Merseyside and Cheshire Palliative Care Network Audit Group

Standards and Guidelines Fourth Edition 2010

CONTENTS

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Editorial Team

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PREFACE TO THE FOURTH EDITION

We are pleased to introduce the fourth edition of the Merseyside and Cheshire Palliative Care Network Audit Group Standards and Guidelines. Since the publication of the third edition in 2006, every chapter has been extensively reviewed by members of the group and experts from across the United Kingdom. This edition sees the inclusion of six new guidelines: drugs at the end of life; interventional pain techniques; major haemorrhage; spiritual care; substance misuse and urinary incontinence.

As the list of subjects continues to grow, the emphasis of the audit programme has developed to reflect the importance of closing the audit loop, by re-auditing and updating guidelines. Over the past three years this has included: agitation / delirium, antibiotics, bisphosphonates blood transfusions, constipation, corticosteroids, diabetes, hydration at the end of life, opioid substitution and pleural effusions. Standards and guidelines which have not been re-audited since the last publication have been extensively updated and reviewed for inclusion in this the 4th edition. A full description of the audit programme is now included in Appendix C.

The referencing for each chapter is comprehensive. The Scottish Intercollegiate Guidelines Network system has been introduced and there are now levels of evidence throughout the guidelines and grades of recommendation for all the standards in each of the 43 chapters.

This book is intended as an information resource for qualified medical staff and other health professionals caring for patients where palliative care is appropriate. The guidance is applicable to patients with cancer and other forms of advanced disease. It is important that health care professionals ensure that the information is suitable before using it in any clinical situation.

The book encourages the setting and monitoring of standards in palliative care and promotes clinical excellence in end of life care. We are very grateful for the motivation, dedication and commitment of the group members and our external experts and would like to thank them for making this book possible.

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Editorial Team
December 2009

INTRODUCTION

This book represents the collaborative work of the Merseyside and Cheshire Palliative Care Network Audit Group. One of the main objectives of the group is to use audit projects to develop standards and guidelines, which can be in turn be used to support specialist palliative care professionals and empower those working in other areas of health care.

Initially formed in 1995, the group consists of individuals involved in specialist palliative care across the network in home, hospital and hospice settings. The strength of the group lies in the multidisciplinary representation and the willingness of individual units and services to participate in the audit programme. Over the past fourteen years the group has continued to expand and develop and now holds bimonthly audit meetings throughout the year. In May, the whole group plans the audit programme for the coming twelve months, thus helping to maintain ownership of the audit process and enthusiasm for the projects. Five audit projects are chosen, three of which are identified as regional audits and based on a previously audited topic. One of these audits may be expanded to include the wider locality as a 'supra-regional' audit. There are a further two new audit topics, one of which is designated as non-symptom control.

Each audit meeting attracts approximately 60 health care professionals from across the network. The meetings begin with the presentation of a literature review of the designated topic, followed by results from the individual audit. An open discussion then allows the group to formulate standards and guidelines. An external expert is invited to contribute to both the presentation and discussion. The guidelines are formatted, fully referenced, and the evidence is graded before a final review by the group and the external expert.

Regional audits complete the audit cycle by assessing the group's performance against previously developed standards. Dissemination of the audit projects has been achieved by presentations and publications at national and international level.

The aim of this book is to collate the work undertaken by the group. It is designed both for the purposes of education and to facilitate the production of other group standards and guidelines. The guidelines are not standard protocols and are by no means prescriptive.

Experts from across the UK have externally reviewed all of the standards and guidelines and their comments have been incorporated. The group aim to update the book every three years. Suggestions and comments are welcomed for the next edition which is due in 2012.

DISCLAIMER

The editors cannot be held responsible for any liability incurred as a consequence of the use or application of any contents of this book. Recommendations contained in this book cannot be appropriate for every situation and so professionals using this book should make their own decisions regarding safe and appropriate patient care.

The editorial team make no representation, express or implied, that the drug dosages in this book are correct. Readers must therefore always check the product information and data sheets provided by the manufacturers and the most recent codes of conduct and safety regulations. Mention of specific product brands does not imply endorsement.

Every effort has been made to ensure the accuracy of this text. However the editorial team do not accept responsibility or legal liability for any errors in the text, or for the misuse or misapplication of material in this work.

December 2009

LIST OF ABBREVIATIONS

General

ACE	Angiotensin converting enzyme
ADRT	Advance Decision to Refuse Treatment
AED	Anti-epileptic drugs
AEDs	Automated external defibrillators
BNF	British National Formulary
BP	Blood pressure
BUN	Blood urea nitrogen
Ca^{2+}	Calcium
CBG	Capillary blood glucose
CBT	Cognitive behaviour therapy
CKD	Chronic kidney disease
CNG	Cancer Network Group
CNS	Central nervous system
CQC	Care Quality Commission
COPD	Chronic Obstructive Pulmonary Disease
COX	Cyclo-oxygenase
CPR	Cardiopulmonary resuscitation
CSCI	Continuous subcutaneous infusion
CSM	Committee on Safety of Medicines (now part of Commission on Human Medicines)
CT	Computerised tomography
CXR	Chest X-ray
D_2	Dopamine type 2 receptor
DIC	Disseminated intravascular coagulation
DM	Diabetes mellitus
DNACPR	Do Not Attempt Cardiopulmonary Resuscitation
DNAR	Do Not Attempt Resuscitation
DSM	Diagnostic and Statistical Manual of Mental Disorders

DVT	Deep venous thrombosis
e/c	Enteric coated
ECG	Electrocardiogram
ECT	Electroconvulsive therapy
ECOG	Eastern Cooperative Oncology Group
eGFR	Estimated Glomerular Filtration Rate
FBC	Full blood count
FDA	Food and Drug Administration (USA)
FEV_1	Forced expiratory volume in one second
GABA	Gamma-aminobutyric acid
GI	Gastrointestinal
Hb	Haemoglobin
HbA1c	Glycosylated haemoglobin
H_1, H_2	Histamine type 1, type 2 (receptor)
HR	Heart Rate
5HT	5 hydroxytryptamine
HIV	Human Immunodeficieny Virus
ICD	International Classification of Diseases
ICN	Integrated Care Network
IMCA	Independent Mental Capacity Advocate
INR	International Normalised Ratio
IVI	Intravenous infusion
LCP	Liverpool Care of the Dying Pathway
LFT	Liver function test
LMWH	Low molecular weight heparin
LPA	Lasting Power of Attorney
MAOI	Mono-amine oxidase inhibitor
MARI	Mono-amine oxidase re-uptake inhibitor
MCV	Mean cell volume
MDT	Multidisciplinary team meeting
MEN	Multiple endocrine neoplasia
MHRA	Medicines and Healthcare products Regulatory Agency
MRI	Magnetic resonance imaging
MRSA	Methicillin-resistant staphylococcus aureus
MSCC	Malignant spinal cord compression

MSSU	Midstream specimen of urine
Na Cl	Sodium chloride
NaSSA	Noradrenergic and specific serotoninergic antidepressant
NBM	Nil by mouth
NICE	National Institute for Health and Clinical Excellence
NMDA	N-methyl-D-aspartate
NSAID	Non-steroidal anti-inflammatory drug
O_2	Oxygen
OTC	Over the counter
PCV	Packed cell volume
PE	Pulmonary embolism
PEG	Percutaneous endoscopic gastrostomy
PEJ	Percutaneous endoscopic jejunostomy
PG(s)	Prostaglandin(s)
PICC	Peripherally inserted central catheter
PPI	Proton pump inhibitor
REM	Rapid eye movement
SPC	Summary of Product Characteristics
SSRI	Selective serotonin reuptake inhibitor
SVCO	Superior vena cava obstruction
TCA	Tricyclic antidepressant
TENS	Transcutaneous electrical nerve stimulation
TFT	Thyroid function test
U and E	Urea and electrolytes
UTI	Urinary tract infection
VAS	Visual analogue scale
VIP	Vaso-active intestinal polypeptide
WBC	White blood count
WHO	World Health Organisation

Drug Administration

bd	twice daily
im	intramuscular
iv	intravenous
ivi	intravenous infusion
m/r	modified release or slow release

nocte	at bedtime
od	once daily
po	per os, by mouth
pr	per rectum
p.r.n	rescue medication (as needed / required)
pv	per vaginum
qds	four times a day (per 24 hours)
sc	subcutaneous
sl	sublingual
stat	give immediately
TD	transdermal
tds	three times a day (per 24 hours)
WFI	water for injection

Units

g	Gram(s)
Gy	Gray (s), a measure of radiation
h	Hour(s)
IU	international units
kg	kilogram(s)
L	Litre(s)
mcg	microgram(s)
mg	milligram(s)
ml	millilitre(s)
mm	millimetre(s)
mmol	millimole(s)
min	minute
sec	second(s)

1. GUIDELINES FOR THE MANAGEMENT OF AGITATION IN ADVANCED CANCER

1.1 GENERAL PRINCIPLES

* There are many causes of agitation in palliative care patients, which makes recommendations for treatment difficult. [1]

* Agitation in the dying phase is well recognised but poorly defined and management can be very difficult. Reversible causes should be corrected where possible. The aim of treatment should always be to control the agitation or restlessness. [2, 3, 4, 5]

* Management of a patient who is agitated may include non-pharmacological and pharmacological measures. [1]

* Medication used should be titrated to control the agitation and not with the intention of sedation. Medication can be administered intermittently or via a continuous infusion. The effect of sedating medication on the conscious level will vary between individual patients. [6, 7]

* Sedation can be defined as: "A medical procedure used to palliate symptoms refractory to standard treatment by intentionally diminishing the conscious level." [8]

1.2 GUIDELINES

* It may be difficult to differentiate between delirium and agitation. Delirium should be excluded by using the DSM IV criteria for the diagnosis of delirium (see Guidelines for the Management of Delirium in Advanced Cancer). [9] [Level 4]

* Common causes of agitation in palliative care patients are listed in Table 1.1

Table 1.1 Causes of agitation [1, 10] [Level 4]

Anxiety	Dyspnoea
Biochemical abnormalities	Pain
Cerebral tumour	Psychiatric illness
Constipation	Terminal agitation
Depression	Urinary retention
Drugs	Withdrawal of alcohol / nicotine /sedative drugs

* Drugs are a common cause of agitation and include: corticosteroids; benzodiazepines (paradoxical agitation) and opioids. Dopamine antagonists such as haloperidol, levomepromazine and olanzapine (akathisia) may also cause cognitive decline and dementia due to the acetylcholine effects. [1] [Level 4]

* If a patient is agitated it is important to exclude reversible causes and treat where appropriate.[4, 5] [Level 4]

* Non-pharmacological measures are important in the management of an agitated patient. These may include reassurance, presence of familiar faces and use of a well-lit and quiet room. Psychological and spiritual support should be offered where appropriate. [10] [Level 4]

* Nicotine replacement therapy may be used where agitation is secondary to nicotine withdrawal. [4, 5] [Level 4]

* Midazolam is the drug of choice for the management of agitation or restlessness at the end of life. [11] [Level 3]

* The intention of treatment should be to control the symptom of agitation or restlessness. However, at times this may result in a decreased level of consciousness. The drug doses should be titrated to achieve symptom control of the agitation. [6] [Level 4]

* The aim of treatment, and any expected change in level of consciousness, should be discussed with the patient, relatives and multi-disciplinary team where possible.[7] [Level 4]

* The aim of treatment, and any expected change in the level of consciousness, should be documented in the case notes.[7] [Level 4]

* Where treatment of agitation results in continuous sedation, the underlying disease process should be advanced and irreversible, and death expected in hours to days. [6] [Level 2++]

* Table 1.2 lists the pharmacological options for the symptomatic management of agitation. [4, 5, 12, 13] [Level 4]

* Figure 1.1 illustrates a suggested approach to the pharmacological management of terminal agitation. [4, 5] [Level 4]

* Where the patient is shown to lack the capacity to consent to treatment, the Mental Capacity Act 2005 must be followed. The Lasting Power of Attorney, Advance Decisions and Independent Mental Capacity Advocates should be utilised where appropriate. [12] [Level 4]

Figure 1.1 Pharmacological management of terminal agitation in advanced cancer [4] [Level 4]

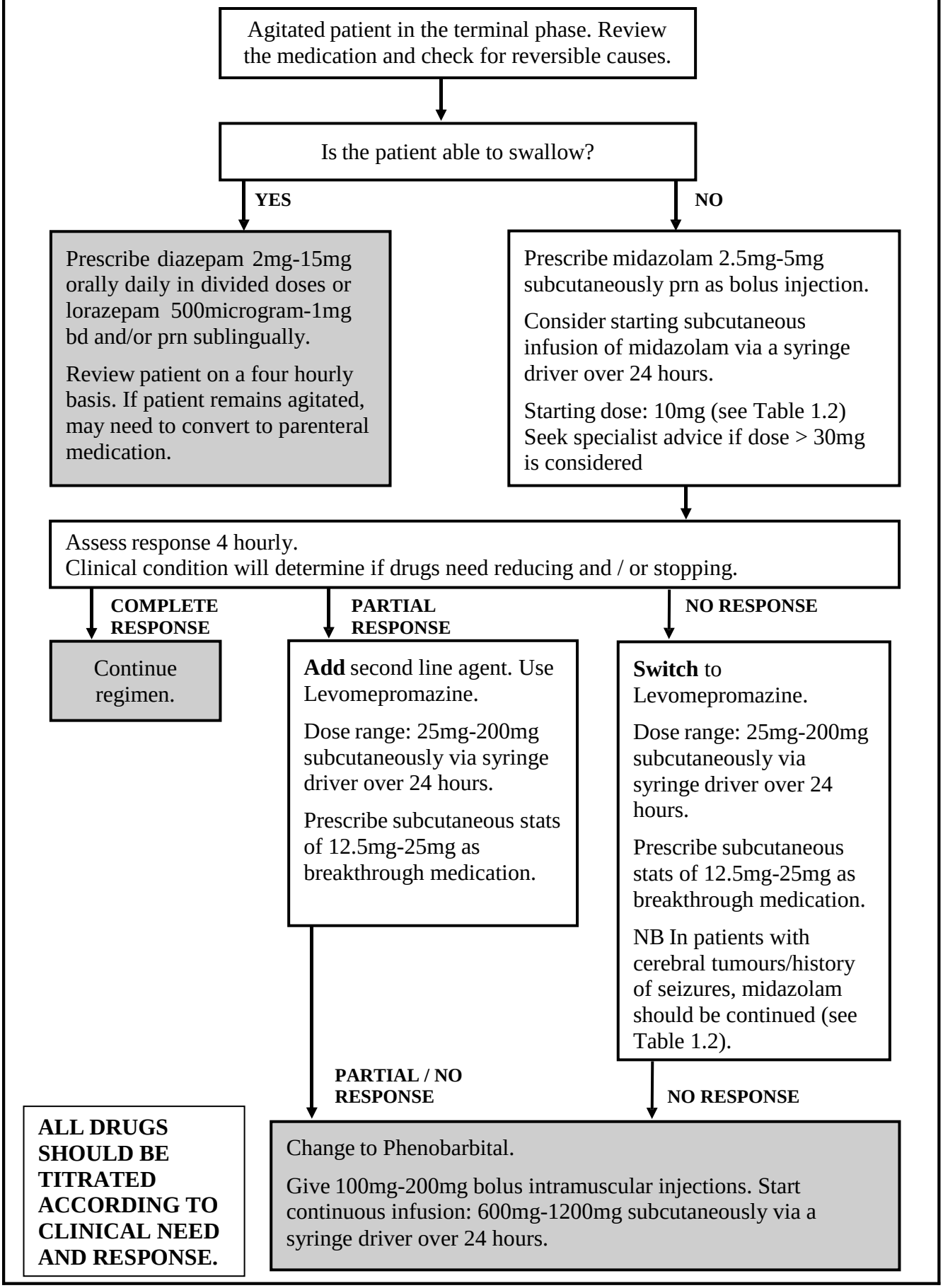

Table 1.2 Pharmacological options for the symptomatic management of agitation in advanced cancer [4, 5, 12, 13, 14] [Level 4]			
Name of drug / Class of drug	**Dose and route of administration**	**Side effects**	**Comments**
Lorazepam *Short acting benzodiazepine*	500 microgram-1mg bd and prn sublingually. Maximum dose is 4mg per 24 hours.	Possible risk of paradoxical agitation.	Not for use in syringe driver. Can develop tolerance.
Diazepam *Long acting benzodiazepine*	2mg-5mg tds and prn orally. 10mg via rectal route prn. 2mg-10mg via intravenous route prn.	Possible risk of paradoxical agitation.	Not for use in syringe driver. Can develop tolerance.
Midazolam *Short acting benzodiazepine*	2.5mg-10mg prn via subcutaneous route. 10mg-30mg ** subcutaneously via syringe driver over 24 hours.	Possible risk of paradoxical agitation.	Will not improve cognition in delirium. Can develop tolerance. Flumazenil is the reversing agent. [14] **If a dose > 30mg / 24 hours is being considered, seek specialist palliative care advice. Doses of up to 100mg / 24 hours have been used but only when the addition of an antipsychotic such as levomepromazine is inappropriate. If patient has received an enzyme inducer such as carbamazepine or phenytoin the dose may need reducing after 3- 5 days as the enzyme induction wears off.
Levomepromazine *Long acting phenothiazine*	12.5mg-200mg subcutaneously over 24 hours for management of agitation. Stat doses can vary between 12.5mg-50mg subcutaneously. Can also use orally for the control of agitation.	High doses may precipitate seizures.	May lower the threshold for seizures. Therefore in patients with a history of seizure / cerebral tumours consider the addition of midazolam in a CSCI.
Phenobarbital *Long acting barbiturate*	Usually given via parenteral route in this situation. Use 100mg-200mg intramuscular stat injections. Can use 600mg-2400mg subcutaneously via syringe driver over 24 hours.		Use intramuscular injections for breakthrough medication. Do not mix with other drugs in a syringe driver. There is anecdotal evidence that get fewer site reactions if use sodium chloride 0.9% as diluent, although water can be used. Can be given intravenously.

1.3 STANDARDS

1. Reversible causes of agitation should be treated where appropriate. [4, 5] [Grade D]
2. All patients should have a clinical examination at the initial assessment of agitation.[4, 5] [Grade D]
3. All patients should have a review of medication at the initial assessment of agitation.[4, 5] [Grade D]
4. The reason for the use of psychotropic medication should be documented in the case notes. [7] [Grade D]
5. Patients should be reviewed every four hours to ensure adequate symptom control.[7] [Grade D]
6. If a health care professional feels they may be shortening life by the use of sedation they should contact senior / specialist help for advice. [7, 13] [Grade D]

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2. GUIDELINES FOR THE USE OF ANTIBIOTICS IN PALLIATIVE CARE

PLEASE REFER TO LOCAL GUIDANCE

2.1 GENERAL PRINCIPLES

* Before starting antibiotic treatment, consider the goals of treatment and whether they are appropriate for that individual patient. The goals of treatment with antibiotics may be:
  - Symptomatic relief of the unpleasant symptoms of sepsis, **or**
  - Cure of reversible infective complications to maintain quality of life. [1]
* The goal(s) of treatment will determine the need for laboratory investigations. [1]
* It may be appropriate to discontinue antibiotics within 48 hours of having achieved a good clinical response in certain types of infections e.g. respiratory and urinary tract infections. Soft tissue and deep seated infections are an exception to this advice and often need a longer duration of treatment. [2]
* If a patient is unable to take oral antibiotics, a period of 24-48 hours of intravenous antibiotics may be indicated. These can be administered within the hospice setting if staff are adequately trained. It is preferable to choose an antibiotic that can be given once daily as either a bolus injection or a brief infusion. Transfer to an acute unit is an alternative option. [2]
* If a patient is unwell and / or pyrexial, and has recently received chemotherapy, consider the possibility of neutropenic sepsis. [3]
* Patients with neutropenic sepsis should be discussed with the appropriate oncologist as a matter of urgency. If antibiotics are commenced in the specialist palliative care unit, clinicians should follow the locally agreed policy. [3]
* Hospital antibiotic policies vary and the choice of antibiotic may need discussion with the microbiologist. Locally agreed policy will take precedence over these guidelines. It is important that there is access to follow up advice from microbiologists in the event of non-response to treatment or troublesome side effects. [4]
* All antibiotics carry a risk of side effects and it is important that the risk is minimised. Inappropriate prescribing should be avoided. Gastrointestinal upset is a particular problem with some antibiotics e.g. co-amoxiclav. [4]
* All staff should be educated about the importance of ward cleaning and hand washing. [5]

2.2 GUIDELINES

2.2.1 Cellulitis

* If a patient is systemically unwell, they may require an initial course of intravenous antibiotics before conversion to oral therapy.[6] [Level 4]
* If a patient has rapidly spreading cellulitis or cellulitis with lymphoedema, consider an intravenous regimen and review after 24- 48 hours (see Table 2.2). [6] [Level 2]

* If a patient has lymphoedema and cellulitis, it may be necessary to continue prophylactic low dose antibiotics after the initial antibiotic course is complete, e.g. Penicillin V 500mg od (1g if weight>75kg). The dose may be reduced to 250mg od after 12 months of successful prophylaxis.. For those allergic to penicillin consider Erythromycin 250mg od. If this is not tolerated an alternative would be Clarithromycin 250mg od. Prophylaxis needs to be life long if relapse occurs when antibiotics are discontinued after a two year period of successful prophylaxis [6, 7, 16] [Level 2]

2.2.2 Chest infections

* Send sputum for microbiology as soon as possible. If there is no response to antibiotics and cultures are negative, consider atypical organisms such as *Chlamydia* or *Mycoplasma*.[8] [Level 2]
* Physiotherapy, bronchodilators, corticosteroids and hydration are important options in the management of chest infections. [8] [Level 4]

2.2.3 Neutropenic sepsis [2, 3, 4, 6] [Level 3]

* Table 2.1 gives some useful definitions for febrile neutropenia and neutropenic sepsis.

Table 2.1 Definitions used in neutropenic sepsis

Febrile neutropenia	Neutropenic sepsis
Temperature ≥ 37.9 °C on at least one occasion PLUS Neutrophil count of ≤ 1x 10^9/l	As for febrile neutropenia Additional clinical features may include: − Rigors − Confusion − Hyperventilation − Hypotension

* Neutropenic sepsis may occur during or following chemotherapy, classically 7-10 days after treatment.
* All patients with suspected neutropenic fever should undergo clinical assessment and have a full blood count taken as a matter of urgency. It is important to know the treatment cycle day and details of the specific chemotherapy regimen to allow determination of the risk.
* Always discuss the patient with the appropriate medical oncologist.
* If a patient has a prolonged neutropenia and a significant life expectancy, the use of antifungal prophylaxis should be considered and discussed with the microbiologist/ oncologist.
* Patients should be assigned a risk index to determine optimum treatment. Details of risk categories can be obtained from the local chemotherapy unit. If there is any doubt it is preferable to manage patients as high risk in the first instance. These guidelines only give details for managing high risk patients. Management of patients deemed low risk and borderline risk will be detailed in local policies. High risk patients should receive intravenous therapy. Low risk patients receive oral therapy and it may be possible to facilitate an early discharge. [3] [Level 4]
* The patient may need urgent transfer to an acute unit.

* If treatment is appropriate:
  - Arrange a full septic screen including blood cultures, sputum, urine, faeces and throat swabs.
  - Check electrolytes, liver function and creatinine.
  - Start antibiotics.
* If deemed high risk and not allergic to penicillin give:
  - Piperacillin / tazobactam (Tazocin®) 4.5g tds intravenously plus stat dose of 5mg/kg gentamicin (lean body weight or total body weight if this is lower). Maximum dose is 400mg. Note that the first dose of gentamicin is irrespective of renal function.
  - If a venous cannula is in place add vancomycin or teicoplanin in addition to the above (see Table 2.2).
* After 24 hours review results of cultures and clinical response. If gentamicin is to be continued, drug levels and renal function must be monitored.
* If allergic to penicillin, substitute intravenous ciprofloxacin for piperacillin / tazobactam (Tazocin®) and add gentamicin
* It is important to try and prevent the occurrence of neutropenic sepsis. Patients who have received chemotherapy, and who are anticipated to develop a neutropenia which persists for more than 10-14 days, should receive elective prophylaxis against endogenous enteral flora. The choice of antibiotic will vary according to local policy, but will typically be an oral quinolone antibiotic such as ciprofloxacin.

2.2.4 Urinary tract infections [9] [Level 3]

* Only 50% of episodes of dysuria and/or frequency are caused by bacterial infection of the bladder.
* Before commencing antibiotic treatment, dipstick the urine for leucocytes and nitrites. If negative for both, the probability of infection is low. If positive, then send a midstream sample of urine for culture. It is reasonable to start first line antibiotics without waiting for the result (see Table 2.2).
* If the patient does not respond to the initial course of antibiotics, the regimen should be altered according to sensitivities from microbiology.

Vulvo-vaginal candidiasis

* Vulvo-vaginal candidiasis may be a cause of dysuria and / or frequency. It may not be associated with irritation or discharge. It should be considered in women with persistent symptoms of cystitis who have a laboratory urinalysis showing white cells but no significant bacterial growth. The diagnosis is made by a low vaginal swab as a high vaginal swab is not necessary.

Catheterised patients

* Catheterised patients often have bacterial colonisation of the lower urinary tract which is impossible to eradicate. Antibiotic treatment should be reserved for patients with symptoms of bladder wall inflammation and/or a kidney infection.
* Dipsticks are unhelpful in catheterised patients. Nitrites will be positive from bacterial colonisation and pyuria is often present simply because of the presence a foreign body. If a patient is thought to have a urinary tract infection then a sample of urine from the catheter should be sent for culture.

* The routine use of antibiotics during catheter changes is not indicated. The only exceptions are if the patient is neutropenic or at risk of endocarditis.

2.2.5 Wound odour

* Foul odours due to anaerobic infections often respond to metronidazole therapy. [10] [Level 4]
* If systemic metronidazole is used, the correct dose is 400mg tds, reducing to 200mg tds after 7-14 days. [6] [Level 3]
* Topical metronidazole (0.8% metronidazole in an aqueous base) is expensive and may cause skin irritation with long term use. Use should be restricted to patients for whom systemic metronidazole is ineffective. [10] [Level 4]
* For medical and surgical wounds that look infected the antibiotic of first choice is flucloxacillin (or erythromycin if the patient is allergic to penicillin). If the patient is septicaemic consider adding metronidazole. [6] [Level 2] (see Table 2.2 for further details)

2.2.6 Methicillin Resistant Staphylococcal Aureus (MRSA)

* MRSA is a bacterial organism resistant to methicillin and other groups of antibiotics. It can cause significant infections e.g. urinary tract infections, wound infections, pneumonia and overwhelming sepsis. [11] [Level 3]
* Staff education regarding the importance of hand washing and high standards of ward cleanliness is a priority. [12] [Level 2]
* There is no definitive evidence on the long term benefits of decolonisation because MRSA is now generally regarded as "for life." [13] [Level 4]
* If there is evidence of MRSA infection, consider seeking the advice of a microbiologist. [13] [Level 4]
* The treatments vary in efficacy, expense and potential for causing side effects. There is reason for remaining optimistic when talking to patients and carers about the likely success of treatment and also to emphasize the benign nature of MRSA in patients without wounds or intravascular devices. [13] [Level 4]
* Leaflets on MRSA should be provided. [14] [Level 4]
* Patients with MRSA bacteraemia may require transferring to an acute setting but this decision will need to be made on an individual patient basis. [11] [Level 3]
* Glycopeptide antimicrobials remain the mainstay of treatment e.g. vancomycin or teicoplanin. [12] [Level 2]
* A variety of oral agents are available to treat MRSA once intravenous therapy has secured an initial clinical response. This helps avoid the need for prolonged iv access and the attendant complications. [13] [Level 4]

2.2.7 Clostridium Difficile

* Prevention is better than cure. It is important to maintain good environmental hygiene and ensure good antibiotic management in accordance with local antibiotic policies. [5] [Level 3]
* Staff and visitors should ensure strict personal hygiene is observed. Hands should be washed with soap and water as alcohol washes do not kill the spores. Hand washing prevents cross infection. [5] [Level 3]
* Isolation should be considered for patients who are faecally incontinent.[5] [Level 4]

* The use of antibiotics should be rationalised. If possible antibiotics should be discontinued. [5] [Level 3]
* Patients may require supportive care with hydration and correction of electrolyte imbalance, depending on their clinical condition. Good nutrition should be centred on a balanced diet which includes soluble fibre to sustain colonic colonisation by friendly bacteria (probiotic approach). There is no evidence that prebiotics are of any benefit. [15] [Level 3]
* First line treatment is oral metronidazole 400mg tds or oral vancomycin 125mg qds for 10-14 days. [6] [Level 2]
* There is no requirement to repeat a stool culture at the end of the treatment. [6] [Level 3]
* The relapse rate is 25%. If this occurs, investigation and management should be based on a multidisciplinary review. [15] [Level 3]

2.2.8 Suggested antibiotic regimens

* Current recommended antibiotic regimens are listed in Table 2.2. These will vary according to local policies.

2.3 STANDARDS

1. Specimens for culture and sensitivity should be sent to microbiology before the initiation of antibiotic treatment whenever possible. [6] [Grade D]
2. Antibiotic guidelines should be updated every 2-3 years. [2] [Grade D]
3. Any known allergies to antibiotics should be clearly recorded in the patient notes and on the medication chart. [6] [Grade D]
4. Inappropriate prescribing of antibiotics should be avoided. [6] [Grade D]
5. All inpatient palliative care units should have a MRSA policy. [13] [Grade D]
6. All staff should be educated about the importance of ward cleaning and hand washing.[5] [Grade D]
7. Information leaflets on MRSA should be available for patients/families. [10] [Grade D]
8. Any patient with diarrhoea and known antibiotic use should have a stool sample sent urgently for screening for C difficile toxin. [5] [Grade B]
9. In patients with *Clostridium difficile* there should be an urgent review / discontinuation of any antibiotics prescribed. [5] [Grade B]
10. Patients with *Clostridium difficile* infection should be isolated and barrier nursing / gloves used wherever possible. [5] [Grade B]
11. Intravenous therapy should be reviewed every 24 hours with a view to oral stepdown at the earliest opportunity. [6] [Grade D]
12. Where intravenous antibiotic therapy is anticipated to be required for ≥5 days, early consideration of placement of a midline or PICC line should be considered for patient comfort and the possibility of home IV therapy. [2] [Grade D]

Table 2.2 Suggested antibiotic management for specific infections [3, 4, 6] [Level 2]
(NB: Recommendations may vary according to local policy)

Problem	Causative organism(s)	First line antibiotics	Additional notes
Spreading Cellulitis	*Streptococcal*	Ceftriaxone 1-2g iv od initially. Oral stepdown to amoxicillin 500mg tds or if allergic to penicillin clindamycin 300mg orally tds. Review after 24- 48 hours.	If there is no breach in the skin, swabbing for microbiology is futile.
Wound infection	*Staphylococcus aureus/ Beta haemolytic streptococci /Anaerobes* (if necrotic, cancerous or malodorous lesion)	Flucloxacillin 500mg orally qds. If septicaemic / anaerobes add metronidazole 400mg orally tds. If allergic to penicillin use erythromycin 500mg orally qds.	Always swab before starting treatment as sensitivities are unpredictable.
Exacerbation of COPD / Lower Respiratory Tract Infection	*Haemophilus / Strep pneumoniae Moxarella catarrhalis*	Doxycycline 200mg as a loading dose then 100mg bd or moxifloxacin 400mg orally od for 5 days. If there is a poor response add amoxicillin 500mg tds. If allergic to penicillin use erythromycin 500mg qds for 7 days.	
Bronchopneumonia / Hospital acquired chest infection	*Strep pneumoniae / Haemophilus / Gram negative / Staph aureus* (post influenza) and atypical bacteria (*Mycoplasma Legionella*)	The choice depends on whether community / hospice / hospital acquired infection and on clinical severity / signs of respiratory distress. Refer to local guidelines for antibiotic choice.	Send sputum and blood cultures for culture and sensitivity before starting antibiotics where possible
Aspiration pneumonia	*Strep pneumoniae / Staph aureus / Gram negative bacteria / anaerobes*	Co-amoxiclav 1.2 g tds or piperacillin / tazobactam 4.5g iv tds for 5 days depending on clinical background.	Prophylactic antibiotics following an episode of aspiration are of no benefit.
Urinary tract infections	*E coli / Proteus / Klebsiella / Enterococcus*	Non catheterised (* waiting for culture) Nitrofurantoin 50mg qds **or** Trimethoprim 200mg bd **or** Cefalexin 500mg-1g orally bd (all for 3-5 days). Catheterised (* waiting for culture) Ciprofloxacin500mg orally bd **or** Gentamicin 5mg / kg- one dose intravenously.	If pseudomonas infection use ciprofloxacin 250mg-500mg bd orally. The dose of gentamicin will depend on weight, renal function and subsequent gentamicin levels if appropriate. It is important to check renal function prior to using gentamicin.
CDT Positive Diarrhoea	*Clostridium difficile Toxin*	Metronidazole 400mg orally tds for 10-14 days or Vancomycin 125mg orally qds for 10-14 days.	Stop all other antibiotics if possible
Neutropenic sepsis.	Gram negative and Gram positive bacteria. Atypical bacteria.	Piperacillin / tazobactam (Tazocin®) 4.5g iv tds plus stat dose of gentamicin 5mg/kg iv. If allergic to penicillin use ciprofloxacin 400mg iv bd to replace Tazocin® and add gentamicin. If there is evidence of central line tunnel infection add vancomycin and consider stopping gentamicin.	Check gentamicin levels 6-14 hours post dose. Review after 48 hours on regimen. If prompt intravenous therapy is not feasible, a starting dose of 5mg / kg gentamicin may be given intramuscularly. Certain drugs may contribute to gentamicin toxicity especially loop diuretics.

