CLINICAL GUIDELINE TITLE	**Pain management for adult inpatients with acute or chronic pain**

1) SUMMARY

This guideline covers the management of acute and chronic pain for adult patients.

It does NOT cover the management of paediatric pain, cancer pain associated with palliation or end of life care. Please see separate guidelines. Other pain guidelines exist for patient-controlled analgesia, epidural analgesia, low-dose ketamine, local anaesthetic infusions and entonox administration.

There are separate pain guidelines for patients with renal impairment.

The following document has been used to inform the evidence in this guideline:
Faculty of Pain Medicine of the Royal College of Anaesthetists Core Standards for Pain Management Services in the UK (2015) [1]

2) INTRODUCTION

This guideline has been developed to ensure that we **'get on top of the patient's pain**' and that unnecessary pain and suffering do not occur. Our aim is that patients' report having no more than mild pain whilst in hospital. Acute pain should be managed promptly, safely and effectively in order that the development of persistent, chronic pain is prevented and that function is restored or optimised.

Reduction of the patient's pain should be achieved by continued assessment, logical prescribing and timely administration of analgesia.

The guideline will assume that prescribers will use a drug's summary of product characteristics (SPC) and the British National Formulary (BNF) to inform decisions made with individual patients (this includes obtaining information on special warnings, precautions for use, contraindications and adverse effects of pharmacological treatments).

3) DEFINITIONS

Pain – pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [2].

Acute pain - pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease [4].

Chronic pain – commonly persists beyond the time of healing of an injury and frequently there may not be any clearly identifiable cause [4]

Persistent post-surgical pain – pain persisting at least three months after surgery (various authors propose thresholds of duration from two to six months). Pain not present before surgery or that has different characteristics or increased intensity from preoperative pain. Pain is localized to the surgical site or a referred area. Other possible causes of the pain are excluded (e.g., cancer recurrence, infection). [5]

Nociceptive pain – pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors [2]

Neuropathic pain - pain caused by a lesion or disease of the somatosensory nervous system [2].

Allodynia - pain due to a stimulus that does not normally provoke pain [2].

Hyperalgesia - increased pain from a stimulus that normally provokes pain [2].

Pain assessment – a systematic, clinical process of describing the magnitude and characteristics of the patient's pain.

Analgesia – absence of pain in response to stimulation which would normally be painful [43].

Analgesic – a medicine that relieve pain.

4) SCOPE

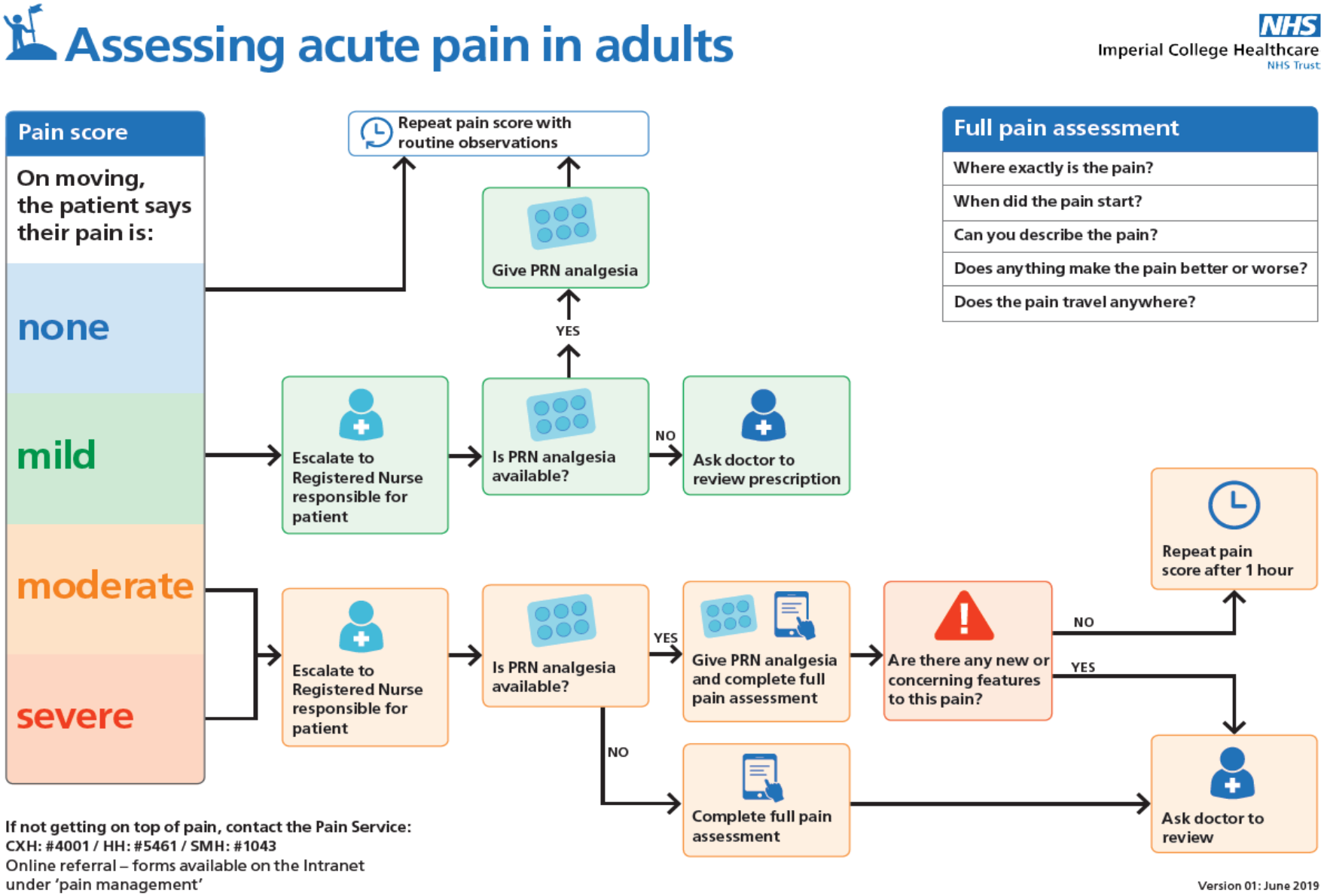
This guideline has been produced through the work of the multidisciplinary Pain Task & Finish Group which met from September 2018 to May 2019. It is designed to help the multidisciplinary team to assess the patient's pain and to provide analgesia relevant to the degree of pain that the patient is experiencing.

It consists of two parts and section 1 contains:

- A flow diagram entitled 'Assessing acute pain in adults'.
- A guide to logical prescribing entitled 'Getting on top of pain: acute pain in adults (Pain Mountain)
- A document containing frequently asked questions entitled 'Pain Myth Buster'.
- Information on how to contact the pain service.

Section 2 consists of more in depth information regarding the medications used to manage pain.

