Gateshead Clinical Commissioning Group

Strong Opioid Guidelines for the treatment of chronic non-malignant pain

Effective Date: December 2011

Reviewed: March 2014

Next review date: March 2016

This guideline has been prepared and approved for used within Gateshead in consultation with NHS Gateshead CCG and Secondary Care Trusts.

Approved by:

Committee	Date
Gateshead Medicines Management Committee	12th March 2013
Alliance Medicines Optimisation, Pathways and Guidelines Committee	27th March 2014

Equality & diversity statement: this guideline will aim to be fair to all patients regardless of age, disability, gender, race, sexual orientation, religion/ belief or any other factor that may result in unfair treatment or inequalities in health/ employment.

This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Strong Opioid guidelines for the treatment of chronic non-malignant pain

Publication Date: December 2011
Reviewed: March 2014

1. Development

This guideline was developed by the joint consensus of the Gateshead Prescribing and Medicines Management Committee and the Gateshead Health NHS Foundation Trust Drug & Therapeutics Committee.

The sub-group that developed this guideline were as follows;
Dr Chris Jewitt (GP and Gat Net CCG Prescribing lead), Dr M Sherratt (GP), Mrs Anne-Marie Bailey (Associate Lead for Medicines Management), Dr J Anto (Consultant Anaesthetist), Dr Ola Olukuga (Consultant Anaesthetist), Dr Helen Groom (GP), Mrs Catherine Armstrong (Pharmacist) and Mr Peter Clarke (Pharmacist).

The key primary care contact for information is Mrs Anne-Marie Bailey, Senior Medicines Optimisation Pharmacist NECS (lead pharmacist for Gateshead and Newcastle CCGs) 0191 2172811.

The key contact for GHFT for information is Mr Gavin Mankin, Medicines Governance Pharmacist Tel. 0191 445 2818

2. Background

Persistent pain is common, affecting around 5 million people in the UK. For many sufferers, pain can be frustrating and disabling, resulting in functional impairment physically, emotionally and vocationally. Medications and other treatments that aim to reduce pain intensity play a role in the management of symptoms, but should be provided as part of a wider management plan focused on reducing disability and improving overall quality of life.

Opioid drugs are increasingly being used to treat persistent pain. Opioid drugs have a well-established role in the management of acute pain following trauma (including surgery) and in the management of pain associated with terminal illness. There is evidence from clinical trials that opioids can be effective, in the short and medium term, in providing symptomatic improvement in a variety of non-cancer pain conditions. However, the safety and efficacy of opiates in the long term is uncertain as is the propensity for these drugs to cause problems of tolerance, dependence and addiction.

The benefits of opioid treatment for the patient must be balanced against burdens of long term use as therapy for persistent pain may need to be continued for months or years. The position of opioid treatment must also be considered within a wider social context and issues such as diversion must be addressed.

3. Aim

The aim of this guideline is to collate simple and sensible advice, based on the best evidence available, and agreed by local healthcare professionals.

Its purpose is to give practical advice to enable potent opioids to be used in the most appropriate, safe and effective way for chronic non-malignant pain.

4. Implications

Implementation of the attached guidance will aim to improve the safe and effective use of opioid analgesics in Gateshead, thus improving the management of patients with pain. There will be an improvement in the management of these patients in primary care resulting

in a reduction of significant events related to use of these drugs and less referral to secondary care.

5. Implementation & Audit

Copies of the guidelines will be widely circulated across Gateshead and will be made available on the Gateshead Information Network (GIN). It is intended that various components of these guidelines will be audited over the next 6 months.

6. References

Opioids for persistent pain: good practice. The British pain Society Jan 2010
http://www.britishpainsociety.org/book_opioid_main.pdf

World Health Organisation Pain Ladder
http://www.who.int/cancer/palliative/painladder/en

Recommendations for the appropriate use of opioids for persistent non-cancer pain
http://www.painclinic.org/pdf/painbooklets/info-med-opioidsnoncancerpain.pdf

