Renal Supportive Care – an overview.
Frank Brennan, Palliative Care Physician.
Renal Palliative Care – Caring for adult patients with ESKD – an overview

Frank Brennan
Palliative Care Consultant
Department of Nephrology
St George Hospital Sydney, Australia

British Columbia Kidney Days, Vancouver, British Columbia, Canada
October 2014
A 53 year old woman

- Type 2 Diabetes Mellitus
- Hypertension
- OA – mild
- ESKD – Diabetic Nephropathy
- HD 3/week for 5 years
• Shuffled in to the clinic room

• Head down

• No eye contact
“My legs move all through the night” – Severe Restless Legs Syndrome - 2 years
“I itch all the time… often it becomes ferocious”
Severe uraemic pruritus – 3 years
“My feet and calves burn and get pins and needles – it is awful”

Severe diabetic peripheral neuropathy – 18 months
And sleep?
“I don’t sleep… I doze in 5 minute lots…

“I sit on a chair and put my elbows on my knees to hold them still…

and I pray to die.”
Overview

What is Palliative Care?
What role does Palliative Care have in Nephrology?
Withholding and withdrawing from dialysis
What exactly is the conservative, non-dialytic management of ESKD?
Symptom management
Care of the dying patient with ESKD
Creating and nurturing a Renal Supportive Care service
What is Palliative Care?
WHO definition (2002)

Palliative Care is an approach which improves the quality of life of patients and their families facing life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
Myths

There is virtually no common ground for active treatment of disease and palliative care.
Myths

That palliative care is simply the care of the dying
Myths

That palliative care means giving up hope
Modern view of Palliative Medicine

A. Early involvement: “There is wide recognition that the principles of palliative care should be applied as early as possible in the course of any chronic, ultimately fatal illness.”
B. The concept of concurrent care: that active care and palliative care can and should occur together.
C. That bringing in a palliative approach as the person is dying is a set of missed opportunities.
Benefits of early involvement—
- reinforcement of idea of comfort.
- that symptom control is impeccable throughout.
- establishing a rapport/trust
- demystifying analgesia (opioids)
- introducing idea of Community Care
- helps avoid sense of abandonment
D. That palliative care can be applied to all life-limiting illnesses
What possible role does Palliative Care play in End Stage Kidney Disease?
1. Epidemiology
In developed nations the characteristics of patients on dialysis have changed over the years.

Essentially more elderly patients with co-morbidities.
Number Starting Renal Replacement Therapy
Dialysis or Transplantation
Australia and New Zealand

New Patients, Australia

New Patients, New Zealand
In western nations the mean age of commencement on Renal Replacement Therapy is 60 - 65 years.

Increasing number of patients returning to dialysis after transplant failure.
The age cohort that has the greatest prevalence is the 65-84 year old group.

Canadian Organ Replacement Register (CORR) Report 2014
The other aspect of this change which will be a rising challenge globally is the rise of Diabetes Mellitus
In Canada - Prevalent ESKD by primary diagnosis

Diabetes – 27.1 %

CORR Report 2014
Does everyone who has ESKD commence dialysis?
In Australia, for every one patient with ESKD receiving Renal Replacement Therapy (RRT) there is another who does not receive RRT

Australian Institute of Health and Welfare Research, 2011
2. Mortality
ESRD patients

Overall patients with ESKD with or without RRT have a reduced life expectancy compared to age-matched controls.
For patients on dialysis 15.7 % die each year (CORR Report 2014)
For those aged 75 years and older that figure is 25 %

(CORR Report 2014)
3. Symptomatology
Patients with ESKD have a significant symptom burden related to both the disease itself and other co-morbidities.
What are the common symptoms associated with ESKD?
The Prevalence of Symptoms in End-stage Renal Disease: A systematic Review

Murtagh FE et al. *Advances in Chronic Kidney Disease* Vol 14, No 1 (January) 2007; pp 82-99
A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis

# Symptom Prevalence

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dialysis</th>
<th>Conservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/Tiredness</td>
<td>71%</td>
<td>75%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>55%</td>
<td>74%</td>
</tr>
<tr>
<td>Constipation</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>49%</td>
<td>47%</td>
</tr>
<tr>
<td>Pain</td>
<td>47%</td>
<td>53%</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>44%</td>
<td>42%</td>
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</table>
## SYMPTOM PREVALENCE

