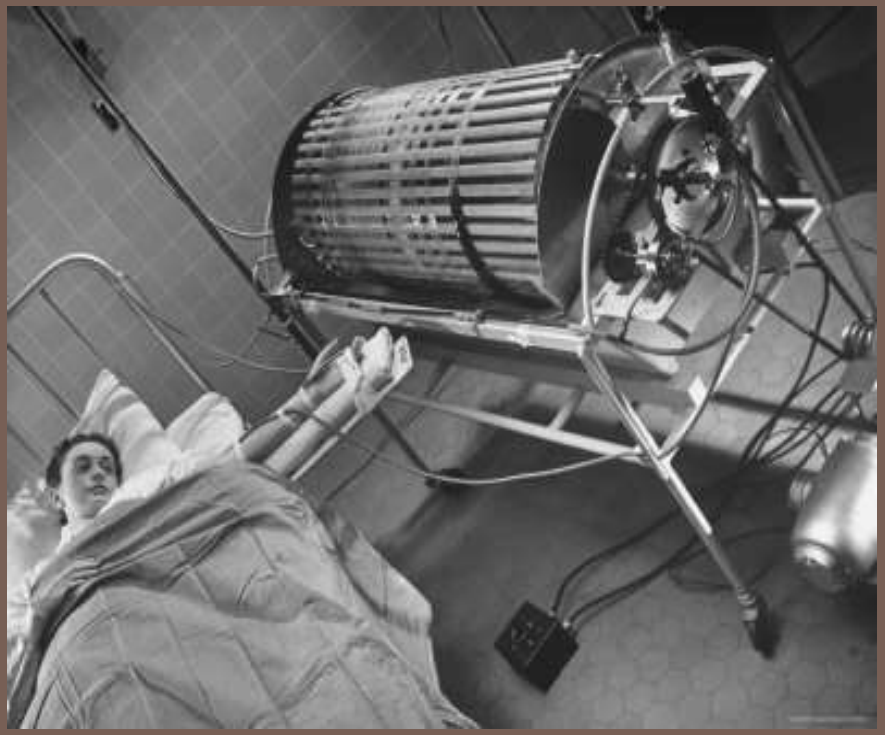

END STAGE RENAL DISEASE AND THE DISCONTINUATION OF DIALYSIS

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December 8, 2014

Disclosures:

- I listen to Taylor Swift (Don't lie so do you)

CASE STUDY: Mrs. S

- 83 yo F from LTC referred to nephrology for ESRD, poorly controlled pain and pruritus
- PMhx: Htn, type II DM, Afib, CHF, COPD, vascular dementia, PVD, depression, chronic pain
- Pt unable to participate in assessment d/t CI
- Family wishes to help her live as long as she can, be symptom free and maintain current QOL

Objectives:

- Would this patient benefit from a palliative approach to care?
- Will dialysis impart a survival benefit?
- What symptoms may this patient experience and how can they be managed?
- How can you help in advance care planning?
- If this patient were to forgo or discontinue dialysis what can you expect?
  - The who, how, when and where of discontinuing dialysis

End Stage Renal Disease:

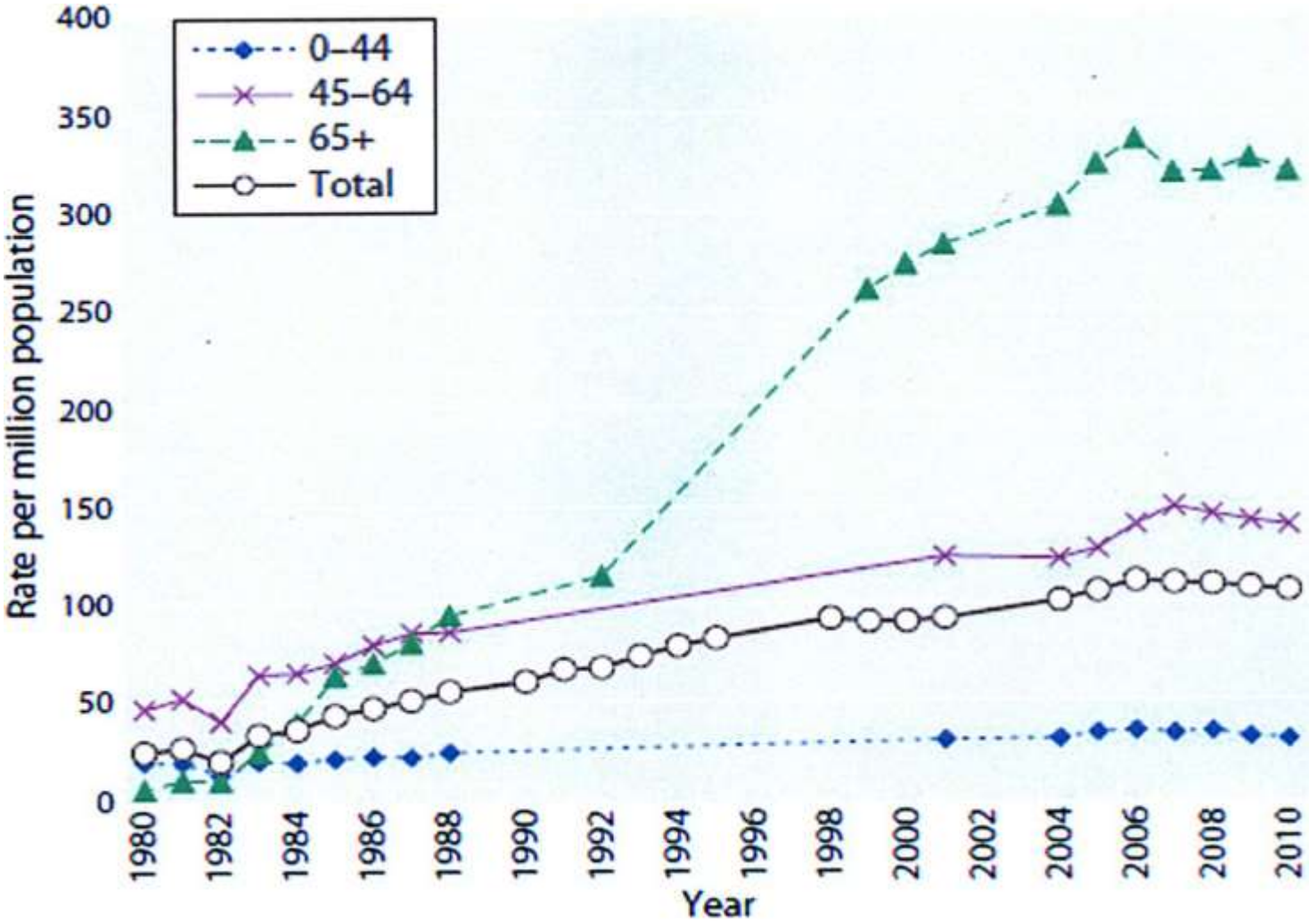
Stage	GFR (ml/min)	Description
1	>90	Normal kidney function, but urine findings, structural abnormalities or genetic trait point to kidney disease
2	60–89	Mildly reduced kidney function, but other findings (as for stage 1) point to kidney disease
3	30–59	Moderately reduced kidney function
4	15–29	Severely reduced kidney function
5	<15	End-stage kidney failure (established renal failure)

GFR = glomerular filtration rate.

End-stage renal disease: Epidemiology and Impact

- ESRD is a serious illness with significant health consequences and high-cost treatment options
- # pts with ESRD has increased 3x in Canada last 20 years with largest cohort of incident dialysis patients being > 65yo
- Critical increase easily attributable to increasing prevalence DM and HTN in an already aging population
- Result is a large subpopulation of unwell, frail, elder dialysis pts with high symptom burden and high health care needs
  - Estimated 1000 hrs/yr in tx
- Among all dialysis patients, regardless of vintage, yearly mortality is ~25% (>breast, ovarian, prostate, colorectal ca)
- Symptom burden comparable to advanced cancer yet under-recognized and undertreated

Renal Registry data indicating increasing dialysis take-on rates over time by age group



Davison R , and Sheerin N S Postgrad Med J 2014;90:98-105

Identifying Patients: Criteria for a Palliative Care Assessment at the Time of Admission

A potentially life-limiting or life-threatening condition and . . .