5) FULL GUIDELINE
5.1 Section 1



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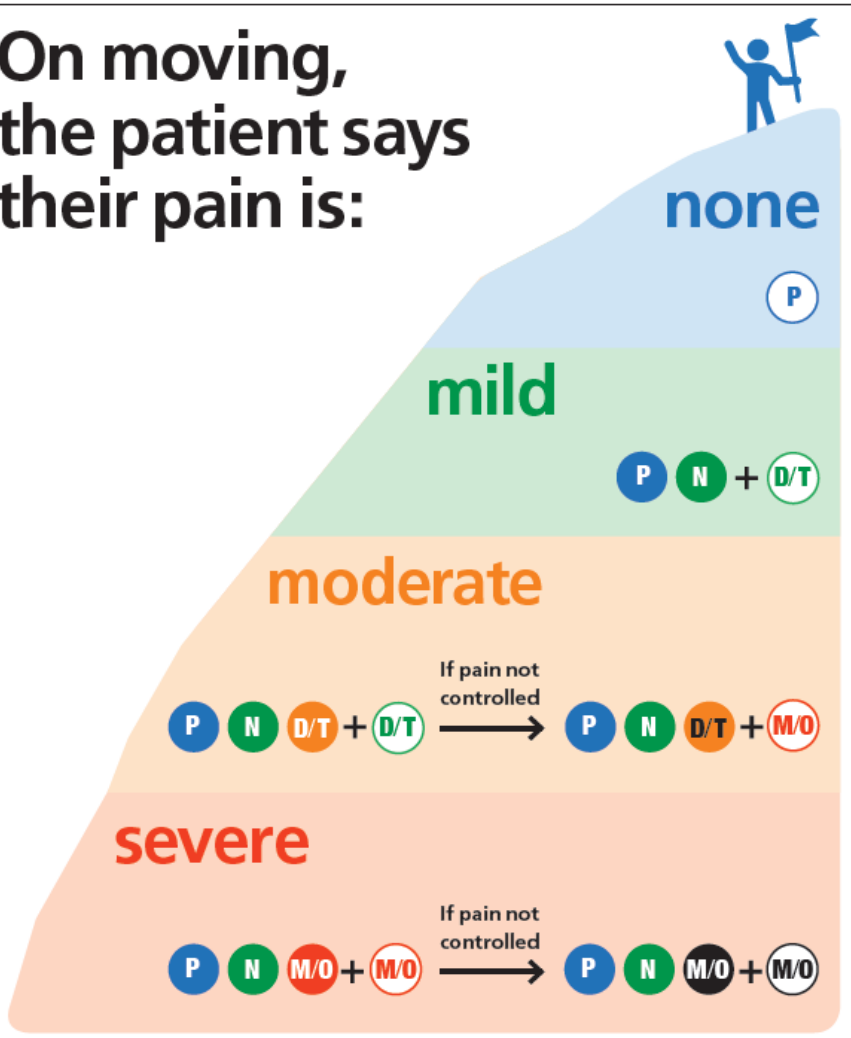

P — PRN **Paracetamol** *1g PO 6°*

P — REGULAR **Paracetamol** *1g PO 6°*

N — REGULAR **+/– NSAID PO**
Ibuprofen *400mg 8°* **or**
or Naproxen *250mg 6–8°*
CAUTION IN THE ELDERLY

D/T — PRN **Dihydrocodeine** *30mg PO 6°* **or** **Tramadol** *50mg PO 6°*

D/T — REGULAR **Dihydrocodeine** *30mg PO 6°* **or** **Tramadol** *50mg PO 6°*

D/T — REGULAR **Dihydrocodeine** *60mg PO 6°* **or** **Tramadol** *100mg PO 6°*

M/O — PRN **Morphine** *10mg PO 4°* **or** **Oxycodone IR** *5mg PO 4°*

M/O — REGULAR **Morphine** *10mg PO 4°* **or** **Oxycodone IR** *5mg PO 4°*

M/O — PRN **Morphine** *20mg PO 4°* **or** **Oxycodone IR** *10mg PO 4°*

M/O — REGULAR **Morphine** *20mg PO 4°* **or** **Oxycodone IR** *10mg PO 4°*

If not getting on top of pain, contact the pain service
CXH: #4001 / HH: #5461 / SMH: #1043

Elderly patients
Start doses low, go slow!

Renal impairment
→ *local guidelines*

Sickle cell disease
→ *local guidelines*

Maternity
→ *local guidelines*

Trauma
→ *local guidelines*

Epidural/ PCA
→ *local guidelines*

Severe liver impairment
→ *pain guideline*

Neuropathic pain
→ *pain guideline*

DON'T FORGET PRN CO-PRESCRIPTIONS

Naloxone *100–200microgram (1.5–3microgram/kg)* IV
If respiratory rate is <10
Repeat if needed at 2 minute intervals

Antiemetic
Ondansetron *8mg PO 8°* **or**
Cyclizine *50mg PO 8°*

Laxative
Senna *15mg ON* **and/or**
Docusate *200mg 12°*

Refer to 'Pain management for adult inpatients with acute or chronic pain' guideline and additional resources e.g. Summaries of Product Characteristics (SPCs) for a full list of cautions, contraindications and side-effects when making a clinical decision.

Version 01: June 2019

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BASICS OF OPIOID PRESCRIBING	
Is it okay to prescribe two different weak opioids together?	It's preferable to select either dihydrocodeine or tramadol.
Is it okay to prescribe a weak opioid and a strong opioid together?	Yes In most situations one should be a regular prescription and the other should be PRN.
Is it okay to prescribe two different strong opioids together?	In general, you should select either morphine or oxycodone.
Is it okay to prescribe a short-acting breakthrough opioid with a regular fentanyl patch?	Yes Prescribe either morphine or oxycodone as a 4-hourly PRN dose
How do I convert IV/SC/transdermal opioids to oral dose equivalents?	Use conversion chart **(LINK)** If there is any uncertainty please contact the pain team
What is the preferred route of administration for an opioid?	Prescribe orally unless contraindicated as effects are longer lasting.
Is there a maximum opioid dose?	No Acute pain: titrate to effect and side effects. Chronic pain: up to 120mg oral morphine or equivalent per day.
Should I prescribe long-acting opioids for acute pain?	It is preferable to use short-acting opioids to titrate to best effect.
If the patient has a regular opioid prescription, when can I give a PRN opioid dose?	Treat regular and PRN opioids as two separate prescriptions. PRN opioids can be given as required but ensure 4-hourly intervals between PRN doses.
Should I prescribe anti-emetics and laxatives PRN when prescribing opioids?	Yes Refer to local protocols **(LINK TO PAIN GUIDELINE SECTION ON ANTIEMETICS)**
How can I ensure an admitted patient is not receiving opioids via a transdermal patch?	Review regular analgesia and check the body for a transdermal patch.

PRINCIPLES OF ANALGESIC PRESCRIBING	
What analgesia should I prescribe if a patient has renal impairment?	Refer to the renal pain guideline **(LINK)**
Who should review and prescribe analgesia when a patient is transferred to another ward area?	Junior doctors should review analgesia when the patient arrives in a new area.
How should I titrate analgesia in someone with moderate or severe pain?	Prescribe PRN immediate release 4-hourly opioids and review regular analgesia dose. **(LINK TO PAIN MOUNTAIN)**
How often should I review analgesia prescriptions?	Review on the daily ward round and if the patient's situation changes.
Should I continue the patient's normal analgesia when they are admitted?	Yes Review the doses if the patient is sedated or clinically unwell e.g. renal impairment. Take into account reason for admission e.g. is the patient having a procedure with specific analgesic requirements?
When should I administer regular analgesia?	No later than 15 minutes from when it is due
Should I ask the patient if they would like their regular prescribed analgesia?	Give patients their regular analgesia as this is what is keeping them comfortable. Review prescription if the patient is refusing doses or appears drowsy.
If the patient is going to be moved/have physio/ a procedure do I need to give additional analgesia?	Yes Give immediate release PRN analgesia 30 minutes beforehand.

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PCAs (patient controlled analgesia) AND EPIDURALS	
Is it okay for me to prescribe a PCA?	PCAs should only be prescribed under supervision from the pain team.
Is it okay for me to give other opioids with a PCA or a epidural containing fentanyl?	No Only paracetamol or NSAIDs (beware of contraindications) can be prescribed alongside a PCA.
Is it okay for me to give anti-neuropathic drugs e.g. gabapentin, pregabalin, amitriptyline with PCAs, epidurals, or other analgesics?	Yes
Is it okay for me to prescribe opioids with a plain local anaesthetic infusion or plain local anaesthetic epidural infusion?	Yes

LOCAL ANAESTHESIA	
What do I prescribe when giving local anaesthetic for a painful procedure?	The maximum dose of lidocaine is 3mg/kg The maximum dose of lidocaine with adrenaline is 7mg/kg Deliver the minimum volume of local anaesthetic necessary for analgesic effect to avoid causing excessive and painful tissue distension.
Should I prescribe lidocaine patches for pain?	No The use of lidocaine patches is restricted to specialist practitioners.