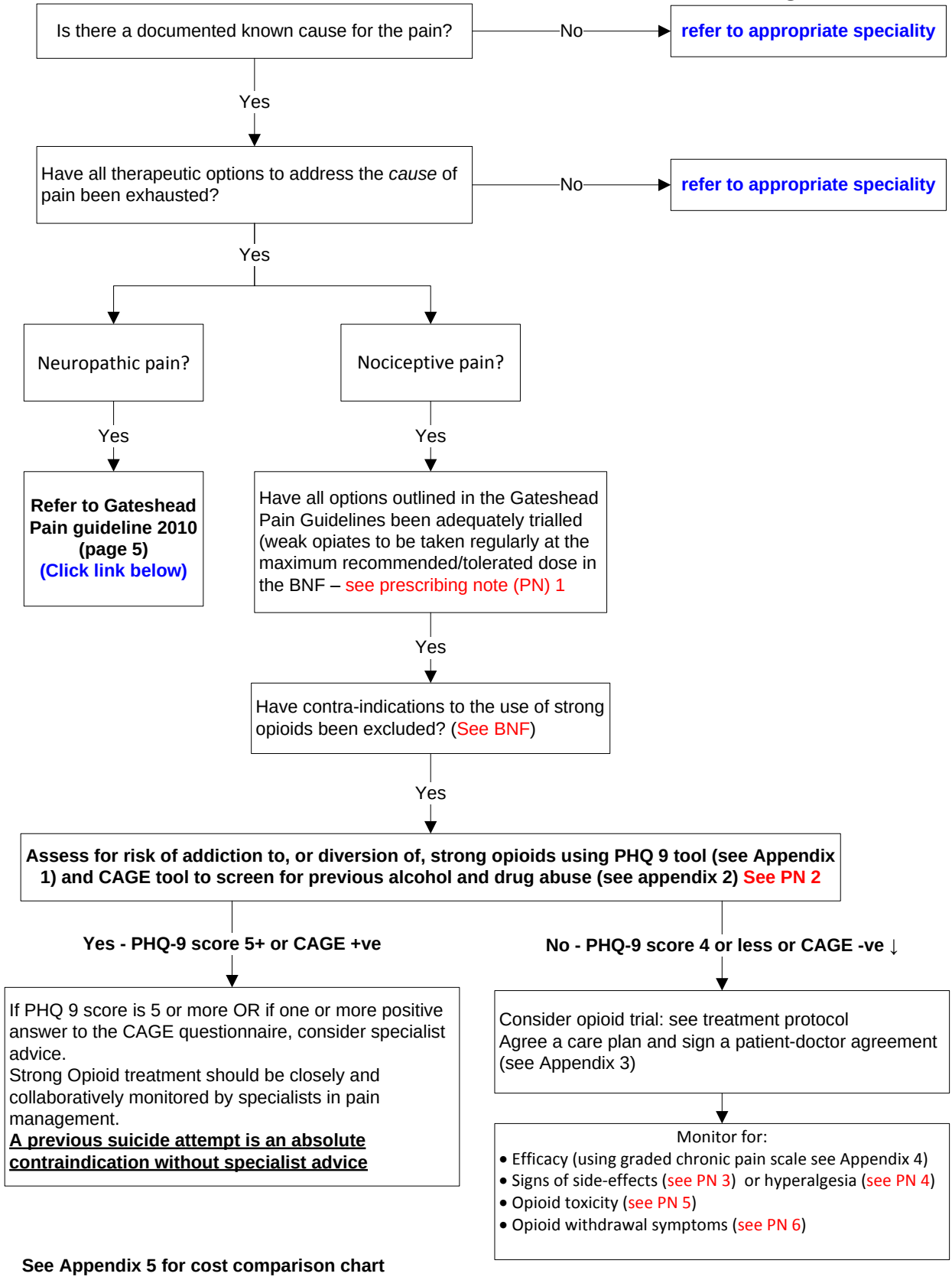
NPS: Prescribing Practice Review 51: Opioids in chronic non-cancer pain
http://www.nps.org.au/health_professionals/publications/prescribing_practice_review/current/prescribing_practice_review_51

Von Korff M. Chronic Pain Assessment in Epidemiologic and Health Services Research: Empirical Bases and New Directions. Handbook of Pain Assessment: Third Edition. Dennis C. Turk and Ronald Melzack, Editors. Guilford Press, New York., In press

North of Tyne Area Prescribing Committee Chronic & Palliative Care Guideline: Strong Opioids 2011