Primary Criteria

- The "surprise question": You would not be surprised if the patient died within 12 months
- Frequent admissions
- Admission for difficult-to-control symptoms
- Complex care requirements
- Decline in function, feeding intolerance, or unintended decline in weight

Secondary Criteria

- Admission from LTC
- Elderly pt, CI, with acute hip fracture
- Metastatic/incurable cancer
- Chronic home oxygen
- Out-of-hospital cardiac arrest
- Enrolled in PCBP or known to palliative care
- Limited social support
- No history of ACP discussions/documents

Identifying patients with palliative care needs:

- Goal is early identifications of pts at high risk for unmet palliative care needs
- Serves as trigger to include a palliative care approach in daily care and consider palliative referral in more complex cases
- High risk patients specific to ESRD include:
  - Pts with ESRD + any high risk factor (primary or secondary criteria)
  - Pts with ESRD who have opted for conservative management
  - Pts with ESRD who are considering discontinuing RRT or have no options for ongoing dialysis access
  - Pts who are unwell or with high symptom burden at the onset of dialysis

Advanced Care Planning: What?

- Process of shared reflection, discussion and decision making for purpose of clarifying values, tx preferences, and goals of care
- Dynamic process requiring constant reassessment
- Patient-centered approach to individualize care
- Uses open-ended questions
- Provides outcome data + personal opinion
- Ultimate decision for dialysis lies with medical team in taking best interest of pt into account

Advanced Care Planning

Examples of Open-Ended Questions to Promote Discussions

Addressing goals of care when prognosis is uncertain
What are your most important hopes?
What concerns you most about your illness?
What is your quality of life like now?
How do you think about balancing quality of life with length of life?
Is it more important for you to live as long as possible, despite some suffering, or to live without suffering but for a shorter time?
What are your biggest fears?
Given the severity of your illness, what is most important to you to achieve?
What do you understand about your illness?
How much do you want to know?

Advance-care planning and end-of-life issues
Values
What makes life most worth living for you?
Are there circumstances in which you would find life not worth living?
Have you seen or been with someone who had a particularly good (or difficult) death?
What have been the worst and the best things about this illness for you?

Directives
If you are unable to speak for yourself in the future, who would be best able to represent your views and values? (proxy directive)
Have you given any thought to what kinds of treatment you would want or not want if you become unable to speak for yourself in the future? (instruction directive or living will)
Have you considered circumstances in which you would want to stop dialysis?
Where would you like to be and who would you like to be there when you die?

Adapted from the Renal Physician Association and American Society of Nephrology,7 Weiner et al,26 and Quill.27