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3. GUIDELINES FOR THE USE OF ANTICOAGULATION IN PALLIATIVE CARE

3.1 GENERAL PRINCIPLES

* Venous thromboembolism is relatively common in patients with advanced cancer, many of whom remain asymptomatic. [1]
* Patients receiving palliative care present particular problems when considering treatment with anticoagulation. Advanced cancer and immobility are persistent risk factors that may require long-term treatment. The use of warfarin may be complicated by factors such as liver metastases, vomiting or drug interactions e.g. antibiotics, NSAIDs, corticosteroids and anticonvulsants. General frailty may make repeated blood tests inappropriate and venous access may be limited. [1, 2]
* It is important for the clinician to decide whether anticoagulation is appropriate on an individual patient basis. [3]
* Recurrent thromboembolism occurs in 27% of patients, despite a therapeutic INR (International Normalised Ratio). [4]
* Low Molecular Weight Heparin (LMWH) is an alternative to warfarin in palliative care patients and can be used for prophylaxis of deep venous thrombosis (DVT) in high-risk patients. [5]
* LMWH may be superior to warfarin in the treatment of thromboembolism in patients with cancer. [3, 4, 6]
* Poor INR control may subject the patient to an increased risk of bleeding without adequately treating the venous thrombosis. [4, 6]
* The National Patient Safety Agency has issued guidance on the safe prescribing of anticoagulants. [7]

3.2 GUIDELINES

3.2.1 General management of suspected Deep Venous Thrombosis (DVT) / Pulmonary Embolism (PE)

* Decisions surrounding the use of anticoagulation in patients with advanced cancer should be discussed with a senior physician. Figure 3.1 illustrates some general guidelines regarding the investigation and management of thrombo-embolic disease. [8] [Level 4]

3.2.2 Aims and duration of anticoagulation

* Table 3.1 illustrates:
    - The suggested duration of treatment for patients on warfarin and LMWH, **and**
    - The target INR for patients on warfarin. [9, 10] [Level 4]

* Oral anticoagulation may be stopped abruptly when the duration of therapy is completed. [10] [Level 2]

* Advice on the management of bleeding and /or high INR is given in Table 3.2. [9, 11, 12] [Level 3]

Figure 3.1 Management of suspected DVT / PE in palliative care [8] [Level 4]

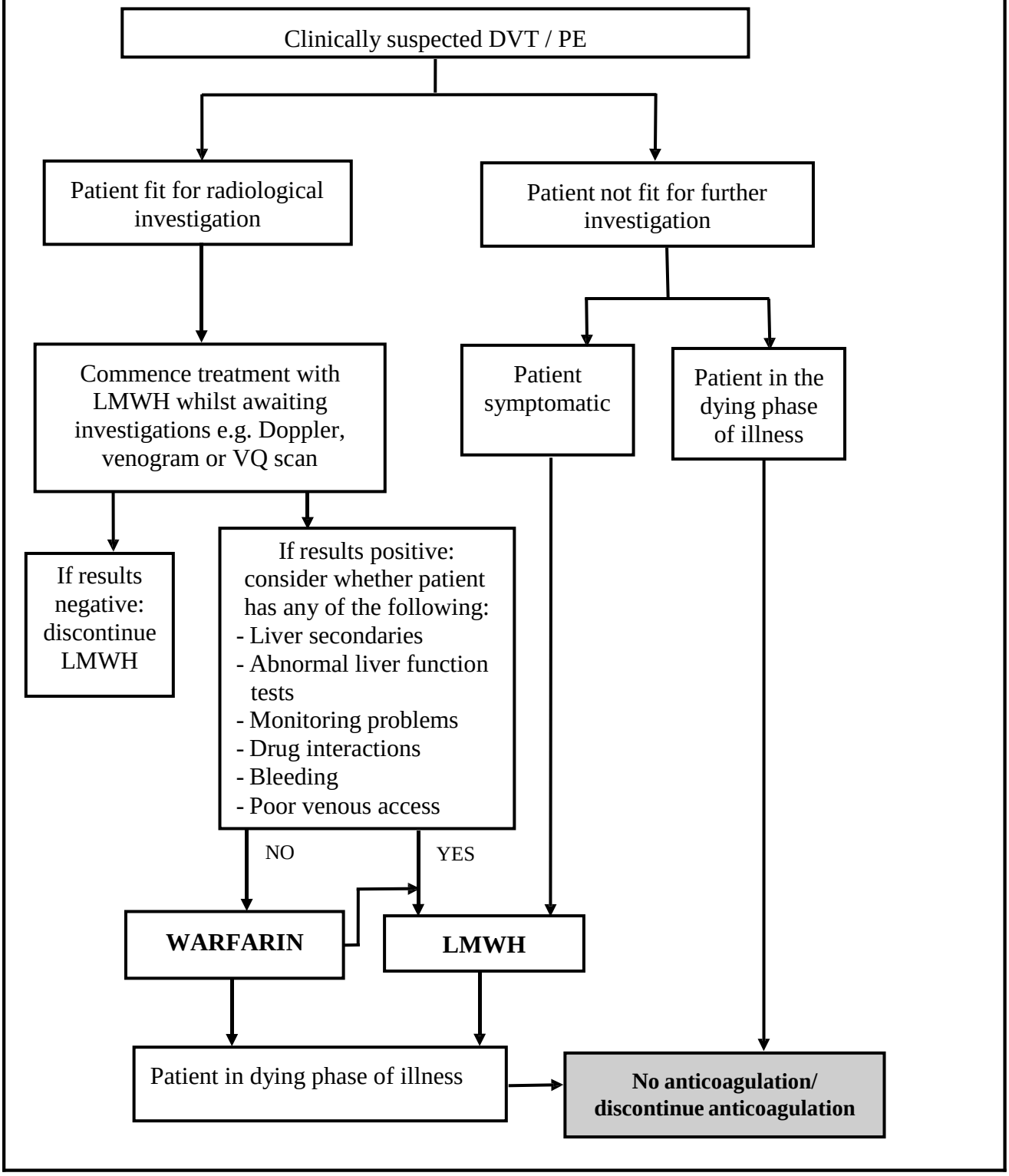

Table 3.1 Indications, duration of treatment, and target INR for patients receiving anticoagulation [9, 10]

Diagnosis	Target INR for patients on warfarin	Duration of treatment with anticoagulants
Pulmonary embolus		
Temporary risk factors; low recurrence risk	2.5	3 months minimum [Level 1+]
If idiopathic or permanent risk factors	2.5	6 months minimum [Level 1+]
Proximal deep vein thrombosis (above knee)		
Temporary risk factors; low recurrence risk	2.5	3 months minimum [Level 1+]
If idiopathic or permanent risk factors	2.5	6 months minimum [Level 1+]
Calf vein thrombosis	2.5	6 weeks minimum [Level 1+]
Recurrence of venous thromboembolism when **no** longer on warfarin therapy	2.5	6 months minimum [Level 1+]
Recurrence of venous thromboembolism **whilst on** warfarin therapy	3.5	6 months minimum [Level 2+]
Atrial fibrillation (all causes)	2.5	Indefinite [Level 2+]
Cardiomyopathy	2.5	Indefinite [Level 2+]
Mural thrombus	2.5	Indefinite [Level 2++]
Mechanical heart valves	For patients in whom valve type and location are known, there are specific target guidelines.[10] If valve type not known the target INR is: Aortic valves: 3.0 Mitral valves: 3.5	Indefinite [(Level 2++]

Table 3.2 Management of bleeding and / or high INR [9 11, 12] [Level 3]	
Major bleeding	Omit warfarin. Give Vitamin K 1mg via slow intravenous injection or 1mg oral Vitamin K. Consider prothrombin complex concentrate (factors II, VII, IX, and X) 30-50 units/kg or if no concentrate available use fresh frozen plasma 15ml/kg.
INR>8.0. No bleeding or minor bleeding	Omit warfarin. Restart when INR<5.0. If there are other risk factors for bleeding give Vitamin K 1mg via slow intravenous injection or 1mg oral Vitamin K. Repeat doses of Vitamin K if INR still too high after 24 hours.
6.0 < INR < 8.0. No bleeding or minor bleeding	Omit warfarin. Consider reversal with 1mg slow intravenous Vitamin K or 1mg of oral Vitamin K particularly if there are additional risk factors for bleeding. Check for bleeding, haematuria or significant bruising. Restart warfarin when INR<5.0.
INR<6.0 but more than 0.5 units above target value	Omit warfarin for 2 days. Recheck INR. Restart when INR<5.0.
Unexpected bleeding at therapeutic levels	Always investigate possibility of underlying cause e.g. unsuspected renal or gastro-intestinal tract pathology. If bleeding is severe, the INR should be reversed.

3.2.3 Low Molecular Weight Heparin (LMWH)

* In some patients LMWH may be a better choice for patients than warfarin. Possible clinical indications for use of LMWH include:
  - Treatment of thromboembolic disease e.g. DVT / PE whilst warfarin therapy is being initiated. Heparin treatment is usually temporary and is stopped when adequate anticoagulation with warfarin is achieved i.e. INR >2. [13] [Level 4]
  - Long term treatment of thromboembolic disease where warfarin therapy is not appropriate e.g. liver disease, unstable INR, difficult venepuncture (see Figure 3.1). [5] [Level 4]
  - Extension of the thrombus despite the use of warfarin. [4] [Level 1+]
  - Prophylaxis of DVT in appropriate patients e.g. first five months of treatment with thalidomide in patients with additional thrombotic risk factors;[15] in patients taking diethylstilboestrol there is a significant increase in the risk of deep vein thrombosis and decisions should be made on an individual patient basis.[16][Level 3] Daily injections are more acceptable to patients than anti-embolic stockings. [14] [Level 2++]
* There are a number of Low Molecular Weight Heparins available. They include Dalteparin, Enoxaparin and Tinzaparin. Choice will vary according to local policies. They are all given using a once-daily administration schedule via the subcutaneous route. There may be clinical situations where a split twice-daily dose schedule gives better symptom control. [11] [Level 4]
* Renal function should be checked prior to, and during treatment with LMWH. Renal impairment may require dose adjustment. [11] [Level 4]
* All LMWH treatment doses are calculated according to the weight of the patient. Table 3.3 gives the dosing schedule for dalteparin. Other drug doses are available in the BNF. [11] [Level 3]

Table 3.3 Recommended treatment dose of Dalteparin (subcutaneous) [11] [Level 3]	
Weight (kg)	**Dose of Dalteparin (units/day)**
<46	7 500
46 – 56	10 000
57 – 68	12 500
69 – 82	15 000
≥ 83	18 000

* The recommended **prophylactic** dose of dalteparin is 5000 units daily via the subcutaneous route. [5, 11] [Level 3]

* Contraindications to treatment with LMWH are listed in Table 3.4. [11] [Level 3]

Table 3.4 Contraindications when considering the use of treatment with LMWH [11] [Level 3]
Acute bacterial endocarditis
Haemophilia and other haemorrhagic disorders
History of heparin-induced thrombocytopenia
Known hypersensitivity to heparin or LMWH
After major trauma
Peptic ulcer
Recent cerebral haemorrhage
Recent injury or surgery to central nervous system / eyes/ ears
Severe hypertension
Severe liver disease (including oesophageal varices)
Spinal or epidural anaesthesia
Thrombocytopenia

* The risk of heparin-induced thrombocytopenia is low with LMWH but may occur after 5-10 days. Platelet counts should be measured just before commencing treatment with heparin. Regular monitoring of the platelet count is recommended if it is given for longer than 4 days. If there is a 50% reduction of the platelet count, heparin should be stopped. [11] [Level 4]

* Inhibition of aldosterone secretion by heparin can result in hyperkalaemia. Patients with diabetes mellitus, chronic renal failure, acidosis, raised plasma potassium or those taking potassium-sparing drugs seem to be more susceptible. The risk appears to increase with the duration of therapy. Plasma potassium concentration should be measured in patients at risk of hyperkalaemia before starting LMWH. It should then be monitored at regular intervals, especially if the heparin is to be continued for longer than 7 days. [11] [Level 3]

* For patients requiring long-term therapy with LMWH, monitoring anti-factor Xa activity levels may be advisable and it is best to seek advice from the local haematologist. This especially applies especially to patients who are under or over-weight, those with renal impairment and those at risk of bleeding. [11][Level 4]

* Treatment should be kept under regular review as continuation of LMWH may not be appropriate in certain circumstances e.g. if the patient is in the dying phase. [8] [Level 4]

3.3 STANDARDS

1. The following information should be documented in the case notes: [8-11] [Grade D]

All patients on anticoagulation	- Indication for anticoagulation
	- Intended duration of treatment
Patients commencing warfarin	- Target INR
	- Daily warfarin dose and INR when checked (inpatients)
Patients commencing on LMWH	- Weight (kg)
	- Renal function
	- Platelet count

2. The full blood count, urea and electrolytes should be checked as follows: [8, 11] [Grade C]
   - Prior to commencing treatment with LMWH.
   - Seven days after starting treatment with LMWH.
   - Every 4 weeks during treatment with LMWH (if appropriate).
3. All patients receiving anticoagulation should be issued with the standard anticoagulation booklet. [11] [Grade D]
4. For patients on warfarin, clinician responsibility for both INR monitoring and patient follow-up should be clearly documented in the case notes and the patient-held anticoagulation booklet.[8] [Grade D]

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4. GUIDELINES FOR THE USE OF ANTI-EPILEPTICS IN PALLIATIVE CARE

4.1 GENERAL PRINCIPLES

* Anti-epileptic drugs should be considered in all patients with primary or secondary brain tumours who have a history of one or more seizures. [1, 2]
* The acute management of seizures includes maintaining the airway, emergency drug treatment and a reassessment of the anti-epileptic drugs prescribed. [3]
* A prolonged seizure in a patient who is not in the terminal phase requires immediate emergency management, resuscitation and possible admission to hospital. [3]
* A clear distinction should be made between anti-epileptic drugs for the control of seizures and corticosteroid medication for control of symptoms due to tumour oedema e.g. headaches / vomiting due to raised intracranial pressure or focal neurological signs. [4]
* Increasing the dose of corticosteroid is not recommended for seizures in the absence of new neurological symptoms / signs or evidence of raised intracranial pressure. However, as seizures may increase cerebral oedema, patients who develop new seizures in spite of anti-epileptic drugs may need optimization of anti-oedema therapies before modifying anti-epileptic drugs. [4]
* In the terminal phase, the aim is to prevent and control seizures with the minimum of disruption for the patient. Midazolam or clonazepam may be given without the need for transfer to hospital. [5, 6]
* Corticosteroids can be discontinued in the terminal phase unless they are required for control of raised intra-cranial pressure e.g. headaches/vomiting or seizures. [5, 6, 7]

4.2 GUIDELINES

* Table 4.1 illustrates the World Health Organisation classification of seizures. [8] [Level 4]

4.2.1 Antiepileptic medication

* The ideal drug for controlling seizures in palliative care patients is not easy to establish due to the variety of metabolic interactions and potential side effects. [4] [Level 4]
* There are a variety of anti-epileptic drugs available and Table 4.2 gives further details.[6, 9] The choice of drug will depend on the type of seizure. [3, 6] [Level 4]
* Clinical assessment should be used to optimise the dose of the anti-epileptic drug with the minimum of side effects. [3, 9, 10] Monotherapy should be used whenever possible. [3] [Level 4]
* It has been considered appropriate to use only new anti-epileptic drugs when the older drugs (e.g. carbamazepine, sodium valproate) have been unsuccessful, or where they are unsuitable due to contraindications or drug interactions. However, lamotrigine or carbamazepine are now considered first line therapy for partial onset epilepsy, and lamotrigine has the advantage of being better tolerated with few drug interactions. [11] [Level 4]
* Clobazam and clonazepam can be used for myoclonic or generalised tonic-clonic seizures. They will be effective for short-term use but patients may develop tolerance to the anti-

epileptic effects of the benzodiazepines. In addition, any benefit may diminish over time although this may not always be relevant in the palliative care setting. Despite the possibility of tolerance with benzodiazepines many patients do get a sustained response to drugs such as Clobazam. [3] [Level 4]

* The metabolism of dexamethasone is accelerated by carbamazepine and phenytoin which reduce the steroid effect. The metabolism of phenytoin can be either increased or decreased by dexamethasone so altering the anti-epileptic effect. When using these drug combinations it may be necessary to increase the dose of anti-epileptic and / or corticosteroid. Drug levels are useful for patients on phenytoin. Levels can be used to guide dose titration if seizures are poorly controlled or side effects become apparent. [9, 10, 12, 13] [Level 3]

Table 4.1 International Classification of Seizures [8] [Level 4]	
1. Generalised (involving the entire cortex).	Tonic-clonic seizures (grand mal). Absence seizures (petit mal). Myoclonic seizures. Atonic seizures.
2. Partial/focal (involves a localised area of brain). Note: May spread to involve the whole cortex i.e. secondary generalisation.	Simple (no effect on conscious level). Complex (interrupt consciousness to varying degree). Secondary generalised tonic-clonic seizures.

4.2.2 Management of seizures

* An acute seizure may settle spontaneously. Intranasal, buccal or subcutaneous midazolam should be available for the control of prolonged or recurrent seizures. Alternatively, lorazepam 2mg-4mg can be given intravenously or subcutaneously. [6, 10] [Level 4] For more information on intranasal midazolam see Figure 4.1.

* If seizures continue despite above measures, consider transfer to hospital for emergency management. A secure airway should be established, oxygen should be administered, cardio-respiratory function should be assessed and intravenous access should be established. Administer diazepam 10mg-20mg rectally and repeat 15 min later if status continues to threaten. Alternatively, consider giving midazolam 10mg via the buccal route or intravenously. [3] [Level 4]

* Clusters of seizures (i.e. with recovery in between attacks) may respond to oral clobazam. Starting dose is 10mg per day and the usual maintenance dose is 10mg-20mg twice daily. The maximum dose is 30mg twice daily. This drug can be used for a short period if required e.g. a few days. [10] [Level 4]

4.2.3 Use of anti-epileptics in the terminal phase

* In the terminal phase convert oral anti-epileptics to a continuous subcutaneous infusion of midazolam 30mg-60mg/24 hours. Clonazepam is an alternative and will require less volume. [3-5, 6, 9, 10] [Level 4]

* If seizures are not controlled with midazolam / clonazepam, consider a change to phenobarbital 200mg-600mg/24h via a continuous subcutaneous infusion. Phenobarbital can be mixed with sodium chloride 0.9% or water, although anecdotal evidence suggests that may get less site reactions with sodium chloride 0.9%. It is generally recommended that a separate syringe driver should be used because of the high pH of the drug.[6] [Level 4]

* Discontinue oral corticosteroids unless needed for control of symptoms due to raised intracranial pressure e.g. headaches, vomiting, seizures. Dexamethasone may be administered by subcutaneous bolus injection (for doses <8mg daily) or by a CSCI. [7, 10, 14] [Level 4]

Table 4.2 Antiepileptic drugs available [6, 9, 10, 15] [Level 4]			
Drug Name	**Indication**	**Dose of drug**	**Additional comments**
Carbamazepine	Partial onset	Starting dose 100mg-200mg od-bd. Increase by 100mg-200mg every two weeks. Usual dose is 800mg-1.2g daily in divided doses. Maximum dose is 2g daily.	Titrate slowly to avoid drowsiness and rash. Beware of drug interactions.
Clobazam	Partial onset Generalised onset including myoclonus	20mg-30mg daily orally. Maximum dose is 60mg daily.	Not licensed for monotherapy.
Clonazepam	Myoclonic / tonic-clonic	1mg-8mg daily in divided doses orally. 1mg- 8mg via CSCI.	Can be given subcutaneously via a syringe driver. May be useful in the terminal phase.
Diazepam	Acute treatment of tonic-clonic	10mg stat. Orally / intravenously / rectally.	There are many drug interactions. Useful for emergency management of seizures.
Lamotrigine	Partial onset Generalised onset	Seek specialist advice.	Complicated titration regime. Do not use for myoclonus.
Midazolam	Tonic-clonic	10mg-60mg over 24 hours via a subcutaneous infusion.	Useful in the terminal phase. Can also be given intranasally.
Phenobarbital	Generalised / Partial	60mg-180mg nocte orally. For stat dose give 100mg via an intramuscular / intravenous injection. Give 200mg-600mg over 24 hours via a subcutaneous infusion.	Can get problems on withdrawal. Can be given orally, im, sc, iv. Anecdotal evidence suggests may get fewer site reactions if use sodium chloride 0.9% as diluent although water can also be used.
Phenytoin	Partial Acute treatment for tonic clonic	Starting dose is 150mg-300mg daily orally. Increase gradually in 50mg increments. Give either as single dose or twice daily. Usual maintenance dose is 200mg-500mg/day.	Can be used for rapid control of seizures. Can be given intravenously. Beware of drug interactions. Potent enzyme inducer.
Sodium Valproate	Generalised / Focal	Starting dose is 300mg bd. Increase by 200mg/day at 3 day intervals. Usual maintenance dose is 1g-2g/day. Maximum dose 2.5g/day.	Has a better side effect profile compared to some of the other anti-epileptics. Can be given intravenously.
Topiramate	Partial onset / Generalised onset	Seek specialist advice.	Mainly used by neurologists only.
Levetiracetam	Partial onset Generalised onset including myoclonus	Starting dose is 250mg bd. Increase by 250mg bd every two weeks. Usual maintenance dose is 1000mg-3000mg daily.	Generally well tolerated but can cause mood disturbance.
Oxcarbazine	Partial onset seizures	Starting dose 150mg- 300mg bd. Increase by 150mg-300mg every one to two weeks. Usual maintenance dose is 600mg-900mg bd.	May be better tolerated than carbamazepine. May cause hyponatraemia.

Figure 4.1 Using intranasal midazolam [2, 16, 17] [Level 4]

* Paediatrics has developed the use of intranasal midazolam for sedation and the management of seizures.
* Studies on seizure control in children demonstrate that it is as effective as intravenous diazepam. There is a shorter time to starting treatment and to control of seizures.
* The dose used in adults is determined by weight, i.e.

  <50kg 5 mg intranasal midazolam.

  >50kg 10 mg intranasal midazolam.

* Advantages of intranasal midazolam include:
  - The drug is lipid soluble and will cross the nasal mucosa and blood-brain barrier.
  - There is a rapid rise in blood and cerebrospinal fluid levels.
  - Peak plasma concentrations are reached in 5-12 minutes.
  - There is no need for intravenous access.
  - The drug can be administered by a trained carer.
  - It may be more acceptable than the rectal route.
* The buccal route can be used as an alternative to the intranasal route if there is excessive head movement due to seizures.
* The injection solution 10mg/2ml is used. The required dose is drawn up in a 2ml syringe and given via a Mucosal Atomization Device.
* Half of the dose is given in each nostril.
* For patients at home, the dose can be drawn up by the nurse and kept in the fridge for up to one month. It can then be given by a trained carer if the need arises.
* The Mucosal Atomization Device can be washed and reused but should only be used for a single patient.
* The intranasal route is an unlicensed route for administration of midazolam and the prescriber takes responsibility for its use.
* An information leaflet regarding intranasal midazolam for patients and carers is available on request from The Hospice of the Good Shepherd, Chester.

4.3 STANDARDS

1. For all patients with primary or secondary brain tumours, the following information should be documented in the case notes: [14] [Grade D]
   - History of seizures including the frequency and type.
   - Anti-epileptic drug(s) used and the dose(s).
2. The dose of corticosteroids should not be increased if seizures occur in the absence of new neurological symptoms / signs or evidence of raised intracranial pressure, unless the patient is also taking phenytoin or carbamazepine. [4, 13, 14, 18, 19] [Grade D]

3. All patients with a history of seizures should have access to medication that can be given in the event of an episode of prolonged seizures. [3, 14] [Grade D]

4. If a patient is in the terminal phase, oral anti-epileptic drugs should be converted to midazolam / clonazepam via a continuous subcutaneous infusion. [3-5, 6, 9, 10] [(Grade D]

5. If a patient is in the terminal phase and unable to take oral medication, corticosteroids should be discontinued unless they are needed for control of symptoms related to raised intracranial pressure. If they are required, they can be given via the subcutaneous route. [6, 14] [Grade D]

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5. GUIDELINES FOR THE MANAGEMENT OF MALIGNANT ASCITES IN PALLIATIVE CARE

5.1 GENERAL PRINCIPLES

* Ascites is the accumulation of fluid in the peritoneal cavity. [1, 2]
* Malignancy is the underlying cause in approximately 10% of all cases of ascites. About 15-50% of patients with malignancy will develop ascites. [3]
* Cancers commonly associated with the development of ascites include breast, colorectal, endometrial, gastric, ovarian and pancreatic. [3]
* Non-malignant causes of ascites include liver disease, congestive cardiac failure, nephrotic syndrome, pancreatitis, tuberculosis and bowel perforation. [2, 3]
* Several different pathophysiological mechanisms are implicated in the development of malignant ascites. These include: [4]
    - peritoneal lymphatic obstruction.
    - hypoalbuminaemia leading to a reduction in oncotic pressure.
    - increased capillary permeability.
    - increased portal vein pressure with activation of the renin-angiotensin pathway.
* Symptoms resulting from an accumulation of ascitic fluid include abdominal bloating / swelling, pain, nausea and vomiting, anorexia, fatigue, peripheral oedema, heartburn and dyspnoea. [5]
* Malignant ascites carries a poor prognosis. Management should be aimed at maximising patient comfort and quality of life. [7]
* Management options for malignant ascites include diuretic therapy, therapeutic paracentesis and peritoneovenous shunts. [8] Oncological interventions may be helpful in ovarian carcinoma and lymphoma. Hormonal therapy may be useful in hormone sensitive malignancies such as some breast cancers. [2, 7]
* There is no evidence that any particular therapeutic option is more effective than another.[9]

5.2 GUIDELINES

5.2.1 Diuretic therapy

* Diuretic therapy should be considered in every patient with malignant ascites particularly those with a prognosis of greater than 4 weeks. Urea and electrolytes should be checked before starting treatment and during treatment as appropriate. [8, 10] [Level 4]

Spironolactone

* Spironolactone is the diuretic of choice in malignant ascites.[11] It works by competitively blocking aldosterone leading to an increase in sodium excretion. It is a potassium sparing diuretic. Patients with raised plasma concentrations of renin and massive liver metastases are most likely to respond. [10, 11, 12] [Level 2]

* Dose: 100mg-400mg daily. For elderly patients consider a lower starting dose and titrate according to individual response. It may take 3-5 days to get a response. The dose should be increased every 3-7 days in 50mg-100mg increments. The maximum dose is 400mg/day. However, many patients will be too frail to tolerate such large doses. [10, 11, 12] [Level 2]

* Side effects include nausea, headache, lethargy, delirium, hyperkalaemia, skin rashes, diarrhoea and hyponatraemia. [10, 11, 12] [Level 2]

Furosemide

* Furosemide is a loop diuretic and should be added if there is an inadequate response to spironolactone. Dose: 40mg-80mg/day. Side effects include electrolyte imbalance, hypotension and gastrointestinal disturbance. [10, 12] [Level 3]

5.2.2 Therapeutic paracentesis [Level 3]

* Paracentesis is the removal of fluid from the peritoneum via a catheter / venflon inserted through the abdominal wall. [13]

* Paracentesis is a useful procedure for the control of acute symptoms, or in those patients who are resistant to diuretics. It provides relief in about 90% of cases. [13]

* Paracentesis can be performed in a variety of settings and should ideally be within 48 hours of presentation. [14, 15]

* Diagnostic imaging is not necessary prior to paracentesis if clinical examination demonstrates the presence of a large volume of ascitic fluid. Ultrasound evaluation may be required prior to paracentesis if there is diagnostic uncertainty or suspected loculation of fluid. Loculation is especially common in ovarian carcinoma. [6]

* Consider checking a full blood count and clotting screen prior to paracentesis if the patient is bleeding, has liver metastases, is jaundiced, or is on anticoagulant therapy. Biochemistry should be checked if there is a history of renal impairment. [16]

* Before undertaking paracentesis it is important to gain informed consent from the patient and document this in the case notes. [16] [Level 4]

* Practice varies as to the volume of ascitic fluid removed and the rate of fluid removal. Clamping of the drain is often not required. Fluid should be drained as quickly as is comfortable for the patient, limited only by their clinical condition. [17, 18]

* The bladder should be emptied before paracentesis. Analgesia should be available before, during, and following the procedure. [16]

* Ascitic drains should be removed when no longer in use due to the risk of infection. [19]

* There is no evidence to support the use of albumin infusions either during or after paracentesis for malignant ascites. Use of intravenous fluids is not recommended. [14, 19]

* It may be necessary to repeat the paracentesis for ongoing symptom control.[16]

* Absolute contraindications to paracentesis include disseminated intravascular coagulation and clinical evidence of fibrinolysis. Relative contraindications include severe bowel distension and previous extensive abdominal/ pelvic surgery. [20]

* Possible complications include secondary peritonitis, pulmonary emboli and hypotension.[7]

5.2.3 Peritoneovenous shunts

* Peritoneovenous shunts drain ascitic fluid from the peritoneal space into the internal jugular vein. Shunts should be considered if recurrent ascites is the main clinical problem and the prognosis is measured in months rather than weeks. [13] [Level 3]

* Shunts may limit the need for diuretics and paracentesis. The two main types of shunts are Denver and Le Veen. [21] [Level 4]

* Shunts can be inserted under local anaesthetic. The complication rate following shunt insertion is high and includes shunt malfunction, leakage, sepsis, gastrointestinal bleeding, thromboembolism and pulmonary oedema. [21, 22] [Level 3]

5.2.4 Octreotide

* This is a synthetic somatostatin analogue which acts by reducing the volume of fluid secretion by the intestinal mucosa and by increasing the rate of resorption. It can be useful in chylous ascites. The dose is 200microgrammes-600microgrammes via a continuous subcutaneous infusion over 24 hours. [23] [Level 4]

5.2.5 Cytotoxic Therapy

* Systemic therapy may be of benefit if the primary disease is known to be responsive to cytotoxics e.g. breast, ovary. Intraperitoneal therapy has been shown to be of benefit in some tumour types but its use is limited to small volume / micrometastatic intraperitoneal disease. [2, 24] [Level 3]

5.3 STANDARDS

1. Patients who have acute symptoms attributable to ascites should have paracentesis within 48 hours of presentation. [16] [Grade D]
2. All patients should have baseline urea and electrolytes checked prior to commencing and whilst taking diuretic therapy. [16] [Grade D]
3. Intravenous fluids/ albumin should not be used routinely during or following therapeutic paracentesis but may be appropriate in severe hypovolaemia. [14, 19] [Grade D]
4. Abdominal drains should be removed within 24 hours of insertion if there is limited drainage, unless there is a clinical indication for leaving them in situ for a longer period of time. [24] [Grade C]

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6. GUIDELINES FOR BEREAVEMENT SERVICES IN PALLIATIVE CARE

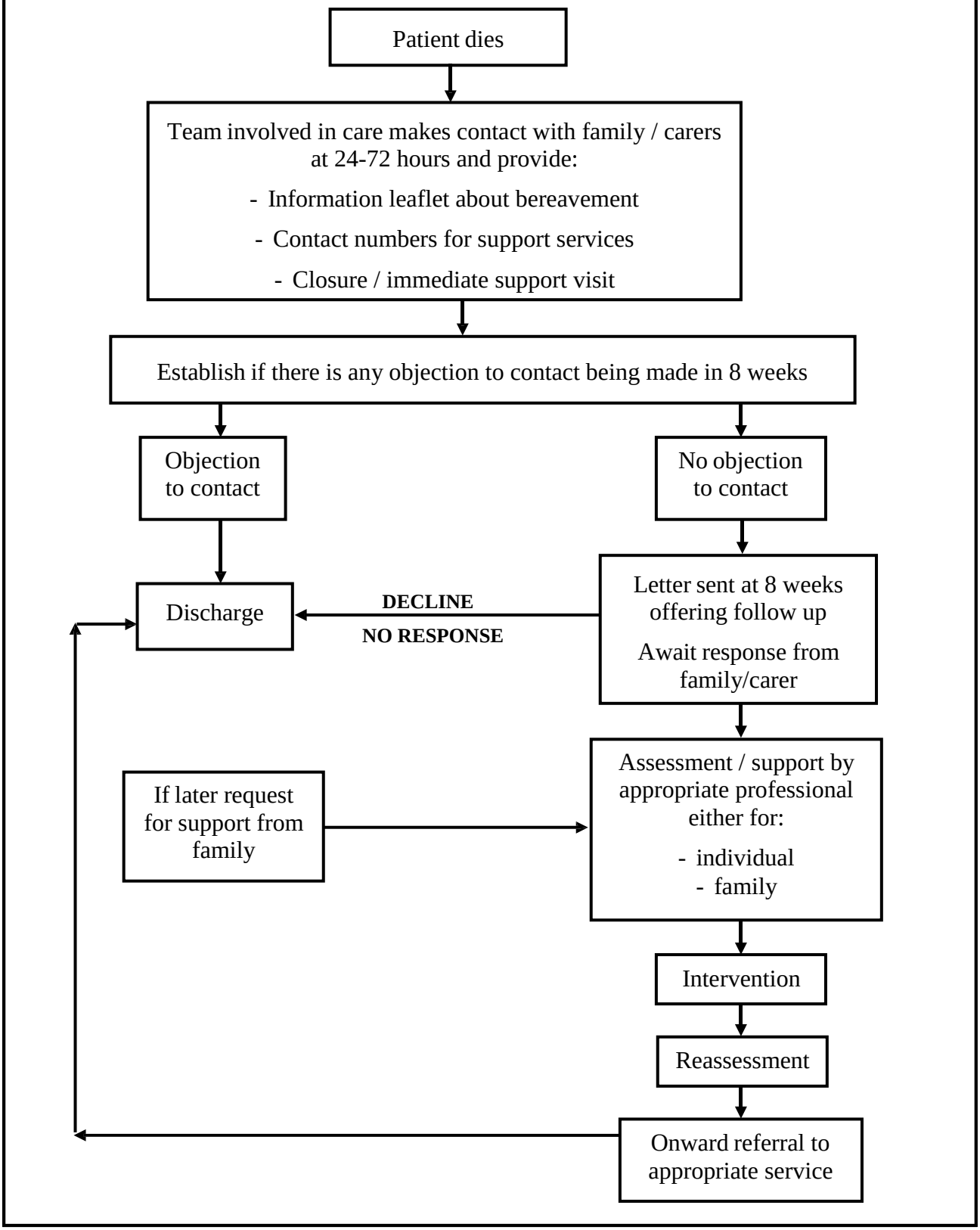
6.1 GENERAL PRINCIPLES

* Bereavement may be defined as: "the situation of anyone who has lost a person close to them through death." [1]
* Grief is now recognised to be much more than a psychological process. It is multi-dimensional and diverse in its expression. Grief has psychological, emotional, physical, spiritual, economic, behavioural and social dimensions. The expression of grief is influenced by culture and ethnicity. [2]
* Grief is a normal response to human loss. The majority of people have sufficient internal and external resources to manage their grief. However, some might find it too difficult or traumatic without additional support. [2]
* Although grief is normal, it may be associated with anxiety and depression for a substantial minority of bereaved people. Early identification of individuals at risk is important. [3]
* Approximately 5-33% of people will develop complicated grief. Many other people will experience great distress over a lengthy period and over 33% will have symptoms of anxiety and depression. [4]
* Providing information about grief and how to access resources of help promotes resilience. [5]
* Factors that influence the course of grief include: [6, 7, 8]
  - The degree of distress associated with the illness and death.
  - The personality of the bereaved person.
  - The coping style of the bereaved person and their relationship with the deceased.
  - The quality of social support available.
* Estimates of the need for additional support vary. About 33% of bereaved people may benefit from support and 5-10% will need therapeutic interventions from health care professionals. [3, 7]
* Types of intervention include: written information, one-to-one supportive or therapeutic counselling, telephone counselling, befriending, referral to professionals, social and therapeutic groups, drop in events and remembrance services. [6, 8, 9]

6.2 GUIDELINES

* Figure 6.1 gives a suggested model for bereavement care.
* The initial contact regarding bereavement support should be made by the clinical team involved in caring for the dying patient. [2] [Level 4]
* All bereaved families / carers, independent of where the bereavement occurs, should receive an information booklet about bereavement and the services that are available locally and nationally for bereaved adults and children. This may include details of appropriate websites. [2] [Level 4]

Figure 6.1 Flowchart of suggested model for bereavement care [11] [Level 4]



* When a family is well-known to palliative care services, the need for additional bereavement support may be assessed by looking at associated risk factors and the multidisciplinary team's knowledge of the family pre-bereavement. [7, 10] [Level 4]

* Independent of initial contact following a bereavement, written contact regarding bereavement support should be made at around eight weeks after the death unless the family / carer clearly state they do not wish to be contacted. [1] [Level 4]
* Health professionals involved in bereavement support should receive adequate education and supervision to ensure they provide an effective service. [3] [Level 4]
* The use of bereavement pathways / flowcharts should be encouraged (see Figure 6.1). [3] [Level 4]
* Clinical teams providing bereavement support should clearly outline the remit of the services they provide. [3] [Level 4]
* All services should have adequate documentation of service provision and feedback from service users should be encouraged. [3] [Level 4]
* If required, bereaved relatives / carers should be referred on to an appropriate specialist bereavement service. [2, 3] [Level 4]
* Memorial services have been shown to be useful in a hospice setting. [1] [Level 4]

6.3 STANDARDS

1. All families / carers should receive an information booklet about bereavement and the support available within 72 hours of the bereavement. [2] [Grade D]
2. Families / carers should be made aware that written contact will be made and given the opportunity to decline this service. [1, 2] [Grade D]
3. Proactive or outreach offers of bereavement support should be made 8 weeks after bereavement. [2] [Grade D]
4. Bereaved relatives / carers should be referred on to an appropriate specialist bereavement service where appropriate. [2, 3] [Grade D]
5. Each organisation involved in bereavement support should ensure that providers are adequately trained and supervised. [1] [Grade D]

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7. GUIDELINES FOR THE USE OF BISPHOSPHONATES IN THE MANAGEMENT OF MALIGNANT BONE DISEASE

7.1 GENERAL PRINCIPLES

* Bisphosphonates are synthetic analogues of pyrophosphate, a natural regulator of bone metabolism found abundantly in bone matrix. They inhibit differentiation of osteoclast precursors and induce osteoclast apoptosis leading to a decrease in bone resorption. [1, 2]

* Bisphosphonates may be classified into two main groups:

  - The more potent nitrogen-containing bisphosphonates inhibit osteoclast bone resorption by inhibition of the mevalonate pathway. They include zoledronic acid, disodium pamidronate and ibandronic acid.