OPIOID OVERDOSE	
What do I do for an acute opioid overdose?	100-200 micrograms of naloxone every 2-3 minutes until respiratory depression reversed. Take care with patients on long term opioids as they are at risk of acute withdrawal syndrome. **(LINK TO NPSA GUIDANCE)**
Should I prescribe naloxone?	Yes PRN naloxone should be prescribed if prescribing strong opioids.
What do I prescribe if a patient takes methadone? Refer to opioid dependency management guidelines **(LINK)**	Verify a regular opioid substitution prescription with a GP, community prescriber, or the community addiction service. If there are no concerns and no clinical contraindications prescribe the opioid substitute. If any of the above conditions are not met then do a urine toxicology screen – if this is negative then do not prescribe an opioid substitute but continue to monitor for signs of withdrawal. If the urine toxicology screen is positive and they show signs of withdrawal but you cannot confirm their regular prescription then prescribe up to 30mg in the first 24 hours of admission (usually given in 5-10mg PRN methadone doses).

KETAMINE	
Do I need to wean ketamine before discontinuing?	No
Can ketamine be given alongside other analgesics?	Yes Ketamine can be prescribed alongside PCAs, epidurals, local anaesthetic infusions, opioids and anti-neuropathic agents. Ketamine is opioid sparing.

Contacting the pain service

If you are having difficulty getting on top of the patient's pain, please contact the pain service on the bleep numbers given below during normal working hours (Monday to Friday). Outside of these hours the site practitioners should be contacted first for any problems related to epidural infusions or patient-controlled analgesia (PCA). The on-call anaesthetist should be contacted for all other problems.

The clinical nurse specialists will routinely review all patients with epidural infusions and most patients with PCA. For acute and chronic inpatient referrals, please use our Inpatient Pain Service Referral Form, which can be downloaded from the pain management site on the intranet. (This can be found by clicking A-Z on the home page). Completed forms must be emailed to the pain service's email address: imperial.inpatient.painservice@nhs.net

The pain service should be contacted if the:

- patient has moderate or severe pain at rest or moving and the analgesic regimen outlined in the pain mountain is not working.
- patient has uncontrolled acute neuropathic pain +/- allodynia and hyperalgesia.
- patient has an opioid tolerance
- patient has acute on chronic pain
- patient has drug dependency syndrome

Hospital	Bleep	Contact	Hours
CXH	4001	Nurse specialist	09:00 – 17:00
	8111	On-call anaesthetist	17:00 – 20:30
	1438	Site practitioner	20:30 – 07:00
HH	5461	Nurse specialist	09:00 – 17:00
	9313	On-call anaesthetist	17:00 – 20:30
	9335	Site practitioner	20:30 – 07:00
SMH	1043	Nurse specialist	08:00 – 17:00
	1213	On-call anaesthetist	17:00 – 20:30
	1065	Site practitioner	20:30 – 07:00

5.2 Section 2

5.2.1 The assessment of pain

Pain can only be scored by the patient [6]

Our aim is that patients should have no more than mild pain

Refer to the pain assessment algorithm in section 1.

All patients should be asked the same question when their routine observations are completed and recorded in their electronic record(s):

'On moving would you say your pain is none, mild, moderate or severe?'

Some patients may be unable to complete a verbal pain rating scale due to being unconscious or because they have dementia. Under these circumstances specialist pain assessment scales can be used. The Critical Care Pain Observation Tool (CPOT) is used in critical care for unconscious patients [7]. The Pain Assessment in Advanced Dementia (PAINAD) scale for patients with dementia [8].

Patients who report moderate or severe pain should have a full pain assessment completed. Patients should be asked the following questions:

- Where exactly is the pain?
- When did the pain start?
- Can you describe the pain (what does the pain feel like: sharp, dull, burning etc.)?
- Does anything make the pain better or worse?
- Does the pain travel anywhere?

Whilst nociceptive pain, which is usually described as sharp, dull or throbbing pain predominates in the acute setting, neuropathic pain can also be present. This type of pain does not normally respond to opioids and needs to be treated with specific medications (see section 5.2.8). Features in the pain history that may suggest a diagnosis of neuropathic pain include [4]:

- Patients at a high risk of nerve injury, due to the type of surgery or disease process
- Describing the pain as burning, shooting or the feeling of ants crawling under the skin
- The presence of abnormal sensations, such as allodynia (pain caused by light touch) or hyperalgesia (increased response to a painful stimulus).
- Pain that is spontaneous or paroxysmal; it comes on without there being any apparent cause, such as movement.

Please remember that new or acute pain is often a warning sign and should be fully investigated.

5.2.2 Medications given for mild pain

Paracetamol

Paracetamol is an analgesic, anti-pyretic and anti-inflammatory medication that can be prescribed for patients with mild pain. It may be given in conjunction with non-steroidal anti-inflammatory drugs (NSAIDs). The combination of paracetamol and an NSAID is more effective than either paracetamol or NSAID alone [9]. It can also be given with other medications on the pain mountain. Combinations of paracetamol with opioids such as dihydrocodeine, tramadol and patient-controlled analgesia (PCA), show increased efficacy [6].

The mechanism of action of paracetamol remains unclear. It is absorbed rapidly from the small intestine after oral administration with a bioavailability of between 63 and 89% [4]. Early postoperative oral administration can result in plasma concentrations that can vary enormously after the same dose and may remain sub therapeutic in some patients [10].

Paracetamol	
Normal oral dose	1 gram, every 4 - 6 hours
Maximum oral daily dose	4 grams
Types of preparations	Tablet/Caplet Soluble tablet Oral suspension Suppository Intravenous infusion
Oral NNT Paracetamol 500mg: 3.5 (2.7 - 4.8) [11]. Oral NNT Paracetamol 1g: 3.6 (3.2 – 4.1) [11].	

The British National Formulary (BNF) recommends that dose requirements should be based on weight and should be prescribed with a minimum of four hours between each administration [12]. Extra care should be taken with adults weighing less than 50 kgs and those patients with chronic alcohol consumption, chronic dehydration, chronic malnutrition and hepatocellular insufficiency [12]. Please see the altered dose intravenous (IV) dosing requirements for adults weighing less than 50kgs below.

Intravenous Paracetamol		
	Adults weighing>33 kg to 50 kg	**Adults weighing 50 kg and above**
IV Dose per administration	15mg/kg every 4 – 6 hours	1 g every 4 - 6 hours
Max daily dose	60mg/kg, not exceeding 3 grams	4 grams

Adverse effects with paracetamol are rare. The proportion of participants reporting an adverse event with paracetamol ranged between 7% and 18%, and with placebo between 6% and 16% [13].

Liver damage and less frequently renal damage can occur following overdose [12]. Please see BNF for dosing advice in patients with risk factors for hepatotoxicity.

Non-steroidal anti-inflammatory drugs (NSAIDs)
The term NSAID refers to both non-selective and selective NSAIDs. NSAIDs have a spectrum of analgesic, anti-inflammatory and anti-pyretic effects and are effective analgesics in a variety of pain states. They can be prescribed for people with mild to moderate pain, but their application may be limited because of adverse effects and contraindications [4].

NSAIDs inhibit the release of prostaglandins in peripheral tissues by inhibiting the actions of cyclooxygenase enzymes I and II (COX-1 and COX-2). The selective coxibs inhibit the release of COX – 2 enzyme.

The National Institute for Clinical Excellence (NICE) recommends that NSAIDs should not be given to patients with [14]:

- Hypersensitivity/severe allergic reaction to an NSAID (including aspirin).
- Asthma (NSAIDs can cause a severe exacerbation in some asthmatics).
- Severe heart failure.
- Liver fibrosis, cirrhosis, or acute liver failure.
- Severe hepatic impairment (e.g. liver enzyme levels more than three times the upper limit of the normal range; serum albumin less than 25g/L).
- Gastrointestinal bleeding, symptomatic peptic ulcer, or gastrointestinal perforation or obstruction.
- Coxibs and diclofenac are also contraindicated in people with ischaemic heart disease, cerebrovascular disease, peripheral arterial disease, mild, moderate, or severe heart failure.