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dialysis</th>
<th>Conservative</th>
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</thead>
<tbody>
<tr>
<td>ANXIETY</td>
<td>38 %</td>
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<tr>
<td>DYSPNEA</td>
<td>35 %</td>
<td>61 %</td>
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<tr>
<td>NAUSEA</td>
<td>33 %</td>
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<tr>
<td>RESTLESS LEGS</td>
<td>30 %</td>
<td>48 %</td>
</tr>
<tr>
<td>DEPRESSION</td>
<td>27 %</td>
<td></td>
</tr>
</tbody>
</table>
• Symptoms are prevalent

• Symptoms are multiple

• Symptoms are burdensome
The management of symptoms are challenging with the altered pharmacokinetics of most medications in renal impairment.
4. Quality of life
QOL - St George dialysis
(SF-36 Scores)

Mean score (max 100)

PF  RP  BP  GH  VT  SF  RE  MH


Aust Norms
5. The “quality” of dying
Realistically, given issues of manpower, it may not be possible for a Palliative Care health professional to be present in every Renal Unit.
What are the core competencies in a “Palliative approach” to patients with ESKD for medical practitioners?
4 Pillars of a Palliative approach

- Communication
- Symptom management
- Psychosocial support
- Care of the dying patient
Communication
Once ESRD is diagnosed it is important examine the various options
RRT

Conservative
Decision making around dialysis
Survival
Dialysis or not? A comparative study of survival of patients over 75 years with CKD Stage 5.

Survival

Survival benefit lost if Co-morbidities include IHD

RRT v Conservative
Chandra et al NDT Nov 2010
Change in Functional Status after Initiation of Dialysis

3702 Nursing home residents mean age 73
Mean eGFR 10
Female 60%
Diabetes 68%
CHF 66%
CHD 44%
Cerebrovascular dis. 39%
Depression 35%
Dementia 22%

Kurella Tamura et al. 361 (16): 1539, October 15, 2009
Smoothed Trajectory of Functional Status before and after the Initiation of Dialysis and Cumulative Mortality Rate

[Nursing home residents mean age 73]
Clinical Practice Guidelines on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

Renal Physicians Association of the USA 2010.
Recommendation No. 6

It is reasonable to consider forgoing dialysis for … ESRD patients who have a very poor prognosis or for whom dialysis cannot be provided safely.
1. Those whose medical condition precludes the technical process of dialysis because the patient:

(a) is unable to co-operate (eg. Advanced Dementia)
(b) unstable medically (eg. Significant hypotension)
2. Another life-limiting illness – although this may be negotiated
3. Over 75 years
   with 2 or more of the following statistically
   significant criteria predictive of very poor
   prognosis:

   (a) Surprise question.
   (b) High Co-morbidity Score
   (c) Significantly impaired Functional status
       such as Karnofsky < 40,
   (d) Severe chronic malnutrition (s. Albumin
       < 25.)
Conservative management of ESRD
This may be decided in consultation with a Nephrologist, or

The patient is not referred to a Nephrologist in the first place
What level of care occurs for this group?
If this is being raised as an option:

What does a Conservative pathway mean?

What is its content?

Can we make predictions about their course?
Challenge is to ensure that this pathway of management is not seen as “second best” or inadequate but is thorough, systematic and evidenced-based.
Renal Medicine

Blood Pressure
Calcium/Phosphate
Anaemia
Fluid balance

Palliative approach

Symptom management
Psychosocial support
Care of the dying
There is a modest, but growing body of literature of research on this cohort of patients.
Longitudinal study of conservative stage 5 CKD

- Included patients with Stage 5 Chronic Kidney Disease with definite decision for conservative (non-dialysis) management, and with capacity for consent
- 73 participants (response rate 62%)
- 49 (66%) died during follow-up
  - mean age 81 years, range 58-95 yrs
  - 24 (49%) men
  - median follow-up 8 months (range 1-23 months)
- Outcomes measured monthly until death or study end
  - Symptoms (MSAS-SF)
  - Palliative needs (POS)
  - Functional status (KPS)
Trajectory of functional status:

KPS (%)

Time before death (months)

n=10  n=43

mean KPS  95% confidence intervals
Trajectory of symptom distress:

MSAS-Global Distress Index (0-100 scale)

Time before death (months)

n=10  n=43

mean MSAS-GDI  95% confidence intervals
Trajectory of palliative needs:

Palliative outcome scale
(0-100 scale)

- mean POS score
- 95% confidence intervals

Time before death (months)

n=10

n=43

www.kcl.ac.uk/palliative
Symptom management
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Symptom control is challenging
Symptoms interact and compound each other
Nocturnal:

U. Pruritus

RLS, Insomnia, Fatigue

Pain
Symptoms may derive from the co-morbidities
ESKD constrains the use of medication
Pharmacology in the context of CKD is complex
Multiple gaps in knowledge
Recommendations in published data occasionally conflict on the specific doses of medications to be used.
Principles of symptom management

1. Think of the cause(s).

2. Be meticulous

3. Principle of non-abandonment
PAIN
Impact on QOL

Davison (2002)
69 dialysis patients

62% stated that pain interfered with their ability to participate and enjoy recreational activities.