  - The less potent non-nitrogen containing bisphosphonates form cytotoxic ATP analogues interfering with cellular metabolism. They include disodium clodronate and disodium etidronate. [1, 2]

* Zoledronic acid, disodium pamidronate and ibandronic acid are the most potent and widely used bisphosphonates for the management of metastatic bone disease. [3]

* Ibandronic acid is available in oral and intravenous preparations. It is only licensed for the management of metastatic bone disease in patients with metastatic breast cancer. [4, 5] Local policies may dictate which bisphosphonate is available for clinical use.

* Bisphosphonates, and in particular the aminobisphosphonates, are known to have a number of side effects. These include a rise in body temperature and accompanying flu-like symptoms that resemble a typical acute phase response. Other side effects include renal toxicity, hypocalcaemia and osteonecrosis of the jaw. [6]

7.2 GUIDELINES

7.2.1 Initiation, dosing and duration of treatment

* Treatment with opioids and NSAIDs should be optimised before using bisphosphonates for pain relief. Consider referral for radiotherapy or orthopaedic interventions where appropriate.[7] [Level 4]

* Bisphosphonates should be considered where clinically appropriate for the prevention of skeletal related events and treatment of malignant bone pain in patients with bone metastases from breast cancer or hormone refractory prostate cancer and in patients with multiple myeloma. [1, 7-9, 10] [Level 1+] Decisions to treat should be based on an assessment of their general medical condition and expected survival time. [11] [Level 4]

* In patients with lung, renal or solid tumours (other than breast or prostate) metastasizing to bone, the strongest evidence is for the use of zoledronic acid to delay the onset of skeletal related events. [11] [Level 2]

* Zoledronic acid should be the current bisphosphonate of choice for patients with hormone refractory prostate cancer with bone metastases. This is for both prevention of skeletal related events and palliation of bone pain. [6] [Level 2++]

* If using zoledronic acid, the datasheet recommends the use of oral calcium supplements 500mg daily plus vitamin D 400 IU daily. This will reduce the risk of hypocalcaemia. Monitoring of serum calcium and phosphate levels is also required. [7, 12] [Level 4]

* Sodium clodronate is an alternative for bone pain in patients with breast cancer and myeloma. [7, 8] [Level 2++] Oral administration is often poorly tolerated. It may be given intravenously or subcutaneously. [5, 13] [Level 4]

* Ibandronic acid is currently only licensed for the management of bone metastases in patients with metastatic breast cancer. It may be administered orally or intravenously. [4, 14] [Level 4]. It may have a better renal profile than zoledronic acid. [15] [Level 2+]

* Patients should be warned of the possibility of a 'flare' of bone pain and transient 'acute phase reactions' characterized by fever and myalgia which occur in 15-30% of patients. These generally occur after the first infusion of nitrogen containing bisphosphonates and less frequently after following infusions. [6] [Level 4]

Table 7.1 Use of bisphosphonates in the management of metastatic bone disease [5, 6, 7, 8, 13, 15] [For level see text]

Drug	Dose	Route of administration	Diluent	Rate of infusion
Zoledronic Acid	4mg	Intravenously	100ml sodium chloride 0.9% or dextrose 5%	15-30 minutes Repeat every 4 weeks
Disodium Pamidronate	90mg	Intravenously	250-500ml sodium chloride 0.9%	Rate not exceeding 1mg/min
Ibandronic Acid	6mg 50mg	Intravenously Orally	100ml sodium chloride 0.9% or dextrose 5% Not applicable	15 minutes Repeated every 4-6 weeks Not applicable
Sodium Clodronate	600mg-1500mg	Intravenously	500ml sodium chloride 0.9% or dextrose 5%	Depends on dose. Range 2-4 hours

* If effective, bisphosphonate infusions should be repeated at regular intervals. [4, 7, 13, 14, 16] [Level 4]

* A patient who fails to respond to the first dose of a bisphosphonate used for the treatment of pain should, if clinically appropriate, receive a further two consecutive doses at 4-weekly intervals before being considered a non-responder. [7] [Level 2+]

* In patients with disease progression in the skeleton and who are experiencing pains despite the use of oral bisphosphonates or disodium pamidronate, changing to zoledronic acid or ibandronic acid can improve pain control. [6] [Level 2+]

* Since the risk of skeletal related events is continuous, treatment if tolerated should be continued for at least 2 years, even if a patient experiences a bone event. Continuation of treatment beyond 2 years should be based on an individual risk assessment. [6] [Level 4]

* Bisphosphonates should not be discontinued once skeletal events occur (unless for other clinical reasons) as continuing use significantly reduces the risk of subsequent skeletal events. [6] [Level 2+]

* Table 7.1 gives further details of the dosing regimens for the commonly used bisphosphonates.

7.2.2 Bisphosphonates in renal failure

* Hypocalcaemia is a well recognised electrolyte abnormality associated with bisphosphonates. Renal failure and other electrolyte abnormalities, particularly hypomagnesaemia, frequently coexist with hypocalcaemia. [3] [Level 4]

* To avoid renal toxicity with bisphosphonates, serum creatinine should be checked and hydration status clinically assessed, prior to each treatment. The serum calcium should also be checked prior to every infusion. [6, 17] [Level 4]

* The risk of renal failure is directly related to drug infusion time and dosage. The use of high dose zoledronic acid with a short infusion time is especially nephrotoxic. [3] [Level 4]

* Treatment with zoledronic acid and disodium pamidronate should not be initiated in patients with severe renal impairment (Cr Cl<30mls/min) unless in cases of life-threatening hyperalcaemia where the benefits are judged to outweigh the risks. [7, 12, 16] [Level 4]

* When using bisphosphonates for the treatment of bone pain, and where there is persistent renal deterioration but a need for treatment, it may be appropriate to consider either a dose reduction or a longer infusion time. Close monitoring is essential. [6] [Level 4]

* There is a growing body of evidence showing that ibandronic acid is better tolerated in renal failure compared to other bisphosphonates. [24] [Level 2+] However, dose reduction, monitoring, and longer infusion times are still required if there is severe renal impairment.[20] [Level 4]

* Table 7.2 gives details of the bisphosphonate dose adjustments required in renal impairment.

7.2.3 Osteonecrosis of the jaw (ONJ)

* Osteonecrosis of the jaw has been reported in cancer patients whose treatment regimens include intravenous bisphosphonates. A very small number of cases have also been reported in patients receiving oral bisphosphonates for non-cancer indications. Clinical features include exposed bone in the maxillofacial area, which occurs in association with dental surgery or can occur spontaneously, with no evidence of healing.[19, 20, 21] [Level 4]

* A working diagnosis is made when there is no evidence of healing after 6 weeks of appropriate evaluation and dental care and no evidence of metastatic disease in the jaw or osteoradionecrosis. If osteonecrosis does occur, invasive dental procedures should be avoided if possible. [19] [Level 4]

* Where clinically appropriate, patients should have a dental examination and any dental treatment required before starting bisphosphonate treatment. [3-5, 7, 13, 14, 16, 19] [Level 4]

* Patients should be educated regarding the importance of good oral hygiene to reduce the risk of dental infection and periodontal infections. They should be encouraged to advise their dentist they are receiving bisphosphonate treatment. [19] [Level 4]

* Length of exposure to bisphosphonates is strongly associated with development of ONJ. It is extremely rare for those patients receiving less than 12 treatments to develop ONJ. Therefore if a patient has a poor prognosis and it is anticipated that they are only going to receive a few infusions for bone pain, dental checks may not be essential or appropriate.[19] [Level 4]

* Written information regarding bisphosphonate therapy and preventative measures for ONJ should be made available to patients. [22] [Level 4]

* In patients who develop ONJ whilst receiving bisphosphonates, the decision to stop or continue treatment should be made on a case by case basis. Cessation of therapy may not have an effect on established osteonecrosis. Referral to the local dental hospital, an oral surgeon or dental oncologist should be considered for further management. [6, 19] [Level 4]

* Patients receiving bisphosphonates and who have dental problems other than ONJ should receive the least invasive dental treatment. [6] [Level 4]

Table 7.2 Dosage adjustments for use of bisphosphonates in patients with impaired renal function [4, 5, 7, 12, 13, 14, 16, 18] [Level 4]

Creatinine Clearance (ml/min)	Zoledronic Acid	Disodium Pamidronate	Intravenous Ibandronic Acid	Oral Ibandronic Acid	Intravenous Sodium Clodronate
>60	4mg	90mg over 4-6 hours.	6mg over 15 minutes.	50mg daily.	600-1500mg.
50-60	3.5mg	90mg over 4-6 hours.	6mg over 1 hour.	50 mg daily.	25% dose reduction recommended.
40-49	3.3mg	90mg over 4-6 hours.	6mg over 1 hour.	50mg daily.	25-50% dose reduction recommended.
30-39	3.0mg	90mg over 4- 6 hours.	6mg over 1 hour.	50 mg daily.	25-50% dose reduction recommended.
<30	Not recommended unless benefit outweighs risk.	Not recommended unless benefit outweighs risk.	2mg over 1 hour .	50 mg weekly.	Not recommended especially with creatinine clearance <10ml/min.

7.3 STANDARDS

1. Treatment with opioids and non-steroidal anti-inflammatory agents should be optimised before using bisphosphonates for malignant bone pain. [7] [Grade D]
2. The use of bisphosphonates for the management of malignant bone pain should be clearly documented in the case notes. [22] [Grade D]
3. Subsequent infusions of the bisphosphonate should be given as per the recommended regimen for each drug. [4, 5, 7, 13, 14, 16, 18] [Grade D]
4. A patient who fails to respond to the first dose of a bisphosphonate used for the treatment of pain, should, if clinically appropriate, receive a further two consecutive doses at 4-weekly intervals before being considered a non responder. [7] [Grade B]
5. The serum creatinine and adjusted calcium should be checked prior to each bisphosphonate infusion. [6, 17] [Grade B]
6. Those patients prescribed zoledronic acid should also have calcium and vitamin D supplements prescribed. [12] [Grade D]
7. Patient Information Sheets on the use of bisphosphonates and potential adverse effects should be provided. [22] [Grade D]

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8. GUIDELINES FOR THE USE OF BLOOD TRANSFUSIONS IN PALLIATIVE CARE

8.1 GENERAL PRINCIPLES

* Anaemia commonly occurs in patients with both advanced malignant and non-malignant disease. [1]
* It is important to understand the cause(s) of the anaemia if possible, although investigations to determine the cause may be inappropriate. Table 8.1 shows the major causes of anaemia in patients with advanced disease.[1][Level 4]

Table 8.1 Causes of anaemia in advanced disease [1] [Level 4]	
Acute or chronic haemorrhage	Chronic renal impairment
Anaemia of chronic disease	Haemolysis
Bone marrow failure	Malnutrition

* Symptoms caused by anaemia are diverse and may be very disabling. They include weakness, fatigue, dyspnoea, nausea, angina, oedema, dizziness, anorexia, low mood and headache. [2]
* There is no correlation between the pre-transfusion haemoglobin and the severity of anaemia symptoms. [2]
* Symptomatic improvement following transfusion may be delayed for several days. [2]
* The management of anaemia is influenced by prognosis. Patients who are close to death may not benefit from transfusion. [3]

8.2 GUIDELINES

* Patients receiving palliative radiotherapy should have a Hb>10g/dl. [4] [Level 1+]
* Iron supplements may be used for patients with iron deficiency anaemia. They may be poorly tolerated and prognosis should be considered. [5] [Level 4]
* The following may be used to reduce bleeding in palliative care patients. [5, 6] [Level 4]

1. Tranexamic Acid: An antifibrinolytic agent.

   Dose: 1g tds orally. Reduce to 500mg tds once bleeding has stopped. Crushed tablets may be dissolved in small amounts of water and administered via a PEG tube. Avoid if massive haematuria. The dose should be reduced in renal failure and the drug avoided in severe renal impairment.

2. Etamsylate: A haemostatic agent

   Dose: 500mg qds orally. May cause nausea.

8.2.1 Transfusion of red cells

* Consider transfusion when Hb<10g/dl. The decision to transfuse should be based on the presence of symptoms and not on the Hb level alone. [2] [Level 3]
* If the prognosis is less than 14 days, transfusion for weakness may not be appropriate. [3, 7] [Level 3]
* The patient should give informed consent for the procedure and this should be documented in the case notes. They should also be offered written information regarding their transfusion. [8, 9] [Level 4]
* All patients receiving a blood transfusion should wear a patient identity wristband or equivalent. [8, 9] [Level 4]
* Furosemide (20mg-40mg orally / intravenously with alternate units) should only be prescribed for patients at risk of fluid overload. [9, 10] [Level 4]
* One unit of blood will raise the Hb level by approximately 1g/dl. The pre-transfusion Hb level and other clinical indicators should influence the number of units transfused. [9] [Level 4]
* The red cells should be transfused within 4 hours of removal from cold storage and each unit should therefore be prescribed over 2-3 hours. [9] [Level 4]
* The use of an infusion pump is recommended to ensure the transfusion is completed within safe time limits. [9] [Level 4]
* Pulse, blood pressure and temperature should be recorded at least before and 15 minutes after starting the transfusion. Further observations may be appropriate depending on the clinical situation. [9] [Level 4]
* All staff involved with transfusions should receive competency-based training in line with national targets. [8, 9, 11] [Level 4]

8.2.2 Transfusion of platelets

* Indications for platelet transfusions include:
  - Symptomatic relief in patients with bleeding and thrombocytopenia. [9] [Level 4]
  - Patients with thrombocytopenia undergoing invasive procedures e.g. nerve blocks. [9, 12] [Level 4] For general procedures, patients should have a platelet count >50× 10^9 ml. For procedures involving the CNS e.g. epidurals, aim for a platelet count >100× 10^9 ml.
  - Platelet transfusions may be appropriate in palliative care patients. However, their effect is likely to be short-lived. One adult therapeutic dose (i.e. one unit) raises the platelet count in a typical 70kg patient by 20-40 × 10^9 ml. [9] [Level 4]
* It is important to use the platelets as soon as possible after removal from the transfusion laboratory. If there is a delay in administration the platelets should be moved continuously to prevent clumping. [9] [Level 4]

8.2.3 Transfusion Reactions

* If a patient becomes febrile or develops a mild urticarial reaction, consider stopping the transfusion for a short period of time. The use of intravenous hydrocortisone 100mg or intravenous chlorpheniramine 10mg may be required. If the reaction does not settle, discuss with the local transfusion laboratory and consider stopping the transfusion. [9] [Level 4]

* In the event of a severe transfusion reaction, such as anaphylaxis or shock, the transfusion should be stopped immediately. Emergency treatment with intravenous fluids and adrenaline should be administered as appropriate. The reaction should be reported immediately to the local transfusion laboratory and local procedures followed. Serious adverse reactions and events should be reported via the online SABRE system (Serious Adverse Blood Reactions and Events) which can be accessed via www.shot.org.uk or www.mhra.gov.uk. [4, 9, 11, 12] [Level 4]

8.2.4 Discontinuation of Transfusions

* Some patients with a low haemoglobin level do not respond symptomatically to blood transfusion or may only respond for a short period of time. Decisions regarding the continuation of blood transfusions should be made on an individual basis, taking into account symptoms, prognosis, response to previous transfusions and patient wishes.[2] [Level 3]

* Where possible, response to transfusion and discussions regarding future transfusions should be recorded in the case notes to aid future decision-making.[10] [Level 4]

8.2.5 Erythropoietin

* Erythropoietin is a glycoprotein produced mainly by the kidneys, which stimulates red cell production. The production of erythropoietin is reduced in advanced malignancy and this contributes to the anaemia experienced by cancer patients.[13] [Level 4]

* Treatment with erythropoietin may reduce the requirement for a blood transfusion and may improve quality of life in palliative care patients.[14] However, up to 50% of patients do not respond to treatment,[15] and there may be a significant increase in the risk of thrombosis.[16, 17] It is therefore not recommended at the present time as an alternative to blood transfusion for palliative care patients. [Level 4]

8.3 STANDARDS

1. It is important to identify, document and treat the cause of anaemia if possible.[1, 8] [Grade D]
2. Symptoms should be recorded before and after the transfusion to determine whether there has been any benefit. This will facilitate decision-making regarding future transfusions.[2, 8] [Grade D]
3. The patient should give informed consent for the procedure and this should be documented in the patient notes. [8, 9] [Grade D]
4. Patients should be offered written information regarding their transfusion.[8, 9] [Grade D]
5. All patients receiving a blood transfusion should wear a patient identity wristband or equivalent.[8, 9] [Grade D]
6. Each blood unit should be transfused within 4 hours of removal from cold refrigeration.[9] [Grade D]
7. An infusion pump should be used to control the rate of transfusion.[9] [Grade D]
8. All staff involved with transfusions should receive competency-based training in line with national targets. [8, 9, 11] [Grade D]

9. Serious adverse reactions and events should be reported via the online SABRE system (Serious Adverse Blood Reactions and Events). [8, 9, 12, 13] [Grade D]

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9. GUIDELINES FOR THE MANAGEMENT OF BOWEL OBSTRUCTION IN ADVANCED CANCER

THIS SECTION HAS BEEN UPDATED
PLEASE SEE A-Z SECTION FOR UPDATED GUIDELINES

9.1 GENERAL PRINCIPLES

* The term "bowel obstruction" covers a range of clinical situations and diagnosis may be difficult. Bowel obstruction may be permanent or intermittent; complete or partial; acute or chronic and may occur at any point along the gastrointestinal tract. [1]
* Bowel obstruction may be caused by intrinsic or extrinsic mechanical obstruction or an abnormality in gut motility. [1]
* Patients with small bowel / high intestinal obstruction are likely to experience the symptoms of vomiting and abdominal colic. [2]
* Patients with large bowel / low intestinal obstruction are likely to experience the symptoms of abdominal distension and constipation. [2]
* If the lumen of the gastrointestinal tract is occluded, fluid secreted by the bowel wall accumulates within the lumen. This results in bowel distension and stimulates release of further fluid from the gastrointestinal tract. [1, 2]
* The management of bowel obstruction in advanced cancer may be medical or surgical, or a combination of both approaches. The aim is to control symptoms including nausea, vomiting and abdominal pain. [1]
* If the obstruction is thought to be complete, prokinetic agents and stimulant laxatives should be discontinued. [3, 4] If the obstruction is sub-acute or incomplete, then it may be appropriate to use prokinetic agents, rectal measures and softening laxatives providing the patient is not describing abdominal colic. [5]
* During the medical management of bowel obstruction, the majority of patients may be adequately hydrated with small amounts of oral fluid. If a patient develops persistent thirst, parenteral fluids may be an option. [6]
* Surgical intervention may involve: the formation of a stoma, bypass, resection, stenting or a venting gastrostomy. [7]
* Self-expanding metallic stents can alleviate malignant bowel obstruction and should be considered for patients with single level obstruction distal to the splenic flexure. [7, 8, 9]

9.2 GUIDELINES

9.2.1 Initial management

* Rectal examination should form part of the initial assessment of any patient with suspected bowel obstruction. Constipation should be excluded. If the rectum is empty an abdominal radiograph should be considered if appropriate. [1, 2] [Level 4]

* In obstruction of the small bowel, the bowel contents are liquid. In partial large bowel obstruction, the use of Movicol® or Idrolax® may be helpful. However they should be discontinued in complete obstruction. Faecal softeners / gentle stimulants such as sodium docusate should be considered for partial obstruction. Stimulant laxatives should be discontinued. (see *Guidelines on the Management of Constipation*). [10] [Level 4]

* If the history is suggestive of low bowel obstruction, a trial of metoclopramide should be considered to control symptoms of nausea and vomiting. [6] [Level 3] It should not be used if there is intestinal colic. In patients where metoclopramide is contraindicated, alternative anti-emetics to be considered are cyclizine / haloperidol or levomepromazine.[11] [Level 4]

* Hyoscine butylbromide may be used to reduce gastrointestinal secretions and abdominal colic.[12] [Level 3] Glycopyrronium is an alternative to hyoscine butylbromide.[13] [Level 3]

* Octreotide may also be useful in reducing gastrointestinal secretions and is recommended as a second line option. Octreotide may have a more rapid effect than hyoscine butylbromide. [11, 14, 15] [Level 3]

* In a patient with a high intestinal obstruction, consider the use of an intravenous proton pump inhibitor as this may reduce the volume of gastrointestinal secretions e.g. omeprazole 40mg intravenously once daily. Ranitidine via a continuous subcutaneous infusion has also been shown to reduce secretions. [11] [Level 4]

* Corticosteroids may also help to achieve symptom control. Consider a trial of dexamethasone 8mg subcutaneously for 5 days. Corticosteroids may have a favourable impact on the outcome of the episode of malignant bowel obstruction. [16] [Level 2+]

* Opioid analgesia and anti-spasmodics should be titrated to achieve good pain relief.[3, 17] [Level 4]

* Table 9.1 illustrates the drug options available for the management of bowel obstruction (***see*** *Guidelines on the Management of Nausea and Vomiting*).

* A surgical opinion should always be considered as part of the management of any patient with bowel obstruction. Factors associated with a more favourable outcome following surgery include:

  - Single level of obstruction.
  - Albumin >30g/l.
  - Absence of ascites.
  - No previous oncological treatments in the last 6 months. [18] [Level 2+]

9.2.2 Management of resolving bowel obstruction

* If symptoms are controlled for 48 hours, or appear to be resolving, then medication should be reduced to the lowest dose possible to maintain good symptom control. [17][Level 4]

* Prokinetic agents and laxatives may be considered at this stage. [11] [Level 4]

* Laxatives are only of value in large bowel obstruction. Bowel contents are liquid in small bowel obstruction. [1] [Level 4]

* Prokinetic agents such as metoclopramide may help promote gastric motility. [11] [Level 4]

* Some patients may be able to recommence oral medication if the obstruction is relieved. [17] Level 4]

Table 9.1 Drug options for the management of bowel obstruction [For Levels- see table]			
Indication(s)	**Drug Name**	**Dose (subcutaneously via syringe driver over 24 hours)**	**Notes**
Relief of colic Reduce volume of gastrointestinal secretions	Hyoscine butylbromide [11, 12] [Level 3] or Glycopyrronium [13] [Level 4]	60mg-240mg 600microgrammes-2.4mg	NB. Do not combine cyclizine and hyoscine butylbromide in a syringe driver as may get crystallisation.
Reduce volume of gastrointestinal secretions	Octreotide [18, 19] [Level 3]	300microgrammes-600microgrammes	Consider compatibility with other drugs.
Relief of pain	Diamorphine / Morphine [Level 4]	Dependent on previous opioid dose	
Reduce nausea and vomiting	Cyclizine [Level 4] Haloperidol [Level 4] Levomepromazine [17] [Level 4] Metoclopramide [6] [Level 3]	150mg 1.5mg-5mg 6.25mg-25mg 30mg-60mg	Do not use cyclizine in severe cardiac failure. [20] [Level 3] Contraindicated in complete obstruction. Dose may be increased to 120mg but need to watch closely for increasing abdominal colic.
Reduce tumour oedema. Reduce nausea and vomiting.	Dexamethasone [4, 16] [Level 2+]	8mg	May be given as a stat subcutaneous injection. Discontinue if no improvement in symptom control after 5 days.

9.2.3 Use of a nasogastric tube

* Consider a wide bore nasogastric tube for patients with upper gastrointestinal obstruction and / or intractable large volume vomiting. [2, 6, 7] [Level 4]

9.2.4 Venting gastrostomy

* A venting gastrostomy can improve the symptoms of malignant bowel obstruction. It should be considered in patients with intractable symptoms who have a prognosis of >2 weeks. If a nasogastric tube has helped improve symptom control it is possible that a venting gastrostomy may also be effective. [21] [Level 4]

9.3 STANDARDS

1. The multidisciplinary notes should record:
   - The finding of the rectal examination on initial assessment.
   - The presence and severity of abdominal colic, nausea and vomiting.
   - The number of vomiting episodes in 24 hours. [17] [Grade D]
2. Consideration of a surgical opinion and the decision made should be documented in the case notes. [17] [Grade D]
3. Medication should be delivered by continuous subcutaneous infusion. Breakthrough medication can be given by stat subcutaneous injections. [11] [Grade D]
4. If a patient is experiencing abdominal colic, prokinetic drugs and stimulant laxatives should be discontinued. [11] [Grade D]
5. The frequency of vomiting should be reduced to one episode per 24 hours. [17] [Grade D]

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10. GUIDELINES FOR THE MANAGEMENT OF INTRACTABLE BREATHLESSNESS IN PATIENTS WITH MALIGNANT DISEASE

10.1 GENERAL PRINCIPLES

* Breathlessness is a common symptom in patients with advanced malignancy. Approximately 70% of patients experience breathlessness during the last six weeks of life. [1]

* Breathlessness in the patient with advanced cancer is usually multifactorial. It is important to consider potentially reversible causes of breathlessness and treat where appropriate (see *Guidelines on Antibiotics, Ascites, Blood Transfusions, Corticosteroids, Fatigue, Pleural Effusions*). Table 10.1 includes some of the common causes of breathlessness in patients with advanced cancer. [2]

Table 10.1 Common causes of breathlessness in patients with advanced cancer [2]

Anaemia	Iatrogenic e.g. chemotherapy	Pericardial effusion
Anxiety	Infection	Pleural effusion
Ascites	Intrathoracic malignancy	Pneumothorax
Bronchospasm	Ischaemic heart disease	Pulmonary embolism
Chronic obstructive pulmonary disease	Lymphangitis carcinomatosis	Pulmonary fibrosis
Congestive cardiac failure	Neuromuscular disorders	Stridor
Fatigue / cachexia	Pain	Superior vena cava obstruction

* Intractable breathlessness can be defined as breathlessness where active management of the cause is no longer possible and / or appropriate. [1]

* The mechanisms involved in the sensation of breathlessness are poorly understood. Physical, psychological, social and spiritual factors may all contribute to the experience of breathlessness. It is important to adopt a multi-disciplinary approach to the management of this difficult symptom. [3]

* Management approaches will include both pharmacological and non-pharmacological measures. [3, 4]

* Benzodiazepines, opioids and oxygen are the mainstay of medical management for intractable breathlessness. Therapeutic trials of medications, either singly or in combination, may be necessary to determine an effective management strategy for an individual patient. [3]

10.2 GUIDELINES

10.2.1 Non-pharmacological options

* These are important and should not be overlooked. They may be used alone or in conjunction with medication. [5, 6, 7] [Level 4]

* They include:
  - Reassurance and explanation.
  - Use of a fan or cool air across the face.
  - Adequate positioning of the patient to aid breathing.
  - Breathing exercises and relaxation training.
  - Advice on modifying lifestyle.
  - Acupuncture, aromatherapy and reflexology.

10.2.2 Pharmacological options

Benzodiazepines [Level 3]

* Benzodiazepines may be useful especially if there is coexisting anxiety and / or fear.[8]
* Lorazepam is suggested for episodes of paroxysmal breathlessness.
  Dose: 0.5mg-1mg sublingually as required (maximum dose is 4mg daily). [9]
* In patients unable to tolerate oral medication or those in the dying phase, subcutaneous midazolam 2.5mg-5mg as required may be appropriate. [2] If effective, this can then be incorporated into a 24 hour subcutaneous infusion via a syringe driver. [9]

Nebulised medication [Level 4] / [Level 1-]

NB: **The first administration of any nebulised medication, including saline, must be monitored for adverse effects such as bronchospasm. [9]**

* Nebulised non-opioids
  - Nebulised sodium chloride 0.9% may help as a mucolytic. Consider a trial for 24 hours.
    Dose: 5ml via a nebuliser 4 hourly or as required. [10] [Level 4]
  - A trial of a nebulised bronchodilator should be considered if there is evidence of airways obstruction.[11][Level 4] Commonly prescribed bronchodilators are Salbutamol and Ipratropium Bromide.
    Dose: Salbutamol 2.5mg-5mg up to 4 times in 24 hours. [9]
    Dose: Ipratropium bromide 500micrograms up to 4 times in 24 hours. [9]
* There is no current evidence to support the use of nebulised lignocaine in the management of intractable breathlessness and therefore it is not recommended for use at present.[12, 20] [Level 4]
* Nebulised opioids
  - Current evidence does not support the use of nebulised opioids in the management of intractable breathlessness. [13] [Level 1-]

Systemic opioids [Level 1]

* Morphine is the most commonly prescribed oral opioid in the management of intractable breathlessness. [13]
* The prescribing of oral opioids on an "as required basis" may be appropriate for paroxysmal breathlessness. [13]
* A trial of morphine sulphate solution should be considered for patients who are opioid naïve.
  Dose: Morphine Sulphate solution 2.5mg-5mg every four hours, or as required.[13]
* There is some evidence that the use of a short-acting opioid is more effective at relieving breathlessness. It may be necessary to prescribe on a regular basis in addition to any long-acting opioid that the patient may be taking. If a patient is already established on opioids it may

be appropriate to increase the dose of the long acting opioid by 25-50%, This would not be appropriate if the patient is experiencing intermittent periods of breathlessness as they may then get an increase in side-effects [14, 15, 16]

* Diamorphine / morphine are the strong opioids of choice in patients who are unable to swallow. Dose: Diamorphine 1.25mg-5mg as required subcutaneously if the patient is opioid naive. If diamorphine is unavailable then morphine may be used as an alternative. Dose: Morphine 2.5mg-10mg as required subcutaneously. If effective, the appropriate dose can be incorporated into a 24 hour infusion via a syringe driver.[13, 16]

Oxygen [Level 3]

* The evidence for efficacy is limited. [2, 17]

* A trial of oxygen should be considered in patients known to be hypoxaemic (i.e. oxygen saturation less than 90%). Care is required in patients with known COPD and Type 2 respiratory failure.
  Dose: Oxygen 24-28% in patients with known COPD.
  Oxygen 24-60% for other patients.[17]

* The use of continuous oxygen should be avoided if possible as this may lead to patient dependence, reduced mobility and give limited benefit. Intermittent use is the preferred mode of administration. [2]

* Oxygen administered via a mask may be claustrophobic, cause a barrier between the patient and family and result in dryness of the mouth. Nasal prongs are often better tolerated than masks. Humidified oxygen may be more comfortable for the patient. [2]

Corticosteroids [Level 3]

* Corticosteroids may help in patients with tumour compression or lymphangitis carcinomatosis. They are also used in exacerbations of obstructive airways disease. There is no evidence of their benefit in non-specific dyspnoea. If there is no improvement, they should be discontinued (see Guidelines on the Use of Corticosteroids). [2, 3]

  Dose: Dexamethasone 4mg-8mg daily administered before 2pm. Occasionally higher doses (8mg-16mg) are used e.g. lymphangitis, superior vena cava obstruction.

Anti-cholinergic medications [Level 4]

* Anti-cholinergic medications are the drugs of choice in the management of respiratory secretions in the dying phase. Hyoscine hydrobromide and glycopyrronium are the two most commonly used drugs. [18]

  Hyoscine hydrobromide: 400micrograms subcutaneously as required. Prescribe 1.2mg-2.4mg subcutaneously via a syringe driver over 24 hours.[21]

  Glycopyrronium: 200micrograms subcutaneously as required. Prescribe 600micrograms - 2.4mg subcutaneously via a syringe driver over 24 hours.[22]

Other medications [Level 4]

* There is anecdotal evidence that phenothiazines, antihistamines, cannabinoids and nebulised furosemide may be useful in the management of intractable breathlessness. [2] [Level 4]

10.3 STANDARDS

1. Reversible causes of breathlessness should be identified and treated where appropriate. [2] [Grade D]

2. Patients with anxiety should be considered for a trial of relaxation therapy and / or anxiolytics. [18] [Grade C]

3. All patients with breathlessness should have access to non-pharmacological interventions. [6, 7, 19] [Grade C]
4. Breathlessness should be controlled in all dying patients. [20] [Grade D]
5. All patients prescribed nebulised medication should first receive a test dose. [10] [Grade D]
6. Any adverse reactions to nebulised medication should be clearly documented in the clinical notes. [20] [Grade D]
7. Diamorphine / morphine are the opioids of choice if patients are unable to swallow. [13] [Grade A]
8. Midazolam is the benzodiazepine of choice in patients who are unable to swallow. [2] [Grade D]
9. Nebulised opioids should not be used in the management of intractable breathlessness. [14] [Grade C]

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11. GUIDELINES FOR CARDIOPULMONARY RESUSCITATION IN PALLIATIVE CARE

11.1 GENERAL PRINCIPLES

* Cardiopulmonary resuscitation (CPR) includes all life support measures which are applied in the event of a cardiac arrest in the endeavour to restart circulation and breathing. It is comprised of basic life support and advanced life support. [1, 2, 3, 4]

* Basic Life Support aims to maintain adequate circulation and oxygenation until action can be taken to reverse the underlying cause of the cardiopulmonary arrest. It includes external cardiac massage and rescue breathing, via mouth to mouth or by use of a pocket mask or bag valve and mask. [4, 5]

* Advanced Life Support represents a continuation of basic life support and involves the use of a defibrillator, venous cannulation, intubation, advanced airway management, appropriate intravenous drugs and other advanced therapies to provide definitive treatment for reversible causes of cardiac arrest. [1, 4]

* Basic and advanced life support was originally intended to be administered to otherwise healthy people with reversible pathology, which left untreated would lead to cardio-respiratory arrest and sudden death. [2, 6, 7]

* CPR is **not** indicated in certain circumstances including:

  - If CPR is not predicted to restart the heart and breathing.

