun turrets of the *Indomitable* in 1918.
Talk Outline

- Pathways & Definitions
- Guideline recommendations
- Some trends over time
- Late referral versus early referral
- Early dialysis initiation versus late
- Models of CKD care
Pathways to Renal Replacement Therapy

- **Undiagnosed Community CKD**
  - Timely Referral to Kidney Care
  - CKD or AKI in Secondary Care
  - Centre/Satellite HD ± Transplant
  - Home HD/PD ± Transplant
  - Conservative Care

- **Known Community CKD**
  - AKI
  - Late Referral
  - Timely Referral to Kidney Care
Late presentation for renal replacement therapy

Progressive CKD referred late

- Avoidable - CKD known to healthcare providers

Acutely presenting AKD

- Unavoidable - unpredictable CKD progression or unknown to healthcare providers

- AKI or AKI on CKD

Adapted from Udayaraj et al NDT 2011
Guideline Recommendations

<table>
<thead>
<tr>
<th>Guideline Groups</th>
<th>1. Referral Guidance</th>
</tr>
</thead>
</table>

2. Early Dialysis Initiation

<table>
<thead>
<tr>
<th>Guideline Groups</th>
<th>2. Early Dialysis Initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSN (2008)</td>
<td>Consider if GFR &lt;20 mL/min plus clinical indications</td>
</tr>
<tr>
<td>EBPG (2002), KDOQI (2006), UKRA (2009)</td>
<td>Evaluate risks, benefits etc at GFR &lt;15 mL/min when clinical indications are present</td>
</tr>
<tr>
<td>CARI (2005)</td>
<td>GFR &lt;10 mL/min plus clinical indications</td>
</tr>
</tbody>
</table>

3. Late Dialysis Initiation

<table>
<thead>
<tr>
<th>Guideline Groups</th>
<th>3. Late Dialysis Initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBPG (2002), UK RA (2009), CARI (2005)</td>
<td>Before GFR &lt;6 mL/min even if asymptomatic</td>
</tr>
</tbody>
</table>
Should We Follow Guidelines?

“We’ll think about it.”
Trends in Late Referral by Year

Late referral defined as \( \leq 3 \) months before RRT start

Data from Canadian, UK and ANZDATA Renal Registries
GFR at Initiation of HD & PD by Year: UK

UK Renal Registry 13th Annual Report
GFR at Initiation of Dialysis by Year: USA

USRDS ADR 2010
Adjusted US Incident ESRD Mortality

Adjusted for age, gender, race and primary diagnosis

USRDS ADR 2010
# Early Referral Versus Late Referral

<table>
<thead>
<tr>
<th>Consequences of Late Referral</th>
<th>Benefits of Early Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia and bone disease</td>
<td>Delay need to initiate RRT</td>
</tr>
<tr>
<td>Severe hypertension &amp; fluid overload</td>
<td>↑ proportion with permanent access</td>
</tr>
<tr>
<td>Low prevalence of permanent access</td>
<td>Greater choice of treatment options</td>
</tr>
<tr>
<td>Delayed referral for transplant</td>
<td>↓ need for urgent dialysis</td>
</tr>
<tr>
<td>↑ initial hospitalisation rate</td>
<td>↓ hospital LOS and costs</td>
</tr>
<tr>
<td>↑ 1-year mortality rate</td>
<td>Improved nutritional status</td>
</tr>
<tr>
<td>↓ patient choice of RRT modality</td>
<td>Better CVD and comorbid condition management</td>
</tr>
<tr>
<td>Worse psychosocial adjustment</td>
<td>↑ patient survival</td>
</tr>
</tbody>
</table>
### Studies Comparing Early & Late Referral (1)