The Renal drug Handbook Third Edition Radcliffe Publishing Oxford

Patient Assessment for Treatment of Chronic Non-malignant Pain



See Appendix 5 for cost comparison chart

Link to Gateshead Pain Guideline 2010 http://ginportal.info/2010/12/chronic-pain-guidelines-2010-pdf/

Chronic Non-malignant Pain Guideline: Strong Opioid treatment protocol

All Patients	▪ Stop all other weak opioids (e.g. codeine, dihydrocodeine, tramadol) See PN 5. ▪ Paracetamol and NSAIDs can be continued, where appropriate. ▪ Discuss goals, potential problems and issues and sign a doctor/patient agreement ▪ An opioid trial is needed prior to a decision to continue treatment in the longer term. The duration of the trial is usually 2-4 weeks. ▪ When a dose increase is required, increase by 30-50% of previous dose. Do **not** increase by more than 50% of previous dose. ▪ Intervals between dose titration should allow time for the patient to build a tolerance to some of the side-effects. Suggest reviewing patient every 7-14 days and titrate dose until pain relief is achieved. **More rapid titration may be required in severe pain.** ▪ Short-acting preparations can be used for breakthrough pain. ▪ Warn the patient not to drive at start of therapy until stable and feels fit to drive and that it is their responsibility to inform DVLA. Document on the patient record (Read code 8CA9).
1st Line	**Oral Morphine** ▪ Start with low doses modified-release morphine (5-10mg twice daily) and titrate accordingly, particularly in patients with chronic renal impairment. ▪ **Note.** If eGFR is 20-50ml/min/1.73m^2**,** 75% of normal dose is required

2nd Line (1st line for patients with significant or unstable renal impairment eGFR 10 to 30ml/min/1.73m^2)	**Oral Oxycodone**
	▪ Before switching from morphine, have you:
	  ▪ Allowed time for tolerance to adverse effects?
	  ▪ Adequately treated adverse effects?
	  ▪ Excluded other causes of new problems?
	▪ In mild to moderate renal impairment, start with low dose (Oxycodone MR 5mg twice daily) and titrate accordingly to achieve pain relief
	▪ **Note** Oxycodone is contra-indicated in severe renal impairment (eGFR < 10ml/min/1.73m^2)

3rd Line	**Consult the chronic pain team for specialist advice** ▪ For patients not benefiting from analgesia after four dose increases, review the type of pain being treated and consider seeking specialist advice. ▪ Patients on greater than 120mg oral morphine (or equivalent) daily should also be referred. ▪ For patients with severe renal impairment, seek renal specialist advice

Breakthrough Pain Doses

A dose equivalent to between one tenth and one sixth of the total daily dose should be prescribed for breakthrough pain.

Equivalent doses for Opioids

Oral Codeine, Dihydrocodeine	**These are all 1/10th as potent as morphine**
Oral Tramadol	**Oral Tramadol is 1/5th as potent as morphine**

	Conversion ratio from oral morphine	**Example**		
		Approximate 24 hour dose equivalent	Approximate 12 hourly dose equivalent	Approximate breakthrough dose equivalent
PO Morphine	**Multiply by 1**	**30mg**	**10mg**	**5mg**
PO Oxycodone	**Divide by 2 ***	15mg	5mg	2.5mg

*Morphine and oxycodone are equipotent given parenterally. However, due to greater bioavailability of oral oxycodone, a smaller oral dose is required compared to morphine

NB. Conversions are in line with the North of England Palliative Care Guidelines. Dose adjustments may be required following conversion. Advice may be sought from the specialist chronic pain team, if required.

Prescribing Notes (PNs)

1. **'Strong' and 'weak' opioids** (see table 1). Patients with chronic non-malignant pain are often prescribed weak opioids, such as codeine and dihydrocodeine (WHO Step 2), but some patients continue to experience pain, and there is growing evidence that *selected* patients can respond well to potent opioids (WHO step 3). Morphine is the most commonly used strong opioid.

