

# Pain and ESKD

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**Renal Supportive Care Master Class**  
**Oxford, UK.**  
**November 1 2019**

1

- Pain is a perfect misery, the worst of evils.

John Milton (1608-1674)

- Pain is a more terrible lord of mankind than even death itself.

Albert Schweitzer (1875-1965)

- Pain lengthens time.

Anita Hart Barter 1990.

2

# Epidemiology of pain in CKD

Haemodialysis patients – 68.9 %

Pooled mean weighted prevalence of 19 studies since 2000

Davison S, Brennan F. Pain in CKD. In : *Evidence Based Nephrology*. In Press.

3

40.4 % reported the pain as moderate to severe.

Davison S, Brennan F. Pain in CKD. In : *Evidence Based Nephrology*. In Press.

4

Data on conservatively managed patients  
is more limited  
but shows similar prevalence and severity  
figures.

Murtagh FEM et al. A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis.  
*J Pall Med* (2007) 10;6:1266-1276.  
Brennan FP. et al. Symptoms in patients with CKD managed without dialysis. *Progress in Palliative Care* 2015;  
23 (5): 267-273.

5

Impact on function and QOL

6

Data from 9 studies representing approximately 2100 HD patients found that pain was associated with lower HR-QOL.

Table 2 in Davison S, Koncicki H, Brennan F. Pain in Chronic Kidney Disease : A Scoping Review. *Seminars in Dialysis* 2014; 27(2): 188-204.

7

## Impact on QOL

Davison (2002)

69 dialysis patients

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

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51 % stated that pain caused them “extreme suffering”

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41 % stated that pain caused them to consider  
ceasing Dialysis

10

Independently associated with:

- Missed or shortened dialysis sessions
- A+E presentations
- Hospitalisations.

Weisbord SD et al. *Clin J Am Soc Nephrol* 2014; 9(9): 1594-1602.

11

Positive correlation with depression

Davison S, Jhangri GS. *J Pain Symptom Management* 2005; 30(5): 465-473

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## Causes of Pain

ESRD  
and its treatment

Co-morbidities

13

### 1. Pain related to the disease:

- Polycystic Kidney Disease
- Renal Bone Disease
- Amyloid – including Carpal Tunnel Syndrome
- Calciphylaxis

14

## 2. Pain secondary to treatment :

- PD pts with recurrent abdominal pain
- AV Fistulae > 'Steal syndrome'
- Cramps
- Intradialytic headaches

15

## 3. Pain related to co-morbidities

- OA
- Diabetic peripheral neuropathy
- PVD / IHD

16



## Pain etiquette

- ENQUIRE REGULARLY
- RESPOND COMPASSIONATELY
- TREAT COMPETENTLY
- REFER WISELY

17

## Pain assessment

18

# I-POS –S (Renal)


19

**IPOS-Renal Patient Version**

Patient name : .....

Date (dd/mm/yyyy) : .....

Patient number : ..... (for staff use)

  
www.pos-pal.org

**Q1. What have been your main problems or concerns over the past week??**

1. ....

2. ....

3. ....

**Q2. Below is a list of symptoms, which you may or may not have experienced. For each symptom, please tick the box that best describes how it has affected you over the past week?**

	Not at all	Slightly	Moderately	Severely	Overwhelmingly
Pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness or lack of energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea (feeling like you are going to be sick)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vomiting (being sick)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Poor appetite	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sore or dry mouth	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Drowsiness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Poor mobility	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Itching	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Difficulty Sleeping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Restless legs or difficulty keeping legs still	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Changes in skin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diarrhoea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Please list any other symptoms not mentioned above, and tick the box to show how they have affected you over the past week?**

1. ....

2. ....

3. ....