<table>
<thead>
<tr>
<th>Definition, Studies &amp; Number of patients</th>
<th>Mortality: LR vs ER</th>
<th>Temporary Access &amp; Hospitalisation: LR vs. ER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>≤ 3 months pre-RRT</strong>&lt;br&gt;21 studies, n=15,655&lt;br&gt;25-57% late referral</td>
<td>26-40% vs. 13-28%&lt;br&gt;HR for LR 1.19-2.77</td>
<td>Temp. access 34-70% vs. 6-48%&lt;br&gt;HR for LR 1.42-2.89</td>
</tr>
<tr>
<td><strong>≤ 4 months pre-RRT</strong>&lt;br&gt;10 studies, n=10,142&lt;br&gt;22-49% late referral</td>
<td>28-35% vs. 6-16%&lt;br&gt;HR for LR 1.37-2.7*</td>
<td>Temp. access 34% vs. 6%</td>
</tr>
</tbody>
</table>

*2 studies recorded no significant difference in mortality
### Studies Comparing Early & Late Referral (2)

<table>
<thead>
<tr>
<th>Definition, Studies &amp; Number of patients</th>
<th>Mortality: LR vs ER</th>
<th>Temporary Access &amp; Hospitalisation: LR vs. ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 6 months pre-RRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 studies, n=141,565</td>
<td>37-65% vs. 21-28%</td>
<td>Temp. access 83% vs. 45%</td>
</tr>
<tr>
<td>30-72% late referral</td>
<td>HR for LR 1.50-1.58</td>
<td>HR for LR 1.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LOS: 18 d vs. 4 d</td>
</tr>
<tr>
<td>Not specified</td>
<td>12-45% vs. 5-24%</td>
<td>Temp. access 69-96% vs. 17-36%</td>
</tr>
<tr>
<td>16 studies, n=7,161</td>
<td>HR for LR 1.2-1.52*</td>
<td>HR for LR 1.67</td>
</tr>
<tr>
<td>22-58% late referral</td>
<td></td>
<td>LOS 17-25 d vs. 3-12 d</td>
</tr>
</tbody>
</table>

*2 studies recorded no significant difference in mortality*
Meta-analysis of Late Referral

- 22 studies from 10 countries
- 7 <1/12, 8 <3/12, 5 <4/12, 2 < 6/12 prior to RRT
- 12,749 subjects, age 55.6 y, 57.3% male

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Referral</th>
<th>Late Referral</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, % (SD)</td>
<td>11 (3)</td>
<td>23 (4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospital LOS, days (SD)</td>
<td>13.5 (2.2)</td>
<td>25.3 (3.8)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Serum albumin, g/L (SD)</td>
<td>3.62 (0.05)</td>
<td>3.40 (0.03)</td>
<td>0.001</td>
</tr>
<tr>
<td>Haematocrit, % (SD)</td>
<td>30.54 (0.18)</td>
<td>29.71 (0.10)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Kent New Referrals by CKD Stage

Stage 4 R/E% = 48%
Stage 5 R/E% = 48%

Stage 4 R/E% = 102%
Stage 5 R/E% = 82%

National eGFR reporting & P4P introduced

Hobbs et al, NDT 2009 Nov;24(11):3411-3419
Conceptual Model of Referral Decision Making

**Patient (age, gender, race, education level)**

- Disease-specific factors, symptoms
- Comorbidities, cognitive & functional impairment
- Preferences, anxiety

**Patient- Primary Care Provider Relationship**

- Duration
- Frequency of visits
- Trust

**Primary Care Provider (age, gender, race)**

- Experience, CKD patients, skills
- CKD knowledge & awareness of guidelines
- Relationship with local renal unit
Health System Barriers

Things are looking up Kay, you’re next in line for a fistula

You know that kidney you were waiting for

Good news Phil, they’ve just opened a new dialysis station
Early Versus Late Dialysis Initiation
Benefits of Early Dialysis Initiation

• Over a 15 y period 82 patients had ‘early start’ dialysis and 308 ‘late start’
• Mean CrCl at dialysis initiation 12.9 ml/min (ES) vs. 2.1 ml/min (LS)
• 12 y survival 77% (ES) vs. 51% (LS)
• LOS 7 (ES) vs. 16 (LS) days/patient/y
• Employment 72% (ES) vs. 42% (LS)

Protein Malnutrition and Progression of Renal Failure

• Spontaneous decline in DPI
  – 1.1 g/kg/d above CrCl 50 ml/min
  – 0.85 g/kg/d at CrCl 25-50 ml/min
  – 0.7 g/kg/d at CrCl 10-25 ml/min
  – 0.54 g/kg/d below CrCl 10 ml/min

• Ideal body weight fell by 0.38% for each 10 ml/min fall in CrCl

Ikizler et al. JASN 1995;6:1386-1391
Studies that have examined the role of ‘early’ versus ‘late’ dialysis have consistently shown a better outcome in the patients starting early.”