  - Where successful resuscitation would probably result in a quality of life previously deemed unacceptable by the patient, recognising that the focal point of any such decision would be the views of that patient.

  - If it is contrary to the wishes of the patient with capacity for that decision, as previously expressed in a written, valid and applicable Advance Decision to Refuse Treatment (ADRT). [7, 9, 11, 12]

* Decisions about CPR must be made on an individual basis. Advance care planning, including decisions about CPR, is an important part of good clinical care for those at risk of cardio-respiratory arrest. [2, 10, 12]

* The purpose of Do-Not-Attempt Cardiopulmonary Resuscitation (DNACPRR) orders is to allow dying patients to die peacefully without undergoing futile attempts at resuscitation prior to death.[11] If the patient is in the dying phase and has a prognosis of days to weeks, CPR would not be appropriate and a DNACPR order should be considered. [13]

* A DNACPR decision only applies to CPR and not to any other aspects of treatment. [2, 7, 8]

* A DNACPR decision does not override clinical judgement in the unlikely event of a reversible cause of the patient's respiratory or cardiac arrest that does not match the circumstances envisaged.

* A patient with capacity has the right to be involved in decisions that affect and involve them.[10, 14] A patient with capacity for that decision has the right to refuse treatment including CPR, but

not to demand treatment that is clinically inappropriate.[2, 8, 10, 11] If a patient lacks capacity, those close to the patient should be involved in discussions to explore the patient's wishes, feelings, beliefs and values.[2]

* Any CPR decision must depend on the individual circumstances of the patient. A blanket do-not-attempt-cardiopulmonary resuscitation policy on the basis of a particular patient group, such as the elderly, disabled or residents of a nursing home or hospice, is not permissible. [2, 9, 12, 13, 15]

* Wherever possible, discussions about CPR should be carried out by an experienced senior clinician. [2]

* The BMA / RCN Joint Statement outlines three patient scenarios relating to CPR decisions and the actions that should be taken i.e.

  - An arrest cannot be anticipated in the current circumstances.
  - An arrest can be anticipated but there is **no** realistic chance that CPR could be successful.
  - An arrest can be anticipated and there **is** a realistic chance that CPR could be successful.

  The Joint Statement should be reviewed for guidance in the three scenarios.[2]

* Hospitals and hospices should have a CPR policy which all staff are aware of, and appropriate information for patients and relatives about resuscitation policies and facilities available within the establishment. [2, 5, 10, 16, 17, 18]

* Policies and decisions about CPR need to be compatible with the Human Rights Act 1998, implemented in 2000, and with the Mental Capacity Act 2005. [10, 12, 14, 20]

* CPR is rarely appropriate for patients with a terminal illness.[3, 7] However, palliative care units now treat patients earlier in their disease and also patients with non-cancer diagnoses whose prognosis may be less clear. In some units, procedures are performed such as interventional pain techniques where cardiac arrest may be a rare but recognised complication. Prompt intervention may be successful in reversing the underlying cause. Therefore there may be a small subgroup of hospice patients for whom consideration of CPR may be appropriate.[9]

* It has been suggested that palliative care units may need to consider whether they should have automated external defibrillators (AEDs) which could also be brought into use should staff or visitors suffer cardiac arrest. However cardiac arrest is such a rare event in this setting that it is not feasible to expect that hospices could be providers of comprehensive advanced life support over and above appropriate use of AEDs as it would be impossible to maintain the necessary skills. Speedy transfer of these patients to hospital for intensive treatment and monitoring should be of paramount importance in the event of an arrest. The focus of training should be on maintaining skills in Basic Life Support so this can be implemented until paramedics arrive to transfer the patient to hospital.[15, 21]

11.2 GUIDELINES

* The BMA / RCN Joint Statement provides comprehensive guidance on decisions relating to CPR. Practitioners are advised to consult this document for further information. [2] [Level 4]

* All hospices are governed by NHS or Care Quality Commission (CQC) regulations. The latter clearly states that health establishments must base their CPR policy on Resuscitation Council policy. This includes inpatients, outpatients and patients attending day therapy.[2, 23, 24] [Level 4]

* Decisions regarding CPR must involve the multi-professional team alongside the patient, relatives and carers where appropriate. The most senior clinician in charge of the patient's care will have ultimate overall responsibility for the decision, and for ensuring adequate documentation of that decision. Documentation should include: how the decision was reached;

the date of the decision; reasons for the decision and the name and position of the person responsible for making the decision. [2, 8, 17, 19] [Level 4].

* If a clinical decision is made that an arrest can be anticipated but there is no realistic chance that it could be successful, it is not appropriate offer CPR. Careful consideration should be given to whether to inform the patient of the decision. The situation should be reviewed regularly. [2, 10, 11, 13] [Level 4]

* When appropriate, patients and relatives should be given information, including written material, to supplement face-to-face discussions. [2, 5, 10, 17] [Level 4].

* Patients should be offered the opportunity to discuss CPR in more detail if they wish. Where discussions take place they must be approached with sensitivity and tact. [2] [Level 4]

* If there is no Advance Decision to refuse Treatment or DNACPR order and the wishes of the patient are not known and cannot be identified, resuscitation should be the default position in the event of a cardiac or respiratory arrest, unless the patient is clearly dying or until further information is obtained that makes continued CPR inappropriate e.g. a DNACPR order or clinical information indicating that CPR will not be successful. [2] [Level 4]

* If CPR might re-start the pulse and respiration, the benefits to the patient of prolonging life must be weighed against the potential burdens. This should incorporate consideration of the patient's best interests and wishes in addition to clinical factors. Sensitive but realistic discussion with the patient of the facts, potential risks and adverse effects and their wishes should be undertaken unless they indicate that they do not want to discuss CPR. [2, 5, 13] [Level 4]

* If a patient with capacity wishes to be a candidate for CPR in the event of cardiac arrest and CPR has a chance of restarting the pulse and respiration, their wishes should be clearly documented and the MDT must be aware of this decision. This wish should be reviewed with the patient at regular appropriate intervals as their condition advances. [8, 17] [Level 4] IF the patient wishes to have CPR, the team and patient may wish to consider whether they should be transferred to an appropriately equipped unit for ongoing acute medical care. [9, 12] [Level 4]

* Although patients or their advocates with Lasting Power of Attorney (LPA) can refuse treatment, they cannot demand treatment assessed by the healthcare team to be clinically inappropriate. If they do not accept a DNACPR decision and wish a second opinion, this should be arranged. Where possible, the clinician providing the second opinion should review the patient in their current place of care. [2] [Level 4]

* A competent refusal of CPR must be respected, even if this will result in the patient's death, without the need for the patient to justify their decision. Such a refusal may be documented in the form of a formal Advance Decision to Refuse Treatment and to be legally binding should be set out as described in the Mental Capacity Act i.e. it must be in writing, signed either by the patient, or by another person on his behalf, and signed by a witness. It must state that the advance decision is to apply even if the patient's life is at risk. If an Advance Decision to Refuse Treatment is found to be not legally binding, it must still be taken into account when assessing the patient's best interests. [2, 14] [Level 4]

* If a patient lacks capacity, CPR can be withheld if it would not be in the patient's best interests as assessed by the MDT and those close to the patient. [2, 10, 14, 17] [Level 4]

* If a patient lacks capacity and has formally appointed an advocate with Lasting Power of Attorney to make welfare decisions and their authority includes making clinical decisions about life-sustaining treatment on the patient's behalf, or if the court has appointed a deputy or guardian with similar authority, this person should be consulted about a decision concerning CPR. The Advocate with LPA or deputy cannot demand treatment that is clinically inappropriate. However, if it is thought that CPR may succeed in restarting the pulse and respiration for a prolonged period, a decision about the appropriateness of CPR should be made

in the patient's best interests. This should be informed by the views of the MDT, those close to the patient and advocates with LPA where those have been appointed. [2, 14] [Level 4]

* If a patient lacking capacity has no family, friends / advocate and it is not clear whether or not CPR would have a realistic chance of success, or if a DNACPR decision is being made on best interests grounds, then an independent mental capacity advocate (IMCA) must be consulted at the earliest opportunity. [2, 14] [Level 4]

* DNACPR decisions should be recorded on a clearly identifiable document which should cross care settings. [22] [Level 4]

* If a DNACPR document goes home with the patient, then the decision and the reason for it should be discussed with the patient and those close to them. This should form part of discussions about the patient's awareness of their illness and facilitation of advanced care planning. [22] [Level 4]

* Healthcare organisations should ensure that their clinical staff maintain knowledge and skills to undertake discussions and decision making about CPR. [2] [Level 4]

11.3 STANDARDS

1. Hospitals and specialist palliative care units should have a resuscitation policy and all staff should be aware of this policy. [2, 5, 10, 16, 21] [Grade D]

2. Designated staff should receive regular training to ensure that they maintain competency in performing basic CPR. Clinical staff should update their skills on an annual basis. [2, 9, 10, 12, 21] [Grade D]

3. Any decisions about CPR must be clearly documented. This includes: how the decision was reached; the date of the decision; reasons for the decision and the name and position of the person responsible for making the decision. [2, 17, 19] [Grade D]

4. Decisions about CPR should be shared with all health care professionals who may need to know e.g. hospitals, hospices, nursing homes, GPs, other community health care professionals, out-of-hours medical services and ambulance staff. [13] [Grade D]

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12. GUIDELINES FOR THE MANAGEMENT OF CONSTIPATION IN PALLIATIVE CARE

12.1 GENERAL PRINCIPLES

* Constipation is defined by the patient and is a symptom not a disease. [1, 2]
* Patients with ECOG performance status 3 or 4 are at a high risk of developing constipation (i.e. patients confined to bed or chair for more than 50% of waking hours). [1, 3, 4]
* Patients on weak or strong opioids are at high risk of developing constipation. [1, 3, 4, 5]
* There is no evidence to suggest the superiority of any one laxative in resolving constipation.[1]
* Table 12.1 lists common causes of constipation in advanced cancer.

Table 12.1 Common causes of constipation in advanced cancer [1, 3, 6, 7, 15]

Bowel obstruction	Depression	Immobility
Concurrent disease	Drugs	Poor food intake
Confusion	Environmental	Spinal cord compression
Dehydration	Hypercalcaemia	Weakness

12.2 GUIDELINES

* To identify patients at risk of constipation, an assessment of performance status should be undertaken.[1, 15] [Level 4]
* A digital rectal examination should be carried out on the first assessment, if appropriate. [6] [Level 4]
* Bowel obstruction should be excluded (*see Guidelines on the Management of Bowel Obstruction*). [6] [Level 4]
* General management includes encouraging fluid intake, particularly fruit juices. [1,7,15] [Level 4]
* Oral laxatives should be reviewed every 3 to 4 days using stool consistency (e.g. Bristol Stool Chart) [8] and ease of defecation as guides to dose titration. [1] [Level 4]
* The laxative dose should be titrated upwards until constipation is controlled. Oral laxatives should initially be given at night. [4, 6, 7, 9] [Level 4]
* If strong opioid induced constipation is severe, then consider substitution to transdermal fentanyl (*see Guidelines on Opioid Substitution*). [10, 11] [Level 2+]
* Oral laxatives may be subdivided into different groups according to their mode of action. Tables 12.2a and 12.2b feature the laxatives and rectal interventions commonly used in palliative care. [7, 9] [Level 4]
* Figure 12.1 outlines the steps for increasing the dose of codanthramer. [1] [Level 4]

* The use of rectal interventions will be guided by the findings on rectal examination (see Figure 12.2). [2, 12] [Level 4]
* If rectal intervention is required for management of constipation, the oral laxative dose should also be increased. [4] [Level 4]
* In patients with spinal cord compression or cauda equina syndrome, alternate day suppositories should be considered, in addition to a review of the current oral laxative therapy. [4] [Level 4]
* Methylnaltrexone (Relistor®) is licensed for the treatment of opioid induced constipation in patients with advanced disease receiving palliative care, when response to the usual laxative therapy has not been sufficient. It is a peripheral μ-opioid antagonist which is given subcutaneously. It is supplied in 12mg/0.6 mL single-use vials. It must not be used in patients with known or suspected mechanical bowel obstruction, or patients with an acute surgical abdomen. The onset of action is between 30-60 minutes. Side effects include bloating, flatulence, cramps and nausea. Table 12.3 details recommended doses of methylnaltrexone. [13, 14] [Level 1+]
* If constipation remains a significant problem, consider the use of further investigations e.g. abdominal X-ray. [6, 12] [Level 4]

Table 12.2a Oral laxatives commonly used in palliative care [7, 9] [Level 4]

Type of laxative	Drug name	Starting dose	Additional notes
Combination laxatives	Codanthramer capsules	1-2 caps at night	Take 6 -12 hours to have effect. Urine coloured red; warn the patient.
	Codanthramer suspension	5ml-10ml at night	Only licensed for use in terminally ill patients of all ages. May cause abdominal colic.
	Codanthramer strong capsules	See Figure 12.1	May cause painful rash around rectum and buttocks which should be treated with a barrier cream, such as Metanium®.
	Codanthramer strong suspension	See Figure 12.1	Caution in patients with urinary and / or faecal incontinence.
	Docusate sodium	100mg tds	Takes 24 - 48 hours to have an effect. Mainly acts as softener, but doses over 400mg may have weak stimulant action. Syrup is available but the taste is extremely unpleasant.
Stimulant laxatives	Senna tablets	1-2 tabs at night	Takes 8 - 12 hours to have effect. May cause abdominal colic.
	Senna syrup	5ml-10ml at night	Reduce dose of senna, if colic develops.
	Bisacodyl tablets	1-2 tabs at night	
Osmotic laxatives	Magnesium hydroxide	10ml-20ml bd	Should be avoided in patients with cardiac disease or poor renal function.
	Lactulose	10ml-20ml bd	Can be associated with flatulence / abdominal colic. Can take 48 hours to have an effect.
	Movicol®	1 sachet tds	Movicol® may be used to treat faecal impaction. Give 8 sachets in 1 litre of water, over 6 hours. Contraindicated in complete bowel obstruction.

Table 12.2b Rectal interventions commonly used in palliative care [7, 9] [Level 4]

Rectal Laxatives

Type of laxative	Drug name	Dose	Additional notes
Stimulant rectal intervention	Bisacodyl l0mg Suppository	1 or 2 when necessary	Takes 15-60 minutes to have effect. Use when there is soft loading of the rectum.
	Glycerol 4g Suppository	1 or 2 when necessary	Takes 15-60 minutes to have effect. Useful softening action. Use when there are hard stools.
	Docusate sodium - 120mg enema	1 when necessary	Takes 5-20 minutes to have effect. Softener and mild stimulant. Useful for hard stools
Others	Arachis oil enema	1 when necessary	Warm before use. Takes up to 1 hour to have effect. Caution in patients with peanut allergy.
	Sodium citrate enema (e.g.Micralax ®)	1 when necessary	Small volume (5ml). Takes 30-60 minutes to have effect.
	Phosphate enema	1 when necessary	Large volume (120ml-130ml). Stronger than citrate enema.

Figure 12.1 Increasing the dose of Codanthramer [1] [Level 4}

(Only for use in terminally ill patients)

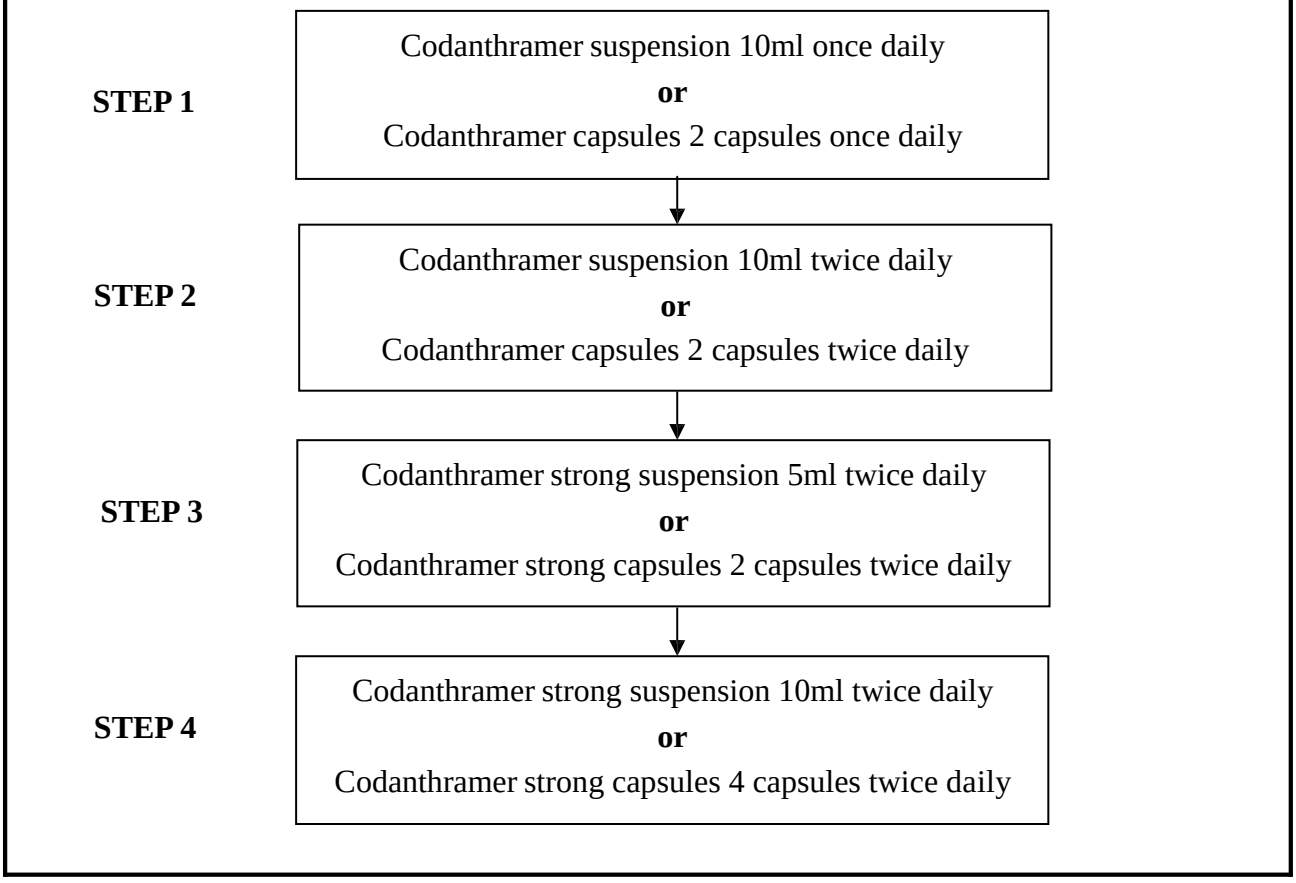

Figure 12.2 Rectal interventions for constipation [4, 7] [Level 4]

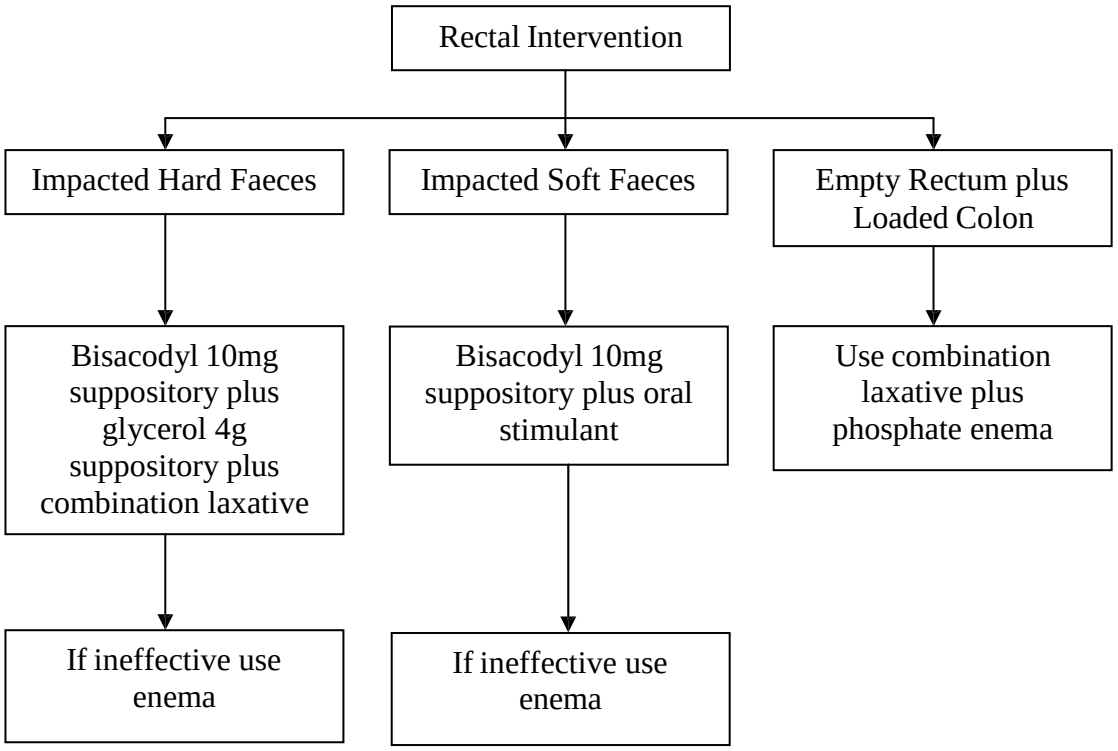

Table 12.3 Recommended doses of methylnaltrexone (Relistor®) for opioid induced constipation [13, 14] [Level 1+]

Patient Weight	Dose	Additional notes
38kg to <62kg	8mg (0.4ml) (0.075mg/kg in severe renal failure)	Given as a single subcutaneous dose on alternate days. Patients may receive two consecutive doses 24 hours apart, only when there has been no response (bowel movement) to the dose on the preceding day. Doses may also be given with longer intervals, as per clinical need.
62kg to 114kg	12mg (0.6ml) (8mg in severe renal failure)	
< 38kg or > 114kg	0.15 mg/kg (0.075mg/kg in severe renal failure)	In severe renal impairment, (creatinine clearance < 30ml/min) the dose should be reduced. Data is limited for use in end stage renal or severe hepatic failure.

12.3 STANDARDS

1. Identify the cause of constipation, treating reversible causes and managing bowel obstruction where appropriate (*see Guidelines on the Management of Bowel Obstruction*). [6] [Grade D]
2. Patients commencing opioid therapy should also be offered a combination laxative. [1, 4] [Grade D]
3. Changes in laxatives should be documented in the patients' notes. [1] [Grade D]

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13. GUIDELINES FOR THE USE OF CORTICOSTEROIDS IN PALLIATIVE CARE

13.1 GENERAL PRINCIPLES

* Corticosteroids have been shown to be effective for a variety of uses in the palliative care setting. (see Table 13.1) As many as 50% of patients with advanced disease may be prescribed systemic corticosteroids during their illness. [1]

Table 13.1 Indications for systemic corticosteroids

Anorexia [2, 3, 4]	GI obstruction [8, 9]	Post radiotherapy [12]
Bone pain [5, 6]	Liver capsular pain [2]	Raised ICP [13, 14]
Dyspnoea [7]	Lymphangitis carcinomatosis [10]	Spinal cord compression [15]
General well-being/ weakness [2, 4, 6]	Nausea [2, 7]	SVCO/IVCO [16]
	Neuropathic pain [1, 5, 11]	Tracheal obstruction [17]

* The most commonly used systemic corticosteroids in clinical practice are prednisolone and dexamethasone. 40mg of prednisolone is equivalent to 6mg of dexamethasone. [18]
* Topical and rectal preparations of corticosteroids are also available for treatment of local inflammation. [18]

13.2 GUIDELINES

* Table 13.2 indicates suggested starting doses of systemic corticosteroids which are used in palliative care.
* It is important to limit the risk of inducing adrenal insufficiency. Therefore all patients prescribed corticosteroids should be given treatment for the shortest time using the lowest effective dose. [19] [Level 1+]
* The need for corticosteroids should be reviewed on a regular basis. [2, 7] [Level 3]
* Corticosteroids should be discontinued if there has been no clinical response within 5–7 days. [5, 7] [Level 4]
* Unless given in an emergency, corticosteroids should be administered once daily in the morning, or twice daily with the last dose before 2.00pm. This reduces suppression of the hypo-pituitary-adrenal axis and may prevent corticosteroid-induced insomnia. [18, 19] [Level 1+]
* In the event of a deterioration in the patient's symptom control, or the presence of an intercurrent illness, the corticosteroid dose may need to be increased for 5-7 days to maintain symptom control. Any subsequent reductions in dose may have to be made more slowly. [20, 21] [Level 4]

* All patients who are anticipated to require corticosteroids for longer than 3 weeks should be given a steroid card. [19] [Level 4]

Table 13.2 Suggested starting doses for systemic corticosteroids [24] [Level 4]

Suggested starting dose	Clinical indication	Mechanism of action	Additional notes
2mg-4mg	Anorexia General well-being	Uncertain	If patient has diabetes or a prognosis greater than 3 months, consider using megestrol acetate 160mg-320mg orally daily for appetite. [3, 8, 9]
4mg-8mg	Nausea Dyspnoea	Uncertain	
8mg	GI/GU obstruction Bone pain Neuropathic pain Liver capsule pain Post-radiotherapy	Reduction of tumour oedema/ anti-inflammatory effect	
16mg	Spinal cord compression Raised ICP SVCO/IVCO Tracheal obstruction Lymphangitis carcinomatosis	Reduction of tumour oedema/ anti-inflammatory effect	

* The need for gastroduodenal cover with systemic corticosteroids is uncertain. A proton pump inhibitor or H_2 antagonist should be co- prescribed with the corticosteroid for all patients taking NSAIDS [22] or those with two or more of the following risk factors. [23] [Level 2+]
  - Advanced malignancy.
  - Previous history of peptic ulcer disease.
  - Anticipated cumulative dose of corticosteroid equivalent to or greater than 140mg dexamethasone.
* It may also be worth considering gastric protection for the following patients: [23, 24] [Level 4]
  - Concurrent use of SSRIs, aspirin, anticoagulants, bisphosphonates.
  - Where the starting dose of corticosteroid is equivalent to or greater than 8mg dexamethasone.

* If a patient is taking anti-epileptics such as phenytoin, carbamazepine or barbiturates there is a possibility of enzyme induction. Phenytoin in particular, has been shown to reduce the bioavailability of dexamethasone by as much as 75%. Patients may therefore require a 2-4 fold increase in their dexamethasone dose to achieve adequate symptom control. [25] Dexamethasone may also affect plasma phenytoin concentrations. [26] [Level 1-]

13.2.1 Corticosteroid Side Effects

* Side effects of corticosteroids include candida infection, weight gain, bruising, thinning of the skin, diabetes mellitus, proximal myopathy and cushingoid features. Patients on long-term corticosteroids should be maintained on the lowest possible corticosteroid dose and monitored for side effects. [12, 14, 23] [Level 3]

* Due to immunosuppression, patients on long-term corticosteroids also have an increased risk of developing new infections, or reactivating dormant infections such as TB or herpes zoster. Signs of infection may be masked by steroid use and patients should therefore be closely monitored. [21] [Level 4]

* If a patient develops a proximal myopathy secondary to the use of dexamethasone, it may be worth considering changing to a non-fluorinated corticosteroid (e.g. prednisolone), as these are thought to cause less myopathy. [27] [Level 3]

* Hyperglycaemia is a recognised side effect of corticosteroid therapy, in both diabetic and non-diabetic patients. [1, 2, 7, 28] It is therefore important to monitor glucose levels in all patients receiving corticosteroid therapy. Figure 13.1 gives guidelines for the monitoring and management of blood glucose in patients on corticosteroids. (*see also Guidelines for the Management of Diabetes Palliative Care*) [Level 4]

* Megestrol acetate may be an appropriate alternative for appetite stimulation in patients who develop hyperglycaemia or other toxicities due to corticosteroids. [3] [Level 4]

* Prolonged treatment with systemic corticosteroids is known to increase the risk of osteoporosis and fractures. This risk escalates rapidly within the first 3 months of treatment. Calcium and Vitamin D supplementation may be required for all patients taking corticosteroids with a deficient dietary intake. Bisphosphonates have been shown to be effective for the secondary prevention of fractures in some high-risk patients. Patients who are anticipated to require corticosteroids for longer than 3 months should be considered for prophylactic treatment with bisphosphonates at the time of commencing corticosteroids. Oral bisphosphonates may cause oesophageal/ gastric irritation. [29, 30, 31] [Level 4]

13.2.2 Withdrawal of Corticosteroids

* Corticosteroids should be discontinued once symptoms have resolved, or reduced to the lowest effective dose required to maintain symptom control.[19] [Level 1+]

* Any medications co-prescribed to prevent side effects should be stopped once corticosteroids have been discontinued. [24] [Level 4]

* The Committee on Safety of Medicines (CSM) has recommended that systemic corticosteroids should be gradually withdrawn in patients who have received treatment for longer than 3 weeks. [18, 19, 31] [Level 1+]

* Gradual withdrawal should also be considered in those patients who have received <3 weeks of treatment, but who are considered high-risk for developing adrenal insufficiency (see below). [18, 19, 31] [Level 4]

* The CSM has recommended that systemic corticosteroids may be stopped abruptly in those whose disease: [18, 19, 31] [Level 1+]

    1. is unlikely to relapse **and**
    2. who have received treatment for less than 3 weeks **and**
    3. who are not included in one of the high- risk groups (described below)

* Patients at high risk of developing adrenal insufficiency include the following: [18, 19, 31] [Level 4]

    1. Have recently received repeated courses of corticosteroids. (especially if taken for longer than 3 weeks)
    2. Are taking a short course of corticosteroids within one year of stopping long-term therapy.
    3. Have other possible causes of adrenal suppression.
    4. Have received more than prednisolone 40mg daily or the equivalent e.g. dexamethasone 4mg-6mg
    5. Have received repeat doses in the evening.

* If stopping steroids gradually, the dose may be reduced rapidly if symptoms allow, until a physiological level (7.5mg prednisolone / 1mg dexamethasone) is reached. This may involve halving the dose daily. The dose should subsequently be reduced more slowly to allow the adrenals to recover and to prevent a hypo-adrenal crisis. During the withdrawal of corticosteroids it is important to monitor the patient for deterioration of symptoms. [18, 19, 31] [Level 4]

* At the present time, dexamethasone 0.5mg tablets are in limited supply in the UK. Dexamethasone liquid is a suitable alternative. [31] [Level 4]

* If steroids are administered continuously via a syringe driver, the patient is at greater risk of adrenal insufficiency if the steroids are discontinued abruptly. In these circumstances, unless the patient is in the dying phase, corticosteroids should be withdrawn gradually. [19, 24] [Level 4]

13.2.3 Corticosteroids in the Last Days of Life

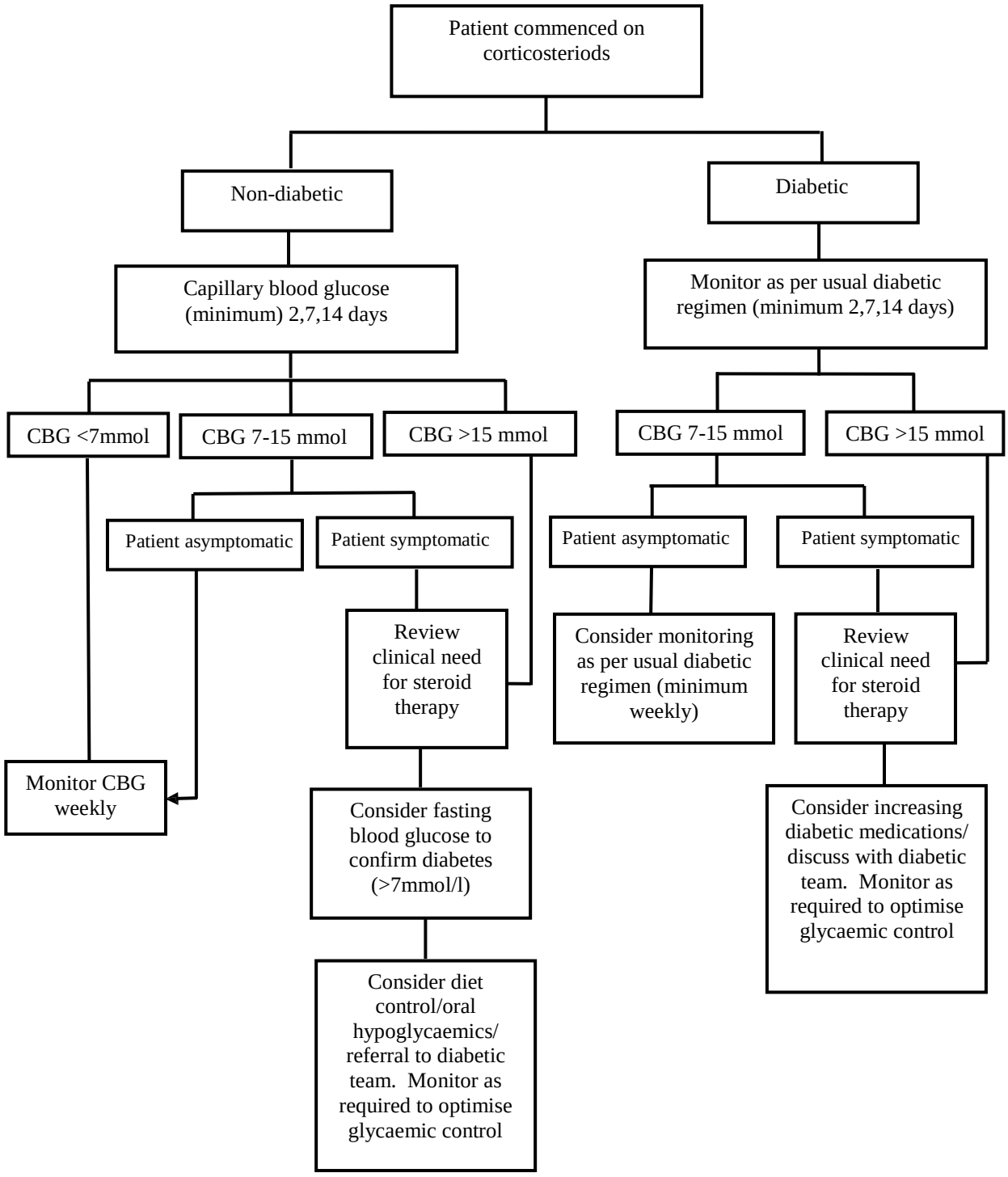
* It is usually appropriate to discontinue corticosteroids in the dying phase unless they have been necessary in achieving good symptom control for the patient e.g. to treat: [18, 24] [Level 4]

    - headaches
    - seizures
    - pain

* For patients unable to take oral dexamethasone, doses <8mg may be given by bolus subcutaneous injection: [18, 31] [Level 4]

* If a continuous infusion is necessary, dexamethasone should be administered via a separate driver to prevent precipitation.