**Over the past week:**

	Not at all	Occasionally	Sometimes	Most of the time	Always
Q3. Have you been feeling anxious or worried about your illness or treatment?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q4. Have any of your family or friends been anxious or worried about you?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q5. Have you been feeling depressed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Always	Most of the time	Sometimes	Occasionally	Not at all
Q6. Have you felt at peace?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q7. Have you been able to share how you are feeling with your family or friends as much as you wanted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q8. Have you had as much information as you wanted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Problems addressed/ No problems	Problems mostly addressed	Problems partly addressed	Problems hardly addressed	Problems not addressed
Q9. Have any practical problems resulting from your illness been addressed? (such as financial or personal)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	None at all	Up to half a day wasted	More than half a day wasted		
Q10. How much time do you feel has been wasted on appointments relating to your healthcare, e.g. waiting around for transport or repeating tests	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
	On my own	With help from a friend or relative	With help from a member of staff		
Q11. How did you complete this questionnaire?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		

*If you are worried about any of the issues raised on this questionnaire then please speak to your doctor or nurse*

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## Modified Edmonton Symptom Assessment System (mESAS)

11x VAS

21

Brief pain inventory

22

## **Pain management in patients with CKD**

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The traditional approach to the pharmacological management of pain has been to use the WHO Analgesic Ladder.

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Certainly, the WHO Ladder  
has been validated in the context of ESKD  
and it remains a very useful construct.

Barakovsky AS et al. *J Am Soc Nephrol* 2006; 3198-3203

25

Is an approach based on the WHO Analgesic Ladder  
the most appropriate approach  
in the specific context of CKD ?

26

Towards a strategic approach  
to pain management  
in patients with CKD

27

That approach is based on three considerations.

28

1. There are few studies examining pain management in the specific context of CKD

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2. There are international evidence based guidelines and consensus statements on pain management of specific pain syndromes for the whole population.

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- Osteoarthritis
- Painful diabetic peripheral neuropathy
- Post herpetic neuralgia
- Cancer pain

31

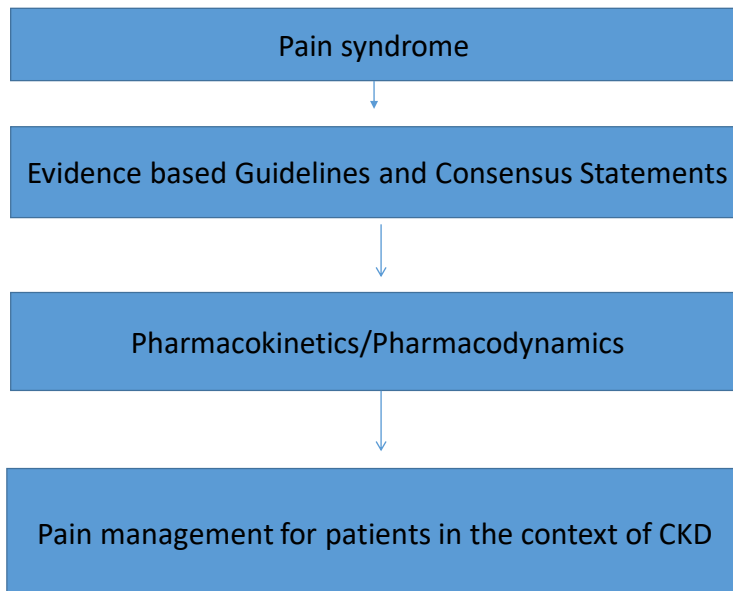
3. There is an increasing, although not complete, understanding of the pharmacology of analgesic medications in the cont.ext of CKD and their dialysability

32



These recommendations could be filtered through the known pharmacology of medications in the context CKD and their dialysability.

33

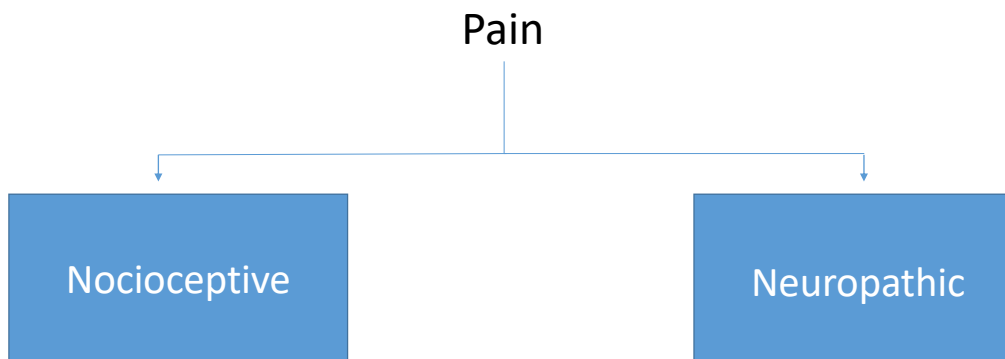


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A similar, but alternative approach...