Where possible NSAIDs should be avoided in the following situations [14]:

- Renal failure, with estimated glomerular filtration rate (eGFR) less than 30–15 mL/min/1.73 m2, or creatinine clearance less than 30–20 mL/min.
- Dehydration - can provoke acute renal failure if given to someone who is dehydrated, especially if they have diabetes.

NSAIDs should be used with caution in the following situations [14]

- The elderly — increased risk of serious adverse effects, such as gastrointestinal bleeding and perforation, which may be fatal.
- People with a history of peptic ulceration, or those at high risk of gastrointestinal adverse effects.
- People with inflammatory bowel disease — may cause exacerbations of ulcerative colitis or Crohn's disease.
- People with hepatitis or cholestasis — increased risk of gastrointestinal bleeding and fluid retention.
- People with hypertension.
- Women trying to conceive – impair female fertility

There are long-standing and well-recognised renal safety concerns with all NSAIDs. Patients with conditions such as hypovolaemia, congestive heart failure, liver cirrhosis, or multiple myeloma are at particular risk. Contributing risk factors include the concurrent administration of medicines such as angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptors antagonists, and diuretics [14].

There is also substantial evidence confirming an increased risk of cardiovascular events with many NSAIDs, including COX-2 inhibitors and some traditional NSAIDs such as diclofenac and high-dose ibuprofen. All NSAIDs have the propensity to cause fluid retention and to aggravate hypertension, although for certain agents this effect appears to

be larger (etoricoxib). Increasingly a pro-thrombotic risk (including myocardial infarction and stroke) has been identified with COX-II selective agents in long-term studies and there does seem to be some evidence for a dose effect [14].

Current prescribing advice includes [14]:

- The decision to prescribe an NSAID should be based on an assessment of a person's individual risk factors, including any history of cardiovascular and gastrointestinal illness.
- Naproxen (1,000 mg a day or less) and low-dose ibuprofen (1,200 mg a day or less) are considered to have the most favourable thrombotic cardiovascular safety profiles of all NSAIDs.
- The lowest effective dose should be used for the shortest duration necessary to control symptoms. A person's need for symptomatic relief and response to treatment should be re-evaluated periodically.

Oral diclofenac is no longer recommended by the Trust and is not included in the North West London integrated formulary. The preferred alternative is Ibuprofen as first line choice of NSAID, with naproxen as second line preference. Diclofenac suppositories and intravenous preparations are still available to use when there is no suitable alternative and it is deemed clinically necessary.

Ibuprofen	
Normal oral dose	200 – 400 mg, 8 hourly
Maximum daily dose	2.4 grams (ideally keep to 1.2 grams)
Types of preparations	Tablets Oral suspension
Oral NNT for 200mgs 2.9 (2.7-2.9). NNT for 400mg 2.5 (2.4-2.6) [11].	

Naproxen	
Normal oral dose	500 mg, twice daily 250mg, 6-8 hourly
Maximum daily dose	1.25 grams, ideally keep to 1 gram
Types of preparations	Tablet
Oral NNT for 500mgs 2.7 (2.3 – 3.3) [11].	

Adverse effects

Dyspepsia and other upper gastrointestinal complications, such as ulcer, perforation, obstruction or bleeding. Patients are high risk if they have one or more risk factors (e.g. use high doses, aged over 65 years) [14].

Renal function – With careful patient selection and monitoring the incidence of NSAID-induced perioperative renal impairment is low. All patients receiving NSAIDs need to have their renal function monitored [4].

Cardiovascular effects – These risks are mainly derived from the medications taken regularly in long-term treatment and may not reflect the risk of short-term use in acute pain [4]. All NSAIDs approximately double the risk of congestive cardiac failure [4]. Other complications include: myocardial infarction, stroke and hypertension [14].

Platelet inhibition – Non-selective NSAIDs may increase the risk of bleeding, particularly after surgery [14].

Asthma — NSAIDs may exacerbate or precipitate asthma. Stop the NSAID if it is suspected to have precipitated bronchospasm [14].

Skin reactions and angioedema — stop the NSAID.

Hepatic reactions such as hepatitis, liver necrosis, or hepatic failure can occur but are rare.

5.2.3 Medications given for moderate pain

Weak opioids can be prescribed for patients with moderate pain and may be given in conjunction with paracetamol and NSAID's. Please note that the analgesic action of codeine depends on metabolism via the CYP2D6 cytochrome, P450 isoenzyme [4]. In Caucasian populations, 8% to 10% of people are poor metabolisers, whereas 3-5% are ultra-rapid metabolisers and have significantly higher levels of morphine and morphine metabolites after the same dose of codeine [4]. **Due to this metabolic uncertainty it is better to avoid the use of codeine phosphate and to prescribe dihydrocodeine instead.**

It is better to prescribe a weak opioid and paracetamol separately. Co-analgesic drugs, such as co-dydramol (10/ 500) and co-codamol (8/ 500), can give sub-optimal doses of dihydrocodeine or codeine and their use should be avoided.

Only one step-2 analgesic should be prescribed; therefore dihydrocodeine and tramadol should not be prescribed together. If a step-2 analgesic does not give a clinically meaningful reduction in the patient's pain, then the regimen should move up to step-3, please see the pain mountain in 5.1 Section 1.

Dihydrocodeine tartrate	
Normal oral dose	30 - 60 mg, 6-hourly
Maximum daily oral dose	240 mg
Types of preparations	Tablets Oral solution
Oral NNT for 30 mgs 8.1 (4.1-540) [11]	

Tramadol	
Normal oral dose	50 - 100 mg, 6-hourly
Maximum daily oral dose	400 mg
Types of preparations	Capsule MR tablet Oro-dispersible tablet Soluble tablet Injection
Oral NNT for 50mg 8.3 (6.0-13) [15] Oral NNT for 100 mgs 4.8 (3.8–6.1) [15]	

Tramadol is a centrally acting analgesic which acts as an opioid agonist and a serotonin and noradrenaline re-uptake inhibitor [16]. Please note that paracetamol has synergistic benefits, when given with tramadol as the NNT for tramadol reduces from 4.8 to 2.8 (2.1 - 4.4) [17]. Tramadol lowers the seizure threshold and should not be given to patients with epilepsy. The seizure threshold is also reduced in patients taking tricyclic anti-depressants (TCAs) and serotonin reuptake inhibitors (SSRIs) [18].

5.2.4 Medications given for severe pain

Oral opioids are prescribed for patients with severe pain. If regular tramadol or dihydrocodeine is insufficient, they should be stopped and an opioid prescribed in its place, please see the pain mountain in 5.1 Section 1. Patients who are receiving regular full dose tramadol or dihydrocodeine, may also require a strong opioid pro re nata (PRN), for breakthrough or procedural pain.

Oral opioids are prescribed in preference to intramuscular or sub-cutaneous opioids, when an oral route is available. This is more acceptable to the patient and has a longer duration of action. Ideally pain should be controlled with a short acting, 4-hourly, preparation.

Patients with acute, post-operative pain will experience pain which progressively recedes and should be weaned off strong analgesics prior to discharge. If patients are discharged with a prescription for strong opioid analgesia, then advice should be given to the GP on when to stop it. Prescriptions should not be continued without review in the community. The Trust's patient information leaflet entitled 'Controlling your pain with opioids' is dispensed with all outpatient opioid prescriptions.

The use of strong opioids for persistent non-cancer is not advised, as treatment can be associated with additional side-effects such as endocrine impairment, hyperalgesia and immunomodulation [19]. For further information please see the section on long-term opioids in persistent non-cancer pain (see section 5.2.6).

Morphine remains the most widely used opioid for the management of pain and the opioid against which other opioids are compared.

Morphine sulphate	
Starting oral dose	10 mg, 4-hourly To be given at 0200, 0600, 1000, 1400, 1800 and 2200 hours. Do not omit the 0200 hours dose.
Maximum daily oral dose	Increase until pain is controlled
Types of preparations	Liquid – Morphine oral solution Immediate release tablet - Sevredol Modified release: tablet, capsule, granules

Please note that morphine oral solution (10 mg/5 mls solution) is a schedule 5 controlled drug. This means it can be stored in the medicine trolley and does not need to be checked out by two nurses. This facilitates ease of timely administration for patients.