Figure 13.1 Guidelines for the monitoring and management of blood glucose in patients on corticosteroids [24] [Level 4]



13.3 STANDARDS

1. Corticosteroids should be given once daily in the morning, or twice daily with the last dose being given before 2.00 pm, unless there is an emergency situation.[19] [Grade A]
2. All patients taking corticosteroids should be monitored for corticosteroid induced side effects and if identified they should be documented in the case notes. [12, 14, 24] [Grade D]
3. Corticosteroids should be discontinued if the patient has shown no clinical response after 5–7 days. [5, 7] [Grade D]
4. Patients should be maintained on the lowest effective dose of corticosteroid for the shortest possible time. [19] [Grade A]
5. All patients who are anticipated to require corticosteroids for longer than 3 weeks should be given a steroid card. [19] [Grade D]
6. An H_2 antagonist or PPI should be co-prescribed with corticosteroids for all patients on NSAIDS and for patients with 2 or more of the following risk factors for gastro-intestinal bleeding. [20] [Grade B]
   - Advanced malignancy.
   - History of peptic ulcer disease.
   - Anticipated cumulative dose of dexamethasone $\geq$ 140mg.

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14. GUIDELINES FOR THE MANAGEMENT OF DELIRIUM IN ADVANCED CANCER

14.1 GENERAL PRINCIPLES

* Delirium can be defined as: "A transient organic brain syndrome characterised by the acute onset of disordered arousal and cognition, accompanied by disturbances of perception and psycho-motor behaviour." [1]
* The prevalence of delirium in advanced cancer is between 25-80%. It often has multiple aetiologies. [2, 3]
* Delirium is often unrecognised in patients with advanced cancer but early detection may lead to improved patient outcomes. [3, 4]

14.2 GUIDELINES

14.2.1 Assessment of Delirium

* Delirium is a clinical diagnosis. Table 14.1 outlines the DSM IV criteria necessary for diagnosis and some of the commonly listed clinical features. [1] [Level 4]

Table 14.1 Diagnosing delirium

Clinical Diagnosis	Associated Clinical Features
All of the following should be present: - Disordered conscious level - Change in cognition - Fluctuation - Developing over a short period - Aetiologically related to a medical condition	Some of the following may be present: - Poor concentration - Disorientation - Loss of short term memory - Hallucinations - Paranoid ideas - Restlessness or aggression

* Delirium may be hyperactive or hypoactive. Hypoactive delirium is more common than hyperactive delirium in palliative care patients, although is often not diagnosed. [5] [Level 4]
* Features of hypoactive delirium include slowed motor function, lethargy, confusion and decreased awareness and interaction with their surroundings. These features may mimic depression. [5] [Level 2-]
* The role of neuroleptic medication in hypoactive delirium is uncertain at present. [5] [Level 4]

14.2.2 Reversible causes of delirium

* Delirium is often reversible although this may not apply in the last 24-48 hours of life. [4] [Level 2-]
* Some of the potentially reversible causes of delirium are listed in Table 14.2. [2, 6] [Level 4]

Table 14.2 Reversible causes of delirium

Alcohol	Haematological causes
Biochemical abnormalities e.g. hypercalcaemia, uraemia	Infections
Cardiovascular causes	Nutritional deficiencies
Cerebral pathology	Withdrawal from alcohol / nicotine
Constipation	Withdrawal from drugs e.g. antipsychotics, opioids, benzodiazepines
Drugs	

14.2.3 Management of delirium

* It is important to use both pharmacological and non-pharmacological measures in the management of a patient with delirium. [2] [Level 4]
* Non-pharmacological measures may include: a well-lit and quiet room, familiar faces, explanation, reassurance and the avoidance of isolation and loneliness. [2] [Level 4]
* Drugs, in particular opioids, are a common cause of delirium. A review of medication, including drugs recently discontinued, should be performed. [4] [Level 2-]
* If the patient is distressed, delirium may require specific drug management. Table 14.3 lists the pharmacological options. [7, 8, 9, 10] [Level 2+]
* Neuroleptics such as haloperidol and atypical antipsychotics remain the drugs of choice. [6] [Level 2++]
* Benzodiazepines may exacerbate delirium and should be used with caution. [6, 7, 8] [Level 2++]
* The aim of treatment should be to control the delirium. The treatment may at times cause a reduction in the level of consciousness. [9] [Level 4]
* The aim of treatment and any expected change in level of consciousness should be discussed with the patient, relatives and multi-disciplinary team where possible and documented in the case notes. [11] [Level 4]
* Figure 14.1 outlines a pharmacological approach to the management of delirium. Drugs should only be used when the delirium is causing distress to the patient and should be titrated according to clinical need. The manifestation of distress may influence the treatment used e.g. overlying anxiety may be better treated with benzodiazepines; paranoia may be better managed with neuroleptics. [7, 8, 12] [Level 4]

14.2.4 Committee on Safety of Medicines (CSM) warning for olanzapine and risperidone [13, 15] [Level 2]

* Olanzapine and risperidone are associated with an increased risk of stroke in elderly patients with dementia. The CSM has advised the following:
  - Risperidone or Olanzapine should not be used for treating behavioural symptoms of dementia.
  - In acute psychotic conditions in elderly patients with dementia, risperidone should be limited to short term use under specialist advice. Olanzapine is not licensed for the management of acute psychoses.
  - The possibility of cerebrovascular events should be considered carefully before treating any patients with a history of stroke or transient ischaemic attacks. Risk factors for cerebrovascular disease should also be considered e.g. hypertension, diabetes, smoking, atrial fibrillation.
* Observational studies suggest that similar to the atypical antipsychotics, treatment with conventional antipsychotic drugs may increase mortality.[16] [Level 3]

14.2.5 Mental Capacity

* Where the patient is shown to lack the capacity to consent to treatment, the Mental Capacity Act 2005 must be followed. Lasting Power of Attorney, Advanced Decisions and Independent Mental Capacity Advocates should be utilised where appropriate. [11, 14] [Level 4]

Figure 14.1 Pharmacological management of delirium in advanced cancer [7, 8, 10] [Level 4]

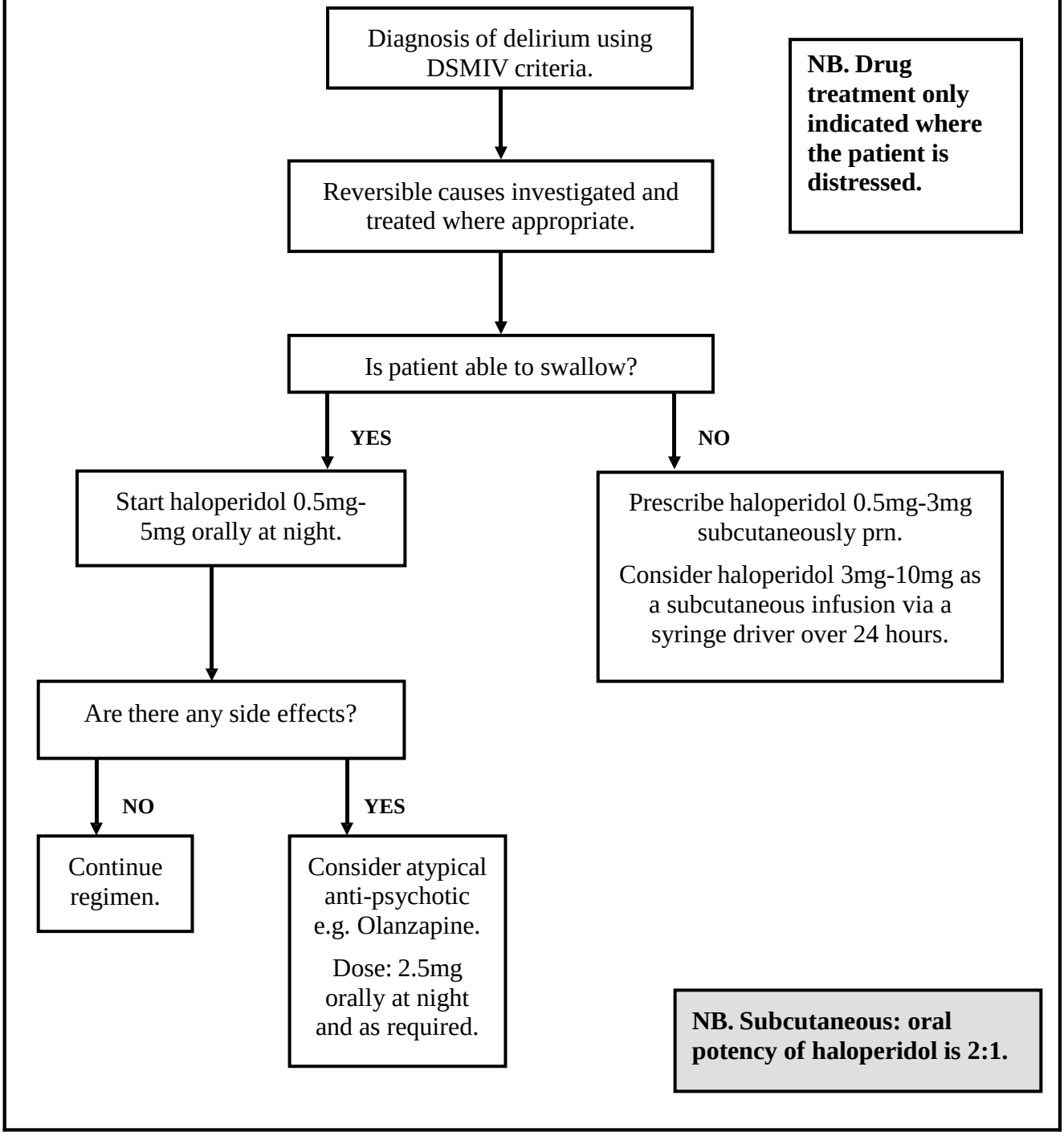

Table 14.3 Pharmacological options for the management of delirium in advanced disease [6, 7, 8, 9] [Level 2+]

Name of drug	Class of drug	Dosage	Side effects	Notes
Haloperidol	Long acting dopamine antagonist.	Oral 0.5mg-5mg tds orally. Maximum dose 30mg/24 hours Subcutaneous 1.5mg-5mg as subcutaneous bolus dose every 8 hours 5mg-10mg subcutaneously via syringe driver over 24 hours. Maximum parenteral dose is 18mg in 24 hours.	Extra-pyramidal reactions.	First line treatment for delirium. **Note.** The parenteral dose should be lower than the corresponding oral dose because of the absence of first pass metabolism. The same dose should not be prescribed for both routes.
Levome-promazine	Long acting phenothiazine.	Oral 12.5mg-50mg orally daily. Subcutaneous 6.25mg-25mg as subcutaneous bolus dose every 6-8 hours 12.5mg-200mg subcutaneously via syringe driver over 24 hours.	High risk of sedation High doses may precipitate seizures.	In a patient with a history of seizures consider the addition of midazolam. **Note.** The parenteral dose should be lower than the corresponding oral dose because of the absence of first pass metabolism. The same dose should not be prescribed for both routes.
Olanzapine	Atypical antipsychotic.	Usually given orally 2.5mg-10mg daily Can be given by CSCI but specialist advice should be sought	Weight gain, drowsiness, dry mouth. See guidelines for CSM warning.	
Risperidone	Atypical antipsychotic.	500micrograms orally initially. Increase by 500micrograms bd alternate days. Maintenance dose usually 1-3mg / day. Maximum dose is 4mg daily.	Weight gain, drowsiness, dry mouth. See guidelines for CSM warning.	May need lower starting dose and slower titration in elderly patients and patients with renal impairment. Interacts with CYP2D6 inhibitors e.g. fluoxetine so some drug interactions may be significant.
Midazolam	Short acting benzo-diazepine.	2.5mg-10mg as subcutaneous bolus doses. 10mg-100mg subcutaneously via syringe driver over 24 hours.	Possible paradoxical agitation.	Will not improve cognition in delirium.
Diazepam	Short acting benzodiazepine.	2mg-15mg orally daily in divided doses. 10mg via rectal route prn. 5mg-10mg intravenously prn.	Possible paradoxical agitation.	Will not improve cognition in delirium.
Phenobarbital	Long acting barbiturate.	100mg-200mg as bolus intramuscular injections. 600mg-2400mg subcutaneously via syringe driver over 24 hours.		Used in the dying phase to as third line agent to control agitation/delirium. Can use sodium chloride 0.9% or water as diluent but anecdotal evidence suggests may get fewer site reactions with sodium chloride 0.9%.

14.3 STANDARDS

1. The DSM IV criteria should be used in the diagnosis of delirium. [1] [Grade D]
2. Reversible causes of delirium should be treated where appropriate. [3, 4] [Grade D]
3. All patients should have a clinical examination at initial assessment of delirium. [3, 4] [Grade D]
4. All patients should have a review of medication at initial assessment of delirium. [3, 4] [Grade D]
5. The reason for the use of psychotropic medication should be documented in the case notes. [11] [Grade D]
6. Haloperidol is the drug of choice for the management of delirium where the cause is unknown. [6, 7] [Grade C]
7. Inpatients with delirium should be reviewed every four hours to ensure adequate symptom control. [11] [Grade D]

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15. GUIDELINES FOR MANAGING DEPRESSION IN PALLIATIVE CARE

15.1 GENERAL PRINCIPLES

* Depression is a common problem in patients with advanced cancer. [1, 2, 3, 4]
* Depression often is undetected, undertreated, or treated at a stage when there is insufficient time for medication to be effective. [1, 2, 4]
* In patients with advanced cancer it may be very difficult to distinguish depression from physical symptoms of their illness and/or adjustment to significant life changes. [1, 2]
* Hopelessness, feelings of guilt and worthlessness, lack of self esteem, loss of energy, insomnia and appetite disturbance are characteristic symptoms of depression. [2]
* Anhedonia is the marked loss of pleasure, interest and enjoyment in normally pleasurable activities. If present it is helpful in differentiating major depression from the `normal` reaction to major physical illness and may help to identify those patients who may respond to antidepressants. [5]
* Many of the antidepressants available currently have acceptable side effect profiles and are usually well tolerated. Depressed patients may benefit from treatment with antidepressant medication even within the last weeks of life. [2, 4]

15.2 GUIDELINES

15.2.1 Diagnosing depression

* Brief screening measures may be useful for identifying depression. The NICE guidance on management of depression recommends the use of at least 2 questions regarding mood and interest e.g.
  - During the last month, have you often been bothered by having little interest or pleasure in doing things?
  - Have you felt low, depressed or hopeless?
  - Do you want help with the way you are feeling? [4, 6, 7, 8] [Level 3]
* Alternatively consider using specific screening tools such as the Hospital Anxiety and Depression Scale (HADS) or the Edinburgh Depression Scale (EDS). The validated cut-off thresholds for palliative care patients should be used. [4] [Level 3] The Brief Edinburgh Depression Scale (BEDS) has been developed as a screening tool in patients with advanced cancer. [4, 9, 10, 11] [Level 3]
* Table 15.1 gives the ICD-10 criteria for depression.[11, 12]

* The severity of depression may be determined by considering the actual symptoms experienced by patients. Further details can be seen in Table 15.2. [1, 11, 12] [Level 4]

* Patients who are depressed should be questioned about suicidal thoughts or intent. Antidepressant use has been associated with thoughts and intent of self harm particularly in patients <30 years old. Assessment of suicidal risk is particularly important when treatment is commenced or the dose adjusted. [1, 2, 6, 13] [Level 4]

* If a patient expresses thoughts or intent of suicide, the issues and meaning behind this should be fully assessed. Optimising physical symptom control and psychological support in such patients is particularly important and it is important to consider increased support from the primary health care team, including direct contact. If a patient is assessed to be at considerable immediate risk of harm to themselves or others, urgent referral to mental health services should be arranged. [6] [Level 4].

Table 15.1 ICD-10 Criteria for depression [11, 12] [Level 4]

	Mild depression	**Moderate depression**	**Severe depression**
Clinical significance	Some difficulties in continuing with ordinary work and social activities but will probably not cease to function completely.	Considerable difficulty in continuing with social, work or domestic activities.	Considerable distress or agitation. Unlikely to continue with social, work or domestic activities.
Duration of symptoms	Duration of at least 2 weeks.	Duration of at least 2 weeks.	Duration of at least 2 weeks.
Severity (see Table 15.2 below)	Two of most typical symptoms plus two of the other symptoms.	Two or three of most typical symptoms plus three of the other symptoms. If four or more of the somatic symptoms are present the episode is diagnosed.	All three of typical symptoms plus at least four other symptoms of severe intensity.

Table 15.2 Symptoms of depression [1, 11, 12] [Level 4]

Typical symptoms	**Other symptoms**	**Somatic symptoms**
Depressed mood.	Reduced concentration and attention.	Loss of interest or pleasure in activities that are normally enjoyable.
Loss of interest.	Reduced self esteem and self-confidence.	Lack of emotional reactivity to normally pleasurable surroundings and events.
Reduced energy levels leading to increased fatigue and reduced activity.	Bleak and pessimistic views of the future.	Waking 2 hours or more before usual waking time.
	Ideas or acts of self harm or suicide.	Objective evidence of psychomotor retardation or agitation.
	Disturbed sleep.	Marked loss of appetite.
	Diminished appetite.	Weight loss.
		Marked loss of libido.

15.2.2 Treatment of depression

* Both pharmacological and psychological interventions should be considered. [1, 14] [Level 2+].
* Patients who are prescribed antidepressants should be informed about:
  - Potential side-effects.
  - Possible delay in onset of action.
  - Likely duration of treatment.
  - Importance of compliance.
  - Possible symptoms that may be experienced on stopping or withdrawal from the antidepressant medication. [6] [Level 4]
* Patients should be advised about the likely delay in onset of any beneficial effect from antidepressant medication although the length of delay is difficult to estimate. Previous guidance has suggested a delay in onset of 4-6 weeks but new evidence suggests that benefit may be seen within a shorter timescale. [15] [Level 3]
* The dose of antidepressant medication should be increased more slowly than in physically well patients. It is important to monitor side effects and clinical response and to consider factors that may influence the response. This may include the physical condition of the patient, or treatment with drugs which may predispose to depression, such as corticosteroids. [1, 2, 3] [Level 4]
* Prescribers should consider clinically significant interactions when prescribing antidepressants and should consult the British National Formulary, Appendix 1 for further guidance. [6] [Level 4]
* If there is an inadequate response to the standard dose and no side-effects, the dose may be increased in accordance with the Summary of the Product Characteristics, but it may be advisable to increase the dose more slowly than in physically well patients. If there has been no response within 4-8 weeks, consider changing to an antidepressant from a different therapeutic group. [6] [Level 4]
* If appropriate, antidepressants should be continued for at least 6 months after remission of a first episode of depression, to ensure adequate treatment and reduce the risk of relapse. If there are recurrent episodes, treatment should be continued for longer. [6] [Level 1+]
* In patients with reduced life expectancy consider the use of psychostimulants, such as methylphenidate, where the onset of action is very rapid. [6, 14] [Level 4] (see *Guidelines on the Use of Psychostimulants*).
* The Committee on Safety of Medicines (UK) advises that hyponatraemia has been associated with all classes of antidepressant drugs. [16] [Level 3] It is more common in the elderly and may be due to inappropriate anti-diuretic hormone secretion. Hyponatraemia should be considered as a possible aetiology in all patients who develop drowsiness, confusion or fits whilst taking antidepressant medication. [16] [Level 4]
* Information leaflets appropriate to the needs of the patient should be provided. [6] [Level 4]

15.2.3 Antidepressants

General Points

* Antidepressants generally reduce the seizure threshold. Caution is required with other pro-convulsive drugs such as antipsychotics or with conditions that predispose to seizures e.g.

cerebral tumours. Tricyclics are often more problematic compared to SSRIs. Citalopram is usually considered the drug of choice in patients vulnerable to seizures. [21] [Level 4]

* When choosing an antidepressant it is also useful to consider the available formulations other than tablets/ capsules. Fluoxetine is available as a liquid. Paroxetine comes as an oral suspension. Citalopram and escitalopram come as oral drops and mirtazapine is available as a melt. [20] [Level 4]

* Table 15.3 illustrates some antidepressants in common use. [17, 23]

Selective serotonin re-uptake inhibitors

* Selective serotonin re-uptake inhibitors (SSRIs) are not superior in efficacy to tricyclic antidepressants but there is evidence that they are better tolerated. They should be considered as first-line treatment for depression. [6] [Level 1-]

* SSRIs have the potential to increase the risk of bleeding from the upper gastrointestinal tract in all patients. The risk is increased for patients with other risk factors such as receiving non steroidal anti-inflammatory agents (including aspirin), liver failure, peptic ulcer disease or oesophageal varices. [6, 17] [Level 4]

* If SSRIs are co-administered with tramadol there is a theoretical risk of serotonin syndrome and therefore this combination must be used cautiously. [3] Characteristics of the serotonin syndrome include restlessness, tremor, shivering, myoclonus, confusion, convulsions and extreme cases may result in death. Other antidepressants may also trigger serotonin syndrome. Serotonin syndrome rarely occurs after taking only 1 drug with serotonergic activity and is more likely to occur when 2 or more drugs with serotonergic activity are taken together. [1, 3, 6, 18, 19] [Level 4]

Tricyclic antidepressants

* Tricyclic antidepressants (TCA) such as amitriptyline, are an alternative option but are more likely to be associated with side effects e.g. the increased risk of cardiotoxicity; greater toxicity in overdose than agents of similar potency. [6, 20] [Level 3]. Tricyclics other than lofepramine should not be prescribed for patients at high risk of serious cardiac arrhythmias or patients who have recently suffered a myocardial infarction. [20] [Level 4]. Lofepramine has a relative lack of cardiotoxicity compared to other tricyclics but should still be used with caution in such patients. [6] [Level 4]

* Tricyclic antidepressants may be useful in patients who have co-existing neuropathic pain. [3, 17] [Level 4]

* The side effect profiles of individual antidepressants may influence the choice of drug. Some side effects of tricyclic antidepressants, such as constipation, dry mouth, cognitive impairment and confusion, may be problematic in palliative care patients, but others, such as sedation and reduced secretions, may be helpful in certain situations. [3, 14] [Level 4]

Venlafaxine

* Venlafaxine inhibits the reuptake of serotonin and noradrenaline, and lacks the sedative and antimuscarinic effects of the tricyclics. Venlafaxine should not be prescribed for patients who have had a recent myocardial infarction or those at high risk of serious cardiac arrhythmias. It should also be avoided in patients with uncontrolled hypertension. Blood pressure should be checked on initiation and regularly during treatment. If a sustained increase in blood pressure occurs the dose should be reduced or venlafaxine discontinued. Patients prescribed venlafaxine should also be monitored for signs and symptoms of cardiac dysfunction. Venlafaxine is more dangerous in overdose than other antidepressants of similar efficacy. [6] [Level 4]

Mirtazapine

* Mirtazapine is a noradrenergic selective serotonin antagonist. The speed of onset may be a little quicker than for SSRIs but there is no difference when compared to tricyclics. [22] [Level 1] It may be associated with sedation, weight gain and blood dyscrasias. Patients should be advised to report fevers, sore throats, stomatitis or other signs of infection during treatment. If any of these symptoms occur a full blood count should be checked and the drug stopped immediately if a blood dyscrasia is suspected. It may be best avoided in a patient who is immunocompromised e.g. having chemotherapy. [5, 17, 20] [Level 1-]

15.2.4 Stopping antidepressants

* If a patient has been taking antidepressants for 6 weeks or more the drug should not be stopped abruptly. Exceptions to this rule are:

  - If the drug has caused a serious adverse effect e.g. a cardiac arrhythmia in association with a tricyclic antidepressant, [6]

  or

  - The patient is entering the terminal phase. [19] [Level 4]

* Antidepressants should be withdrawn slowly, preferably over 4 weeks, by weekly reductions in dose. One exception to this rule is fluoxetine. At a dose of 20mg daily this may be stopped abruptly because of the long plasma half-life and active metabolite, but at higher doses gradual withdrawal is required. [6, 18, 19, 24] [Level 4]

* Symptoms may occur as a direct result of stopping the drug. This usually takes place within 5 days of stopping treatment. The symptoms may vary in form and intensity. They may also occur during the process of reducing a dose or, in the case of drugs with a short half-life, (e.g. paroxetine, venlafaxine) after missed doses. For SSRIs the commonest symptoms include a flu-like illness, dizziness exacerbated by movement, insomnia, excessive (vivid) dreaming and irritability. If these symptoms occur the rate of drug withdrawal should be slowed and the patient reassured. Symptoms usually do not last longer than 1–2 weeks. The drug should only be restarted if the symptoms are severe or prolonged. [6, 19, 24] [Level 4]

* Withdrawal of tricyclic antidepressants can cause cholinergic rebound with symptoms including headache, restlessness, diarrhoea, nausea and vomiting. [24] [Level 4]

15.2.5 Changing antidepressants

* The dose of the original drug should be slowly reduced and the new drug slowly introduced. The speed of the "cross-tapering" may need to be adjusted according to how well the patient tolerates the process. [19, 24] [Level 4]

* Some drugs should never be co-administered and in these cases cross-tapering should be avoided. Potential risks of administering two antidepressants together include pharmacokinetic interaction (e.g. the increase in tricyclic antidepressant level caused by some SSRIs) and pharmacodynamic interactions, such as the serotonin syndrome. [6, 23] [Level 4]

* If changing between two very similar anti-depressants e.g. different SSRIs, cross-tapering may not be required as administration of the second agent is likely to ameliorate the withdrawal effects of the first. [19] [Level 4] An exception to this is fluoxetine. Any switch from fluoxetine to another antidepressant should be done slowly and cautiously (see Table 15.4). This is due to the long half-life and active metabolites. [19, 24] [Level 4]

* Table 15.4 has been adapted from the guidelines of the South Maudsley NHS Foundation Trust, [19] UK Medicines Information [18] and Bazire [24] and gives further advice on how antidepressants should be switched or discontinued. This advice is derived from manufacturer's information

and is partly theoretical. Caution is advised in all cases. The evidence is not specific to palliative care patients. In the palliative care setting it is important to remember that there may be limited time to achieve an improvement in the mood of the patient and hence in their quality of life. A more rapid switch under close medical supervision may be indicated. [19] [Level 4]

* When switching between antidepressants it is important to be aware of gradual and modest incremental increases of dose, interactions and the risk of serotonin syndrome. [6 18, 19, 24] [Level 4]

Table 15.3 Antidepressants in common use [17, 20, 23]

Class of Antidepressant	Drug name	Dose (oral)	Additional Notes
SSRI	Fluoxetine	Usual dose is 20mg-60mg daily. Reduce dose in elderly.	Increased risk of extrapyramidal reactions with haloperidol. Interacts with phenytoin and carbamazepine. More complicated than others to change from if response poor (see Table 15.4). Will reduce analgesic benefit of codeine/tramadol.
	Paroxetine	Usual dose is 20mg-40mg daily. High doses with specialist advice. Reduce dose in elderly.	Licensed for panic disorder and anxiety. These symptoms may get worse when first starting the drug. Need to give in the morning as acts as a stimulant. Withdrawal syndrome reported more often than with any other SSRI. Interacts with phenytoin and carbamazepine. Will reduce analgesic benefit of codeine / tramadol.
	Sertraline	Usual dose is 50mg-100mg daily. Maximum dose is 200mg.	Useful in anxious patients, renal failure or patients with a cardiac history. Does not interfere with the metabolism of anti-epileptic drugs or haloperidol.
	Citalopram	Usual dose is 10mg-20mg daily. Maximum dose is 60mg daily. Reduce dose in the elderly.	Also available as oral drops. Does not interfere with metabolism of other drugs. Licensed for panic disorder. NB: 10mg tablet = 8mg (4 drops) oral drops
Tricyclics	Amitryptyline	10mg- 150mg daily.	Contraindicated in patients with cardiac disease. Useful choice if pre-existing neuropathic pain. Recent studies have shown that lower doses may have antidepressant effect. High incidence of adverse effects
	Lofepramine	Usual dose is 140mg – 210mg daily (divided doses). May need lower doses in the elderly.	Has fewer sedative and antimuscarinic effects compared to amitriptyline.
NaSSA	Mirtazapine	Usual dose is 15mg-45mg at night. Similar dose for elderly patients.	Good anti-emetic receptor profile. Sedative effect at low dose. Fast onset of action. Change antidepressant if no effect within 4 weeks.

Table 15.4 A guide to switching and stopping antidepressants [19, 24] [Table published with the kind permission of South London and Maudsley NHS Foundation Trust. & Oxleas NHS Foundation Trust]

To / From	Citalopram	Fluoxetine	Mirtazapine	Paroxetine	Sertraline	Tricyclic antidepressants
Citalopram		Withdraw then start fluoxetine at 10mg daily.	Cross taper cautiously.	Withdraw and start paroxetine at 10mg daily.	Withdraw then start sertraline at 25mg daily.	** **Either** cross taper cautiously **or** reduce citalopram to minimum dose, stop, then introduce tricyclic**.**
Fluoxetine	Stop fluoxetine.* Wait 4-7 days. Start citalopram at 10mg daily and increase slowly.		**Either** cross taper cautiously **or** stop fluoxetine, start mirtazapine 4-7 days later	Stop fluoxetine.* Wait 4-7 days then start paroxetine at 10mg daily.	Stop fluoxetine.* Wait 4-7 days, and then start sertraline at 25mg daily.	Stop fluoxetine.* Wait 4-7 days. Start tricyclic at very low dose and increase very slowly.
Mirtazapine	Cross taper cautiously.	Cross taper cautiously.		Cross taper cautiously.	Cross taper cautiously.	Withdraw gradually then stop mirtazapine, start tricyclic the following day.
Paroxetine	Withdraw and then start citalopram.	Withdraw and then start fluoxetine.	Cross taper cautiously.		Withdraw and start sertraline at 25mg daily.	** **Either** discontinue paroxetine gradually and stop, start TCA after gap of few days **or** taper paroxetine dose to 10mg/day & introduce TCA at low dose. After several days discontinue paroxetine & increase TCA dose to therapeutic levels.
Sertraline	Withdraw, then start citalopram	Withdraw, then start fluoxetine	Cross taper cautiously	Withdraw, then start paroxetine		Cross taper cautiously with very low dose of tricyclic.
Tricyclics	** **Either** halve dose and add citalopram, then slow withdrawal **or** reduce TCA dose to 25-50mg, start citalopram at usual starting dose, then discontinue TCA over next 5-7 days.	** **Either** halve dose and add fluoxetine then slow withdrawal **or** reduce TCA dose to 25-50mg, start fluoxetine at usual starting dose, then discontinue TCA over next 5-7 days.	Cross taper cautiously	**Either** halve dose and add paroxetine then slow withdrawal **or** reduce TCA dose to 25-50mg, start paroxetine at usual starting dose, then discontinue TCA over next 5-7 days	**Either** halve dose and add sertraline then slow withdrawal. **or** reduce TCA dose to 25-50mg, start sertraline at usual starting dose, then discontinue TCA over next 5-7 days	Cross taper cautiously.
Stopping anti-depressants	Reduce over 4 weeks	*At 20mg/ day just stop. At 40mg daily, reduce over two wks	Reduce over 4 weeks.	Reduce over 4 weeks or longer if necessary.	Reduce over 4 weeks.	Reduce over 4 weeks.

*See stopping antidepressants - fluoxetine **According to clinical judgement

NB .Unless otherwise specified, starting doses are as indicated in Table 15.3. Should not co-administer clomipramine and SSRIs or venlafaxine.

Clomipramine should be withdrawn before starting the other drugs.

Interactions with fluoxetine may occur as long as 5 weeks after it is stopped because of its long half-life.

