



# END STAGE RENAL DISEASE AND THE DISCONTINUATION OF DIALYSIS

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# Disclosures:

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- Nil

# CASE STUDY: Mrs. V

- 83 yo F from LTC referred to nephrology for ESRD
- PMhx: Htn, type II DM, Afib, CHF, CVA, CAD with previous MI, dementia, PVD, chronic back 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 incorporating a palliative approach to care?
- Would dialysis impart a survival benefit?
- What symptoms may this patient experience and how can they be effectively 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.

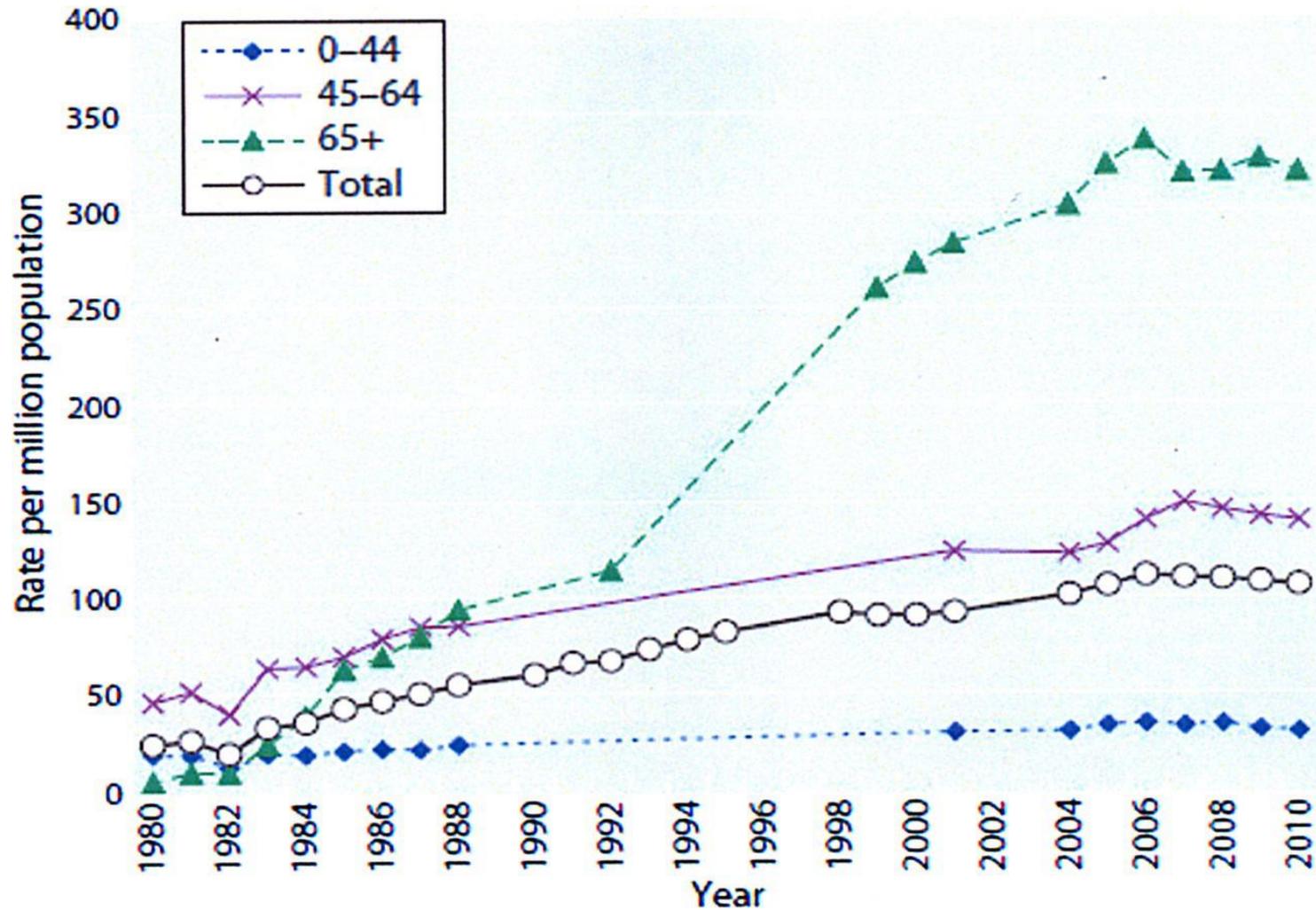
# End-stage renal disease: Epidemiology and Impact