Am J Kid Diseases 2003; 42(6): 1239-1247
51% stated that pain caused them “extreme suffering”
41% stated that pain caused them to consider ceasing Dialysis.
Positive correlation with depression

Causes of Pain

ESRD and its treatment

Co-morbidities
ESRD and treatment

Disease related:
• Polycystic Kidney Disease
• Renal Bone Disease
• Amyloid
• Calciphylaxis

Dialysis-related pain:
• PD pts with recurrent abdominal pain
• AV Fistulae > ‘Steal syndrome’
• Cramps
Co-morbidities

- OA
- Diabetic neuropathy
- PVD / IHD
Pain etiquette

• ENQUIRE REGULARLY

• RESPOND COMPASSIONATELY

• TREAT COMPETENTLY

• REFER WISELY
Principles of pain management

1. Always enquire about pain.
2. Treat the underlying cause of the pain.
3. Treat the pain meticulously.
4. Treat the pain proportionately.
5. Constantly reassess.
Step 1

Acetaminophen
“It is considered the non-narcotic analgesic of choice for mild-moderate pain in CKD patients.”

Acetaminophen at conventional doses is safe
= 1 g qid
Step 2

Tramadol
Step 2

Tramadol “is the least problematic of the Step 2 Analgesics for ESRD patients”

Nevertheless use with caution – use a bd dose.
90 % of Tramadol and its metabolites are Renally excreted
Need for dose adjustment
If on Dialysis or on Conservative pathway eGFR 15-30

Commence 50mg bd

Maximum 100mg bd
If on a Conservative pathway

eGFR < 15

Tramadol 50mg bd (maximum)
Step 3

Morphine
Morphine

Hepatic metabolism

M-3-G    M-6-G

Kidneys
Morphine is not recommended in CKD
Oxycodone

Short-acting
- Endone
- Oxynorm

Long-acting
- Oxycontin
- Oxycontin
“Overall consensus is that Oxycodone is reasonably safe to use in CKD if monitored carefully.”

Davison SN et al *Seminars in Dialysis* 2014
Fentanyl
• Metabolised in Liver

• Inactive metabolites

• 5-10 % excreted unchanged renally

• Fentanyl is not dialysed
Fentanyl is safe to use at standard doses
Methadone
• Metabolised in liver

• Excreted mainly in the feces. Some renal excretion of Methadone and its metabolites

• Not dialysed

• Safe to use, but requires skill in dosing regimen – specialist use.
Davison SN, Konicki H, Brennan FP.

Pain in Chronic Kidney Disease: A Scoping Review.

Seminars in Dialysis 2014; 27(2): 188-204.
RESTLESS LEGS SYNDROME
Definition

1. An urge to move the limbs, usually associated with parasthesias/dysthesias
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.

Incidence in the general population: 2-15 %

Incidence in ESRD: 20-30 %
Mechanism is not completely understood
Management

Clonazapem

0.5mg – 1mg nocte
Dopamine agonists
• Ergot-Dopamine Agonists (Pergolide, Cabergoline)

• Non-Ergot Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)
Gabapentin
Two Level 1 studies have shown efficacy for Gabapentin in the treatment of RLS in Dialysis patients

• Study A – Placebo controlled – Thorp et al (2001)

• Study B – Gabapentin compared to Levodopa – Micozkadioglu et al (2004)
On Dialysis

Gabapentin 100mg after each Dialysis and titrating to effect
On conservative management with eGFR < 15

Gabapentin 100mg every second night and titrating to effect
On conservative management with eGFR > 15

Gabapentin 100mg nocte
and titrating to effect
URAEMIC PRURITUS
Associations

• Poor sleep quality

• Depression

• QOL

• Mortality

The pathogenesis of pruritus
Epidermis

Dermis
Complex neural network within the dermis and nerve fibres enter the Epidermis as free nerve endings
C Fibres
5 - 10% of the C fibres are itch sensitive
For many years the assumption was:

Histamine $\rightarrow$ C Fibres $\rightarrow$ Spinal Cord
Of the C Fibres that are itch-sensitive:

20 % are Histamine-sensitive

80 % are Histamine-insensitive
Myth 1

That all itch is histamine mediated
Myth 2

That the best first line medication for pruritus of whatever cause are Anti-Histamines
Pathogenesis of Uraemic Pruritus
Multiple theories, conflicting findings
“Despite this vast array of possible explanations, none consistently have been demonstrated to be the underlying cause of pruritus associated with CKD. Large epidemiological studies ultimately may facilitate our understanding of the elusive pathophysiological process of this distressing symptom.”