Table 1 Examples of opioids currently available on prescription in the UK
Not all of the drugs detailed below are currently on Gateshead formulary. Those in italics are NOT on the formulary - refer to formulary for more details

STRONG:
Diamorphine Parenteral
Morphine Oral (Oramorph, Sevredol, *MST Continus*, *MXL,* Zomorph), Parenteral
Oxycodone Oral (OxyNorm, OxyContin), Parenteral

Buprenorphine Oral - sublingual (Temgesic) Transdermal (Transtec, BuTrans)
Dipipanone Oral
Fentanyl Transdermal (Durogesic, Matrifen) Oral transmucosal/sublingual (Effentora, Abstral)
Hydromorphone Oral (Palladone, Palladone SR)
Methadone Oral (not on formulary at a strength appropriately licensed for analgesia)
Pentazocine Oral
Pethidine Oral, Parenteral

WEAK:
Codeine Oral
Dihydrocodeine Oral (*DF118 Forte, DHC Continus*)
Tramadol Oral (*Zydol, Zamadol*) Oral, *Parenteral*

Dextropropoxyphene Oral
Meptazinol Oral (Meptid)

2. **Assessing risk of addiction to, or, diversion of strong opioids**
Where possible all patients should be assessed using PHQ-9 and/or CAGE questionnaire, however, if this is not possible or patients refuse assessment, patients meeting the following criteria are more likely to be at higher risk:-
    - Personal history (past/current) of substance misuse (alcohol, illegal drugs, prescription drugs)
    - Family history of substance misuse
    - Psychological disease, inc history of suicide attempts
    - Off work > 6 months due to ill health (if applicable)
    - Poor response to opiates in past

3. **Adverse effects of opioid therapy.** 80% of patients taking opioids will experience at least one adverse effect. Table 2 details the most common adverse effects and the time taken to build a tolerance to these side-effects is stated in brackets. Patients using intermittent dosing schedules may not become tolerant to side effects.

Table 2

Constipation (little or no tolerance)	Somnolence (3-5 days)
Nausea (5-10 days)	Itching (little or no tolerance)
Vomiting (5-10 days)	Dry mouth (little or no tolerance)

Management of constipation

- Prescribe Senna 15mg at night initially increasing to 30mg at night if required. Add a softener, Docusate 100mg twice daily increasing to 500mg daily in divided doses, if required.

Management of nausea and vomiting

- Choice of drug will depend on individual patient assessment and should take into account duration of therapy, other concomitant drugs and other possible causes. First line recommendations are Haloperidol 0.5 – 5mg daily, Cyclizine 50mg up to three times a day and Domperidone 10-20mg three to four times a day.

Management of Itch

- Prescribe a non-sedating antihistamine, Loratadine or Cetirizine 10mg daily.

Management of excessive somnolence.

- Withhold 1 or 2 doses of the strong opiate and consider a dose reduction of 25%.

Persistent adverse symptoms may necessitate discussion with the patient regarding treatment withdrawal or switching to another strong opioid.

Respiratory depression is a feared complication of the use of opioid for acute pain, but is only likely to be problematic in persistent pain if there have been major changes in dose, formulation or route of administration. Accidental overdose is likely to be the most common cause of respiratory depression. Concomitant alcohol can exacerbate this adverse effect. Particular caution is necessary for patients taking more than one class of sedative medication and in those with pre-existing disorders of respiratory control, such as obstructive sleep apnoea

4. **Opioid hyperalgesia.** Prolonged use of opioids might lead to a state of abnormal pain sensitivity, called hyperalgesia. Clinically, the patient on long term opioid therapy presents with increased pain. Pain associated with hyperalgesia is more diffuse than the pre-existing pain and less defined in quality. Hyperalgesia can be managed by either reducing the dose of the opiate or rotating between two different opioids, approximately every 12 months. If hyperalgesia is suspected, please seek advice from the secondary care pain service.

5. **Opioid Toxicity.** Clinical features of opioid toxicity are described in table 3. It is helpful to discuss these features with the patient (or carer), particularly if there is concern regarding adherence with the prescribed regimen. The dose of opioid causing toxicity varies between individuals and depends on medical co-morbidity (particularly renal or hepatic impairment) and concomitant medication therapy, including over the counter medications and illicit drug use.

   To reduce the risk of opiate toxicity, doses should not usually be increased by more than 50% of the previous dose. If a patient is displaying symptoms of opioid toxicity, reduce or stop dose of the opioid and consider further action depending on the severity of symptoms.