Opioids for acute pain should be gradually weaned as the pain diminishes, as opioids for chronic non-cancer pain are not effective [19]. On the rare occasions that patients need to continue with opioids long acting opioids can be used, such as modified release morphine. Please contact the pain service for advice.

If the patient is intolerant of or sensitive to morphine preparations, consider using an oxycodone preparation. **Please note that 5 mg of oral oxycodone (immediate release) is equivalent to 10 mg of oral morphine.** There is no difference in dose equivalence between an injection of oxycodone and an injection of morphine.

Oxycodone	
Starting dose	5 mg, 4-hourly To be given at 0200, 0600, 1000, 1400, 1800 and 2200 hours. Do not omit the 0200 hours dose.
Maximum daily dose	Increase until pain is controlled
Types of preparations	Oxycodone (Immediate release) capsule Oxycodone (Immediate release) liquid Oxycodone (Modified release) tablet
Oral NNT for 5mg oxynorm, plus 1G paracetamol is 1.8 (1.6 – 2.2) [11].	

Buprenorphine is a partial mu-opioid receptor agonist and kappa-opioid receptor antagonist, with high receptor affinity and slow dissociation from the mu-receptor, which leads to a delayed onset and longer duration of action. As a consequence, it is suggested that buprenorphine should **not** be given with other opioids, as it can reverse their action [20], though more recent animal work appears to disprove this assumption [21], though it has yet to be shown in randomised controlled trials in humans. It can be useful in patients with renal impairment, as 2/3rds of the drug is excreted unchanged, mainly in faeces, while the remaining 1/3rd is metabolised in the liver and gut wall to an inactive metabolite [21]. It is also useful for patients with pancreatitis, as it does not increase the Sphincter of Oddi pressure [22].

Buprenorphine	
Normal sublingual dose	200 microgram, 6 - 8 hourly
Maximum daily sublingual dose	2.4mg
Types of preparations	Sublingual tablet Transdermal patch (‘5’, ‘10’, & ‘20’ micrograms) changed weekly. Transdermal matrix (‘35’, 52.5 or 70 microgram) changed every 72 hours
Transdermal buprenorphine patches should only be used in patients with stable, persistent pain, not in acute pain.	

Transdermal opioid patches

Transdermal opioid patches (Buprenorphine & Fentanyl) are used in patients with stable, persistent pain, not acute pain. But patients may have been prescribed these medications prior to admission into the hospital. Please contact the pain service for further advice about these complex patients.

Intramuscular, sub-cutaneous or intravenous opioids
Sub-cutaneous, intra-muscular or intra-venous analgesia is prescribed for patients with severe pain who are unable to tolerate oral preparations, have no oral route, or whose pain is not controlled with oral opioids. Intra-muscular morphine is an effective method of administering pain relief (10 mgs has an NNT of 2.9 range 2.6-3.6) [15]; however, patients find the mode of administration to be painful, which can discourage them from requesting analgesia when needed.

Patients who require frequent, sub-cutaneous (S/C) dosing can have an in-dwelling sub-cutaneous cannula in situ. The use of the cannula avoids the need for frequent injections and is more comfortable for the patient. Due to the risk of respiratory depression, patients receiving their first parenteral dose of opioids should be closely monitored for the first hour (sedation scores, respiratory rate and saturation monitoring.

There is no evidence that pethidine is better than morphine in the treatment of biliary colic. Both exert similar effects on the Sphincter of Oddi and biliary tract. In fact, pethidine injections should be avoided as they are short-acting, produce the metabolite norpethidine, which if present in large doses, can cause the patient to fit [23, 24].

Patient-controlled analgesia
Please see separate guideline entitled: *Patient-Controlled Analgesia PCA for post-operative and acute pain: Clinical nursing guidelines for adult patients.*

Epidural analgesia
Please see separate guideline entitled: *Epidural Analgesia: Continuous Infusions Clinical Guidelines for Adult Patients.*

5.2.5 Common adverse effects of opioids
Opioids, whether by oral or any other route, are associated with side-effects. This section will discuss the common adverse effects associated with opioid use.

Respiratory depression
It is important to monitor respiratory rate in patients receiving opioids. A respiratory rate of <10 breaths per minute is considered to be respiratory depression. However, respiratory depression is almost always preceded by sedation, therefore, the best early clinical indicator is increasing sedation [4]. The most frequently reported risk factors are female gender, sleep-disordered breathing, obesity, renal impairment, pulmonary disease and cytochrome P450 enzyme polymorphisms, but patient without risk factors can also develop respiratory depression [4].

Naloxone is a highly effective antidote for opioids and can be used to reverse the effects of opioid induced respiratory depression. Care must be taken not to use too large a dose as patients may experience intense pain and distress. It is recommended that doses of 100 - 200 mcg of Naloxone are given at 2 minute intervals for the reversal of post-operative respiratory depression [25].

NHS England published advice in 2014 warning about the risk of distress and death from inappropriate doses of naloxone in patients on long-term opioid treatment [26]. The use of inappropriate doses of naloxone can cause a rapid reversal of the physiological effects of long-term opioids used for pain control, leading to intense pain and distress and acute withdrawal syndrome. This can lead to hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest.

Pruritus
Itching is a common side-effect of opioids [27]. An antihistamine, such as chlorphenamine (piriton), should be the first choice when treating these symptoms. A 5-HT3 receptor antagonist such as ondansetron, may also be useful as a second line of treatment;

however these drugs can be constipating. If pruritus persists despite treatment consider switching the opioid. Please contact the pain service for further advice.

Hallucinations and nightmares
Delirium and changes in cognitive function have been observed in patients receiving opioids, particularly in older people [28]. These symptoms can be very distressing and if the patient is experiencing them, opioid switching should be considered. Level II evidence suggests that the rates of delirium and cognitive impairment were lower for patients given fentanyl than for those receiving morphine [29].

Constipation
All opioids cause constipation. Opioid induced bowel dysfunction will prolong post-operative ileus. All patients should be prescribed laxatives PRN. Laxatives should be prescribed regularly, if constipation becomes a problem. Opioid rotation may also help to improve symptoms [30].

Drug Dependence Syndrome
Drug Dependence Syndrome is defined as "A cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state" [31]. The key points for management of these patients are given below:

- Engaging in open and honest discussions with the patient and caregivers to agree to a management and discharge plan with clear, achievable goals.
- Use strategies that both provide effective analgesia and prevent withdrawal syndrome, which are two separate goals.
- The early recognition and treatment of symptoms and behavioural changes that might indicate withdrawal.
- Use tamper-proof and secure analgesia administration procedures.
- Use regional analgesia where possible, although it may be a challenge in patients who have depressed immunity or local or systemic sepsis from injections.

Please seek further advice from the pain service. For information on managing withdrawal in these patients please see the following Trust guideline: Opioid Dependence Management in Hospital Adult in-patients.

Patients who have been taking opioids for longer than two weeks should not stop taking the drug abruptly, because they will experience a withdrawal due to physical dependence. Opioids should be weaned slowly to avoid this complication.

Nausea & vomiting
Opioid induced nausea and vomiting occurs in many clinical settings, the most studied of which is postoperative nausea and vomiting (PONV) [32]. Postoperative nausea and vomiting (PONV) is common and distressing to patients. The general incidence of vomiting is about 30%, the incidence of nausea is about 50% and in a subset of high-risk patients, the PONV rate can be as high as 80% [33,34,35].

The Apfel simplified risk score is based on 4 risk factor predictors and can be used to identify at risk patients [33]:

1. Female
2. History of PONV and/or motion sickness
3. Non-smoker
4. Use of postoperative opioids.

The incidence of PONV has been linked to the number of risk factors present from the 4 listed above [33]:

Number of risk factors	Approx. Incidence of PONV	Risk
0 – 1	10-20%	Low
2	40%	Moderate
>3	60-80%	High

Other recognised risk factors include Age<50years [36] and anaesthesia-related predictors such as the use of a volatile anaesthetic and duration of anaesthetic [37,38].