Hakim & Lazarus JASN 1995;6:1319-1328
Age and comorbidity may explain the paradoxical association of an early dialysis start with poor survival

Mathilde Lassalle¹, Michel Labeew², Luc Frimat³, Emmanuel Villar², Véronique Joyeux⁴, Cécile Couchoud¹ and Bénédicte Stengel⁵,⁶ on behalf of the REIN Registry

Figure 3 | Kaplan-Meier survival curves according to MDRD eGFR in ml/min per 1.73 m² at start of dialysis.
A Situation Far From IDEAL

• **Lead time bias**
  – Extra period of life gained by delaying dialysis not accounted for (biases results in favour of ES)

• **Problems with estimating equations**
  – Low muscle mass = low creatinine generation
  – Fluid overload dilutes serum creatinine
  – Both associated with greater comorbidity

• **Symptoms and/or ↑comorbidity likely to result in early start**

• **Patient included when they started dialysis**
  – those dying before start excluded = survivor bias
• 828 adults with progressive CKD and CrCl 10-15 ml/min/1.73m² randomly assigned to early or late initiation of dialysis
IDEAL Study

- 404 early (planned 10-14 ml/min) and 424 late (5-7 ml/min) initiation of dialysis
- Protocol allowed earlier start where clinically necessary
- PD/HD 195/118 (ES) vs. 171/215 (LS)
- Mean CrCl 12.0 (ES) vs 9.8 (LS) [MDRD 9.0 (ES) vs. 7.2 (LS)]
- HR for death (ES) 1.04; 95% CI, 0.83 to 1.30; P = 0.75
- No difference in other outcomes
Update Guidance for Dialysis Initiation

• Guideline 1.3
  – Prepare for RRT/conservative care before symptoms develop, including access. Supervise in a dedicated clinic (1C, strong recommendation, low quality evidence)
  – GFR<15 ml/min consider dialysis when clinically indicated; note majority will be at 9-6 ml/min (1A, strong rec., high quality evidence)
  – High risk and rapidly deteriorating pts require closer supervision (1C)
  – Asymptomatic patients presenting with advanced CKD may benefit from delaying dialysis to allow adequate preparation (2C, weak rec., poor quality)

Tattersall et al On behalf of ERBP. NDT Advance Access May 5, 2011
“Once exposed to a formal teaching program of the various types of dialysis and transplantation, patients are much less reluctant to start and experience a more positive result, both long and short term. The team approach, including a nephrology nurse, social worker, dietitian, transplant coordinator, and nephrologist, is essential to this process”

Hakim & Lazarus JASN 1995;6:1319-1328
CLINICAL SCIENCE

Early nephrology care provided by the nephrologist alone is not sufficient to mitigate the social and psychological aspects of chronic kidney disease

Ana Amélia Fayer,¹ Rosemeire Nascimento,¹Ⅲ Regina CRM AbdulkaderⅢ

¹ Discipline of Nephrology, Faculdade de Medicina da Universidade de São Paulo. Ⅲ Division of Psychology, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo. Ⅲ Laboratório de Fisiopatologia Renal-LIM16, Hospital das Clínicas Faculdade de Medicina da Universidade de São Paulo.

Multidisciplinary Team Care May Slow the Rate of Decline in Renal Function

Elizabeth A. Bayliss, *† Bharati Bhardwaja, *§ Colleen Ross, * Arne Beck, * and Diane M. Lanese †Ⅱ

Summary
Background and objectives A multidisciplinary team (MDT) approach to chronic kidney disease (CKD) may help optimize care of CKD and comorbidities. We implemented an MDT quality improvement project for persons with stage 3 CKD and comorbid diabetes and/or hypertension. Our objective was to decrease the rate of decline of GFR.