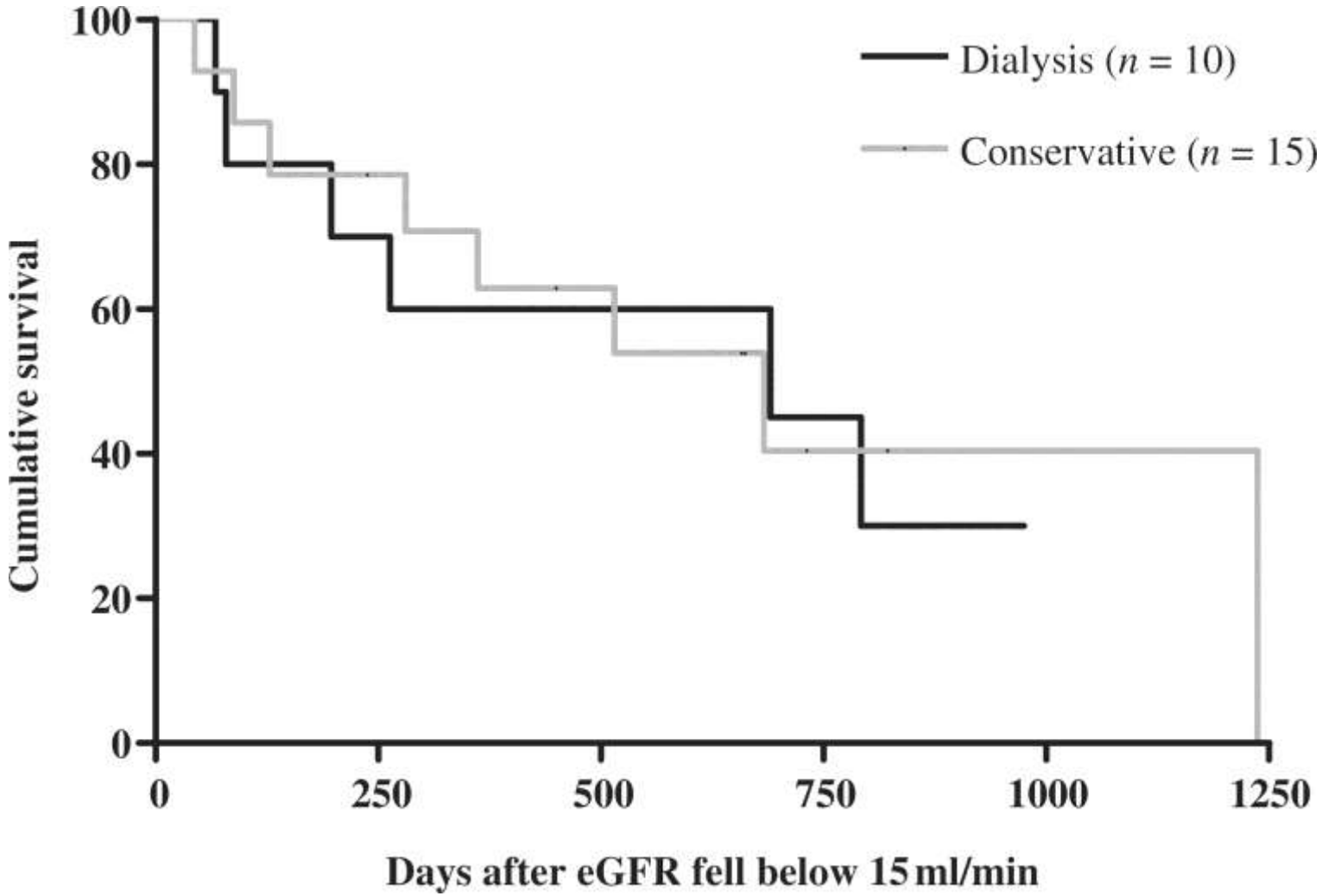
Advanced Care Planning: Why?

- Advanced care planning has been show to:
  - Increase pt/family satisfaction with care
  - Increase likelihood that pt's wishes will be upheld
  - Increase hospice use, reduce hospitalization and lead to "less aggressive" medical care
  - Decrease stress, anxiety, and depression in surviving relatives
- Only 13-35% pts with ESRD complete ACD
- 61% pts regret decision to start dialysis
- ~73% pts on dialysis have significant or moderate CI and 50-80% who discontinue dialysis are incompetent at the time of decision
- 1-time survey of 100 Canadian pts during an initial visit to a nephrology clinic reported that 97% of pts wanted explicit information on prognosis yet over 90% had no such conversation