- 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  $> 65$ yo
- Critical increase easily attributable to increasing prevalence DM and HTN in an already aging population

# End-stage Renal Disease: Epidemiology and Impact

- Result is a large subpopulation of unwell, frail, elder dialysis pts with high symptom burden and high health care needs
  - ▣ 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
- 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 to get to know pt
- Provides outcome data + personal opinion
- Ultimate decision for dialysis lies with medical team in taking best interest of pt into account

# Advanced Care Planning: Open-ended question

- What do you understand about your illness?
- How much do you want to know?
- Given the severity of your illness, what are your biggest concerns? Hopes? Fears?
- What is your quality of life like now?
- How do you view balancing quality of life with length of life?
- Have you considered circumstances in which you would want to stop dialysis?

# 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, reduce costs
  - ▣ Decrease stress, anxiety, and depression in surviving relatives

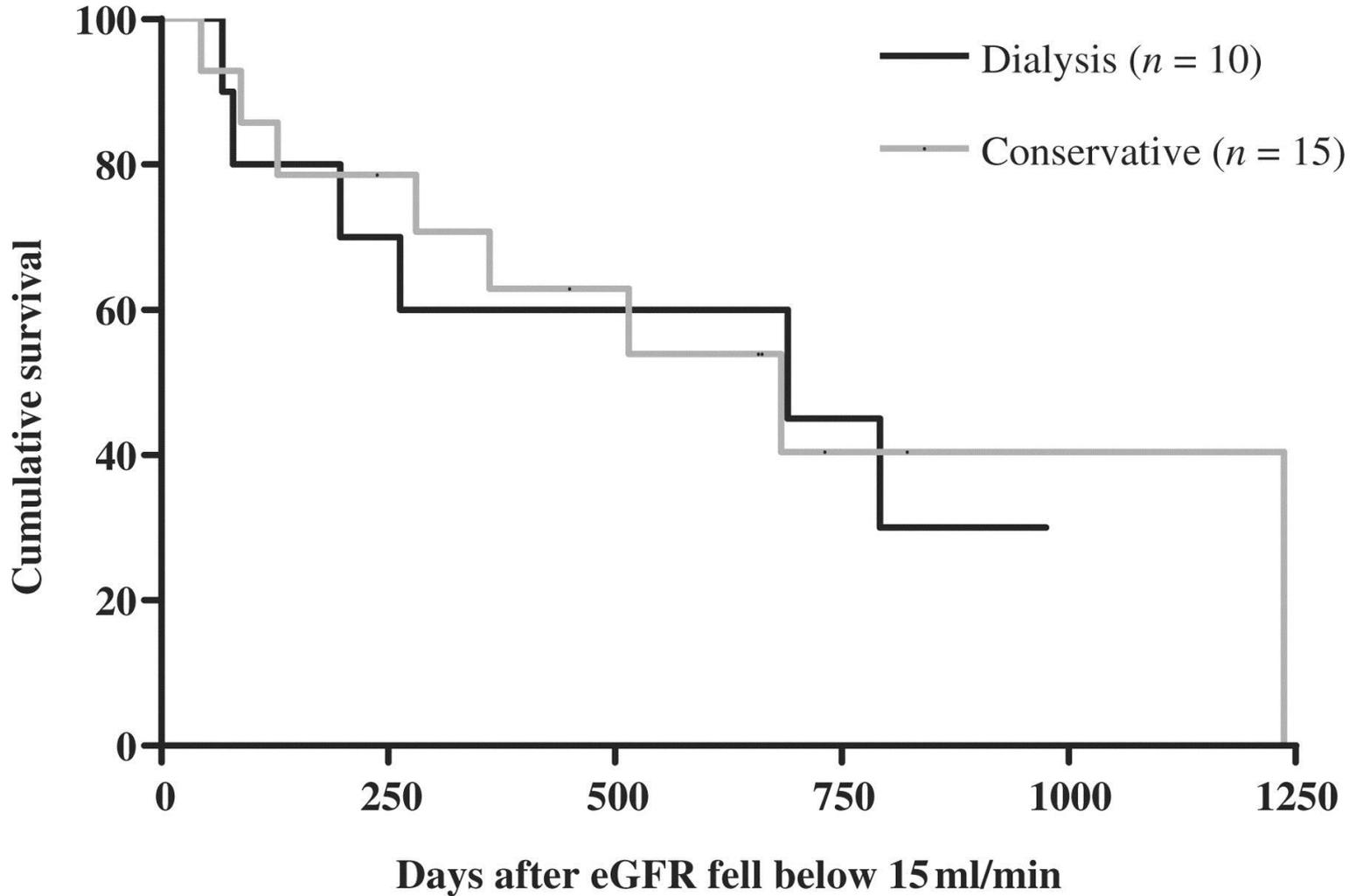
# Advanced Care Planning: Why?