Davison SN. *CJASN* 2019; 14: 917-931.

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36

An example...

## Painful diabetic peripheral neuropathy

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A 68 year old woman

- Type II DM for 12 years.
- ESKD – Diabetic nephropathy. On dialysis.
- Worsening moderate to severe painful diabetic peripheral neuropathy.

38

1. Currently there are no evidence-based or consensus guidelines on the management of painful DPN in patients with CKD.

39

“Clinical evidence regarding the effects of [analgesic agents] to treat DPN in patients on dialysis therapy and those with CKD Stage 4-5 is virtually non-existent.”

Pop- Busui R et al. The Management of Diabetic Neuropathy in CKD. *Am J Kid Dis* 2010; 55(2): 365-385.

40

2. There is a significant body of literature on the management of painful DPN for the general population.

That literature includes several international evidence based guidelines.

41

***Evidence-based guideline : Treatment of painful diabetic neuropathy.  
Report of the American Association of Neurology et al.***

Bril V et al. *Neurology* 2011; 76: 1758-1765.

42

## Level A Evidence - Pregabalin

43

### Novel combination creams

1. Capsaicin 0.025 % and  
Menthol cream 3 %
2. Lignocaine 4%  
Prilocaine 1.5 %  
Tetracaine 4%

44

## **Cramps**

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Prevalence: 33- 78 % in HD

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Associated with premature cessation of dialysis sessions  
→ inadequate dialysis.

47

Causes:

1. Fluid-electrolyte shifts during dialysis.
2. Muscle fatigue → inhibits the mechanism that blocks muscle contraction.

48



## Management:

1. Magnesium -- Crampeze 1-2 bd
2. Quinine -- Tonic water
3. Stimulation of the oropharyngeal reflex that inhibits  $\alpha$ - motor neurons leading to muscle relaxation...Pickle juice / vinegar / yellow mustard / ginger.

49

## Osteoarthritis

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Osteoarthritis Research Society International  
(OARSI) Guidelines 2019

51

**Analgesics in Chronic Kidney Disease**

52

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

53

Paracetamol

54

No dose adjustment = 1g qid

55

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

Davison S, Ferro CJ. Management of Pain in CKD. *Progress in Palliative Care* 2009; 17: 186-195.

56

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Safe to use

57

NSAIDs

58

If on a conservative, non-dialysis pathway –  
do not use.

59

If on dialysis - Consult with the nephrologist.

May use with caution.

Consider increased risks, especially in patients over 75 years,  
of :

- (a) upper GIT bleeding;
- (b) sodium/water retention

60

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

As above.

Avoid in transplant patients

Topical preparations may be preferred over orals.

61

Tramadol

62



63

General concerns regarding Tramadol.

64



## Need for dose adjustment

65

If on dialysis or  
a Conservative pathway eGFR < 15

Tramadol 50mg bd (maximum)

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If on Conservative pathway eGFR 15-30

Commence 50mg bd

Maximum 100mg bd

67

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

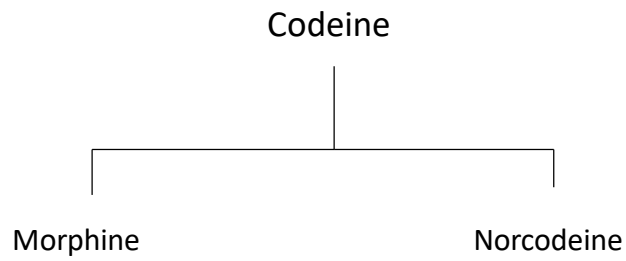
Avoid

68

## Codeine

69

Metabolised in Liver



70

Reports of :  
profound hypotension  
CNS and  
Respiratory depression

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“Not recommended in CKD.”