Advanced Care Planning in ESRD: Providing outcome data

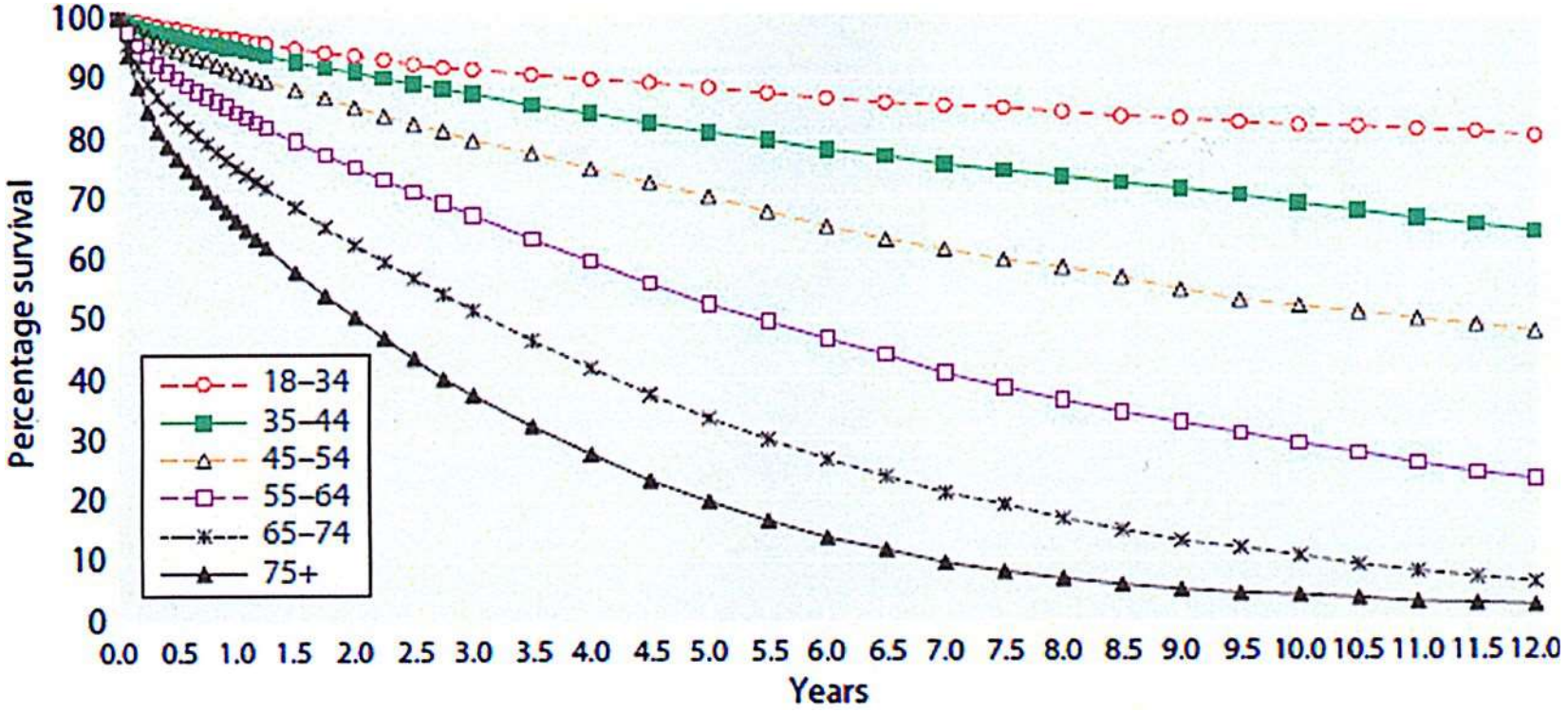
- Largest study to date by Hussain *et al* comparing outcomes in elderly pts choosing between RRT and CM
  - For pts >80 yo, with a poor performance status or high co-morbidity scores the survival advantage of RRT over CM was lost
  - Those accessing a CM pathway had greater access to palliative care services and were less likely to be admitted to or die in hospital (47% vs 69%)
- Murtagh *et al* similar results pts >75 yo and high comorbidity scores OR with IHD alone having no added benefit
- Tamura *et al* found that for LTC residents mortality 58% in the first year of dialysis with only 13% maintaining pre-dialysis functional status

Kaplan–Meier survival curves for those with high comorbidity (score = 2), comparing dialysis and conservative groups (log rank statistic <0.001, df 1, P = 0.98).



Murtagh F E M et al. Nephrol. Dial. Transplant. 2007;22:1955-1962

Kaplan–Meier survival of incident patients 1997–2009 cohort



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Symptom Burden in ESRD:

- Fatigue 12-97%
- Pain 8-82%%
- Pruritus 10-77%
- Dry skin 72%
- Insomnia 20-83%
- Nausea 15-48%
- Anxiety 12-52%
- Depression 5-58%
- Anorexia 25-61%
- Constipation 8-57%
- Muscle cramps 28-60%
- Dyspnea 11-55%
- Headache 18-71%
- Restless legs 8-52%
- QOL 35% lower than age matched healthy population

Uremic pruritis:

- Frustrating, common, and disabling symptom in ESRD
- More common in dialysis (50-90%) vs non-dialysis (25-33%) pts
- Interestingly, not an issue in ARF
- Often generalized but may be localized (back)
- Often worse at night and at end of dialysis
- Pathophysiology multifactorial and poorly understood
- Difficult to treat and may indicate poor prognosis