- Only 13-35% pts with ESRD complete ACD
- 61% pts regret decision to start dialysis
- ~73% pts on dialysis have significant or moderate CI
- 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

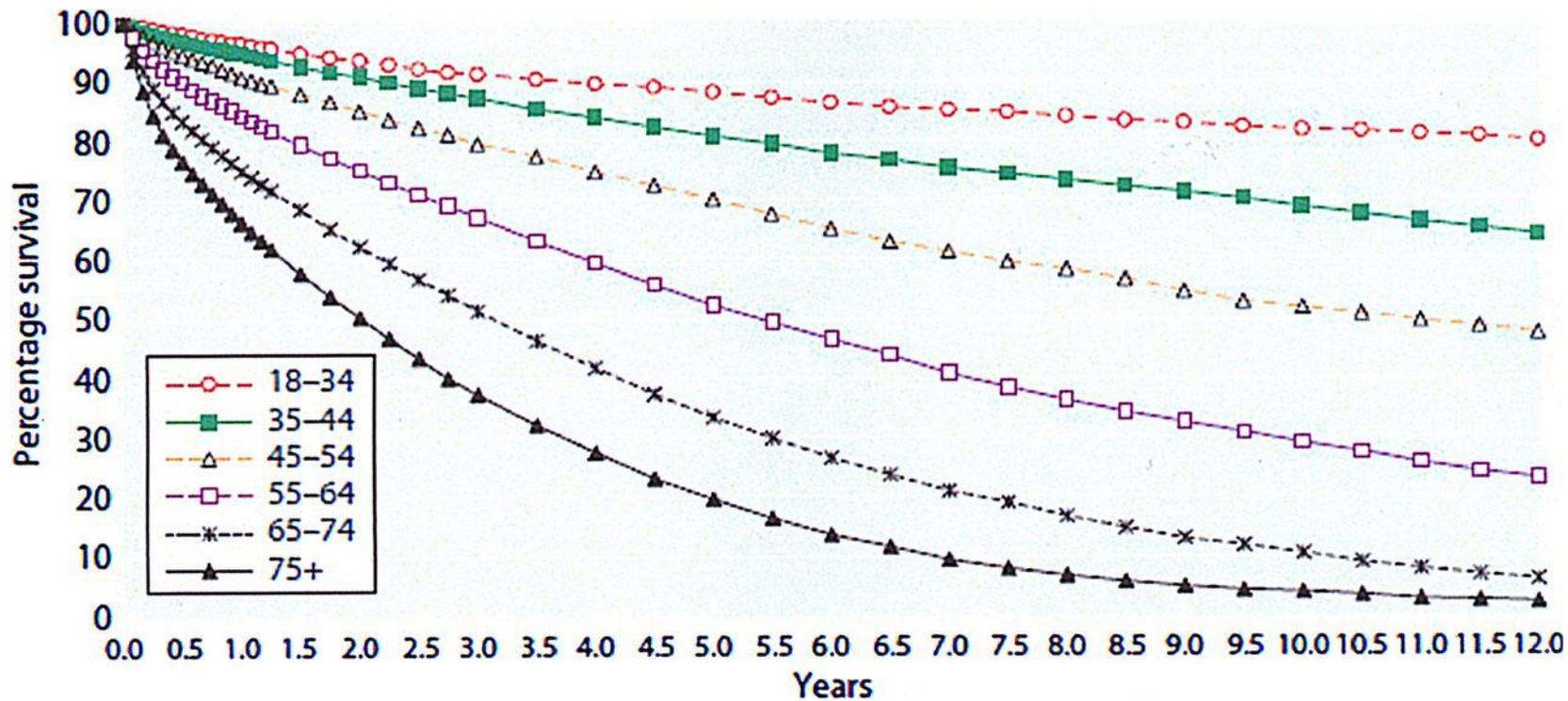
- Largest study to date by Hussain *et al* comparing outcomes in elderly pts choosing between RRT and CM
  - ▣ For pts >80 yo, with a poor performance status or high co-morbidity scores the survival advantage of RRT over CM was lost
  - ▣ Those accessing a CM pathway had greater access to palliative 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