The CKD Chronic Care Model

Community
- Resources and policies

CKD Health Systems
- Organisation of CKD Care
  - Self-management support
  - Delivery system design
  - Decision support
  - Clinical information systems

Improved Outcomes
- Informed activated patient
- Prepared proactive multidisciplinary team

Productive interactions
CKD Models of Care

• Multidisciplinary team
  – dietician, educator, anaemia co-ordinator, pharmacist, social worker, access co-ordinator, counsellor, diabetic nurse, occupational therapist, psychologist, nephrologist

• Shared care scheme
• Low clearance clinics
• Pre-dialysis education programme
Components of Pre-Dialysis Education Programme Provided by 70 UK Centres
“A CKD Care Program is found to help pre-ESRD patients prepare for dialysis initiation and is associated with a reduced probability of emergency dialysis and hospitalization and lowered medical costs”
7 Objectives of CKD Models of Care

1. Provide specific therapy based on diagnosis
2. Slow CKD progression where possible
3. Evaluate and manage co-morbid conditions
4. Prevent and manage CVD
5. Identify, prevent and manage CKD specific complications (e.g. malnutrition, anaemia, bone disease, acidosis)
6. Plan and prepare for RRT (e.g. choice of modality, access-placement and care, pre-emptive transplantation)
7. Psychosocial support and provide conservative care and palliative care options where required.
Some of the Questions

• What are the consequences of late referral and the benefits of early referral?
• What are the factors involved in late referral and how do we improve them?
• Is early dialysis initiation good or bad?
• What’s changed?
• What are the best models of CKD care and how can they be implemented?
• Is there evidence for clinical and cost effectiveness?
• What about the international perspective?
Guideline I.2.3 – When to refer to a nephrology clinic
GFR <30 ml/min and declining should receive nephrologist care and be prepared for RRT (choice of modality & location, discussion with patients & carers, psychosocial support)

Guideline I.3 – When to start dialysis*
GFR <15 ml/min plus symptoms & signs, inability to control hydration status or blood pressure, progressive deterioration in nutritional status
GFR ≥6 ml/min, even if no symptoms and optimal pre-dialysis care, aim to start at 8-10 ml/min (Evidence level: C)

High-risk patients e.g. diabetics may benefit from an earlier start (Evidence level: C)
1.1 Preparation for kidney failure

Patients who reach CKD stage 4 (estimated GFR < 30 mL/min/1.73 m²) should receive timely education .... Patients' family members and caregivers also should be educated about treatment choices for kidney failure. (B)

1.3 Timing of therapy

When patients reach stage 5 CKD (eGFR < 15 mL/min/1.73 m²), nephrologists should evaluate the benefits, risks, and disadvantages of beginning kidney replacement therapy. Particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5. (B)
Guidelines – CSN 2008

Components of care prior to initiation
Patients with eGFR <30 mL/min/1.73m² should receive care in a multidisciplinary setting that includes physicians, nurses, dietiticians and social workers (grade C).

Education program should include lifestyle modification, medication management, modality selection and vascular access as well as options for renal transplantation (grade D, opinion).

Timing of initiation
No evidence to recommend a GFR at which RRT should be initiated in the absence of CKD complications (grade D, opinion).

eGFR < 20 mL/min/1.73m² may require RRT initiation if symptoms, refractory metabolic complications, volume overload or a decline in nutritional status dictates (grade D, opinion).
Guidelines – UK RA 2009

Guideline 1.1&1.2 - RRT: Timely nephrology referral
Refer CKD stage 4-5 or CKD stage 3 and rapidly deteriorating function for assessment by a nephrologist (1B)
Refer at least a year before anticipated RRT (2B)

Guideline 5.2 - RRT: Initiating RRT
Decision to start RRT in patients with CKD stage 5 (eGFR < 15ml/min/1.73m²) based on discussion of risks and benefits of RRT considering symptoms & signs, nutritional status, co-morbidity, QoL, and the physical, psychological and social consequences of RRT (1D)

Guideline 5.3 - RRT: Initiating RRT
Start RRT when eGFR < 6ml/min/1.73m², even if the patient is asymptomatic (2C)

http://www.renal.org/Clinical/GuidelinesSection/RenalReplacementTherapy.aspx#S1
Guidelines – CARI 2005 & 2010

Referral to nephrology (2010)
Patients with an eGFR < 30 mL/min per 1.73 m² should generally be referred to a nephrology service for assessment and multidisciplinary management of chronic kidney disease.