Table 3

Sedation	Slow respiration
Pinpoint pupils	Visible cyanosis e.g. lips, ears,
Myoclonic jerks	Agitation
Vivid dreams, nightmares, hallucinations	Confusion
Snoring when asleep	
In more severe cases:-	
Hypotension	Convulsions
Coma	Cyanosis of the nose

6. **Opioid withdrawal** can occur when an opioid is stopped suddenly, the dose tapered too rapidly or when an opioid antagonist is given. Small doses of opioids may be given to improve symptoms. Tramadol has effects within noradrenergic and serotonergic systems in addition to its μ-opioid receptor actions and can lead to significant withdrawal symptoms even after short periods of dosing. In many cases, Tramadol withdrawal occurs within 12-24 hours after the last dose; it can also occur with modified release formulations.

   Signs of opioid withdrawal are described in Table 4.

Table 4

Sweating	Abdominal cramps, vomiting and diarrhoea
Mydriasis	Bone and muscle pain
Piloerection	Increase in usual pain
Yawning	Restlessness
Rhinorrhoea	Anxiety
Lacrimation	Tremor

Core Principles

Complete relief from pain is rarely achievable and strong opiates should be used after, or in conjunction with a rehabilitation plan with the aim of improving physical and social function. Maintaining fitness, pacing activities and generally healthy lifestyles are important

The Patient care plan should involve clear goals, with a clear plan for progress towards them with the patient taking on some responsibility for their treatment as with all chronic disease states.

The care plan should take into account the following principles:

- Consider non-pharmacological interventions e.g. TENS, acupuncture, physical methods in the reduction of muscle spasm, cognitive behavioural therapy
- A trial of strong opioids, usually for 2-4 weeks, should only be considered for chronic pain after alternative therapies have failed to adequately deliver pain relief
- The patient and prescriber should sign a opiate treatment doctor-patient agreement with clear instructions regarding when to continue maintenance treatment and when to exit from the pathway
- A single prescriber and pharmacy is recommended to facilitate close monitoring of drug use
- The opioid should be titrated to the **lowest effective** dose
- The dose should not exceed 120mg oral morphine (or equivalent) daily without seeking **specialist advice**
- Only use maintenance opioids for long term conditions if pain relief is significant (successful opioid trial) and sustained, and the quality of life has improved
- The prescriber is responsible for routinely monitoring the safety and effectiveness (improved function and pain) of ongoing treatment, and for signs of misuse
- Be cautious when using opiates with conditions that may potentiate opioid adverse effects (including COPD, CHF, sleep apnea, current or past alcohol or substance abuse, elderly, or history of renal or hepatic dysfunction). See BNF for full details of contra-indications and cautions
- Driving: Patients taking appropriate doses of prescribed opioids are permitted by law to drive in the UK if they are using no more than the prescribed dose and feel fit to drive. Patients should be advised to avoid driving at the start of opioid therapy and following dose changes. Patients should be informed that it is their responsibility to advise the DVLA that they are taking opiate medication
- Do not combine opioids with sedative-hypnotics, benzodiazepines or barbiturates for chronic non-cancer pain unless there is a specific medical and/or psychiatric indication for the combination and increased monitoring is initiated.

Appendix 1: Patient Health Questionnaire-PHQ-9

Strong opioids can be considered if the PHQ-9 score is 4 or less. However, some of the questions on the PHQ-9 (e.g. affect on sleep, appetite) could be scored higher than expected due to physical pain rather than psychological problems. Using clinical judgment, if pain is believed to be significantly influencing the score, opiates may be considered for a score of 5-9. If the score is >9, or any uncertainty remains, a psychiatric assessment should be sought.

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✓" to indicate your answer"*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things.....	0	1	2	3
2. Feeling down, depressed, or hopeless.....	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much.....	0	1	2	3
4. Feeling tired or having little energy.....	0	1	2	3
5. Poor appetite or overeating.....	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down.....	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television.....	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual.....	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way.....	0	1	2	3

Column totals ___ + ___ + ____ + ___

= *Total Score* _____

Scoring notes-depression severity

Scores represent**: 0-4 = none 5-9= mild 10-14 = moderate 15-19 = moderately severe 20-27 = severe depression**

Appendix 2 CAGE Questionnaire

Patient Name _____ Date of Visit

When thinking about drug use, include illegal drug use and the use of prescription drug other than prescribed.