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



# 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

# Pain:

- One of the most common symptoms in pts with ESRD yet under-recognized and under-treated
- 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

# Pain

- Has been shown to:
  - Negatively impact quality of life scores
  - Increase use health care system
  - Impair interpersonal relationships
  - Limit function
  - Increase rates of depression, anxiety, insomnia
  - Increase consideration of discontinuing dialysis

# Pain:

- Types: nociceptive, neuropathic, mixed
- Etiology multifactorial:
  - ▣ Comorbidities (DM, PVD)
  - ▣ Primary renal disease (PCKD)
  - ▣ Consequences of CRF (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
- Nortriptyline: 10-25 mg qHS
- Cannabinoids: Nabilone 0.5mg BID
  - ▣ Adjuvant benefits (nausea, appetite) but may be poorly tolerated

## 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](#)

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### IN THIS SECTION

- ▶ [Guidelines, Protocols & Clinical Tools](#)
- ▶ [Disaster Planning](#)
- ▶ [Education and Fellowships](#)
- ▶ [End of Life Resources](#)
- ▶ [Forms](#)
- ▶ [Glomerulonephritis \(GN\) Network and Registry](#)
- ▶ [Handouts](#)
- ▶ [Pharmacy & Formulary](#)
- ▶ [PROMIS Database](#)
- ▶ [Provincial Patient Education Strategy](#)
- ▶ [Research](#)
- ▶ [Vascular Access](#)

# Renal Analgesic Brochure

## Contents

### OPIOIDS

Buprenorphine (BuTrans patch®) .....	1	<a href="#">CLICK HERE</a>
Codeine Contin® or combination of Acetaminophen-Codeine (Tylenol #2, 3, Empracet-15, Empracet-30®) or combination of ASA-Codeine (282, 292®) .....	2	<a href="#">CLICK HERE</a>
Fentanyl (Duragesic Patch®) .....	3	<a href="#">CLICK HERE</a>
Hydromorphone (Dilaudid® and Hydromorph Contin®) .....	4	<a href="#">CLICK HERE</a>
Methodone .....	5	<a href="#">CLICK HERE</a>
Morphine (MOS, MS-IR, Statex, MS Contin, M-Eslon®) .....	6	<a href="#">CLICK HERE</a>
Oxycodone (Supeudol, Oxy-IR, Oxycontin®) or combination of Acetaminophen-Oxycodone (Percocet®) or ASA-Oxycodone (Percodan®) .....	7	<a href="#">CLICK HERE</a>
Tramadol (Ultram®) Tramadol CR (Zytram XL®), Tramadol ER (Ralliva® and Tridural®) or combination of Acetaminophen 325 mg and Tramadol 37.5 mg (Tramacet®) .....	8	<a href="#">CLICK HERE</a>