Large number of therapies described
What therapies have the strongest foundation in evidence-based practice?
• Oral medications

• Topical preparations

• UV Therapy
Gabapentin
There are 3 (three) Level 1 studies showing that Gabapentin has significant efficacy in treating uraemic pruritis

Naini et al (2007)
Razeghi et al (2009)
Evening Primrose Oil
Gabba Linolenic Acid (GLA)
Essential Fatty Acids (EFA) in the epidermis
n-6 EFA

- Linolenic Acid (LA)
  - Gabba –Linolenic Acid (GLA)
    - DGLA
      - Arachidonic Acid
        - Adrenic Acid
          - Docosapentaenoic Acid
n-EFA

Linolenic Acid (LA)

Gabba – Linolenic Acid (GLA)

DGLA

PGE2 ↔ Arachidonic Acid (AA)

Leukotriene B4

Adrenic Acid

Docosapentaenoic Acid
n-6 EFA

Linolenic Acid (LA)

Gabba –Linolenic Acid (GLA)

\[ \text{DGLA} \]

\[ \text{PGE}_1 \]

\[ 15-\text{OH DGLA} \]

Arachidonic Acid (AA)

Adrenic Acid

Docosapentaenoic Acid
So supplementing the Gabba-Linolenic Acid (GLA) has an anti-inflammatory/ anti-itch effect
100mg bd

= Evening Primrose Oil
contains GLA
= 2 capsules bd
Thalidomide  100mg nocte

Silva SR. *Nephron* 1994; 67(3): 270-273
Other oral medications

- Anti-Histamines – evidence does not support use.
- Ondansetron – conflicting results. Not recommended.
- Cimetidine – not recommended
- Naltrexone – conflicting results. Not recommended.

Topical preparations
Capsaicin cream (0.025 %)

Side effect – transient “burning” feeling on the skin
UV-B Therapy
Hassan H et al.

Efficacy and Safety of Gabapentin for Uremic Pruritus and Restless Legs Syndrome in Conservatively Managed Patients With Chronic Kidney Disease

Of all CKD patients on a conservative pathway who presented to the RSC clinic with uraemic pruritus, 47% reported its severity as severe to overwhelming.
At Clinic 4 (median 12.6 weeks) -

85 % reported nil to slight pruritus and no patients reported severe or overwhelming severity.
A 53 year old woman

- Type 2 Diabetes Mellitus
- Hypertension
- OA – mild
- ESKD – Diabetic Nephropathy
- HD 3/week for 5 years
Referred to clinic because of extreme:

1. Uraemic Pruritus
2. Restless Legs Syndrome
3. Diabetic PN
4. Very poor sleep
Gabapentin
Gabapentin commenced for all conditions at 200mg at the completion of each dialysis.
• Complete cessation of all symptoms and a markedly improved sleep

• Sleeping “the best I have for a long time.”
Care of the dying patient with ESKD
ESKD patients may die:

• Having been on dialysis

• Never having been on dialysis
Patients with ESKD on dialysis may die in many different ways
The family’s view of the manner of dying and the care given will have a major effect on their bereavement and will echo down the years in the way they view death.
A major sentinel event → Sudden death
The “negotiated withdrawal”
• George has been on dialysis for 6 months

• He is increasingly fatigued and more frail. No clear reversible cause.

• Further exacerbations of Chronic Airways Limitation.

• NSTEMI

• He presents with a gangrenous toe - post amputation, worsening gangrene… discussion about further surgery.
“It's time to talk to him and his family about the future. We need to be honest. It is right to say to him that he could withdraw from dialysis at any time, that would be OK. We would then speak about what to expect from that point onwards including our care for he and his family.”
Nephrologist 2

“If he brings it up of course I will talk to him…but only if he raises it. It should come from him.”
It is important that any discussion about withdrawal is open and honest at the patient’s own pace and includes the family.
• What should I expect?

• Will I suffer?

• Will I drown in fluids?

• How long will I live?
Patients survive a variable time.