Questions:

1. Have you ever felt that you ought to cut down on your drinking or drug use?
   ……
2. Have people annoyed you by criticising your drinking or drug use?
   ……
3. Have you ever felt bad or guilty about your drinking or drug use?
   ……
4. Have you ever had a drink or used drugs first thing in the morning **to steady your nerves or to get rid of a hangover?**

Scoring: Regard one or more positive responses to the CAGE as a positive screen.

Appendix 3: Opioid Treatment Doctor-Patient Agreement

This form provides information about opioid therapy and seeks your agreement about approach to opioid use.

Potential Benefits
Opioids are used as part of a broad treatment approach rather than as stand-alone therapy. There are a number of potential benefits. These are assessed over a trial period before deciding about maintenance therapy. Specific goals for the opioid trial are:

a. Reduction in my average pain score:
    i. Pain intensity from ___ / 10 to __ / 10
    ii. Pain interfering with ADL from ___ /10 to __ / 10
b. Improvement in the following day to day activities
    i. _____
    ii. _____
    iii. _____
c. Improved performance of the following exercises
    i. _____
    ii. _____
d. Other
    i. _____
    ii. _____

Potential Problems

1. Although medical studies show that opioid medication can reduce persistent pain in the short term, there are no high quality studies looking at the longer-term picture. Further studies are needed.
2. It is possible that you may get initial benefit that wears off over time. This is called tolerance. Sometimes switching to an alternative opioid agent may help. Other pain management strategies may also need to be considered.
3. Dependence and addiction may be problems. All patients on long-term opiates become physically dependent meaning that withdrawal symptoms occur if therapy is stopped abruptly. Addictive behaviour occurs in a small proportion of people and may be minimised by appropriate patient selection.
4. Side effects may include mental clouding and sedation, constipation, nausea, itch, sweating, dry mouth and hormonal problems such as weight gain and sexual dysfunction. Sedation may be more troublesome if opiates are combined with other drugs such as alcohol and benzodiazepines.
5. Lack of alertness may affect driving ability especially in the early stages of therapy or after dose escalation. Generally it is safe to drive once the dose is stable.
6. Babies born to women on opioid therapy may require treatment for opioid withdrawal.

Practical Issues

1. One doctor only is to be responsible for prescribing your opioid medication at any one time. Arrangements can be made for a deputy prescriber to cover medical absences.
2. An initial opioid trial of 2-4 weeks is undertaken to assess your response before a decision is made on whether to begin maintenance therapy. The decision will involve weighing up benefits and side effects. The Graded Chronic Pain Scale can be used before and at completion of the trial to help assess your response.
3. The dose may be adjusted frequently during the trial period. If you progress to maintenance therapy you will need to be reviewed by your doctor on a monthly basis.
4. If your behaviour suggests a problem with drug addiction then your doctor will consider tapering and ceasing your opioid medication. Problem behaviours include giving your medication to others, use of your medication in a non-prescribed way, excessive use of other medications (including alcohol), repeated “loss” of medication, doctor shopping, worsening function at home or at work and frequent complaints about the need for a higher dose.

Agreement
I have read the information provided and agree to participate in the management plan as outlined.
Patient signature: _____
Witness: _____ Date: _____

Appendix 4: ASSESSING FUNCTION AND PAIN

While there is no universally accepted tool to assess opioid therapy's impact on function and pain, this guideline recommends using the two item **Graded Chronic Pain Scale** to assess and monitor response to treatment.

Graded Chronic Pain Scale

Pain intensity and interference

In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be"? [*That is, your usual pain at times you were in pain.*]

No Pain as bad as pain could be

0	1	2	3	4	5	6	7	8	9	10

In the last month, how much has pain interfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities"?