Initiation of dialysis (2005)
GFR < 10 mL/min/1.73 m² and evidence of uraemia ± complications such as malnutrition (Level III evidence)

GFR ≤ 6 mL/min/1.73 m² if no symptoms or complications (Level III)

Educate patients and staff about the strength of the evidence (at best, cohort studies) regarding the rationale for ‘early’ dialysis initiation.

<table>
<thead>
<tr>
<th>Patient Details for RPVGEN TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Last Name</strong></td>
</tr>
<tr>
<td><strong>First Name</strong></td>
</tr>
<tr>
<td><strong>Date of Birth (yyyy-mm-dd)</strong></td>
</tr>
<tr>
<td><strong>NHS Number</strong></td>
</tr>
<tr>
<td><strong>Hospital Number</strong></td>
</tr>
</tbody>
</table>
| **Address** | A nice Flat  
The Village  
Someplace |
| **Postcode** | G4 0SF |
| **Telephone 1** | 01010101010101010101010101010101 |
| **Diagnosis** | No diagnosis stated |
| **Treatment** | Haemodialysis |
| **Transplant Status** | No status uploaded  
(Explain this) |
| **Other Conditions** | |

**From the RPV blog**

**Problems?**
This is a list of medicines as recorded on your renal unit's computer system. IMPORTANT - the list of medicines shown here may not be complete or accurate, because (1) Some renal units do not keep full records of medicines for all patients. (2) Any changes made outside the renal unit - for example any new changes made, or new medicines prescribed by your GP or someone else, will not be shown here. Please point out changes when you next attend a clinic appointment, or send a note or message to your renal unit.

This link to Medline Plus is quite good if you want more information on individual drugs, or on herbs and supplements.

<table>
<thead>
<tr>
<th>Start Date</th>
<th>Medicine Name</th>
<th>Dose</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>28/06/09</td>
<td>Prednisolone</td>
<td>5 mg. Tablet/s Oral Daily For asthma</td>
<td>SGC05</td>
</tr>
<tr>
<td>12/11/08</td>
<td>Ramipril</td>
<td>5 mg. Tablet/s Oral Daily</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/10/08</td>
<td>Darbepoetin alfa</td>
<td>15 micro g Injection Iv weekly. on HD</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/06/08</td>
<td>Lignocaine</td>
<td>as charte Injection sub cut before dialysis 1% if required before AVF cannulation</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/06/08</td>
<td>Folic acid</td>
<td>5 mg. Tablet/s Oral after dialysis</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/06/08</td>
<td>Alfacalcidol</td>
<td>0.25 micro g Capsules Oral after dialysis</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/06/08</td>
<td>Orovite</td>
<td>1 Tablet/s Oral after dialysis</td>
<td>SGC05</td>
</tr>
<tr>
<td>15/06/08</td>
<td>Heparin</td>
<td>as charte Injection Iv during dialysis</td>
<td>SGC05</td>
</tr>
<tr>
<td>05/08/05</td>
<td>Furosemide.</td>
<td>80 mg. Tablet/s Oral Daily</td>
<td>SGC05</td>
</tr>
<tr>
<td>29/07/05</td>
<td>Atenolol</td>
<td>25 mg. Tablet/s Oral Daily</td>
<td>SGC05</td>
</tr>
</tbody>
</table>
International Perspective

Best practice: optimum clinical and cost effectiveness

Gold standard: maximal clinical but reduced cost effectiveness

Acceptable range

Minimum standard

Achievable based on local resource and priorities

Clinical Effectiveness

Cost