- If completely anuric – 7-10 days
- If still passing urine – weeks-months
HOPE
The preservation and maintenance of hope

Resetting the focus of care

I agree that there is no hope for cure, but there is hope that you will be comfortable and supported throughout.
Not be abandoned.

Always be listened to.

All symptoms treated to the best of our ability.

Will not needlessly suffer.

Treated with respect and dignity at all times.
“A crisis withdrawal”
Scenario 1

The major sentinel event occurs …
• Family prepared for imminent death

• Dialysis ceased

• Consensus that there will not be an escalation to ICU etc.
Scenario 2

The major sentinel event occurs…
• No discussion about withdrawal

• Waiting approach

• Patient dies on dialysis, the day of dialysis
This scenario is considerably assisted if there the patient has had prior conversations with their Nephrologist including an Advance Care Plan.
Creating and nurturing a Renal Supportive Care service
St George Hospital, Sydney, Australia

Collaboration between the departments of Renal Medicine and Palliative Medicine.
Formation of a Renal Supportive Care Clinic

March 2009
• Held every week

• Held in the Renal Unit

• Palliative Care Consultant, Advanced Trainee in Renal Medicine, Renal Clinical Nurse Specialist and Renal Social Worker
All patients with ESKD according to needs
Main categories of patients who are referred to the clinic:

• Patients who are on a conservative pathway

• Patients who need assistance in decision making around choosing dialysis or not

• Patients who are on dialysis and have cancer or other terminal conditions.
• Patients on dialysis who are experiencing symptoms which are difficult to manage

• Patients on dialysis who need assistance in decision making regarding withdrawing or continuing with dialysis
• Focus on symptom management

• Psychosocial support

• Preliminary discussions on ACP

• Access to Renal Social Worker and Renal Dietician
**Questionnaire POS-S (renal) — staff version**

Below is a list of symptoms which the patient may or may not have experienced. Please record how these symptoms have affected the patient in the table below. Put a tick in the box to show how you think they have affected how they have been feeling over the last week.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not at all no effect</th>
<th>Slightly but not bothered to be rid of it</th>
<th>Moderately limits some activity or concentration</th>
<th>Severely activities or concentration markedly affected</th>
<th>Overwhelmingly unable to think of anything else</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Shortness of breath</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Weakness or lack of energy</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Nausea (feeling like you are going to be sick)</td>
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<td>□</td>
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<tr>
<td>Vomiting (being sick)</td>
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<td>Poor appetite</td>
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<td>□</td>
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<tr>
<td>Constipation</td>
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<td>Mouth problems</td>
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<td>Poor mobility</td>
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<td>Itching</td>
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<tr>
<td>Difficulty sleeping</td>
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<tr>
<td>Restless legs or difficulty keeping legs still</td>
<td>□</td>
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<tr>
<td>Feeling anxious</td>
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<td>Feeling depressed</td>
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<tr>
<td>Changes in skin</td>
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<td>Diarrhoea</td>
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<td>Any other symptoms?</td>
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Which symptom has affected the patient the most? ............................................................

Which symptom, if any, has improved the most? .............................................................
Teaching programme for Junior Medical Staff, including Nephrology Trainees on all aspects of Renal-Supportive Care
Preparation of documents:

(a) End of Life Pathway for Renal Patients

(b) Commonly used Palliative medications in the context of CKD

(c) A Renal-Palliative Care Reader
Annual Renal Memorial Service
Annual Renal Palliative Care Symposium

2010 - 2014
Renal Supportive Care Curriculum

- Master classes for trainees
What are the best books and materials in this area?
Chambers EJ, Germain M, Brown E (eds)  
*Supportive Care for the Renal Patient*  
2nd edition, 2010  
Oxford University Press
Clinical Practice Guideline on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

Renal Physicians Association of the USA and the American Society of Nephrology. 2010.
Australasian Renal Supportive Care Position Statement

Endorsed by Kidney Health Australia
Endorsed by the Australian and New Zealand Society of Nephrology

Nephrology 2013;18(6)
End-of-life Framework: Recommendations for a Provincial EOL Care Strategy 2009

Work of the BC Provincial Renal Agency
Conclusion

A mutual acknowledgement of need-

The role of Palliative Care/supportive care in ESRD
The last decade has seen considerable levels of advocacy, attitudinal shift, research, publications, and collaboration.
This approach may come at multiple points in the trajectory of the disease.
The core competencies in a “Palliative approach” to patients with ESKD can and should be acquired by all doctors working with these patients.
Applies to patients who are being managed either with dialysis or conservatively
The family will remember forever your involvement, your demeanour and your compassion.
Your patients remain your patients until their death