15.3 STANDARDS

1. Screening for depression and anxiety should be part of every patient assessment. [6] [Grade D]
2. All patients who are depressed should be questioned about suicidal thoughts and intent. [6] [Grade D]
3. Treatment with antidepressants should be discussed with, and offered to, every patient where it is appropriate. [6] [Grade D]
4. The aim of treatment and possible side effects should be explained to the patient and documented in the case notes. [6] [Grade D]
5. Patients started on antidepressants who are not considered to be at increased risk of suicide, should be reviewed after 2 weeks and then regularly thereafter e.g. every 2 – 4 weeks to monitor clinical response. [6] [Grade D]
6. If a patient is assessed to be at increased risk of suicide they should be seen after a week and subsequently frequently as appropriate until they are no longer considered to be at significant risk. If a patient is considered to be a risk to themselves or others it may be necessary to consider urgent referral to Mental Health Care Services. [6] [Grade D]

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16. GUIDELINES FOR THE MANAGEMENT OF DIABETES IN PALLIATIVE CARE

16.1 GENERAL PRINCIPLES

* Diabetes occurs more frequently in palliative care patients than the general population. [1]
* Patients with pancreatic cancer are more susceptible to developing diabetes. [1]
* Management of diabetes in palliative care patients should be adjusted according to individual requirements and may alter depending on the stage of the disease. Complications may usually be managed in a palliative care setting but if severe, admission to an acute unit may be required e.g. for hyperglycaemia associated with ketoacidosis. [1]
* Good diabetic control will help to avoid symptoms of hyperglycaemia or hypoglycaemia and so maintain quality of life. However, strict diabetic control may be less important in palliative care because of a reduced emphasis on avoiding late diabetic complications. [2]
* Diabetic control should be monitored using capillary blood glucose and venous blood glucose. Urinalysis should not be used for monitoring diabetic control. [2]
* Cachexia / anorexia syndrome is common in some malignancies. Affected patients may have a reduced need for hypoglycaemic agents. [2]
* Many of the drugs used in palliative care are diabetogenic and therefore may precipitate diabetes or lead to a reduction in diabetic control e.g. corticosteroids and diuretics. [2]
* Hyperglycaemia may cause symptoms such as:
  - Polyuria
  - Polydipsia
  - Thrush
  - Fatigue
  - Altered conscious level/confusion. [3]

16.2 GUIDELINES

16.2.1 Diet Controlled Diabetes and Type 2 Diabetes Mellitus

* A dietary advice leaflet should be provided but relaxation of dietary restrictions may be appropriate and should be judged on an individual basis. [2] [Level 3]
* Aim for a pre-meal capillary blood glucose of 5-15mmol/l. If a patient has symptoms due to hyperglycaemia at this level then tighter diabetic control may be necessary. [4] [Level 4]
* For patients with recurrent high blood glucose levels (>15mmol), consider increasing current medication/adding insulin. The level of increase should be guided by the body mass index of the patient. [5] [Level 4]
* In non overweight patients, sulphonylureas are recommended as the first line oral hypoglycaemic agent. The oral hypoglycaemic agent of choice is Gliclazide. The initial dose is

40mg-80mg daily with a maximum of 320mg daily. The renal function should be monitored. If this is deteriorating then the dose of gliclazide should be reduced or a change to insulin considered. [4] [Level 2++]

* Early advice from the diabetologists and the Specialist Palliative Care Team should be sought if the patient is symptomatic from hyper/hypoglycaemia or there is evidence of diabetic complications. [2] [Level 4]

* The use of metformin should be avoided as there is an increased risk of lactic acidosis and hypoglycaemic episodes with deteriorating renal function. Unless the patient is well controlled on metformin, he / she should be converted to gliclazide or insulin. [4] [Level 2++]

* There should be a regular review of oral hypoglycaemic agents prescribed for an individual patient. This is particularly important if there is weight loss or a change in dose of any of the diabetogenic drugs such as corticosteroids or diuretics. [2] [Level 4]

* If there is a need to change to insulin, a once daily long acting insulin such as glargine should be used. Long acting insulins result in more stable glycaemic control and have a slightly lower risk of hypoglycaemia than conventional intermediate acting insulins such as Human Insulatard or Humulin I. They may therefore be more appropriate in palliative care patients, especially those with low calorie intake. [6] [Level 2++]

* If there is uncertainty about the choice of insulin or the dose, the diabetic team should be consulted. [1] [Level 4]

* Avoid stat doses of short acting insulin such as Actrapid or Humulin S for episodes of hyperglycaemia. The duration of action of Actrapid is eight hours and its use may precipitate episodes of hypoglycaemia later in the day. There is also the disadvantage of subjecting patients to multiple injections. Instead consider increasing the dose of insulin. [7] [Level 2-]

* Sliding scales of insulin should **not** be used in the management of hyperglycaemia. Instead, the doses of the long-acting insulin should be adjusted [1] [Level 4]

16.2.2 Type 1 Diabetes

* Consider converting to a long acting insulin if the patient is on a different insulin type. [6] [Level 2++]

* The dose of insulin should be reviewed as the patient deteriorates. Consider halving the insulin dose in patients with weeks to live, as their oral intake declines. [6] [Level 3]

16.2.3 Hypoglycaemia

* Causes of hypoglycaemia include: reduced dietary intake, tumour effect, drugs, liver failure, hypoadrenalism and hypopituitarism. Clinical features include agitation, confusion, coma and seizures. Emergency treatment includes administration of sugary drinks/foods; sublingual glucogel®, intravenous 10% dextrose and intramuscular glucagon. [4, 5] [Level 2++]

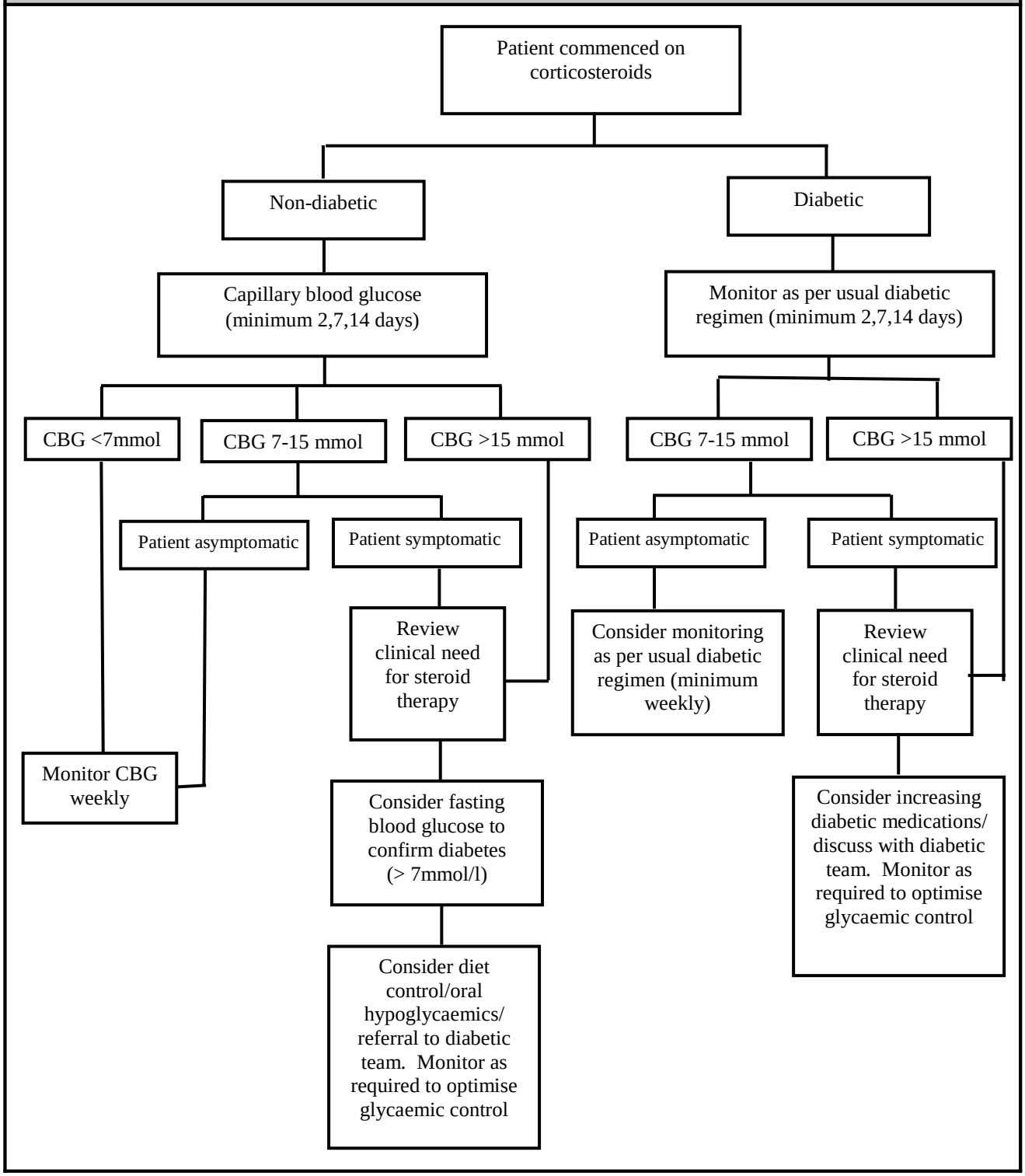
16.2.4 Corticosteroids and Diabetes

* Hyperglycaemia is a recognised side effect of corticosteroid therapy in both diabetic and non-diabetic patients. [1, 2, 7, 8] It is therefore important to monitor glucose levels in all patients receiving corticosteroid therapy. [Level 4]

* Patients who develop diabetes whilst taking corticosteroids should be managed on the lowest effective corticosteroid dose.[11,12] [Level 4]

* Figure 16.1 gives guidelines for the monitoring and management of blood glucose in patients on corticosteroids (*see Guidelines on Use of Corticosteroids in Palliative Care*).

Figure 16.1 Guidelines for monitoring and management of blood glucose in patients on corticosteroids [11] [Level 4]



16.2.5 Diabetic Patients in the Last Days of Life

* It is important that when a diabetic patient is placed on the Liverpool Care Pathway for the Dying Patient (LCP), there is a differentiation made between whether they have Type 1 or Type 2 diabetes. [2, 9, 10] [Level 4]

Type 2 Diabetes and the Last Days of Life

* Hyperglycaemia is unlikely to occur in the dying phase in patients with Type 2 diabetes. [2, 9, 10] [Level 4]
* It is important to have discussions with the patient and/or family about stopping medication and capillary blood glucose monitoring before starting the LCP. [2, 9, 10] [Level 4]
* If the patient is dying and unable to take fluids /medication, stop oral hypoglycaemics and/or insulin in Type 2 diabetes. [2, 9, 10] [Level 4]

Type 1 Diabetes and the Last Days of Life

* If a patient with Type I diabetes is in the dying phase, consider maintaining the patient on insulin at a reduced dose to limit the risk of symptomatic ketoacidosis. [2, 9, 10] [Level 4].
* It may be necessary to check capillary blood glucose to exclude hyper/hypoglycaemia if the patient is symptomatic e.g. agitation, confusion, nausea, thirst. [2, 9, 10] [Level 4]

16.3 STANDARDS

1. Gliclazide is the oral hypoglycaemic of choice. [4] [Grade B]
2. Long acting insulins such as glargine are the insulins of choice. [6] [Grade B]
3. Diabetic control should be monitored using capillary blood glucose and venous blood glucose. Urinalysis should not be used for routine monitoring. [4] [Grade B]
4. Sliding scales of insulin and the use of Actrapid should be avoided in the management of episodes of hyperglycaemia. [1] [Grade D]

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17. GUIDELINES FOR THE USE OF DRUGS IN THE LAST HOURS AND DAYS OF LIFE

THIS GUIDELINE HAS BEEN UPDATED

PLEASE SEE A - Z SECTION FOR UPDATED GUIDELINES

17.1 GENERAL PRINCIPLES

* Symptoms commonly experienced by patients in the last hours and days of life are: [1]
  - Pain.
  - Restlessness / agitation.
  - Excessive respiratory tract secretions.
  - Nausea and vomiting.
  - Breathlessness.
* When managing symptoms, it is important to exclude reversible causes. [2]
* It is important that drugs to control the above symptoms are prescribed in anticipation of the symptoms occurring. [2, 3, 4]
* In the last hours / days of life, all medication should be reviewed and non-essential drugs should be discontinued. [3, 5]
* "As required" doses should be prescribed with a clearly stated maximum dose and frequency where applicable. [6]
* Established medication for currently controlled symptoms should be converted to the appropriate parenteral equivalent as required. [5]
* The subcutaneous route is recommended for parenteral use in the last hours / days of life. A subcutaneous access port, for example butterfly, should be sited to avoid repeated injections.[6]
* If two "as required" doses are needed over 24 hours, a continuous subcutaneous infusion (CSCI) should be commenced, if not already in place. If a syringe pump is not available, it may be necessary to prescribe regular subcutaneous injections. [3]
* The effectiveness of any intervention / medication given should be monitored and recorded in order to ensure symptom control is achieved. [3]
* The Liverpool Care Pathway for the Dying Patient (LCP) contains recommendations for symptom control in the last days / hours of life.[3] Detailed guidance on the management of individual symptoms may also be found in the following chapters of this book i.e. N*ausea and Vomiting, Intractable Breathlessness, Agitation and Delirium.*

17.2 GUIDELINES

17.2.1 Pain

* The distinction between breakthrough pain and poorly controlled background pain is important because a different approach to the management of the pain is required.
* Breakthrough pain (also called episodic pain), is a term used to describe a transient exacerbation of pain that occurs either spontaneously or in relation to a trigger. This may be

either predictable (e.g. movement) or unpredictable (e.g. cough) despite relatively stable and adequately controlled background pain. There are two causes of breakthrough pain:

- incident pain – predictable pain caused by voluntary events (e.g. walking, wound dressing) or involuntary events (e.g. cough)
- spontaneous pain – unexpected pain with no apparent cause.[7] [Level 4]

* Further advice on the distinction between the types of pain and the management of breakthrough pain may be sought from the specialist palliative care team / service.

* Morphine is the parenteral opioid of choice in the last hours / days of life, unless the patient is already established on an alternative opioid for a specific reason.[8] [Level 4] If a patient is opioid naïve, 2.5mg – 5mg subcutaneous morphine prescribed 2-4 hourly is an appropriate starting dose. Diamorphine is also a first line option depending on availability. [3, 6] [Level 4]

* A CSCI should be prescribed according to the need for "as required" doses of opioid. (if not already in place) [3, 6] [Level 4]

* Patients already established on regular oral opioids should be converted to an appropriate parenteral route. This will usually be via a CSCI. [9] [Level 4] Please see "*Guidelines on Opioid Substitution*" for further information.

* Morphine should be used cautiously in patients with renal failure. [6, 11] [Level 4]

* For patients with renal impairment please see *Guidelines on Analgesic Prescribing in Renal Failure* and the LCP Drug Prescribing Guidelines in Advanced Chronic Kidney Disease. [11] Alternatively contact the specialist palliative care team / service for further advice.

17.2.2 Naloxone hydrochloride

* Naloxone hydrochloride, an opioid antagonist, may be required for administration in the event of opioid induced respiratory depression. The half life is 1-1.5 hours and the effect lasts for 45-60 minutes after intravenous administration. . [6, 10] [Level 4].

Bolus injection

Draw up 1ml (400micrograms) naloxone hydrochloride into a 10 ml syringe and dilute with 7ml sodium chloride 0.9%. This results in a concentration of 50microgram/ml. Administer 2ml (100micrograms) by bolus intravenous injection. If no intravenous access, give via the intramuscular route. The dose should be titrated to reverse respiratory depression without reversing analgesia. The usual dose is 100-200micrograms (1.5-3 micrograms / kg).

If there is no response after 2 minutes, repeat to a maximum of 400micrograms. If giving via the intramuscular route, use an alternative injection site. . [6, 10] [Level 4].

Infusion

Alternatively an intravenous infusion can be used. Dilute 2mg (i.e. 5ml of 400 micrograms / ml naloxone hydrochloride) to 500 ml with sodium chloride 0.9% or 500ml dextrose 5%. This provides a concentration of 4micrograms / ml. Administer via a pump. The rate of administration should be titrated in accordance with the patient's response to both the naloxone infusion and to any previous bolus doses administered. The dose should **not** be titrated against the level of consciousness but against respiratory rate. The usual rate is 25-100ml / hour (100-400micrograms / hour). The maximum infusion rate is 220ml / hour (800 micrograms / hour). . [6, 10] [Level 4].

For further information on the use of naloxone in opioid overdose, consult the SPC and the relevant guidelines in the section on "Emergency Treatment of Poisoning" in the current BNF. Use of naloxone in palliative care patients should only be undertaken by specialists. Individual

units should have their own policies for the use of naloxone injections and naloxone infusions. [6, 10] [Level 4]

17.2.3 Transdermal Fentanyl

* If a patient is already stabilised on a fentanyl patch this should be continued in the last hours / days of life with no further titrations in dose. [12] [Level 4]

* For patients on a fentanyl patch, appropriate "as required" doses of immediate release opioid should be prescribed subcutaneously.[15] [Level 4] (*see Guidelines on the Use of Fentanyl in the Dying Phase*)

* If two "as required" doses of opioid are needed in a 24-hour period a continuous subcutaneous infusion of opioid should be commenced alongside the Fentanyl patch. The starting dose of the opioid in the continuous subcutaneous infusion (CSCI) should be equivalent to two breakthrough doses. The patch should continue to be changed as usual i.e. every 72 hours. [12] [Level 4]

* Contact the specialist palliative care team / service for further advice on the use of transdermal fentanyl in patients who have complex or poorly controlled pain in the last days / days of life. There is also further guidance in the appropriate chapter in this book i.e. *Guidelines on Fentanyl in the Dying Phase*.

17.2.4 Agitation

* Please see chapters on Guidelines on the Management of agitation / delirium for further information on the management of these symptoms.

* Possible reversible causes of the agitation should be sought and managed appropriately. Examples include urinary retention, opioids, nicotine withdrawal, constipation and noise. Midazolam 2.5mg as required should be prescribed and administered subcutaneously if a patient is agitated. [2] [Level 4]

* If a reversible cause for the agitation is found, the patient should continue to be monitored for any further agitation and additional "as required" doses of midazolam administered as needed. It may not be necessary to commence a CSCI of midazolam at this stage. [3] [Level 4]

* If a CSCI is required it should be commenced at a dose of midazolam 10mg-30mg over 24 hours, or the dose should be calculated according to the number of "as required" doses given in the last 24 hours. [6, 9] [Level 4]

* If the patient is still agitated at a dose of 30mg of midazolam over 24 hours via a CSCI, specialist palliative care advice should be sought. [15] [Level 4]

* Patients who are paranoid and / or hallucinating may require haloperidol. It is advisable to start with a low dose initially e.g. 2.5mg 12 hourly as required subcutaneously.[13] [Level 3]

* If two or more doses of haloperidol are required in a 24-hour period, commence a subcutaneous infusion of haloperidol 5mg over 24 hours. [9, 13] [Level 4]

* The maximum dose of haloperidol that should be administered subcutaneously over 24 hours is 10 mg. Higher doses of haloperidol risk causing extra-pyramidal side effects. [6] [Level 4]

* Agitated patients who are in renal failure should be prescribed a reduced dose of midazolam. A suitable starting dose would be 1.25mg midazolam "as required" subcutaneously. If this is effective, and two or more doses of midazolam are required in a 24-hour period, commence a subcutaneous infusion of midazolam 5mg over 24 hours. [11] [Level 4]

* Agitated patients who do not respond fully to midazolam may benefit from the addition of levomepromazine. [6] [Level 4]

* In severe cases, phenobarbital may be used for the management of agitation in the last days / hours of life but should only be administered under the guidance of specialist palliative care. [14] [Level 3]

17.2.5 Excessive respiratory tract secretions

* Inability to clear secretions from the oropharynx and trachea often results in noisy respiration as the secretions oscillate up and down with expiration and inspiration. [2] [Level 4]
* Non-pharmacological measures are an important part of the management of respiratory tract secretions and may simply include a change of position. [2] [Level 4]
* It is important to talk to relatives giving explanation and reassurance, as this symptom may cause considerable distress to the family. [15] [Level 4]
* Early use of anti-cholinergic agents may be helpful in patients with cancers known to be associated with an increased incidence of respiratory tract secretions. Examples include primary malignancy of the lung or brain. [16] [Level 4]
* An "as required" dose of an anti-cholinergic drug should be given as soon as respiratory tract secretions develop. They do not relieve symptoms secondary to secretions that are already in place. Regular administration or a CSCI, should be started as soon as possible. [2] [Level 4]
* Hyoscine hydrobromide, glycopyrronium and hyoscine butylbromide are all available for the management of excessive respiratory tract secretions.[16] [Level 4] Table 17.1 gives further details.

Table 17.1 Anticholinergics used in the management of respiratory tract secretions [16] [Level 4]

Drug	As Required Dose	CSCI Dose/24hours	Notes
Hyoscine Hydrobromide	400 micrograms	1200micrograms-2400micrograms	Drug crosses blood-brain barrier. Risk of sedation or agitation. Do not use in renal failure.
Glycopyrronium	200 micrograms	1200micrograms-2400micrograms	Risk of transient bradycardia, followed by tachycardia, with rescue doses of 400 micrograms. This is the preferred drug in renal failure. [20]
Hyoscine Butylbromide	20 mg	60mg-240 mg	Risk of bradycardia. Short duration of action. (60 minutes)

* Pulmonary oedema may be the cause of excessive respiratory tract secretions. Consider the use of parenteral furosemide under the guidance of specialist palliative care.[2] [Level 4]

17.2.6 Nausea and Vomiting

* All patients should be prescribed an anti-emetic to be administered as required in the event of nausea or vomiting developing in the last days / hours of life. [3] [Level 4]Patients who have previously been nauseated and who are established on anti-emetic medication should continue on an anti-emetic. This should be converted to an appropriate equivalent and be prescribed regularly and parenterally. The subcutaneous route is recommended. [3] [Level 4]
* For patients who become nauseous or are vomiting in the last hours / days of life, levomepromazine may be the most effective anti-emetic to prescribe. [17] [Level 3]

* Cyclizine may exacerbate symptoms of heart failure and should be avoided in patients with this condition. [18] [Level 3]

* Patients who are dying with advanced chronic kidney disease should be prescribed haloperidol 0.5mg – 1.5mg subcutaneously "as required" for nausea. If this is effective, and two or more doses of haloperidol are required in a 24-hour period, commence a CSCI of haloperidol 1.5mg to 3mg over 24 hours. [Level 4][11]

* Please see the chapter on *Guidelines on the Management of Nausea and Vomiting* for further information.

17.2.7 Breathlessness

* Benzodiazepines and strong opioids are the drugs of choice in the management of breathlessness in the last days / hours of life**.** [19] [Level 2+]

* Morphine is the first line parenteral strong opioid for patients with breathlessness. In opioid naïve patients the appropriate "as required" dose is 1.25mg–2.5mg subcutaneously prescribed 2-4 hourly. If morphine is effective, a CSCI should be commenced at a dose of 5mg-10mg over 24 hours. Diamorphine would be an alternative first line choice depending on availability.[12, 3, 6, 19, 20] [Level 4]

* Patients who are breathless and already established on a long-acting opioid may benefit from an "as required" dose of opioid that is lower than the usual one sixth of the total daily dose of opioid. [20] [Level 2+]

* Immediate release opioids may be more helpful than long-acting opioids in relieving breathlessness. [19, 20] [Level 3]

* Midazolam is the benzodiazepine of choice for breathlessness in the last days / hours of life. The "as required" dose of midazolam is 2.5mg subcutaneously. A CSCI may be required. Starting dose should be titrated according to need. [2, 3] [Level 4]

* It can be helpful to prescribe and record "as required" doses of opioids for pain and breathlessness separately for those patients who require "as required" doses for both symptoms. This can be useful when titrating the prescribed regular dose of opioids. [16] [Level 4]

* Please see *Guidelines on the Management of Intractable Breathless* for further information.

17.3 STANDARDS

1. In the last hours / days of life all medication should be reviewed and non-essential drugs should be discontinued. [3, 5] [Grade D]

2. All patients should be prescribed "as required" medications for the symptoms most commonly experienced in the last days / hours of life. [3] [Grade D]
   - Pain.
   - Restlessness/ agitation.
   - Excessive respiratory tract secretions.
   - Nausea and vomiting.
   - Breathlessness.

3. Medications should be administered by the subcutaneous route if required.[6, 9] [Grade D]

4. If two or more "as required" doses of the same medication are required in a 24 hour period a CSCI should be considered. If a syringe driver / pump is not available, medication should be prescribed and administered regularly by the subcutaneous route. [3] [Grade D]

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18. GUIDELINES FOR THE MANAGEMENT OF FATIGUE IN PALLIATIVE CARE

18.1 GENERAL PRINCIPLES

* Fatigue may be defined as: "a subjective, unpleasant symptom which incorporates total body feelings ranging from tiredness to exhaustion, creating an unrelenting overall condition which interferes with an individual's ability to function to their normal capacity." [1]
* Fatigue is believed to be the most common and most debilitating symptom experienced by cancer patients. Surveys reveal a prevalence of > 75%. This can increase to > 90% when including patients after treatment with radiotherapy or chemotherapy. [2]
* Despite the prevalence and impact of fatigue the problem has been neglected in clinical and research terms. Reasons for this may include failure of health care professional to offer interventions and patients' lack of awareness of effective treatments. [2]
* Fatigue affects physical, psychological and social well-being. [4, 5, 7]
* Although most of the research is for cancer- related fatigue, it is recognised that fatigue also has a major impact on the quality of life for patients with non-malignant disease. [3]
* Fatigue is a multi-dimensional syndrome and rarely an isolated symptom. It often has multiple contributing causes. [4, 5]
* The multidimensional nature of fatigue makes systematic evaluation essential. All palliative care patients should be screened for the presence of fatigue. Assessment should include a fatigue history, physical examination and appropriate investigations. [4, 6]
* A fatigue history should establish the following information; severity, temporal features (e.g. onset, course, duration and daily pattern), exacerbating and relieving factors, associated distress and impact on daily life. [4, 6]
* The evidence supporting specific management strategies is limited and further research is required. [7]

18.2 GUIDELINES

18.2.1 Assessment

* Assessment of fatigue should depend on self evaluation by the patient. This should only be replaced by estimations from professionals when patient self-assessment is not possible. [5, 7] [Level 4]
* There is no single preferred assessment tool, but it is suggested for clinical purposes, where time may be limited, that a numerical rating scale may be the most practical. [6, 9] [Level 4] This may take the form of a numerical 0-10 scale or a fatigue scoring system based on the Palliative Care Assessment tool (PACA). [9] [Level 4]

  0 = no fatigue.

  1 = fatigue present but not affecting daily life.

2 = fatigue present and having moderate effect of daily life.

3 = fatigue present and having overwhelming effect on daily life.

* Reassessment and evaluation of interventions should take place at regular intervals as clinically indicated. [5, 9] [Level 4]

18.2.2 Management

* The management of fatigue should be tailored to the individual patient using a multi-professional approach. [5] [Level 4]
* Management strategies will vary and may need to be adapted depending on the stage of the illness. It is important to identify when treatment of fatigue is not a priority in order to alleviate distress at the end of life. [7] [Level 4]
* Treatable causes of fatigue should be managed appropriately e.g. anaemia, infection, drug side effects, insomnia, depression. [4, 7] [Level 2++]
* When specific causes of fatigue cannot be identified and corrected, non-pharmacological and pharmacological management should still be instigated if clinically appriopriate.[5] [Level 4]
* Figure 18.1 outlines a management strategy in relation to fatigue in palliative care patients.

18.2.3 Non-pharmacological management

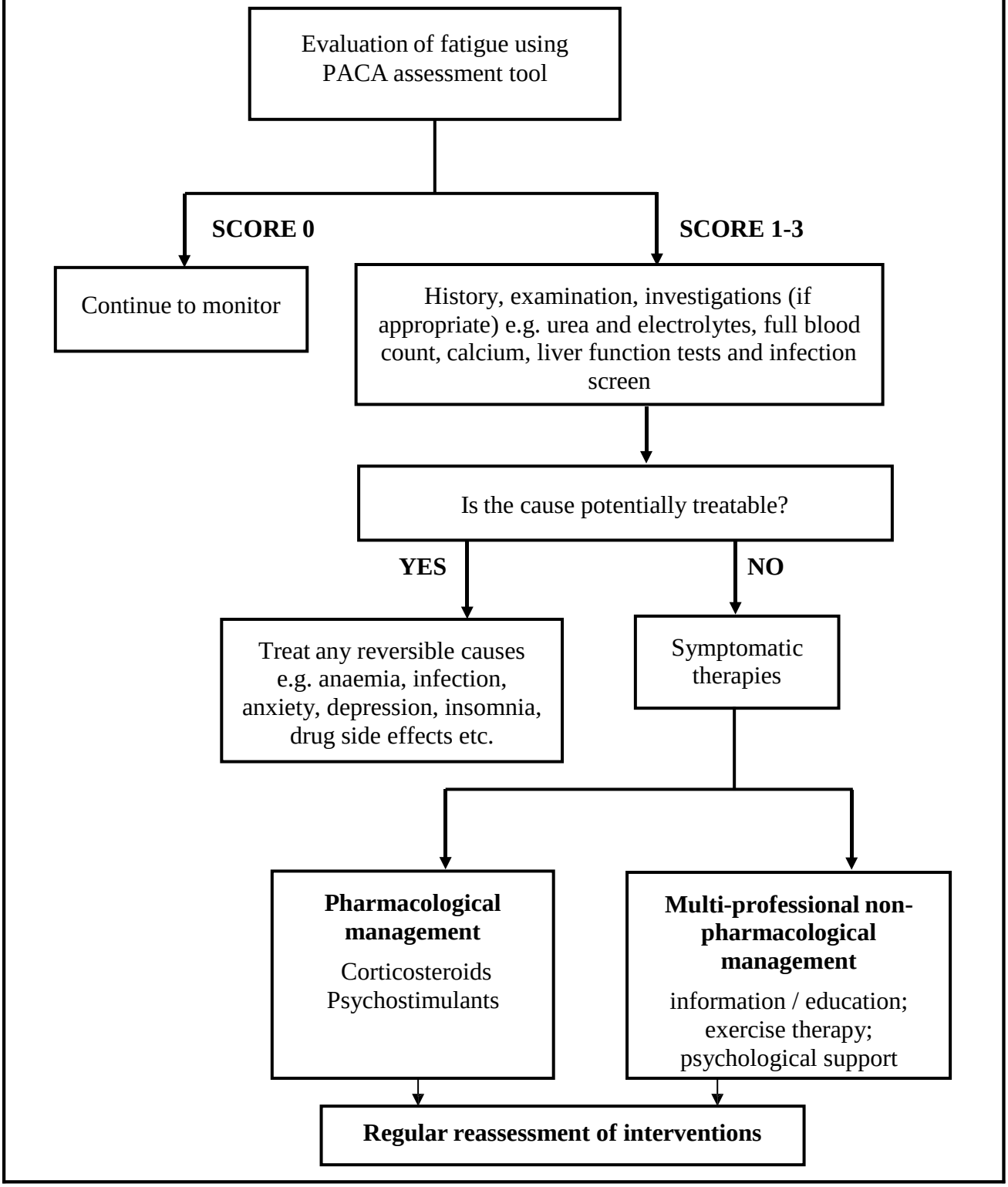
* There is a stronger evidence base for non-pharmacological management strategies in the management of fatigue compared to pharmacological interventions. [9, 10] [Level 4]
* Non-drug management may include: [5, 10, 11]
  - Patient information leaflets, advice on diet, sleep and exercise. [Level 2++]
  - Occupational therapy. [Level 4]
  - Physiotherapy. [Level 2++]
  - Psychological support. [Level 2++]
* Exercise programmes have been shown to be of benefit in the management of fatigue, both during and after cancer treatment. Goal setting can also provide a useful focus for patients. [5, 9, 10] [Level 1+] Further research is required to determine the optimal type, intensity and timing of an exercise intervention. [10] [Level 4]
* Psychosocial interventions specific to fatigue have been shown to reduce the level of fatigue. These may include: educating patients about fatigue, provision of literature, teaching of coping strategies and learned activity management. [5, 11] [Level 2++]

18.2.4 Pharmacological management

* Drug management of fatigue may include the use of corticosteroids, psycho-stimulants or anti-depressants. [4, 7, 12] [Level 2++] *(*see *Guidelines on Psychostimulants, Depression and Corticosteroids*).
* The evidence for the effectiveness of corticosteroids in the management of fatigue is limited. Corticosteroids are often prescribed for co-existent symptoms such as pain and poor appetite. If considering a trial of corticosteroids, dexamethasone is the recommended corticosteroid of choice. The suggested starting dose is 4 mg daily, administered before 2pm. Patients should be reviewed after 5-7 days. If there is no evidence of improvement the corticosteroids should be discontinued. If there is evidence of improvement the patient should be maintained on the lowest effective corticosteroid dose. [7, 9] [Level 4] (*See Guidelines on Corticosteroids)*

* For psychostimulants, the strongest supporting evidence is for methylphenidate hydrochloride. It has been shown to improve cancer related fatigue in some small studies but more research is needed to confirm its role. [12] [Level 4] (*See Guidelines on Psychostimulants).*

Figure 18.1 Management of fatigue in palliative care patients [5, 6, 9] [Level 4]



18.3 STANDARDS

1. All palliative care patients should be screened for the presence of fatigue and the result documented in the case notes.[3,4,5,7] [Grade D]
2. The severity and impact of fatigue on daily life should be assessed in every patient.[3,4,5,7] [Grade D]
3. Patients commenced on corticosteroids for fatigue should be reviewed after 5-7 days.[9] [Grade D]
4. Patient information leaflets regarding the aetiology and management strategies for fatigue should be readily available. [9,11] [Grade C]

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19. GUIDELINES FOR THE USE OF TRANSDERMAL FENTANYL IN DYING PATIENTS

THIS GUIDELINE HAS BEEN UPDATED
PLEASE SEE A-Z SECTION FOR UPDATED GUIDELINES

19.1 GENERAL PRINCIPLES

* These guidelines relate to the use of transdermal fentanyl in dying patients, who are no longer able to take oral breakthrough medication because they are semi-comatosed or comatosed.

19.2 GUIDELINES

* The fentanyl patch should **continue to be changed every three days** unless there are toxic opioid side effects. It should **not** be discontinued. [1] [Level 2+]

* If the patient is experiencing breakthrough pain and requires additional analgesia, a subcutaneous opioid should be given. Table 19.1 shows the appropriate dose of breakthrough diamorphine and morphine according to the strength of the fentanyl patch being used. The breakthrough dose of diamorphine is calculated by the following formula and the accepted conversion from subcutaneous morphine to subcutaneous diamorphine is 3:2.

$$\text{4 hourly dose of diamorphine subcutaneously (mg)} = \frac{\text{Fentanyl patch strength (micrograms / hour)}}{5}$$

(see Guidelines on Opioid Substitution)

Table 19.1 Breakthrough doses of subcutaneous diamorphine and morphine for patients on transdermal fentanyl [4] [Level 4]

Fentanyl patch strength (micrograms / hour)	4 hourly dose of diamorphine subcutaneously (mg)	4 hourly dose of morphine subcutaneously (mg)
25	5	7.5
50	10	15
75	15	25
100	20	30
150	30	45
200	40	60

Note: 25micrograms fentanyl = 60 mg **oral** morphine

* If the patient requires two or more doses of an opioid for breakthrough pain over a 24 hour period, consider commencing a continuous subcutaneous infusion of diamorphine/morphine in a syringe driver over 24 hours. [2] [Level 2+]

* To calculate the dose of diamorphine/morphine in the syringe driver, the breakthrough doses of diamorphine/morphine should be totalled over the previous 24 hours.

  For example, if a patient has received 3 doses of 10mg diamorphine/morphine in the previous 24 hours, the dose of diamorphine/morphine in the syringe driver should be 30mg.

The diamorphine/morphine syringe driver should be used <u>in addition</u> to the fentanyl patch, which continues to be changed every 72 hours. [2] [Level 2+]

* If a decision is made to remove the fentanyl patch it is important to remember that the fentanyl plasma levels will only fall gradually because of continued absorption from the skin.