### NON OPIOIDS

Acetaminophen (Tylenol®) .....	9	<a href="#">CLICK HERE</a>
Non-steroidal anti-inflammatory drugs (NSAIDs) e.g. Ibuprofen (Motrin, Advil®), Diclofenac (Voltaren®), Naproxen (Naprosyn®), COX-2 inhibitors e.g. Celecoxib (Celebrex®) .....	10	<a href="#">CLICK HERE</a>

### ANTICONVULSANTS

Gabapentin (Neurontin®) .....	11	<a href="#">CLICK HERE</a>
Pregabalin (Lyrica®) .....	12	<a href="#">CLICK HERE</a>
Topiramate (Topamax®) .....	13	<a href="#">CLICK HERE</a>
Tricyclic Antidepressants e.g. Amitriptyline (Elavil®), Desipramine (Norpramin®), Nortriptyline (Aventyl®) .....	14	<a href="#">CLICK HERE</a>

### ANTIDEPRESSANTS

Duloxetine (Cymbalta®) .....	15	<a href="#">CLICK HERE</a>
Venlafaxine (Effexor XR®) .....	16	<a href="#">CLICK HERE</a>

### MUSCLE RELAXANTS

Baclofen (Lioresal®) .....	17	<a href="#">CLICK HERE</a>
Benzodiazepines (e.g. Diazepam (Valium®), Lorazepam (Ativan®), Clonazepam (Rivotril®) .....	18	<a href="#">CLICK HERE</a>
Tizanidine (Zanaflex®) .....	19	<a href="#">CLICK HERE</a>

### OTHERS

Clonidine (Catapres®) .....	20	<a href="#">CLICK HERE</a>
Nabilone (Cesamet®) .....	21	<a href="#">CLICK HERE</a>
Tetrahydrocannabinol Cannabidiol THC-CBD (Sativex®) .....	22	<a href="#">CLICK HERE</a>

### TOPICAL

Diclofenac gel (Voltaren Emulgel®) (Cesamet®) .....	23	<a href="#">CLICK HERE</a>
Capsaicin cream or ointment (Zostrix®) .....	24	<a href="#">CLICK HERE</a>
Lidocaine, Prilocaine cream or patch (EMLA®) .....	25	<a href="#">CLICK HERE</a>

### INJECTABLES

# Discontinuing Dialysis: Who?

- 2nd leading cause of death in dialysis pts ~25% (1st CVS ~50%, 3rd infection ~13%)
- Associated factors:
  - Women 25% more likely than men
  - Caucasians 2x more than Asians or African-Americans
  - Age >75
  - LTC resident
  - Presence of progressive illness (dementia, cancer)
  - Poor performance status
  - Lower quality of life scores
  - 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)

# Discontinuing Dialysis: How?

- Dyspnea: fan, opioids, ultrafiltration RARELY required
- Secretions: glycopyrrolate, scopolamine
- Pruritus: ondansetron, gabapentin, mirtazapine
  - ▣ anti-histamines lack evidence but often still used, likely work via sedating properties only
- Agitation:
  - ▣ Haloperidol, loxapine, methotrimeprazine in reduced doses
  - ▣ Benzodiazepines ONLY if intractable and severe

# Discontinuing Dialysis: How?

- Pain: same principles of opioid prescribing with consideration to limited PO route (methadone and oxycodone)
- Nausea: uremia-induced mediated by dopamine
  - ▣ Haloperidol 1st line: 0.5 – 1 mg q8hrs (max 6mg/d)
- 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
  - ▣ 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
  - ▣ 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 EARLIER AND MORE OFTEN

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