No interference									**Unable to carry on any activities**	
0	1	2	3	4	5	6	7	8	9	10

Interpretation of the Two Item Graded Chronic Pain Scale – This two item version of the Graded Chronic Pain Scale is intended for brief and simple assessment of pain severity in primary care settings. Based on prior research, the interpretation of scores on these items is as follows:

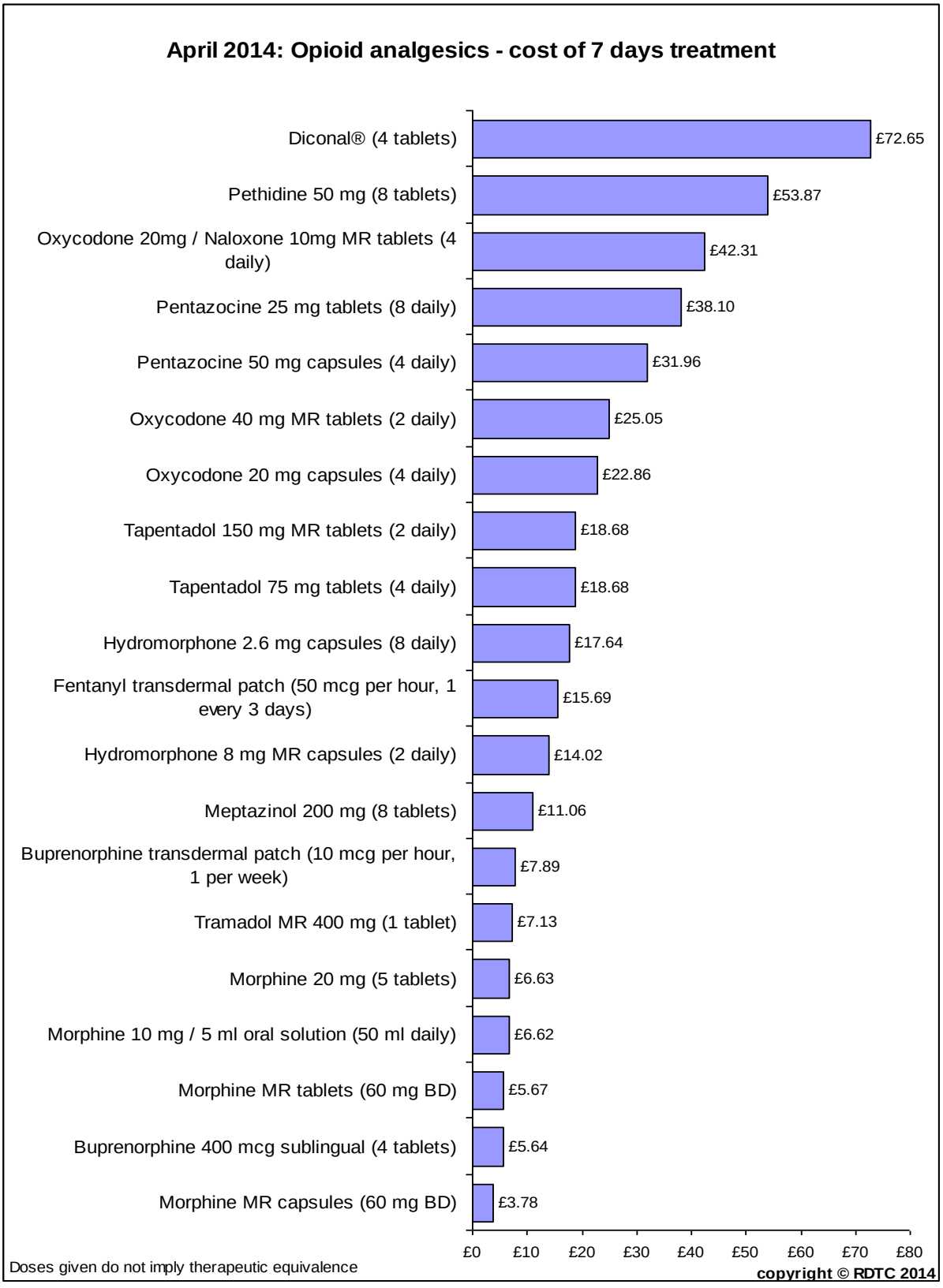
Pain Rating Item	Mild	Moderate	Severe
Average/Usual Pain Intensity	1–4	5–6	7–10
Pain-related interference with activities	1–3	4–6	7–10

Although pain intensity and pain-related interference with activities are highly correlated and tend to change together, it is recommended that change over time be tracked for pain intensity and pain-related interference with activities separately when using these two items.