All patients receiving opioids should be prescribed an anti-emetic on an as required (prn) basis. Patients with a high risk of PONV (Apfel score of 3-4) should have an anti-emetic prescribed regularly during the post-operative period [39].

While antiemetic comparative studies were identified, evidence to support an overall clinically superior antiemetic was lacking. The following options are considered appropriate pharmacologic options, taking into consideration relevant cautions and contraindications:

- First Line: ondansetron
- Second Line: cyclizine
- Third Line: metoclopramide
- Other: prochlorperazine

For full prescribing advice please refer to the BNF.

Antiemetic	Action	Formulations available	Route	Dose	Frequency	Cautions	Notable side effects
Ondansetron* (first line)	$5HT_3$-receptor antagonist which blocks $5HT_3$ receptors in the gastro-intestinal tract and in the CNS.	Tablets: 4mg, 8mg Injection: 4mg/2mL, 8mg/4mL	Oral IV IM	4mg-8mg	TDS	Caution concomitant use with medications prolonging QT or patients who may develop QT prolongation.	Constipation, flushing, headach e,arrhythmias, bradycardia, chest pain.
Cyclizine (second line)	Histamine H_1 receptor antagonist of the piperazine class. The exact mechanism by which cyclizine can prevent or suppress both nausea and vomiting from various causes is unknown.	Tablets: 50mg Injection: 50mg in 1mL	Oral Slow IV IM	50mg	TDS	Caution in patients with glaucoma, urinary retention, obstructive disease of the gastrointestinal tract, hepatic disease, pheochromocytoma, hypertension, epilepsy & avoid in porphyria.	Drowsiness, arrhythmias, antimuscarinic effects, urinary retention, blurred vision, oculogyric crisis, visual hallucinations, bronchospasm. Avoid in heart failure.
Metoclopramide (third line)	Dopamine D2 antagonist; $5HT_4$ agonist (bowel prokinetic).	Tablets: 10mg Injection: 10mg/2mL Liquid: 5mg/5mL	Oral Slow IV IM	>60kg 10mg TDS ≤60kg 500micrograms /kg	TDS TDS	Only prescribe for short term use (up to 5 days) due to risk of neurological effects. Special care should be taken when administering particularly via the intravenous route to the elderly population, to patients with cardiac conduction disturbances (including QT prolongation), patients with uncorrected electrolyte imbalance, bradycardia and those taking other drugs known to prolong QT interval.	May cause extrapyramidal effects – monitor for parkinsonism, tremor, restlessness. Requires dose reduction in severe hepatic impairment and renal impairment (see BNF)
Prochlorperazine (Phenothiazine)	Phenothiazine	Tablet: 5mg Injection: 12.5mg/mL	Oral IM	5-10mg 12.5mg, followed after 6 hours if needed by an oral dose	BD-TDS ONCE	Avoid in hepatic impairment, use small doses in renal impairment (increased cerebral sensitivity).	May cause acute dystonic reactions.

5.2.6 Long-term opioids for persistent non-cancer pain

Opioids are excellent analgesics for acute pain and pain at the end of life, but there is little evidence that they are helpful for long-term pain [19]. A small proportion of people may obtain good pain relief with opioids in the long-term, if the dose can be kept low and especially if their use is intermittent, however it is difficult to identify these people at the point of opioid initiation [19].

The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day [19]. This is equivalent to 20mg Oramorph, 4 hourly; 10mg Oxycodone (immediate release) 4 hourly, 60mg morphine (modified release) 12 hourly; 30mg Oxycodone (modified release), 12 hourly.

If the patient's pain remains severe despite opioid treatment, then it means that the opioids are not working and they should be stopped (by tapering), even if no other treatment is available [19].

Chronic pain is very complex and if patients have refractory pain and disabling symptoms, particularly if they are taking high doses of opioid, a very detailed assessment of the many emotional influences on their pain is essential [19]. This is best done by referring to the inpatient pain service or by getting their GP to refer them to the Pain Management Centre at Charing Cross or to a local pain clinic.

The long-term use of opioids is associated with serious harms, these include:

- Opioid induced hyperalgesia – prolonged use leads to a state of abnormal pain sensitivity, similar to that seen in patients with neuropathic pain [19]
- Endocrine abnormalities due to their effect on the hypothalamic-pituitary adrenal and gonadal axes. This results in low cortisol levels, hypogonadism in men and women, amenorrhea in women, reduced libido in both sexes, erectile dysfunction in men, infertility, depression and fatigue [19].
- Opioids are thought to have an immunomodulating effect and in animal studies have been shown to have an effect on antimicrobial response and anti-tumour surveillance. In human studies opioid users have been found to be more likely to contract pneumonia, but further studies are required to establish the clinical relevance of opioid induced immunosuppression [40].
- Opioids increase the risk and incidence of falls particularly in the elderly [41].
- It is estimated that 8-12% of long term opioid users meet the criteria for a current or past opioid use disorder [19]. The indicators of dependence are provided in full on the opioid aware website [19], and include the following:

    - Long-term prescribing of opioids for non-cancer conditions
    - Current or past psychiatric illness or profound emotional trauma
    - Reports of concern by family members or carers about opioid use
    - Concerns expressed by a pharmacist or other healthcare professionals about long-term opioid use
    - Insistence that only opioid treatment will alleviate pain and refusal to explore other avenues of treatment
    - Refusal to attend or failure to attend appointments to review opioid prescription
    - Resisting referral for specialist addiction assessment
    - The repeated seeking of prescriptions for opioids with no review by a clinician
    - Repeatedly losing medications or prescriptions
    - Taking doses larger than those prescribed or increasing dosage without consulting the clinician; often coupled with seeking early replacement prescriptions. Associated with continued requests for dose escalations
    - Seeking opioids from different doctors and other prescribers. This can take place within GP practices, often identifying locum doctors or doctors unfamiliar with their case. This may be associated with attempting unscheduled visits

- Obtaining medication from multiple different providers, NHS and private GPs, repeatedly and rapidly deregistering and registering with GPs, seeking treatment for the same condition from both specialists and GP; or seeking treatment from multiple specialists. This may be coupled with a refusal to agree to writing to the main primary care provider
- Obtaining medications from the internet or from family members or friends.
- Resisting referrals to acute specialists about complex physical conditions or failing to attend specialist appointments
- Appearing sedated in clinic appointments
- Misusing alcohol or using illicit or over-the counter, internet or other prescribed drugs or a past history of alcohol or other drug dependence
- Deteriorating social functioning including at work and at home.
- Resisting or refusing drug screening
- Signs or symptoms of injecting opioids or snorting oral formulations.

A trial of opioids should be conducted when considering opioids for the management of long-term pain. To identify whether the trial has been successful the patient and prescriber should agree some outcomes. These are usually a reduction in pain intensity of at least 30%, specific functional improvement and if sleep is a problem improved sleep is a reasonable goal [19]. The patient should be encouraged to keep a diary during the trial period, which should include a twice daily report of pain intensity, assessment of sleep and activity levels, along with a record of all opioids taken and any side-effects.

Although the efficacy of opioids may be established with a few weeks during a trial, the more important question is whether the efficacy is maintained past 12 weeks. If the opioid needs to be frequently increased, the dose is over 120mg of oral morphine equivalents and is not providing useful pain relief, then the medication should be tapered and stopped. Opioids should also be tapered and stopped if the underlying painful conditions resolves, the patient received a definitive pain relieving intervention (such as joint replacement), they develop intolerable side-effects or is there is strong evidence that they are diverting their medication. An opioid can be tapered by 10% weekly or two weekly [19].

Patients who are being established on opioid therapy should be regularly reviewed. This is easily done as an inpatient, but they are usually reviewed every 4 weeks as an outpatient whilst medication is being titrated. Once their dose is stable, they should be reviewed every 6 months and this is usually done by their GP [19]. Once discharged from hospital there should only be one prescriber, usually the GP.