Uremic Pruritus: Management

- High quality evidence limited
- Trial of topical emollients and analgesic encouraged
- Pharmacological management:
  - Anti-histamines: lack of evidence but often used, benefit likely d/t sedating properties
    - Hydroxyzine 25 mg qid
  - Gabapentin: 100 – 300 mg after dialysis (low and slow)
  - Ondansetron: 4-8 mg tid
  - Others: Cholestyramine, opioid antagonists (?practical)
- UVB in refractory pruritus
- Renal transplant is definitive tx when possible

Pain:

- One of the most common symptoms in pts with ESRD yet under-recognized and undertreated
- At least 50% of HD pts report pain and 82% of these report pain of moderate to severe intensity
- Dialysis Outcomes and Practice Patterns Study 74% pts reported moderate to severe pain however NO analgesic prescription
- Cohort of Canadian HD pts 75% were found to have a negative Pain Management Index
- Impacts overall QOL, increases use health care system, impairs interpersonal relationships, limits function, increases rates depression, anxiety, insomnia, and increases consideration of discontinuing dialysis

Pain:

- Multifactorial: nociceptive, neuropathic, mixed
- Etiology also multifactorial:
  - Comorbidities (DM, PVD)
  - Primary renal disease (PCKD)
  - Consequences of chronic renal failure (calciphylaxis, renal osteodystrophy)
  - D/t treatment of ESRD itself (dialysis, procedural)
- MSK pain most common (65%), peripheral neuropathy (15%), procedure-related pain (14%), and pain d/t PVD (10%)

Choice of analgesic in ESRD:

Table 2. Modification of the WHO three-step analgesic ladder for ESRD according to Barakzoy and Moss, 2006 [5].

Renal adaptation of the WHO 3-Step analgesic ladder		
	Recommended drugs	Not recommended drugs
Step 1 Mild pain (1 – 3)	Acetaminophen (paracetamol)	NSAIDs COX-2 inhibitors
Step 2 Moderate pain (4 – 6)	*** Tramadol Hydrocodone Oxycodone (plus acetaminophen)	Codeine
Step 3 Severe pain (7 – 10)	Fentanyl Methadone ***Hydromorphone Oxycodone (plus acetaminophen)	Morphine

Buprenorphine

*** Use carefully in low doses

Pain: Principles of pain management in ESRD

- Need to consider renal clearance of the parent compound and their active metabolites
- Is pt on dialysis?
- For drugs with renal clearance GFR approximates renal excretion and dose reductions required
- Within opioid class, lipophilic drugs such as fentanyl, buprenorphine and methadone preferred in dialysis pts
- More water-soluble molecules such as morphine, hydromorphone and oxycodone are removed by dialysis which can precipitate pain crisis and withdrawal

Neuropathic pain:

- Challenging as many drugs CI or cautioned in ESRD
- Methadone remains favorable however current clinical practices unfortunately limit use
- Most traditional antidepressants and anticonvulsants require dose reductions or avoidance
- Gabapentin: 300 mg/d or pregabalin 75 mg/d
  - smaller doses often effective
- Nortriptyline: 10-25 mg qHS
- Cannabinoids: adjuvant benefits (nausea, appetite) but may be poorly tolerated
- Non-pharmacologic modalities (ice, heat, message, acupuncture, TENS, PENS, SCS, HTEMS)

HEALTHCARE PROFESSIONALS

BCPRA provides a number of resources for health professionals, including:

Guidelines, Protocols & Clinical Tools
Chronic disease management initiatives
Disaster planning
Education and fellowships
End of life resources
Forms
Glomerulonephritis (GN) network and registry
Handouts
Patient database (PROMIS) – the Patient Record/Registration and Outcome Management Information System – the renal care community's clinical information system.
Pediatric program planning, to support children at high risk for kidney disease and ensure children in all areas of BC have access to care
Pharmacy & formulary resources, such as a list of essential medications, medication recommendations, and a partnership with community pharmacies
Provincial patient education strategy
Research
Vascular access
Links to other organizations and resources

IN THIS SECTION

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Renal Analgesic Brochure

BC Renal Agency
An agency of the Provincial Health Services Authority

Contents

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OPIOID

Buprenorphine (BuTrans patch®)