  Plasma fentanyl concentrations reduce by approximately 50% in 17 hours (range 12-24 hours). [3] If using a syringe driver, then give subcutaneous stat injections of diamorphine/morphine for the initial 24 hours while the fentanyl plasma level is falling. The syringe driver should then be started after 24 hours. [4] [Level 2+]

19.3 STANDARDS

1. Terminally ill patients who have been treated with fentanyl patches for pain control should have the patch continued in the dying phase. [2] [Grade C]
2. Patients in the dying phase with a fentanyl patch in situ should have an appropriate dose of subcutaneous diamorphine/morphine prescribed for breakthrough pain. [2, 4] [Grade D]
3. A patient who has a fentanyl patch in situ in the dying phase, and who requires two or more doses of diamorphine/morphine for breakthrough pain over a 24 hour period, should be commenced on an appropriate dose of diamorphine/morphine via a continuous subcutaneous infusion over 24 hours. [2, 4] [Grade D]

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20. GUIDELINES FOR THE USE OF GENOGRAMS IN PALLIATIVE CARE

20.1 GENERAL PRINCIPLES

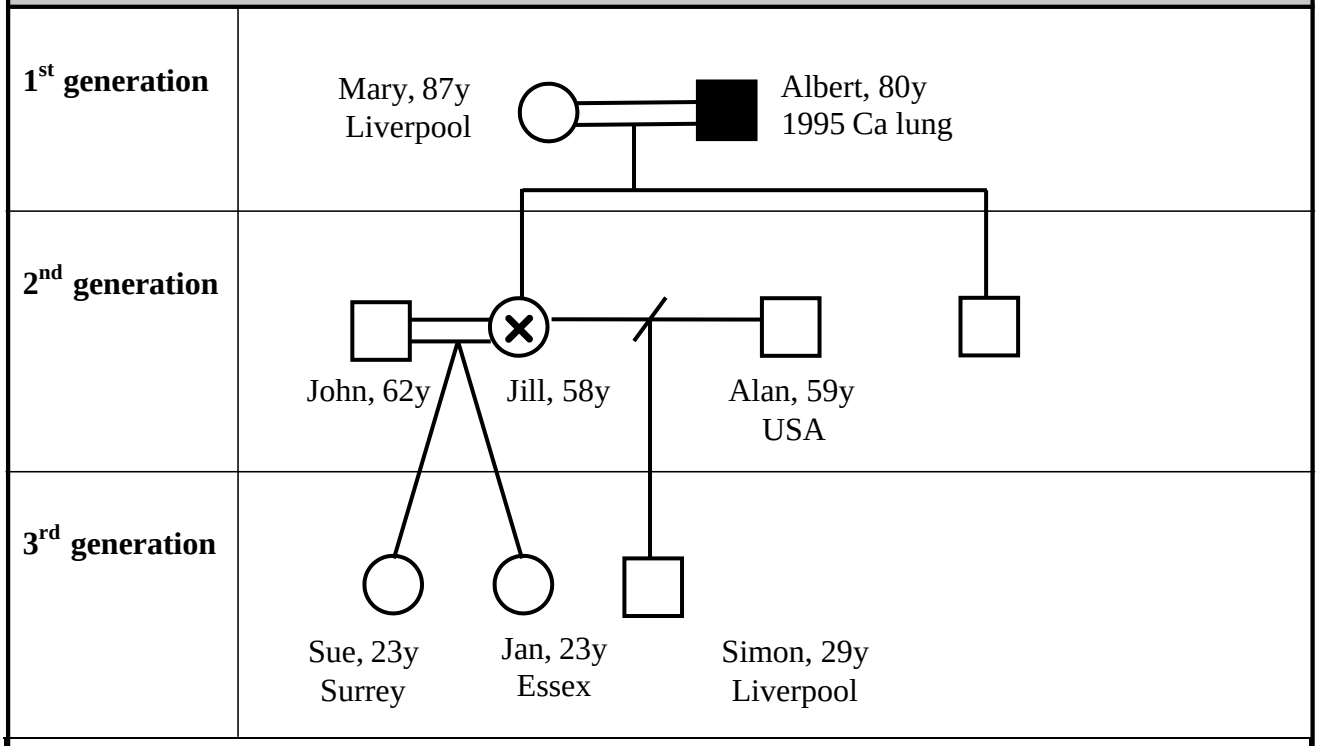
* Specialist palliative care encompasses the social, emotional and spiritual care of the patient and their family, and the physical needs of the patient. Recognition and understanding of the patient's social circumstances may be as influential in the relief of distress suffered by patients and their families/carers as the identification and palliation of physical symptoms. [1]
* The genogram has been widely promoted as a useful tool for gathering, recording and displaying family information in order to practice family centered care. [2, 3, 4]
* Genograms have the scope to record three broad categories of information: [5]
  - Basic family structure (biological and legal relationships across generations).
  - Information about individual family members (demographic data, personality characteristics, emotional, behavioural and medical problems).
  - Family relationships (patterns of closeness, conflict and estrangements amongst family members).
* The benefits of compiling genograms with patients include:
  - Encouraging a holistic comprehensive assessment which encompasses physical and psychosocial aspects. [2, 6]
  - Facilitation of communication with patients, families and other health care professionals.[7]
  - Providing reminiscence opportunities for the patient. [2]
  - Providing a record that consideration has been given to the family unit and its influence on the patient and their needs. This can then be audited in the future. [7]
  - The identification of possible hereditary disease. [5, 8]

20.2 GUIDELINES

* All patients should have the opportunity to compile a genogram with a specialist palliative care worker during their initial assessment. [7] [Level 4]
* The genogram should be recorded in documentation available to all disciplines i.e. the multidisciplinary notes. [6] [Level 4]
* The genogram is a living document that may be updated by any member of the multidisciplinary team on discovery of new information. Any changes or additional information to the genogram should be signed and dated. [6] [Level 4]
* All genograms should include at least three generations and should adhere to the notation / key provided (see Figures 20.1 and 20.2). [Level 4] Notation outside the palliative care setting may differ. [6] [Level 4]

* Negative assessments (such as the absence of children /siblings) should be recorded (see Figure 20.1). [5, 7] [Level 4]

Figure 20.1 Example of a genogram [6] [Level 4]



Please tick if patient has **NO CHILDREN** □

NO SIBLINGS □

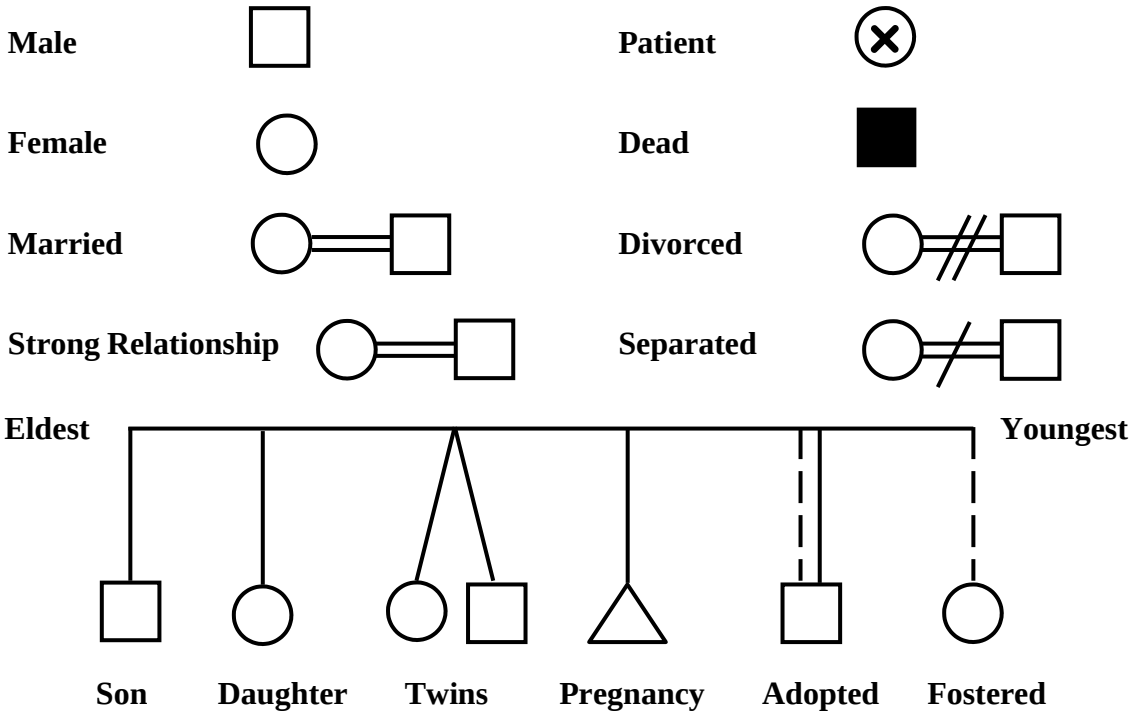
Completed by _____ **Date** _____

Updated by _____ **Date** _____

Updated by _____ **Date** _____

* The patient should be aware that relevant information given during completion of genograms may be shared with other specialist palliative care workers. [6] [Level 4]
* It would be best practice to include a basic genogram in referrals between specialist palliative care settings if the patient gives permission for this. [6] [Level 4]
* Completion of genograms may identify the possibility of a hereditary disease. If this occurs it should be raised with the physician in charge who may need to discuss referral to the Merseyside and Cheshire Clinical Genetics Service with the patient and family. [9] [Level 4]
* Figures 20.3 and 20.4 give further information on the local Clinical Genetics Service and the referral criteria. [Level 4]

Figure 20.2 Annotations commonly used in genograms [10] [Level 4]



Referral Guidelines for Patients Concerned due to Family History

* Patients should initially be referred to the Family History Surveillance Clinic for either breast or bowel cancer if this is available locally.

Referral process

* Following referral the patient has telephone contact or a face to face appointment with a genetic counsellor to collect further information. Further clarification and confirmation of the relevant diagnosis will then occur. This may take several weeks.
* The patient's GP, the referring doctor and the patient all receive information on risk grouping and are advised about screening where appropriate (see Table 20.2).
* Contact details for further information are given in Table 20.3.

Figure 20.3 Cancer Genetics Service - Merseyside and Cheshire Clinical Genetics Service [11]

The functions of the cancer genetics service are:

- To provide risk assessment, information, and psychological, emotional, physical support to individuals with an increased risk of developing cancer due to their family history.
- To use a multidisciplinary team approach to assess the needs of individuals and the appropriate level of intervention and care required.
- To provide support and counselling to the high risk families already identified.
- To provide information, training and support for healthcare professionals who provide genetic information to families through either primary care or cancer clinics.

The genetics clinics provide the following services:

- Time to discuss issues at length.
- Making or confirming a diagnosis.
- Providing understandable information about the condition.
- Discussion of the risks of becoming affected with the condition in the future.
- Discussion of risks to future children.

And where appropriate:

- Follow up of other family members at high risk.
- Storage of DNA from affected individuals and organisation of molecular genetic testing.
- Discussion of the advantages and disadvantages of gene testing options.

Clinical genetics staff include:

- Genetic Counsellors: Nurses with experience in genetic counselling or scientists with a qualification in genetic counselling.
- Physicians: Geneticists are medical consultants who specialise in Clinical Genetics.

Referral categories:

- Only 5-10% of cancers of the breast, ovary and colon are due to an inherited predisposition. **The Family History Breast Surveillance Clinics** supported by the **Merseyside and Cheshire Cancer Genetics Service** assess the risk of cancer based on the reported family history and work with the relevant specialists to recommend further screening strategies where appropriate. The referral criteria suggest who may be at a significantly increased risk of inherited cancer and who may benefit from a referral to the Clinical Genetics Service. This service offers genetic risk assessment and recommendations for clinical surveillance if appropriate. Referrals can be discussed with a member of the genetics team (see Figure 20.4). Types of referral to the cancer genetics services are detailed in Table 20.1

Figure 20.4 Referral criteria for patients with a family history of cancer: Merseyside and Cheshire Clinical Genetics Service [11]

Breast cancer	Breast/ ovarian cancer	Colon cancer	Other cancer syndromes
• One first degree [a] relative diagnosed at ≤40 years old. • Two first degree relatives diagnosed at ≤50 years old. • Three first degree relatives at ≤60 years old (on the same side of the family). • A first degree relative with bilateral breast cancer. NB Breast cancer may also be inherited through the paternal side of the family.	• Minimum: one of each cancer in first degree relatives (if only one of each cancer). • A first degree relative who has both breast and ovarian cancer (breast cancer ≤50 years old). • One relative with ovarian cancer and two relatives with breast cancer at ≤60 years old, who are first degree relatives. • Two or more ovarian cancers; at least one first degree relative affected (on the same side of the family).	• One first degree relative diagnosed at ≤45 years old. • Two first degree relatives (on the same side of the family). • Both parents. • Three relatives, all on the same side of the family (at least one should be a first degree relative). • Familial Adenomatous Polyposis; Familial Juvenile Polyposis; Peutz-Jeghers Syndrome. • Hereditary Non Polyposis Colorectal Cancer (revised Amsterdam criteria [b])	• Patient from a family with a known single gene cancer syndrome: Von Hippel-Lindau disease; Multiple Endocrine Neoplasia (MEN), retinoblastoma. • Related cancers i.e. rare cancer syndromes where a variety of different cancers occur within a family e.g. Li Fraumeni syndrome and Cowden syndrome. If there is a high index of clinical suspicion, the possibility of referral should be discussed on an individual basis.

a) First degree relative = parent or sibling. A second degree relative = uncle, aunt, nephew or grandparent.

b) Revised Amsterdam criteria = 2 relatives with colon cancer (one ≤50 years old) plus one relative with either cancer of the uterus, colon, ureter, stomach or ovary ≤50 years old.

Table 20.1 Types of referral to the cancer genetics service [11]

Breast cancer Ovarian cancer Familial bowel cancer Hereditary non-polyposis colon cancer (HNPCC) Familial adenomatous polyposis (FAP)	Rarer more specific cancer predisposition syndromes i.e. − Von Hippel Lindau disease − Gorlins syndrome − Neurofibromatosis Type 1 and Type II − Li Fraumeni syndrome − Ataxia Telangiectasia and chromosome breakage disorders

Table 20.2 Management of different risk categories [11]		
Low risk	**Moderate risk**	**High risk**
This group of patients are reassured that on the information given their risk is not raised to a significant degree above that of the general population. Extra surveillance is not suggested. It is clearly stated that individuals in this group still have the same risk (or perhaps slightly higher) of cancer as any other individual of the same age in the general population. They should continue the standard health awareness and screening as the general population.	Ongoing management between primary care and appropriate specialist (for example the local Family History Screening Clinic) is recommended. An appropriate referral route is suggested /or discuss options for the GP and patient to consider.	In addition to suggesting the involvement of specialist surveillance, this group will be offered a genetic clinic appointment, and if requested genetic testing may be pursued in some families.

Table 20.3 Contact information [11]	
Family History Breast Screening Clinics	**Various locations including:** Countess of Chester Hospital NHS Foundation Trust North Cheshire Hospitals NHS Trust Royal Liverpool and Broadgreen University Hospitals NHS Trust Southport and Ormskirk Hospital NHS Trust St Helens and Knowsley Hospitals NHS Trust Aintree University Hospitals NHS Foundation Trust
Merseyside and Cheshire Clinical Genetics Service Dr L Greenhalgh Dr I Ellis Dr A Fryer Ms C Benjamin - Genetic Associate	Alder Hey Children's NHS Foundation Trust Eaton Road Liverpool L12 2AP
All Clinical Genetics Enquiries	0151 802 5000
Appointment enquiries	0151 802 5001/5002
Department Fax	Fax: 0151 252 5951 or 8025095/5096
Services Manager Mr Matt Wardle	0151 802 5010
Chester Clinical Genetics Service Mrs S Rowe - Genetic Associate	Mosten Lodge Countess of Chester Hospital NHS Foundation Trust Liverpool Road Chester Tel: 01244 364754 or 01244 364770 Fax: 01244 364770

20.3 STANDARDS

1. All patients referred to a specialist palliative care team (hospital, community or hospice) should have a completed genogram recorded in the multidisciplinary notes as part of the initial assessment. [6, 7] [Grade D]
2. All genograms should be signed and dated at the initial assessment. [6] [Grade D]
3. Genograms should be reviewed and updated as necessary, at a minimum of 3 months following the previous assessment, and signed and dated each time. [6] [Grade D]
4. Genograms should be compiled according to the annotation given in Figure 20.2. [6] [Grade D]
5. The minimum content of the genogram should include 3 generations (children, parents, siblings, grandchildren or grandparents) and should highlight significant relationships (spouse, partner). For these relationships the following should be recorded: [7] [Grade D]
   - Name, age, location, deaths.
   - Age at death, years since death, cause of death (if appropriate).

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21. GUIDELINES FOR THE USE OF HYDRATION IN DYING PATIENTS

21.1 GENERAL PRINCIPLES

* The provision of oral fluids forms part of basic patient care and should not be withdrawn or withheld. [1, 2, 3]
* Artificial hydration, such as intravenous or subcutaneous fluids, has been classified as medical treatment in common law, although this definition has not been universally accepted. [1, 2, 3]
* Blanket policies regarding the use of artificial hydration in dying patients are unhelpful. Decisions regarding hydration should be individualised to each patient. [4]
* There is a lack of good evidence regarding the benefits, burdens and risks of artificial hydration in the dying phase. [5-12, 13, 16]
* It is unclear whether dying patients develop symptoms of dehydration or whether artificial hydration improves these symptoms. [5-11]
* The Mental Capacity Act 2005 highlights important factors that should be considered when making decisions about hydration at the end of life. [14, 15]

21.2 GUIDELINES

* Decisions surrounding the use of artificial hydration should be discussed with the multi-professional team, patients and relatives in accordance with the Mental Capacity Act. [1, 2, 4, 11, 14] [Level 4]
* Decisions regarding the use of artificial hydration should take into consideration the potential harms and benefits to the patient. [1, 2, 4, 11] [Level 4]
* Hydration decisions should be individualised and include the participation of the family, patient and other disciplines. [13] [Level 4]
* A time-limited trial of hydration to assess if it improves symptoms may be appropriate in some patients. [4] [Level 4]

21.3 STANDARDS

1. Decisions surrounding the use of artificial hydration in dying patients should involve the multi-professional team and be clearly documented in the case notes. [1, 3, 4] [Grade D]
2. The use of artificial hydration in dying patients should be reviewed on a daily basis. [4] [Grade D]
3. If artificial hydration is continued in the dying phase, a rate of 1litre over 24 hours intravenously, subcutaneously or via a PEG / PEJ is the recommended regimen. [8] [Grade D]

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22. GUIDELINES FOR THE TREATMENT OF CANCER ASSOCIATED HYPERCALCAEMIA

22.1 GENERAL PRINCIPLES

* The normal range for the serum corrected calcium or albumin-adjusted calcium is 2.2-2.6mmol/l. [1]

* Most laboratories now give corrected calcium results. An uncorrected calcium level may be adjusted for the serum albumin using the following formula:

  Adjusted calcium (mmol/l) = Total calcium + 0.02(40-serum albumin). [1]

* Hypercalcaemia is the commonest life-threatening metabolic disorder associated with malignancy, occurring in approximately 10-20% of patients with cancer. It occurs primarily in those with more advanced disease and is generally indicative of a poor prognosis. [2-7] The incidence of cancer-associated hypercalcaemia is now falling because of earlier and prolonged use of bisphosphonates in cancer patients with metastatic bone disease. [8]

* Symptoms of hypercalcaemia include: fatigue, weakness, constipation, nausea, vomiting, polyuria, polydipsia, cardiac arrhythmias, delirium, drowsiness and coma. [2-4, 7, 9] The severity of symptoms correlates more closely with the rate of increase in calcium rather than the actual level. Other influencing factors include age and the overall medical condition of the patient. [7, 8]

* Treatment of hypercalcaemia includes rehydration and the use of bisphosphonates. [2-5, 7-9]

* Hypercalcaemic patients are dehydrated and sodium depleted. Rehydration with parenteral sodium chloride 0.9% should always be first line management. This may improve some of the symptoms and may reduce calcium levels by 0.4-0.6mmol/l. [5] It has three main effects:

  - Replace lost sodium.
  - Increase the glomerular filtration rate and circulating volume.
  - Promote urinary calcium excretion. [2-5, 10, 11]

* Sodium chloride 0.9% should be used in preference to dextrose as the reabsorption of calcium in the proximal convoluted tubule is linked with that of sodium, hence saline produces a more effective calcium diuresis. [3]

* Bisphosphonates are analogues of pyrophosphate and may be highly effective in the treatment of hypercalcaemia of malignancy.

* Until recently disodium pamidronate was standard treatment for cancer-associated hypercalcaemia. Zoledronic acid is a new aminobisphosphonate which is also licensed for the treatment of cancer-associated hypercalcaemia. Studies have shown it to be superior to pamidronate in terms of a more rapid onset and a longer duration of action. [5] Ibandronic acid is a third generation bisphosphonate which appears to have a better renal profile. Clodronate is less effective than pamidronate [12] but can be given subcutaneously [13] so may be useful for patients in whom venous access is a problem. Local policies may govern which bisphosphonate is available for clinical use.The side effects of bisphosphonates include a transient rise in body temperature, a flu-like syndrome and asymptomatic hypocalcaemia. [9, 11, 14]

* Patients who have undergone thyroid or parathyroid surgery may be particularly susceptible to developing hypocalcaemia due to relative hypoparathyroidism. [14]

* If symptomatic or severe hypocalcaemia occurs post bisphosphonate therapy, then short term supplemental therapy may be required. Although uncommon, renal toxicity has also been associated with bisphosphonate treatment and monitoring of renal function is recommended. [8, 10, 11, 15, 16]

* Osteonecrosis of the jaw has been reported in patients receiving bisphosphonates. [15] (see *Guidelines on the Use of Bisphosphonates in Bone Pain)*

22.2 GUIDELINES

* Clinical assessment of the patient is crucial in determining whether treatment of hypercalcaemia is appropriate. Generally a decision to treat should be motivated by the patient`s symptomatology rather than absolute calcium level. The most important goal of treatment is to improve clinical symptoms. [3, 4, 5, 17] [Level 4]

22.2.1 Rehydration and discontinuation of other drugs

* The patient should be rehydrated with 1-3 litres of parenteral sodium chloride 0.9% before the administration of bisphosphonates. The volume and rate of fluid replacement should be adjusted in each patient according to their age, the severity of hypercalcaemia, the degree of dehydration and the ability of the cardiovascular system to tolerate rehydration. [2, 3, 5] [Level 4]

* Drugs which reduce renal blood flow or renal calcium excretion should be discontinued/avoided where appropriate e.g. non-steroidal anti-inflammatory agents and thiazide diuretics. [3, 7] If a diuretic is needed, a loop diuretic such as furosemide, which inhibits the reabsorption of calcium and sodium in the ascending limb of the loop of Henle, is the drug of choice. [2, 3, 5] [Level 4]

22.2.2 Bisphosphonates

* Please see Table 22.1 and Table 22.2 for details of the bisphosphonates available. Local policies will govern which bisphosphonate is used.

22.2.3 Monitoring of hypercalcaemia

* Corrected calcium levels should be rechecked at 5-7 days after the bisphosphonate infusion. Checking calcium levels prior to this is not appropriate, as the bisphosphonate will not have achieved its maximal effect. [10, 16]

* Calcium levels should be rechecked every 3-4 weeks or when symptoms of hypercalcaemia occur. [1] [Level 4]

22.2.4 Management of treatment resistant hypercalcaemia

* If at 5-7 days post bisphosphonate infusion, the corrected calcium level is greater than 3.0mmol/l or the patients' symptoms of hypercalcaemia persist, it may be appropriate to consider further infusions of bisphosphonates. At least 7 days should elapse before a further treatment is given, to allow maximal response to the initial dose. Options for treatment include: the same dose of bisphosphonate; an increased dose or changing to an alternative bisphosphonate. [10, 16] [Level 4]

22.2.5 Management of recurrent hypercalcaemia

* If the patient experiences subsequent episodes of symptomatic hypercalcaemia, a further infusion of bisphosphonate may be given. Depending on how close the recurrence is to the

original episode, it may be appropriate to give the same dose of bisphosphonate, an increased dose or change to an alternative bisphosphonate. [10, 11, 18] [Level 4]

Table 22.1 Dose of pamidronate in hypercalcaemia

Serum corrected calcium (mmol/l)	Dose of pamidronate sodium (mg)
< 3.0	30-60*
3.0-3.5	60
>3.5	90

* According to clinical judgement

22.3 STANDARDS

1. Patients with proven hypercalcaemia should receive treatment within 24 hours if treatment is appropriate. [2, 5] [Grade D]
2. All patients with cancer-associated hypercalcaemia should be rehydrated with parenteral sodium chloride 0.9% prior to treatment with bisphosphonates. [2, 3, 4, 10, 11] [Grade D]
3. Serum calcium should be checked at 5-7 days. [10] [Grade D]
4. Calcium levels should be rechecked every 3-4 weeks or when symptoms of hypercalcaemia occur. [1] [Grade D]

Table 22.2. Bisphosphonates available for clinical use				
Name of drug	Initial Dose	Route / Diluent / Rate	Contraindications/ Cautions	Notes
Disodium Pamidronate	Dependent on serum calcium see Table 21.1	Intravenous Dilute in 250-500ml of sodium chloride 0.9% Maximum rate:1mg/min. Concentration of solution should not be greater than 60mg/250ml. [14, 16] [Level 4]	In a patient with impaired renal function the infusion rate should not exceed 20mg/hour. Do not use if creatinine clearance is <30ml/min except if there is life threatening tumour induced hypercalcaemia and the benefits outweigh the potential risk. [16] [Level 4]	No dose recommendations for patients with severe renal impairment as only limited pharmacokinetic data. [16] [Level 4]
Zoledronic acid	Recommended dose is 4mg. [6, 8, 9, 11, 15] [Level 1-]	Intravenous Dilute in 100ml of sodium chloride 0.9% or 100ml of 5% dextrose Rate: 15 minutes minimum	Monitor renal function Do not use in patients with severe renal impairment i.e. creatinine clearance <30ml/min as there is no safety data. [11, 14] [Level 4] Use with caution in conjunction with other potentially nephrotoxic drugs plus aminoglycosides or loop diuretics as these may increase risk of hypocalcaemia.[1,.15]	Has been associated with renal dysfunction/ONJ May be a risk of bronchospasm in asthmatic patients. [11] [Level 4] Pancytopenia is a rare side effect. $\geq$ 1 in 10000,<1 in 1000. [15]
Ibandronic acid	Dose varies according to the serum calcium level [5, 18, 21] Corr Ca^{2++} >3mmol/l. Dose is 4mg Corr Ca^{2++}<3 mmol/l Dose is 2mg	Intravenous 500ml sodium chloride 0.9% Rate: at least 2 hours. [18, 21]	Favourable renal safety profile. Deterioration in renal function not associated with use but monitoring of renal function is recommended. [18, 21] [Level 4]	More effective than pamidronate in the treatment of severe hypercalcaemia. [9] [Level 1-]
Clodronate	1500mg [13] [Level 3]	Intravenous or subcutaneous 500-100ml sodium chloride 0.9% Rate:24 hours [12] [Level 3]	Site reactions can be managed with 150-300IU hyaluronidase. [19] [Level 4]	Useful if venous access difficult
Calcitonin	NB Give in addition to the bisphosphonate as calcitonin will give a rapid effect and the bisphosphonate will have a long lasting effect. [5.20] Dose:100IU tds/qds-400IU qds (max)	Subcutaneous Intramuscular Use either human or salmon form(more potent)	Highly emetogenic. Nausea+/- vomiting in 10% of patient. Co prescribe an antiemetic e.g. haloperidol. [20] Other common side effects include rash and flushing. [2, 3, 17] [Level 4]	Only use in exceptional situations when there is the need for rapid reduction of the serum calcium level and the level is very high e.g. symptomatic cardiac arrhythmias. [3, 5, 8, 10] [Level 3]

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23. GUIDELINES FOR THE MANAGEMENT OF INSOMNIA IN PALLIATIVE CARE

THIS GUIDELINE HAS BEEN UPDATED

PLEASE SEE A-Z SECTION FOR UPDATED GUIDELINES

23.1 GENERAL PRINCIPLES

* Insomnia may be a symptom or a syndrome. Definition of the insomnia syndrome (International Classification of Sleep Disorders) requires the presence of all of the following: [1]
  - Difficulties in sleeping characterized by one or both of the following:
  - Difficulty initiating sleep (i.e. taking 30 minutes or more to fall asleep).
  - Difficulty maintaining sleep (i.e. more than 30 minutes of nocturnal awakening) with a corresponding sleep efficiency (i.e. ratio of total sleep time to time spent in bed) of less than 85%.
  - Sleep disturbance occurs during at least three nights per week.
  - Sleep disturbance causes significant impairment of day-time functioning (e.g. fatigue), or marked distress.
* Insomnia is one of the most frequent and distressing symptoms in cancer patients and the clinical impact on patients is often underestimated. [4, 5]
* Insomnia may be transient (< 1 month), short–term (1-6 months), or chronic (> 6 months). [1, 2, 3]
* Insomnia in cancer patients may be linked to uncontrolled physical and/or psychological symptoms. [2, 4, 5]
* Benzodiazepines are the most frequently used drugs in the pharmacological management of insomnia. [2, 3, 4]

23.2 GUIDELINES

* It is important to take a sleep history from all patients. The nature of any disturbance, its duration and effect on every day functioning should be documented in the notes. [3, 4, 5] [Level 4]
* A cause of the sleep disturbance should be identified where possible (see Table 23.1). [3, 4] [Level 4]
* Depression and anxiety are common causes of insomnia and should be identified and treated as appropriate. [3, 4, 5] [Level 4]
* Drugs which may contribute to insomnia (e.g. corticosteroids, diuretics, stimulant antidepressants and other stimulants) should be reviewed and discontinued where possible. If corticosteroids are required they should be administered before 2pm. [3, 4, 6] [Level 4]
* The management of insomnia may include non-pharmacological and pharmacological measures. [3, 4, 5, 6, 7] [Level 4]

* Non-pharmacological measures include: the avoidance of sleep during the day; increasing daytime exercise where appropriate; minimisation of sleep interruption; relaxation techniques; addressing existing fears and anxiety, and improvements in sleep hygiene. Sleep hygiene will consist of simple advice such as: get up and go to bed at same time; keep bedroom dark, quiet and cool; avoid reading or watching TV in bed; don't exercise in the evening; avoid caffeine, alcohol and nicotine in the evening. [4, 5, 6, 7] [Level 4]

Table 23.1 Causes of insomnia [3, 4] [Level 4]

Age-related (i.e. extension of normal physiological changes)	Drug-induced e.g. diuretics, corticosteroids, stimulants, broncho-dilators
Alcohol	Drug withdrawal e.g. benzodiazepines, alcohol
Anxiety	Environmental (e.g. noise levels, light)
Breathlessness	Hallucinations/ nightmares
Bladder/ bowel symptoms e.g. nocturia	Other uncontrolled symptoms e.g. sweating, pruritus
Cognitive impairment / delirium	Pain
Depression	

* Pharmacological measures should be used with caution. Medication should be prescribed at the lowest possible dose and for the shortest period of time. Table 23.2 lists some of the commonly used drugs in the management of insomnia. [3, 4, 5, 6, 8] [Level 4]
* Patients requiring medication should be reviewed at regular intervals. Drugs that are ineffective should be discontinued. [3, 4] [Level 4]
* Caution must be exercised in older patients as many of the drugs used in the management of insomnia cause postural hypotension and urinary retention. These may in turn lead to poor mobility, falls and increasing agitation. [4, 7] [Level 4]
* All benzodiazepines have a significant side effect profile. These include dizziness, confusion, ataxia, dependence, paradoxical agitation and postural hypotension. [4, 6, 8] [Level 4]
* Haloperidol may be used for the management of nightmares and hallucinations but it has little sedative effect. [6, 9] [Level 4]
* The role of antidepressants in the management of insomnia is unclear. If they are used, those with sedative properties should be preferred over drugs such as SSRIs which tend to have more activating properties. The dose should be as low as possible e.g. mirtazapine 7.5mg-15mg; trazodone 50 mg; trimipramine 25mg. [10] [Level 4]
* If mirtazapine is used it is important to remember that it may be associated with blood dyscrasias. Patients should be advised to report fevers, sore throats, stomatitis or other signs of infection during treatment. A blood count should be performed and the drug stopped immediately if a blood dyscrasia is suspected.[9] [Level 4] (For further information on antidepressants please see *Guidelines for Managing Depression in Palliative Care*).

Table 23.2 Drugs used in the management of insomnia [3, 4, 5, 6, 8, 11] [Level 4]			
Medication	**Oral dose**	**Duration of action/ class of drug**	**Notes**
Diazepam	2mg-5mg nocte	Long acting benzodiazepine	Useful if there is coexisting anxiety. Monitor for hangover effect.
Lorazepam	0.5mg-1mg nocte (sublingual)	Short acting benzodiazepine	Little hangover effect, promotes sleep onset and maintenance.
Lormetazepam	0.5mg-1mg nocte	Short acting benzodiazepine	Little hangover effect, promotes sleep onset and maintenance.
Mirtazapine	7.5mg-15mg nocte	Long acting NaSSA	Useful if co-existing depression. Lower doses are more sedative e.g.≤ 15mg.
Nitrazepam	5mg-10mg nocte.	Long acting benzodiazepine	Monitor for hangover effect, promotes sleep maintenance.
Pregabalin	25mg-300mg nocte	Anti-epileptic	Promotes REM sleep. Appears to be useful in patients with anxiety. Withdraw gradually.
Temazepam	10mg-40mg nocte	Intermediate acting benzodiazepine	Monitor for hangover effect, promotes sleep onset and maintenance.
Zolpidem	5mg-10mg nocte	Short acting imidazopyridine	Little hangover effect, promotes sleep onset.
Zopiclone	3.75mg-15mg nocte	Short acting cyclopyrrolone	Little hangover effect, promotes sleep onset.

23.3 STANDARDS

1. Any disturbance in sleep should be documented in the case notes. [3, 4, 5, 8] [Grade D]
2. Reversible causes of insomnia should be identified and treated where appropriate. [3, 4] [Grade D]
3. The regular medication of all patients with insomnia should be reviewed. [3, 4, 8] [Grade D]
4. Current or previous use of night sedation and its effectiveness should be documented. [3, 4] [Grade D]
5. Patients commenced on night sedation should be reviewed within 4 weeks. Ineffective medication should be discontinued. [3, 4, 8] [Grade D]

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24. GUIDELINES FOR THE USE OF INTERVENTIONAL PAIN TECHNIQUES IN PALLIATIVE CARE

24.1 GENERAL PRINCIPLES

* Up to 90% of cancer pain is successfully managed according to the WHO analgesic ladder. [1]
* However 10% of cancer patients with pain do not achieve adequate analgesia e.g. due to incomplete response to opioids or intolerable side effects. [1]
* Up to 90% of non responding patients may benefit from advanced pain management techniques. [1]
* Careful patient selection is important for the success of advanced pain management techniques. [2, 3]
* Joint assessment of patients by pain and palliative care specialists is beneficial for patients and healthcare professionals. It furthers mutual understanding, increases the number of appropriate referrals and improves patient care. [4, 5, 6]
* Commonly used advanced pain management techniques are described in Table 24.1.

24.2 GUIDELINES

* The Merseyside and Cheshire Cancer Network should have a named lead pain clinician. [7] [Level 4]
* Specialist palliative care MDTs should have local access to a named anaesthetist with expertise in nerve blocking. Some patients may require referral to a regional centre for specialised intervention. [7] [Level 4]
* Patients with difficult pain considered for advanced pain management techniques should be reviewed jointly between pain and palliative care specialists. [4] [Level 4]
* Patients with difficult pain should be assessed for an intervention before poor performance status or significant drug toxicities make them ineligible. [8] [Level 3]
* Interventional pain techniques in patients with cancer should be considered if:
  - Pain is not responding to standard treatments.
  - The patient is fit enough for a procedure.
  - The patient is able to give informed consent. [8] [Level 3]
* Careful selection of the type of procedure is important as patients may be only fit enough to undergo one procedure. The procedure with the greatest chance of success should be selected. [5] [Level 4]
* If there is refractory bilateral pain, consider an epidural or intrathecal catheter. [9] [Level 3]
* Patients with refractory pain and a prognosis of at least three months may be suitable for an intrathecal pump device. [10] [Level 1]

* Patients with unilateral pain below the shoulder and a prognosis of 3-12 months should be considered for referral for percutaneous cordotomy. [11] [Level 4]

24.3 STANDARDS

1. The Merseyside and Cheshire Cancer Network should have a named lead pain clinician. [7] [Grade D]
2. Specialist palliative care MDTs should have local access to a named anaesthetist with expertise in performing nerve blocks. [7] [Grade D]
3. All patients considered for interventions should have joint assessments by palliative care and pain specialists. [4, 5, 6] [Grade D]
4. All specialist palliative care services should have local guidelines available for patients who undergo interventional pain management procedures. [8] [Grade D]

Table 24.1 Advanced interventional pain management techniques			
	Indication	**Procedure**	**Comments**
1. **Neuraxial Infusions**	Pain at any level but mainly for pain in lower half of the body.	Insertion of catheters into epidural or intrathecal space. Use strong opioids and local anaesthetic.	High concentration of opioid receptors in spinal cord and therefore local application of opioids with fewer systemic side effects. Smaller dose of opioids required to achieve analgesia than with systemic opioids.
1.1 Epidural catheters [3, 9]	Can remain in situ for months, but if prognosis likely to be more than three months consider referral for implantable intrathecal pump device.	Catheter usually tunnelled into skin to decrease risk of infection and disconnection.	Centres involved in patients with epidural catheters should develop local guidelines for management. These guidelines should address types of medication infused, doses of medication, safe administration of medication, monitoring of epidural catheters in situ and management of complications such as infection or disconnection. Can be cared for in the community, but will require care protocols to be agreed locally.
1.2 Intrathecal catheters [12]	More reliable analgesia in the long-term compared to an epidural catheter (more defined space for drug distribution, no risk of catheter overgrowth).	Volume of infusion and dosage of opioid required smaller than for epidural catheters. Needs to be placed in theatre.	Smaller dose-toxicity range than with epidural catheters. Will require care protocols to be agreed locally.
1.3 Implantable drug delivery systems (IDDS) [10]	For patients with life expectancy of more than three months.	Requires operation to implant pump. Reservoir filled with analgesia.	Requires locally agreed protocols of care when patients are in the community.
2. **Peripheral Nerve Blocks** [2]	Pain in territory of one or more peripheral nerves.	Involves infusion/injection of local anaesthetic and steroid.	Includes femoral nerve block / paravertebral block / brachial plexus block / suprascapular block. Rarely sole or principal treatment
3. **Autonomic blocks** Coeliac plexus bloc [13]	Block inhibits autonomic supply to upper gastrointestinal tract. For pain from pancreatic and upper abdominal malignancies.	Can be performed intraoperatively or under radiological guidance at specialist centres using phenol.	Patient needs to have good performance status. Should be done early in disease course when anatomy not too distorted.
4. **Saddle block** [14]	Indicated for pain in perineal area.	Injection of intrathecal phenol.	Bladder and bowel function can be affected.
5. **Epidural phenol** [15]	Indicated for severe pain not controlled by epidural analgesia.	Injection of 5ml-10ml 6-10% phenol via epidural catheter. The epidural infusion is continued following injection of phenol until the full effect is achieved.	
6. **Percutaneous cordotomy**[11]	For unilateral cancer-related pain e.g. caused by mesothelioma. Suitable for pain below C4 dermatome (below shoulder).	Procedure carried out under local anaesthetic. Patient needs to be able to lie flat for 45 minutes.	80% chance of significant reduction in pain. Life expectancy should be 3-12 months. Side effects are usually temporary and include: occipital headache, mirror pain (pain on side opposite to initial pain), ipsilateral weakness, urinary incontinence or retention.
7. Open cordotomy [16]	For unilateral cancer pain for patients who cannot tolerate percutaneous cordotomy. For pain below T6/7 dermatome.	Performed neurosurgically under general anaesthetic.	As for percutaneous cordotomy.