Opioid rotation or switching can be considered if a patient obtains pain relief with one opioid, but is suffering adverse effects. Switching from opioid to another should only be attempted by a healthcare practitioner with competence and experience or advice should be sought from the pain service. When switching between opioids the calculated dose equivalent should be reduced to ensure safety by 25 to 50% [19]. Please contact the pain service for further advice.

Any patient being discharged from hospital with strong opioids will receive the Trust's opioid leaflet entitled 'Controlling your pain with opioids: Information for patient, relatives and their carers'.

5.2.7 The progression from acute to chronic pain

The aim of acute pain management is not only to relieve the immediate pain and suffering experienced by the patient, but also to prevent the development of chronic or persistent pain. The concept that pain can persist after surgery is relatively new [42,43,44]. Depending on the procedure, persistent post-surgical pain (PPSP) can affect between 5% and 75% of patients with amputation, thoracotomy and mastectomy having the highest incidence [45].

Patient specific risk factors for PPSP are relatively well established and include: female sex, younger age, presence and severity of preoperative pain (both distant and at the surgical site), pre-operative opioid use and preoperative negative disposition such as anxiety, pain catastrophising, depression and a history of post-traumatic stress disorder [45].

Apart from pre-operative risk factors patients can be primed to be susceptible to PPSP in the post-operative period [4]. There is a strong correlation between uncontrolled pain at 24 and 48 hours after surgery and the development of PPSP, therefore we need to ensure that our patients experience none or mild pain post-operatively [4]. Other risk factors include radiation therapy to the area, chemotherapy and nerve damage caused by the surgical procedure [4].

Patients who are identified as having any of the above pre-operative risk factors should be identified at pre-assessment and the pain service alerted in advance. Ideally those patients who are taking high doses of opioid, above 120mg of oral morphine equivalence, should try to reduce their opioids beforehand. One study of patients undergoing primary knee or hip replacement found that patients who weaned their opioids by 50% before surgery had substantially improved outcomes and their outcomes were comparable to patients who used no opioid prior to surgery [46].

Various medications have been used to attenuate the effects of PPSP. In this Trust we use ketamine for these complex patients. Please see the separate Trust guideline: Ketamine low-dose for the treatment of complex pain in adult inpatients.

5.2.8 Treatments for neuropathic pain

Neuropathic pain has been defined as pain caused by a lesion or disease of the somatosensory nervous system [2]. It can be caused by disorders such as diabetes, immune deficiency and space-occupying malignancy. Traumatic and ischaemic conditions may also give rise to neuropathic pain. Lesions may be located at any level from the periphery to the central nervous system. Signs and symptoms of neuropathic pain can include the following:

- Pain described by the patient as hot-burning, lancinating, pins and needles, pricking, tingling, stabbing, shooting, electric-shock or jumping pain
- Sensory loss, either partial or complete, in the painful area
- Allodynia (pain due to a stimulus that does not normally provoke pain) [2]
- Hyperalgesia (increased pain from a stimulus that normally provokes pain) [2]

Gabapentin, pregabalin, duloxetine, nortriptyline or amitriptyline are considered first line medications for the treatment of neuropathic pain (except trigeminal neuralgia) [47,48]. If the initial treatment is not effective or is not tolerated, offer one of the remaining drugs and consider switching again if necessary. For patients with painful diabetic neuropathy, the first-line choice is duloxetine, unless contraindicated [48]. Consider capsaicin cream for patients with localised neuropathic pain who wish to avoid, or who cannot tolerate oral treatments [48].

Opioids are recommended as third-line therapy because of concerns about diversion, misuse, opioid-associated overdose, morbidity and death [47]. The Cochrane review stated there was low or very low-quality evidence related to the use of strong opioids in the treatment of neuropathic pain and stated that their use is subject to considerable uncertainty [49]. Recommendations for many of the neuropathic drugs are outside their licensed indications (off label use).

Start at the low dose and increase to an effective dose, as tolerated by the patient		
Drug	**Starting dose**	**Maximum daily dose**
Amitriptyline	10 mgs, at night	25 - 75mg in 24 hours
Nortriptyline	10 mgs, at night	25 – 75mg in 24 hours
Duloxetine	60 mgs per day	60 mg, twice daily
Gabapentin	300mg three times a day	900 mgs, three times daily
Pregabalin	75 mgs, twice daily	300 mgs, twice daily

Amitriptyline and nortriptyline have an onset of action of less than one week for neuropathic pain, but do not reach their peak for 3-4 weeks. They need to be taken every night. Analgesia is achieved at much lower doses than those given for depression. If these drugs are not working, then consider using a different medication for neuropathic pain. Many patients find nortriptyline easier to tolerate because it has less of a hangover effect the following morning. These medications are usually given at night as they are sedating. Please note it is important the patient understands that they are not being prescribed such medications for depression. The patient should also be warned about possible side-effects, such as dry mouth, drowsiness, blurred vision, constipation and urinary retention. Patients should be advised that as treatment persists, tolerance to the side-effects may develop. Tricyclic anti-depressants are contraindicated in patients with wide-angle glaucoma, recent MI and cardiac arrhythmias. They should not be discontinued suddenly, because the patient is likely to experience withdrawal symptoms (chills, myalgia, sweating, headache and nausea).

Introduction of gabapentin or pregabalin can reduce neuropathic pain after one week. The patient should be warned about possible side-effects, such as cognitive impairment, dry mouth, constipation, drowsiness, blurred vision, dizziness and weight-gain. Men can also experience erectile dysfunction. It is recommended that patients commence on a low dose and titrate as necessary. Pregabalin and gabapentin should be used with caution in patients with renal impairment (please see the Trust's guideline: Analgesia Guideline for the Management of Acute and Chronic Pain for Adults with Renal Impairment). They should not be discontinued suddenly, as the patient is likely to experience withdrawal symptoms.

Please note that Gabapentinoids (Gabapentin and Pregabalin) are schedule 3 controlled drugs. This means they can be stored in a locked medicine trolley and do not need to be checked out by two nurses. This facilitates ease of timely administration for patients. However some ward areas may wish to keep supplies in their CD cupboard.

Capsaicin cream (0.025% or 0.075%) is made from chili peppers and can be used for localised neuropathic pain. It should not be used on broken skin. It needs to be applied 3 to 4 times per day; at this frequency of application it can reduce substance P, but this can take about a month. Patients must wash their hands after application to avoid getting the cream in their mouth or eyes. Avoid hot shower or bath just before or after application as the burning sensation can be enhanced.

Lidocaine plasters are licensed for the use of post-herpetic neuralgia and neuropathic pain associated with evoked allodynia and hyperalgesia. A Cochrane Review found no evidence from good quality randomised controlled studies to support the use of topical lidocaine to treat neuropathic pain, although individual studies indicated that it was effective for relief of pain. Clinical experience also supports efficacy in some patients [50]. There is no evidence for their use for any other condition such as low back pain and therefore they should not be used.

Please contact the pain service for further information.

5.2.9 Pain relief in Chronic Kidney Disease and End Stage Renal Failure

For further information please see the guideline 'Analgesia Guideline for the Management of Acute and Chronic Pain for Adults with Renal Impairment' and the Renal Drug Database [51].

NSAIDs both systemic and topical, should be avoided if possible in patients with chronic kidney disease stage 3b, 4 and 5 (eGFR <45). For acute gout Colchicine can safely be used in place of NSAIDs. If there is no alternative to an NSAID then use the smallest effective dose. A PPI such as Omeprazole 20mg BD, should be co-prescribed for the duration of treatment to prevent gastrointestinal upset and bleeding

In end stage renal failure (Dialysis Patients) an NSAID should only be prescribed under supervision of a nephrologist or pain specialist.

Paracetamol can be prescribed in normal doses, but dose reduction is required for patients with a low body mass index (BMI) and should be based on the patient's dry weight.

Codeine and dihydrocodeine should be avoided in patients with chronic kidney disease stages 4-5 and end stage renal failure. This is because both codeine and its active metabolites are excreted almost entirely by the kidney and they are not removed with dialysis leading to drug accumulation and opioid toxicity.