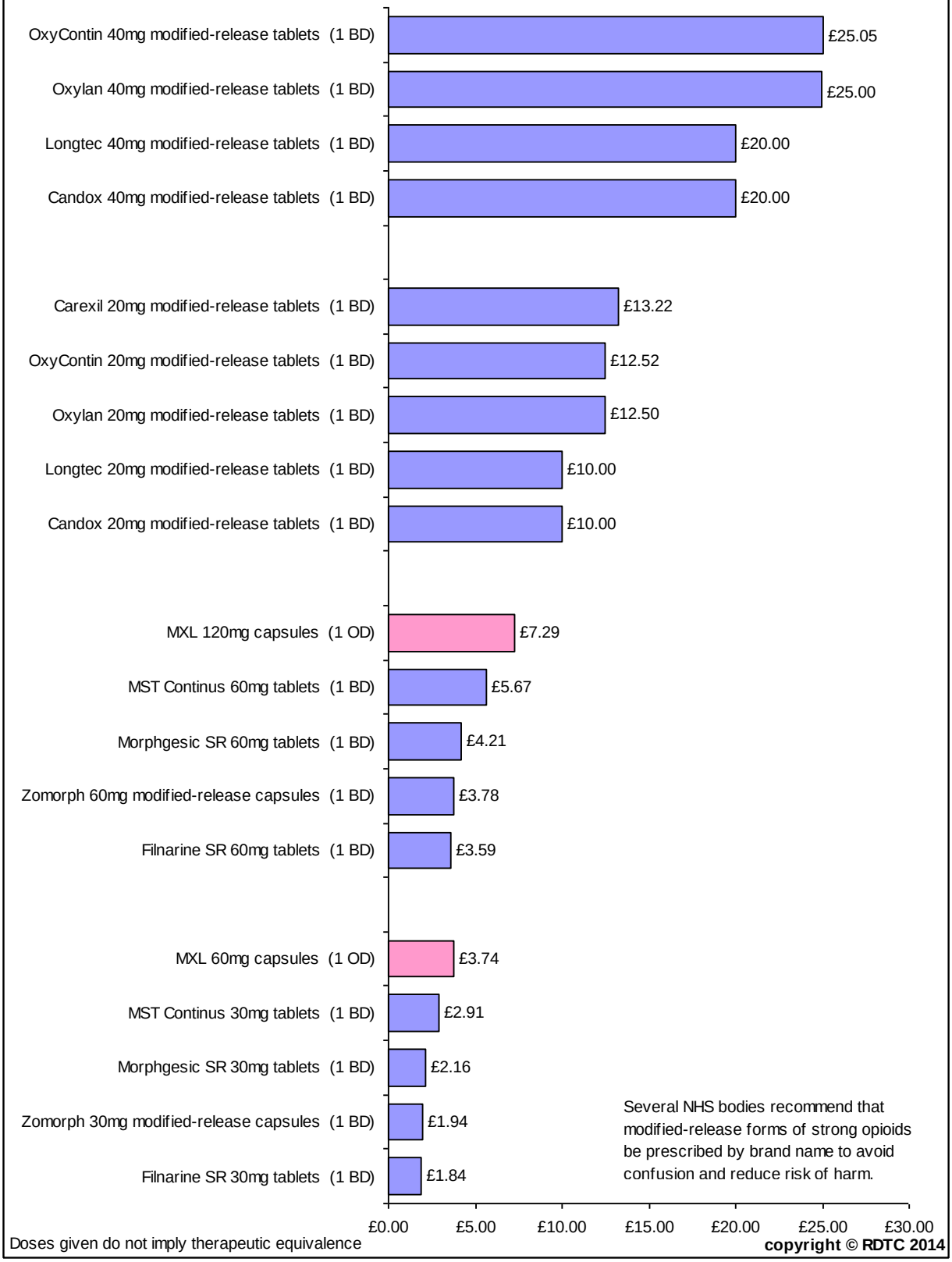
For an individual patient, a reduction in pain intensity and improvement in pain-related interference with activities of two points is considered moderate but clinically significant improvement.

Appendix 5: Cost Comparison Charts for strong opioids

These cost comparison charts are correct as of April 2014, latest charts are available at http://rdtc.nhs.uk/sites/default/files/cost_comparison_charts_0.pdf



April 2014: MR opioid analgesics - cost of 7 days treatment



Doses given do not imply therapeutic equivalence