Davison S et al. *Seminars in Dialysis* 2014; 27(2): 188-204

72

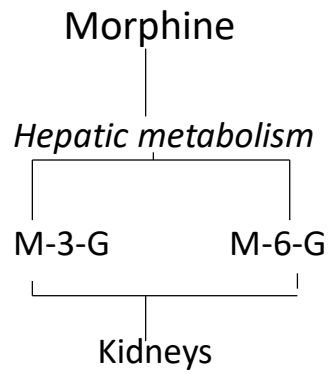
Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Avoid

73

Morphine

74



75

Morphine is not recommended in CKD

Davison S et al. *Seminars in Dialysis* 2014; 27(2): 188-204

76

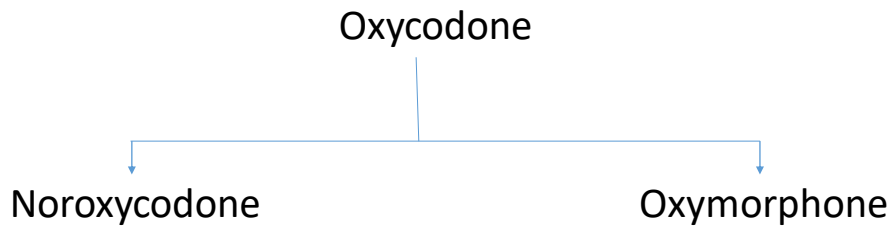
Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Avoid

77

Oxycodone

78



79

- Metabolised by liver
- Active metabolites are eliminated mainly by hepatic metabolism. Less than 10 % parent drug excrete renally.
- Single dose study showed prolongation of oxycodone and its metabolites.
- Dialysability – very limited

80



“Overall consensus is that oxycodone is reasonably safe to use in CKD if monitored carefully.”

Davison S et al. *Seminars in Dialysis* 2014; 27(2): 188-204

81

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Commence with a small dose (1-2 mg bd) and titrate up to max 10mg/24hours. Once pain stable consider switching to Fentanyl or Buprenorphine patches.

82

## Fentanyl

83

- Metabolised in Liver
- Inactive metabolites
- Fentanyl is not dialysed.

84

Fentanyl is safe to use at standard doses

- should monitor carefully.
- do not use in opioid naïve patients

Davison S et al. *Seminars in Dialysis* 2014; 27(2): 188-204

85

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

As above.

86

## Alfentanil

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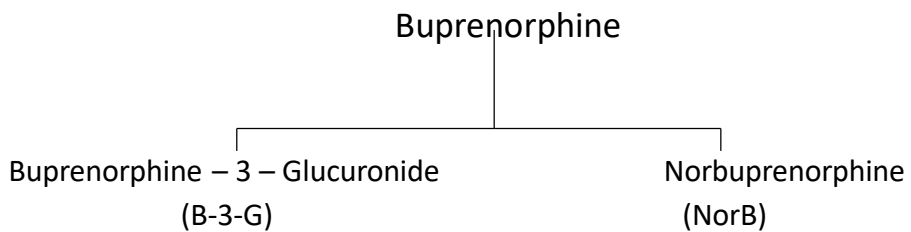
Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Opioid of choice in syringe driver use  
in patients with eGFR < 30 ml/min.

88

## Buprenorphine

89



Both metabolites are mostly fecally excreted.

B-3-G is inactive ; NorB has minor analgesic quality.

Not dialysed

90

“Buprenorphine may be given in standard doses to patients with CKD. Generally considered safe for use in CKD if monitored carefully.”

Davison S et al. *Seminars in Dialysis* 2014; 27(2): 188-204

91

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

Start with smallest dose (5mg)

92

## Methadone

93

- Metabolised in liver
- Mainly fecal excretion.
- Not dialysed
- Safe to use, but requires skill in dosing regimen – specialist use.

94

Oxford University Hospital  
Guideline on the use of analgesia in CKD Stage 4 and 5.

As above.

95

The experience of the Renal Supportive Care Service, St  
George Hospital in pain management.