The preferred alternative is tramadol. This should be prescribed at a maximum dose of 50mg, 8 hourly in advanced chronic kidney disease stages 4/5 and end stage renal failure.

The preferred opioid in chronic kidney disease and end stage renal failure is Oxycodone (immediate release). Oxycodone is metabolised by the liver and its metabolites do not have significant active effects.

Neuropathic pain agents such as gabapentin and pregabalin are excreted by the kidneys and so should be dose adjusted to the patient's renal function. It is advisable to always start with a low dose in renal impairment and slowly increase at 48hr intervals. These medications are also dialysed and so should be administered after haemodialysis with doses generally given in the evening. Consideration should be given to omitting a dose if a patient misses a dialysis session whilst an inpatient due to acute illness.

5.2.10 Pain relief in Severe Liver Impairment

Patients with liver failure have less protein and therefore have less protein binding sites in the plasma. This will affect drugs that are heavily plasma bound, meaning that there is more free drug available. The dose of these drugs therefore has to be decreased.

Drugs that depend of liver metabolism and liver excretion also have to be altered with liver impairment. Many patients with liver failure also have renal failure. An additional problem for patient with severe liver impairment is that they do not manufacture clotting factors and so their clotting may be abnormal.

The use of NSAIDs should be avoided in patients with chronic liver disease (especially cirrhosis and portal hypertension) due to the increased risk of gastrointestinal bleeding [52].

Paracetamol can be used in severe liver impairment and given to liver transplant patients, but the dose should be adjusted [53,54]. The maximum dose for a patient whose weight is >50kg is 3g paracetamol in 24 hours (1g given 8hrly). The maximum dose for a patient whose weight is <50Kg is 2g paracetamol in 24 hours (1g given12hrly). Paracetamol should not be given to patients who have been admitted with liver injury due to paracetamol overdose.

Opioids are metabolised by the liver CYP450 enzyme pathway and should be used with caution in patients with severe liver disease; the use of sedatives can increase the likelihood of encephalopathy. Opioids also slow down gut transit time leading to ammonia retention, which further increases the risk of encephalopathy. Lactulose should be prescribed regularly in these patients.

Codeine and dihydrocodeine should be used only at low doses in patients with severe liver disease, as their active metabolites will accumulate. All opioids should only be prescribed prn (as required) rather than regularly, until further review by a specialist team.

The preferred opioid is Oxycodone (immediate release) in small doses. Oxycodone is metabolised by the liver, but its metabolites do not have significant active effects. It should be commenced at low doses and slowly titrated.

Gabapentin and Pregabalin are not metabolised by the liver and can be used in liver disease [55]. However, they should be initiated at a low dose and slowly increased. These medications can cause pancytopenia in these patients and so the patient's full blood count should be monitored. Tricyclics should be used with caution, as they are liver toxic.

Please seek advice from the pain service or specialist team.

5.2.11 Opioid Conversion Table

This table should be viewed as a guide to opioid equivalence. It is recommended that you discuss opioid conversion with the Pain Service.

Opioid	Daily oral morphine equivalents
Buprenorphine patch 5 micrograms per hour	9 to 14 mg
Codeine 120 mg per day	12 to 18 mg
Dihydrocodeine 120mg per day	As codeine
Oxycodone (MR) 10 mg per day	15 to 20 mg
Buprenorphine patch 10 micrograms per hour	18 to 28 mg
Tramadol 200 mg per day	20 to 50 mg
Codeine 240 mg per day	24 to 36 mg
Dihydrocodeine 240mg per day	As codeine
Oxycodone (MR) 20 mg per day	30 to 40 mg
Fentanyl patch 12 micrograms per hour	30 to 45 mg
Buprenorphine patch 20 micrograms per hour	30 to 56 mg
Tramadol 400 mg per day	40 to 100 mg
Oxycodone (IR) 5mg, 4 hourly	45 to 60 mg
Oxycodone (MR) 30 mg per day	45 to 60 mg
Oxycodone (MR) 40 mg per day	60 to 80 mg
Fentanyl patch 25 micrograms per hour	60 to 90 mg
Buprenorphine patch 35 micrograms per hour	60 to 95 mg
Oxycodone (MR) 60 mg per day	90 to 120 mg
Buprenorphine patch 52.5 micrograms per hour	90 to 145 mg
Fentanyl patch 50micrograms per hour	120 to 180 mg
Buprenorphine patch 70 micrograms per hour	120 to 190 mg

Please note: *Medications which are to be continued by the GP following discharge from hospital should be in line with the North West London integrated formulary. Please contact Pharmacy for further information.*

6) IMPLEMENTATION

Training required for staff	☐ *No* √ *Yes*
If yes, who will provide training:	Dr Gillian Chumbley – Consultant Nurse, Pain Service Pauline Chinn – Lead Nurse, Pain Service Nicola Bourne – Lead Nurse, Pain Service Senior clinical nurse specialists in the Pain Service
When will training be provided?	Training in pain management is provided for nurses and allied health professionals monthly on the pain study day. Training will also be provided for FY1 doctors in training on all Trust sites.
Date for implementation of guideline:	

7) MONITORING / AUDIT

When will this guideline be audited?	The pain service conducts audits every 18 to 24 months to assess pain relief in adult patients. The next audit will be performed in Jan/Feb 2020.
Who will be responsible for auditing this guideline?	Dr Gillian Chumbley – Consultant Nurse, Pain Service Pauline Chinn – Lead Nurse, Pain Service Nicola Bourne – Lead Nurse, Pain Service
Are there any other specific recommendations for audit?	No

8) REVIEW

Frequency of review	**Please indicate frequency of review:** Every 3 years **Person and post responsible for the review:** Dr Gillian Chumbley – Consultant Nurse, Pain Service Pauline Chinn – Lead Nurse, Pain Service Nicola Bourne – Lead Nurse, Pain Service

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10) GUIDELINE DETAIL

Start Date:	**3rd July 2019**
Approval Dates	Drugs and Therapeutics Committee 2nd July 2019 (chair's action 3rd July 2019)
Has all relevant legislation, national guidance, recommendations, alerts and Trust action plans been considered, and included as appropriate in the development of this guideline?	**Please list ALL guidance considered:** Faculty of Pain Medicine, Core Standards for Pain Management Services in the UK (2015). Nice guidance and NPSA Alert appear in the reference list.
Have all relevant stakeholders been included in the development of this guideline?	**Please list all (name and role):** This guideline has been formulated and reviewed by a multidisciplinary Pain Task and Finish group that met between Sept 2018 and May 2019. The following disciplines were represented: nurses, doctors, anaesthetists, educationalists, physiotherapists and pharmacists. All divisions were represented and included representatives from the pain service, surgery, medicine, paediatrics, maternity, therapies, emergency medicine, renal medicine, private patients, Nurse Director's office and pharmacy.
Who will you be notifying of the existence of this guidance?	**Please give names/depts:** It will appear on the Trust Internet, but also be launched as part of the work from the Pain Task and Finish group in September 2019.
Related documents	
Author/further information	**Name:** Dr Gillian Chumbley **Title:** Consultant Nurse – Pain Service **Division:** SCC **Site:** Trust wide **Telephone/Bleep**: 07825 061143 **Trust email address:** gillian.chumbley@nhs.net
Document review history	**Next review due: 3rd July 2022** V5.1 – revised guidelines V5.2 – format changes V5.3 – CD status for gabapentin added V5.4 – changes following comments received at DTC **V6.0 – Finalised version**
THIS GUIDELINE REPLACES:	Pain management guidelines for adult patients with acute or chronic pain

11) INTRANET HOUSEKEEPING

Key words	Pain, acute pain, persistent pain, chronic pain
Which Division/Directorate category does this belong to?	SCC
Which specialty should this belong to when appearing on the Source?	Pain Management

12) EQUALITY IMPACT OF GUIDELINE

Is this guideline anticipated to have any significant equality-related impact on patients, carers or staff? No