Indications	For moderate pain requiring continuous opioid analgesia.
Mechanism of Action	Partial agonist of mu receptor.
Pharmacokinetics	Normal half life 25 to 37 hrs; Extensive hepatic metabolism by CYP 3A4 and potential for drug interactions; 1% excreted unchanged in urine; 27% inactive metabolites excreted in urine.
Adverse Effects	Opioid associated adverse drug reactions (sedation, respiratory depression, nausea and vomiting, constipation, itchiness); irritation/erythema, pruritus at application site. Risk of accidental overdose when used in acute pain, non-tolerant individuals, or through careless disposal. Might precipitate opioid withdrawal symptoms if administered before other opioid agonist effects have subsided (within 4 hours of short acting opioid or 24 hours after long acting opioid).
Dosing Guidelines (Normal Renal Function)	Start low and titrate to effect, e.g. 5 mcg/h buprenorphine patch q7d (max. 20 mcg/h q7d). Previous opioid should be tapered over first 12 hrs of buprenorphine as absorption is delayed. Starting dose for non-opioid naive patient: 5 to 10 mcg/h q 7 d. Adequate breakthrough medication should be provided when switching to buprenorphine as predicted doses are sometimes too conservative. Available: transdermal patch.

Renal Dosing Guidelines GFR (mL/min)	>50 (mL/min)	10 to 50 (mL/min)	<10 (mL/min)
	100%	100%	100%

Supplemental Dose after	IHD	PD
	None	None

Pharmacare Coverage	No
Cost (30 day supply)	4 patches of Buprenorphine 10 mcg/h patch: $95.76

Discontinuing Dialysis: Who?

- Terminology slow to catch up!
- 2nd leading cause of death in dialysis pts ~25% (1st CVS ~50%, 3rd infection ~13%)
- Factors associated with discontinuing dialysis
  - Women 25% more likely than men
  - Caucasians 2x more than Asians (lowest) or African-Americans
  - Age >75
  - More likely to be living in LTC facilities
  - Presence of progressive illness (dementia, cancer)
  - Poor performance status
  - Lower quality of life scores
  - Presence of cachexia
  - Longer duration of dialysis

Discontinuing Dialysis: How?

- Cohen et al: 8 dialysis clinics US and Canada with 137 cases of dialysis cessation
  - 85% had "good" or "very good" deaths
  - 15% had "bad deaths"
  - Pain 40%
  - Agitation 30%
  - Dyspnea 25%
- Others: fatigue, nausea, pruritus, restless legs, myoclonus, muscle twitching and seizures (drug-induced or d/t uremia)
- Research lacking re pts with palliative care involvement but small studies suggest significant decrease in symptom burden

Discontinuing Dialysis: How?

- Dyspnea: fan, opioids, ultrafiltration RARELY required
- Secretions: glycopyrrolate, scopolamine
- Agitation: assure pain and psych issues addressed
  - Haloperidol, loxapine, methotrimeprazine in reduced doses
  - Benzodiazepines if intractable and severe
- Pain: same principles of opioid prescribing with consideration to limited PO route (methadone and oxycodone)
- Nausea: uremia-induced mediated by dopamine
  - Haloperidol 1st line
- Myoclonus, muscle twitching and seizures
  - Rotate medications where applicable and appropriate
  - Benzodiazepines effective at treating symptom

Discontinuing Dialysis: When and Where?

- If no residual renal fxn, mean survival 8-10 days but range 1-100 days
- Much longer and less predictable survival in pts with residual renal function (months – years)
- 73% dialysis pts die in hospital vs 33% who chose conservative management pathway
- <15% dialysis pts die in hospice with pts who choose CM are 4x more likely
- Partially explained by relatively rapid EOL trajectory
  - Average length of time at hospice 1 week and PPS at admission 20%

Summary:

- Critical growing number of unwell pts with ESRD
- End-of life care needs are currently inadequately met
- Morbidity and mortality rates are high
- Effective management strategies exist when appropriate prescribing practices used
- Identifying pts who would benefit from a palliative approach to care is crucial to providing best patient-centered care
- For some pts, not having dialysis is a better option than continuing/initiating
- Dialysis may not improve overall survival and may be detrimental to QOL in elderly patients with multiple medical comorbidities
- WE NEED TO INCORPORATE A PALLIATIVE APPROACH TO CARE MORE

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