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Between March 2009 and October 2019  
596 patients completed a symptom survey at  
their first  
Renal Supportive Care service visit

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Of those 424 patients

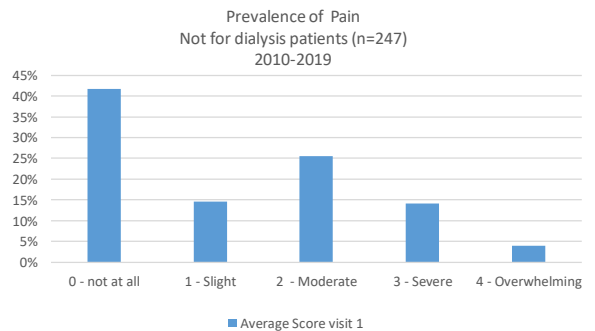
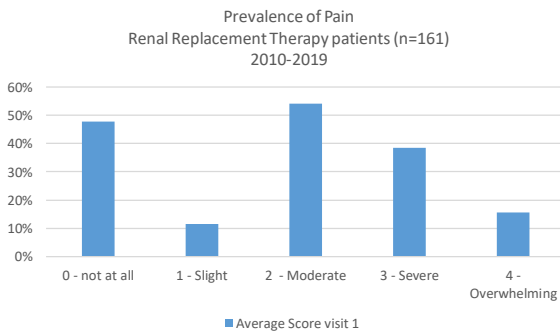
- 35% dialysis patients
- 57% conservatively managed patients
- 2% transplant patients
- 5% Undecided

98

Following those patients  
who had at least 3 clinic visits.

99

Pain Scores reported at first Clinic



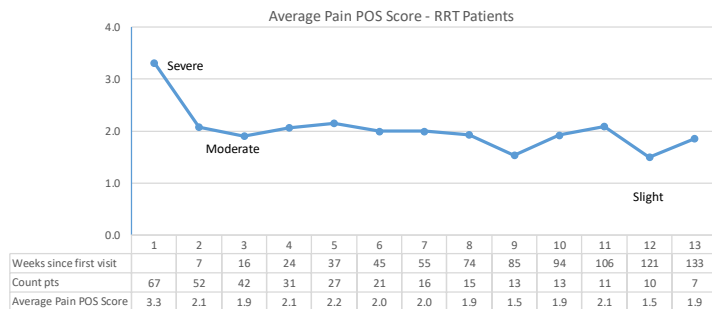
100

Isolating those who presented at first clinic visit with pain that was reported as “severe” to “overwhelming”...  
what happened over time ?

101

#### Pain Score- patterns - (RRT) patients

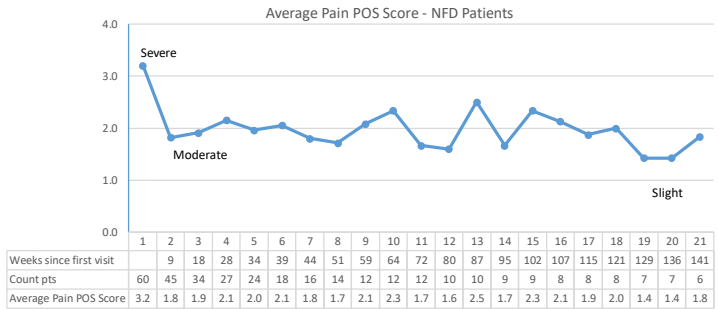
- for patients with more than one visit
- for patients that scored 3-4 for RLS on their first visit (**Severe to overwhelming**)
- for clinic visits where there were 5 or more patients



102

**Pain Score- patterns - Conservative (NFD)**

- for patients with more than one visit
- for patients that scored 3-4 for RLS on their first visit (**Severe to overwhelming**)
- for clinic visits where there were 5 or more patients



103

## Role of Pain Services

104

## **Pain management in patients with ESKD**

A one day Symposium - 2016

St George Hospital, Sydney

105

1. Davison SN, Koncicki H, Brennan F. Pain in CKD : A Scoping Review. *Seminars in Dialysis* 2014; 27(2): 188-204.

2. Davison SN. Clinical Pharmacology Considerations in Pain Management with Advanced Kidney Failure. *CJASN* 2019; 14: 917-931.

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