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25. GUIDELINES FOR THE ASSESSMENT AND MANAGEMENT OF MAJOR HAEMORRHAGE IN PALLIATIVE CARE

25.1 GENERAL PRINCIPLES

* There is no agreed definition regarding major haemorrhage within the palliative care setting.
* The American College of Surgeons Advanced Trauma Life Support Group has developed a classification of haemorrhage. The term major haemorrhage would be Class IV. (see Table 25.1) [1]

Table 25.1 Classification of haemorrhage [1, 2]		
Class I	15% loss of blood volume	No change in vital signs
Class II	15 – 30% loss of blood volume	↓BP ↑ HR Pale cool skin
Class III	30 – 40% loss of blood volume	↓ BP ↑HR Poor capillary refill
Class IV	≥ 40% loss of blood volume	Body can no longer compensate

* Clinically significant bleeding occurs in 6 – 10% of patients with advanced cancer. [2]
* Evidence from an American study suggests that haemorrhage accounts for 6% of all cancer deaths worldwide. [3]
* There are some specific sites, which when they bleed, are more likely to result in a major haemorrhage. [4] (see Table 25.2)
* Major haemorrhage is a very rare event and as a consequence will not be encountered by many health care professionals. [4] Hospitals and hospices should have a policy regarding the management of a patient who has a major haemorrhage.[5]

Table 25.2 Common sites of haemorrhage	
Site	**Comments**
Lung	May asphyxiate with a loss of 400mls [5, 14]
Upper gastrointestinal tract	Usually peptic or gastric ulceration [13]
Lower gastrointestinal tract	
Head and neck	
Urinary tract	

25.2 GUIDELINES

25.2.1 Pre-event assessment of the at risk patient

* Patients who suffer from a malignancy should be assessed for their bleeding risk. [6] [Level 3]

* The factors which are associated with an increased risk of major haemorrhage are in Table 25.3. [7, 8] [Level 3]

Table 25.3 Factors associated with increased risk of major haemorrhage [8, 9, 10] [Level 3]

Category	Risk Factor
Anatomical	Fungating wound Recurrent precursor (sentinel) bleeds Site of lesion close to a major vessel
Systemic disease	Bone marrow failure Coagulation disorders Disseminated intravascular coagulation Infection at the site of the lesion Malabsorption / reduced vitamin K Severe liver disease Uraemia
General	Infection of the fungating wound Platelet count less than 20 000/mm^3 Radiotherapy to a post-operative site
Medication	Chemotherapy causing mucositis Heparin NSAIDs Warfarin

* If the patient is considered to be at risk of a major haemorrhage then a multidisciplinary team decision should be made regarding the future management of the patient. This should be documented in the case notes. [7] [Level 3]

* All medication should be assessed for the risk versus benefit ratio regarding the increased risk of bleeding. The decision and reason to continue to use anticoagulation and NSAIDs should be documented in the notes. [7, 11] [Level 3]

* Referral for assessment of management using specialist techniques may be appropriate. This should be discussed with the patient and the appropriate specialist. Interventions include: [8, 9] [Level 4]
  - Vascular embolisation (interventional radiology).
  - Vascular ligation (palliative surgery).
  - Palliative radiotherapy.
  - Endoscopic interventions (sclerosis, ligation).
  - Cautery with heat or laser treatment.

* The decision regarding active treatment should be discussed with the patient and their significant carers (if appropriate) and this should then be documented in the case notes. This information should be communicated to the relevant health care professionals who are involved in that patient's care. [7, 9] [Level 4]

* The resuscitation status of the patient should be documented in the notes.[12] [Level 4]

* For those patients who are identified as being at risk of bleeding, the decision whether to communicate this information should be made by a senior health care professional and / or the multidisciplinary team. If appropriate, information should be sensitively communicated with the patient and their significant carers. [7] [Level 3]

* The health care professionals involved in the patient's care should organise the prophylactic prescribing of midazolam and arrange for dark towels to be present (to disguise bleeding if it should occur). [2, 7] [Level 3]

* Midazolam should be prescribed at a dose of 5mg to 10mg. The preferred route is intravenous. Alternative routes are deep intramuscular or intranasal. The subcutaneous route should be avoided due to the problems with poor absorption of the medication. [7] [Level 3]

* In the event of a major haemorrhage, two further doses of 10mg midazolam may be administered. The maximum dose is 30mg. The dose should be titrated according to clinical need. [12] [Level 4]

* Morphine sulphate or diamorphine injections are not usually required to manage a major haemorrhage.[12] [Level 4]

* Consider the use of prophylactic medication such as etamsylate and tranexamic acid or haemostatic dressings. [4] [Level 4]

25.2.2 <u>During the major haemorrhage</u>

* If the patient has a major haemorrhage, it is essential that at least one health care professional remains with the patient if at all possible. [7] [Level 3]

* If appropriate, the patient may be placed in the left lateral position to reduce the risk of asphyxia and pressure may be applied to the source of bleeding. [7] [Level 4] Dark towels (green or red) should be used to disguise the amount of bleeding. [7] [Level 4]

* Midazolam should be given via the intravenous, intranasal or deep intramuscular route. The dose of 5mg to10mg may be repeated to a **total maximum dose of 30mg** during an event. The dose should be titrated against the distress of the patient and should be based upon the individual need of the patient.[7] [Level 4]

* The relatives should be involved in the decision as to whether they remain present during the event. [12] [Level 4]

25.2.3 <u>Post major haemorrhage event management</u>

* If the patient recovers, their ongoing management will need to be assessed by the multi-professional team. [12] [Level 4]

* If the patient does not recover, the carers may need increased support following the death. If the fatal haemorrhage occurs in the community, then they may need assistance in cleaning the area where the event has occurred. [7] [Level 3]

* Health care professionals involved may need support after the event. This may include de-briefing sessions. [7] [Level 3]

25.3 STANDARDS

1. All patients at risk of a major haemorrhage should have the risk documented in their case notes. [13] [Grade D]
2. For those patients at risk, the review and rationale of all specific medications that may further increase the risk of bleeding should be documented in the case notes. [12] [Grade D]
3. For those patients who are identified as being at risk of bleeding, the decision whether to communicate this information to them should be made by a senior health care professional and / or the multidisciplinary team. Any discussions of the bleeding risk with the patient and their carers should be documented. If there have been no discussions, then the reason for this should be documented. [7, 12] [Grade D]
4. For patients at risk of bleeding, midazolam should be prescribed prophylactically at a dose of 5mg to 10mg via the intravenous, deep intramuscular or intranasal route. If midazolam is administered, the dose should be titrated to ease distress. The maximum dose is 30mg per episode of major haemorrhage. [7] [Grade D]

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26. GUIDELINES FOR CONVERSION FROM A STRONG OPIOID TO METHADONE

THIS GUIDELINE HAS BEEN UPDATED

PLEASE SEE A-Z LIST FOR UPDATED GUIDELINES

26.1 GENERAL PRINCIPLES

* Methadone may be used as a strong opioid alternative when severe cancer-related pain responds poorly to other opioids, or when there are dose-limiting side effects with other opioids. [1, 2, 3]
* Methadone pharmacology is complex and the use of methadone is associated with a risk of drug accumulation. Conversion to methadone should take place in a specialist unit which is familiar with its use. [1, 2, 4, 5, 6]
* The dose of methadone should always be prescribed in **milligrams (mg)** and **not** millilitres (ml). [5]
* There are three different strengths of methadone solution used for pain control. These are 1mg/ml, 10mg/ml and 20mg/ml. [1]
* Methadone Linctus is a solution of 2mg/5ml. It should **only** be prescribed for patients with intractable cough and should **not** be used for pain control. [5]
* There have been concerns raised about the cardiac toxicity of methadone, specifically related to effects on the QT interval with doses >100mg.[9] However, studies have not shown a link between oral methadone and cardiac toxicity in ambulatory cancer patients. [5, 7, 8, 9]
* These guidelines outline a five day **dose titration phase** using a '**fixed dose'** of methadone before converting to a 12-hourly dosage regimen for **chronic treatment.** [4]
* Methadone can potentially interact with drugs that inhibit CYP3A4 and CYP2B6. This includes erythromycin and azole anti-fungals (although 50mg fluconazole is unlikely to be significant). Clopidogrel is a potent inhibitor of CYP2B6 and may affect methadone plasma levels. [5]

26.2 GUIDELINES

26.2.1 Calculating the "fixed" dose of methadone to be used during the dose titration phase [4] [Level 4]

* The fixed dose of methadone should be 10% of the total oral morphine dose given over the preceding 24 hours. The upper limit of the fixed dose of methadone **should not exceed 30mg.**
  - For example, if a patient is taking MST Continus® 100mg bd, the total 24-hour oral morphine dose is 200mg. The fixed dose of methadone should be 200mg÷10 = 20mg of methadone.

* When converting from diamorphine, oxycodone or hydromorphone, firstly convert the dose to an equivalent 24-hour oral morphine dose. The fixed dose of methadone will again be 10% of this dose with an upper limit of 30mg (see *Guidelines on Strong Opioid Substitution*).
* When converting from transdermal fentanyl, use Table 26.1 to calculate the fixed dose of methadone.

Table 26.1 Converting from transdermal fentanyl to methadone [12] [Level 4]

Fentanyl patch strength	Fixed methadone dose for titration
25 micrograms	6mg
50 micrograms	12mg
75 micrograms and above	18mg

**** This table uses approximations and is for guidance only**

26.2.2 The dose titration phase [4] [Level 4]

* It is important to discontinue any other strong opioid before giving the first fixed dose of methadone.
* Prior to the dose titration phase, patients should be warned that it may take 24-48 hours before there is any significant improvement in pain relief, or any reduction in side effects.
* For the first 5 days, the fixed dose of methadone should be taken orally as required as but **not more frequently than every three hours**. This is due to the risk of toxicity from drug accumulation. If the patient requires analgesia within three hours of the previous dose of methadone, an alternative short acting opioid e.g. morphine sulphate solution, should be used.
* During the dose titration phase, methadone requirements usually drop on days two and three before reaching a steady state on days four and five. On day six, the twice-daily dosage regimen is calculated by dividing the total dose of the previous 48 hours (i.e. days four and five) by **four,** and using this dose 12-hourly for chronic treatment.
* If there is an unexpected escalation in pain during the titration phase, the conversion should be considered to have failed and the patient should return to the initial analgesic regimen. There is no recognised conversion from methadone back to another strong opioid. General advice is to base the dose on previous requirement but use lower doses (i.e. 30-50% lower) and re-titrate. Clinicians need to be prepared to increase the dose and ensure that appropriate rescue doses are available.[10]
* Administration of methadone via a syringe driver is not recommended during the titration phase due to the risk of drug accumulation.

26.2.3 Chronic treatment following dose titration [4] [Level 4]

* Methadone is given every 12 hours during chronic treatment.
* There is little consensus as to what should be used for rescue analgesia during chronic treatment. Success has been reported using oral methadone at a dose of either one sixth or one tenth of the 24-hour methadone dose. The rescue dose should not be given more frequently than every three hours.
* If more than two rescue doses are required over a 24-hour period, the twice-daily dose should be increased by 30-50%.

26.2.4 Routes of administration

* Methadone may be given by subcutaneous infusion if oral administration is not possible. The subcutaneous route is often complicated by site inflammation which may result in frequent site changes. It is possible to give intermittent subcutaneous injections. [1, 11, 12] [Level 4]
* The dose of methadone given in the syringe driver over 24 hours should be half of the 24-hour oral dose. The methadone should be diluted with sodium chloride 0.9% in a 20ml syringe. Syringe driver sites should be changed every 24 hours to avoid local irritation. Hyaluronidase (150IU) can be injected subcutaneously at the syringe driver site to avoid local reaction to the methadone. [1, 12] [Level 4]
* Methadone may be given by suppository twice daily. 50mg suppositories are available. The relative potency of rectal to oral methadone is 1:1. [5] [Level 4]

26.2.5 Discharge of patients on methadone

* If a patient is discharged home on oral methadone, the discharge letter should include a contact name and telephone number for advice on further management. [13] [Level 4]
* Prior to discharge, the designated community pharmacist should be contacted to discuss dose, concentration and the supply of methadone. [13] [Level 4]
* Copies of the discharge letter should be sent to all health care professionals involved in the patient's care. [13] [Level 4]

26.3 STANDARDS

1. The decision to convert a patient to methadone should be clearly documented in the case notes. [13] [Grade D]
2. Methadone should always be prescribed in milligrams (mg). [5] [Grade D]
3. Methadone should be administered orally during the dose titration phase. [4] [Grade D]
4. If administering methadone via a subcutaneous infusion, then sodium chloride 0.9% should be used for dilution. [1, 12] [Grade D]
5. Syringe driver sites should be changed every 24 hours. [12] [Grade D]
6. If a patient is discharged home on methadone, the discharge letter should include a named contact and telephone number for further advice. [13] [Grade D]

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27. GUIDELINES FOR THE MANAGEMENT OF NAUSEA AND VOMITING IN PALLIATIVE CARE

27.1 GENERAL PRINCIPLES

* Nausea and vomiting are experienced by 50-60% of patients with advanced cancer. [1]
* Nausea and vomiting are more common in certain groups of patients i.e. <65 years old, females and certain malignancies e.g. gastric and breast cancer. [1]
* Patients with advanced malignancy may develop nausea and vomiting from causes unrelated to the cancer e.g. gall bladder disease or gastroenteritis. [1]
* Table 27.1 lists some common causes of nausea and vomiting in patients with advanced cancer. [1, 2]

Table 27.1 Common causes of nausea and vomiting in advanced cancer [1, 2]

Anxiety	Gastritis
Autonomic neuropathy	Hypercalcaemia
Biochemical	Infection
Brainstem / meningeal disease	Intestinal obstruction
Constipation	Pain
Cough	Radiotherapy
Drugs	Raised intracranial pressure
Functional obstruction	Renal failure
Gastric outlet obstruction	Vestibular disturbance

* Anti-emetics are neurotransmitter-blocking agents and are effective at different receptor sites (see Figure 27.1). [3]
* The choice of anti-emetic will be influenced by the cause of vomiting. They may be administered by a variety of routes. The oral or subcutaneous routes are the preferred options in palliative care. [4]

27.2 GUIDELINES

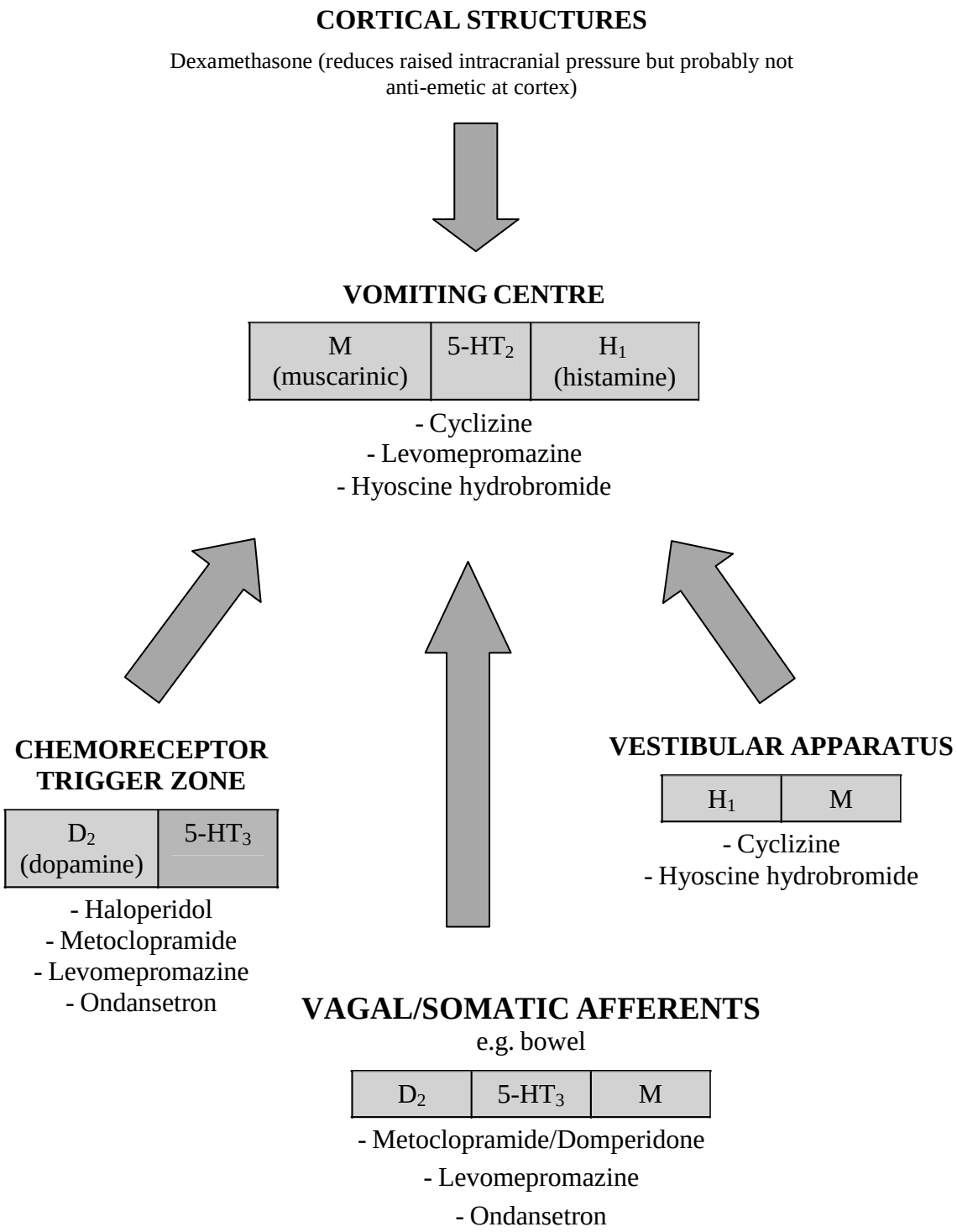
* Table 27.2 lists the pharmacological options for the management of nausea and vomiting in advanced cancer. [3]

Table 27.2 Pharmacological options for the management of nausea and vomiting in advanced cancer [1, 2, 3, 5, 6] [Level 4]						
Drug name	**Type of drug**	**Indication for use**	**Oral dose**	**Parenteral dose (subcutaneously over 24 hours via a syringe driver)**	**Parenteral dose (subcutaneous stat doses)**	**Notes**
Cyclizine	Antihistamine	Central causes. Movement related nausea and vomiting. Bowel obstruction.	50mg tds. Maximum daily dose is 150mg.	100g-150mg	50mg subcutaneous prn.	Dilute with water Side effects include dry mouth, urinary retention and restlessness. Should not be co-prescribed with metoclopramide or domperidone. Avoid in severe cardiac failure. Should not be mixed with hyoscine butylbromide in a CSCI.
Dexamethasone	Corticosteroid	Intracranial disease. Bowel obstruction.	8mg-16mg od Exact dose determined by cause. (See *Guidelines on Use of Corticosteroids*)	8mg-16mg	Not applicable.	Side effects include insomnia, delerium and restlessness. If dose≤ 8mg can give as subcutaneous bolus dose. Use separate syringe driver as does not mix with other drugs.
Domperidone	Prokinetic D_2 receptor antagonist	Useful in gastric stasis.	10mg-20mg tds-qds.	n/a	n/a	Can be given via rectal route. Does not cross the blood-brain barrier so less likely to give extrapyramidal reactions compared to haloperidol.
Haloperidol	Butyrophenone (D_2 receptor antagonist)	Chemical causes e.g. opioids. Metabolic causes.	1.5mg-5mg nocte. (maximum10 mg daily)	1.5mg-5mg (maximum 10mg daily) **NB: Subcutaneous: oral potency of haloperidol is 2:1.**	1.5mg-3mg subcutaneously as required.	Risk of extrapyramidal symptoms. Single daily dose usually sufficient because of long half life. Parental administration is more potent therefore consider starting at a lower dose.

Continued on next page

Table 27.2 (continued) Pharmacological options for the management of nausea and vomiting in advanced cancer [1, 2, 3, 5, 6] [Level 4]						
Drug name	**Type of drug**	**Indication for use**	**Oral dose**	**Parenteral dose (subcutaneously over 24 hours via a syringe driver)**	**Parenteral dose (subcutaneous stat doses)**	**Notes**
Hyoscine Hydrobromide	Anti-cholinergic	Mechanical obstruction Movement-related nausea and vomiting	300 micro-grams - hourly (sublingual)	1.2mg-2.4mg	400microgrammes subcutaneously as required	May cause paradoxical agitation. Has central anti-emetic activity.
Levomepromazine (Methotrimeprazine)	Phenothiazine	Unknown cause of vomiting Usually used as second line therapy due to sedative effect.	6.25mg-25mg od	6.25mg-25g	6.25mg-12.5mg subcutaneously as required	Side effects include dry mouth, sedation and hypotension. Parenteral administration is more potent therefore consider starting at a lower dose. There is a 6mg tablet available (unlicensed).
Lorazepam	Benzodiazepine	Anxiety Anticipatory nausea	0.5mg-1mg sublingually as required or bd	n/a	n/a	Risk of sedation. Often used during chemotherapy.
Metoclopramide	Prokinetic. D_2 receptor antagonist	Useful in gastric stasis/ gastroparesis	10mg-20mg tds	30mg-120mg	10mg-20mg subcutaneously as required	Reduce dose in severe renal failure. Do not use in complete bowel obstruction. May cause extrapyramidal reactions at higher doses. Prokinetic effect may be reduced if anticholinergic drugs are co-prescribed.
Octreotide	Somatostatin analogue	Reduction of gastrointestinal secretions	Not applicable	300microgrammes-600microgrammes	50microgrammes–100microgrammes subcutaneously as required	A long acting depot injection is available.
Ondansetron	$5HT_3$ receptor antagonist	Chemotherapy and radiotherapy induced nausea and vomiting	4mg-8mg bd or tds	8mg-24mg	4mg subcutaneously as required	Side effects include constipation. Dilute with saline.

Figure 27.1 Sites of action of selected anti-emetics [2, 3] [Level 4]



* Patient assessment should include a full history, examination and investigations where appropriate. [1] [Level 4]
* The history should include details of the volume, content and timing of vomiting. Nausea should be specifically enquired for and rated, along with any diurnal pattern or associated features which may suggest a cause. [1] [Level 4]
* A biochemical profile, including corrected calcium, should be checked in patients with nausea and / or vomiting unless they are in the dying phase. [1] [Level 4]
* Reversible causes should be treated where appropriate. These include: drugs, constipation, hypercalcaemia, cough, anxiety and gastric irritation. [3, 4] [Level 4]
* Non-pharmacological measures which may be useful in the management of nausea and vomiting include: psychological measures, transcutaneous electrical nerve stimulation (TENS), complementary therapies and advice on posture and diet. [1, 3] [Level 4]
* Anti-emetics may be given via the oral route for patients with nausea. However, if nausea is severe or protracted, early use of the parenteral route should be considered. Gastric stasis can cause nausea and oral anti-emetics may be ineffective in this situation. [1,3] [Level 4]
* A continuous subcutaneous infusion (CSCI) via a syringe driver should be considered for:
  - Patients who have vomiting lasting more than 24 hours.
  - Patients who have nausea unresponsive to oral anti-emetics for more than 24 hours.[11] [Level 4]
* Various subcutaneous regimens are suggested in Table 27.3.
* A single stat subcutaneous injection should be given at the same time as setting up the CSCI and breakthrough anti-emetics should always be prescribed. [11] [Level 4]
* If using levomepromazine in a syringe driver, the syringe should be shielded from sunlight. [9] [Level 3]
* In cases of inoperable bowel obstruction, a nasogastric tube or venting gastrostomy may be appropriate for symptom control. (see *Guidelines for the Management of Bowel Obstruction*). [1, 10] [Level 3]
* Autonomic neuropathy is common in advanced disease and may cause gastroparesis. This may contribute to terminal restlessness. Consider using a nasogastric tube to remove gas and liquid from the stomach. This may restore comfort and the tube can then be withdrawn. [11] [Level 4]
* If a nasogastric tube is left in-situ, prescribe cyclizine or levomepromazine to alleviate the nausea caused by pharyngeal stimulation. [11] [Level 4]

Table 27.3 Suggested antiemetic regimens via CSCI [2, 3, 6, 7, 8] [Level 4]		
Aetiology	**First line**	**Second line**
Cause unknown	Cyclizine 100mg-150mg +/- haloperidol 1.5mg-5mg via CSCI over 24 hours.	Levomepromazine 6.25mg – 25mg over 24 hours, +/- dexamethasone 4mg–8mg subcutaneously once daily.
Bowel obstruction	See *Guidelines for the Management of Bowel Obstruction.*	See *Guidelines* for *the Management of Bowel Obstruction.*
Chemical/ Metabolic	1.5mg-5mg haloperidol injected subcutaneously once daily or via CSCI over 24 hours.	*Discuss with specialist team*
Gastroparesis	Initial stat subcutaneous injection of metoclopramide 10mg, followed by CSCI of metoclopramide 30mg–60mg over 24 hours. NB Do not use in complete obstruction.	*Discuss with specialist team*

27.3 STANDARDS

1. Any patient with a history of nausea and vomiting should have a full assessment including a history, clinical examination and appropriate investigations to try and identify a cause for the symptoms. [1] [Grade D]
2. Appropriate anti-emetics should be prescribed on a regular **and** as required basis. [11] [Grade D]
3. If a patient is vomiting or nauseated for more than 24 hours, anti-emetics should be given via the parenteral route. [11] [Grade D]
4. If combinations of anti-emetics are required, drugs with different but complementary actions should be used. [2, 3] [Grade D]
5. Metoclopramide should not be prescribed if the vomiting is caused by complete intestinal obstruction. [2, 3] [Grade D]
6. Symptoms of nausea and vomiting should be controlled within 72 hours. [11] [Grade D]

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28. GUIDELINES FOR THE MANAGEMENT OF CANCER-RELATED NEUROPATHIC PAIN

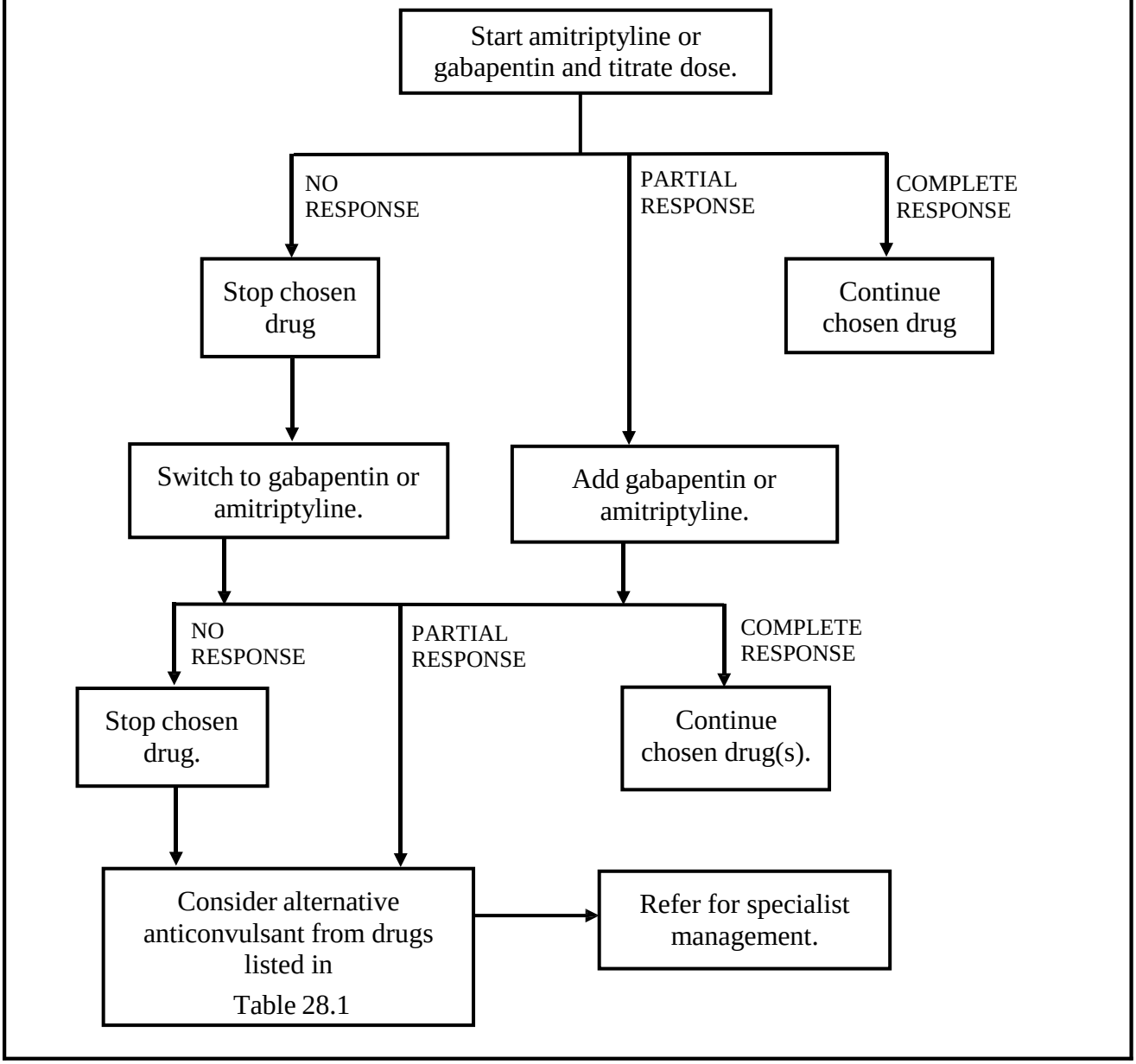
28.1 GENERAL PRINCIPLES

* Neuropathic pain may be relieved in the majority of patients by multimodal management. [1, 2]
* A careful history and examination are essential.[1] Investigations such as computerised tomography (CT) or magnetic resonance imaging (MRI) may be appropriate. [2]
* It is important to have a logical and rational approach to prescribing.
* Chemotherapy or radiotherapy may be indicated if the tumour is chemosensitive or radiosensitive. [3, 4, 5, 6, 7]
* Non-pharmacological approaches should be considered including: transcutaneous electrical nerve stimulation (TENS); acupuncture; hydrotherapy and psychological interventions. [8, 9, 10]
* Interventional techniques may be indicated and should always be discussed at an early stage with an Anaesthetic Pain Specialist. [11, 12]

28.2 GUIDELINES

* The WHO analgesic ladder should be followed. [13] [Level 2-]
* Strong opioids should be titrated against response. Adjuvants and non-opioids should be used as appropriate. [14] [Level 1-]
* The endpoint of titration is pain relief or intolerable side effects. If dose-limiting side effects occur despite the use of adjuvants or other interventions, a switch of opioid should be considered. [15] [Level 3]
* Figure 28.1 features a flow diagram which may be a useful guide for adjuvant prescribing in neuropathic pain. [16, 17] [Level 1+]
* If nerve compression is suspected, a trial of corticosteroids should be considered e.g. dexamethasone 8mg for 5 days. [18, 19, 20] [Level 1-] Pain relief following the use of corticosteroids often predicts a favourable response to radiotherapy. [21] [Level 4]
* Anaesthetic techniques may be indicated. They should always be discussed early with an Anaesthetic Pain Specialist whilst the patient remains fit enough to tolerate any appropriate procedure (see *Guidelines on Interventional Pain Techniques).* [11, 12] [Level 3]
* Topical treatment with capsaicin cream may be of benefit in patients intolerant of other treatments. [22] [Level 1-]
* In patients with symptoms that are difficult to control or who have severe allodynia / hyperalgesia, consider admission to a specialist centre. [23] [Level 4]

Figure 28.1 Approaches to the use of adjuvant analgesics in neuropathic pain [16, 17] [Level 4]



* Methadone is a potent μ agonist and acts as a non-competitive antagonist at the N-methyl-D-aspartate (NMDA) receptor. It has also been shown to inhibit the re-uptake of serotonin and noradrenaline. Morphine, hydromorphone, fentanyl and oxycodone do not exhibit this additional action. Methadone is therefore often used as a broad-spectrum opioid in the treatment of resistant cancer-related neuropathic pain, where there have been dose-limiting side effects and rapid development of tolerance to the previous opioid. Methadone should only be initiated in a specialist unit (see *Guidelines on the Use of Methadone*). [24] [Level 1-]

* Ketamine may be given as an infusion prior to conversion to an oral preparation where appropriate. It should only be initiated under specialist supervision. It can be given intravenously [25] [Level 1-] or subcutaneously. Various regimens have been described and the choice will depend on the preference of the specialist team. [26, 27] [Level 3]

28.2.1 Anaesthetic approaches (see Guidelines on Interventional Pain Techniques)

* If the pain is escalating despite the use of recommended guidelines, or if urgent control is required, consider early referral for an Anaesthetic Pain Specialist opinion. [11] [Level 4]
* The use of peripheral nerve blocks using local anaesthetic and / or corticosteroids may be effective for the relief of pain in the distribution of one or more peripheral nerves. [28, 29] [Level 3]
* Neurolytic procedures such as a saddle block using phenol may relieve some painful sacral neuropathies. [11, 30] However this may cause significant problems with bladder and bowel function. Some experts favour epidural catheters as an alternative. [Level 4]
* Epidural opioids +/- bupivicaine may be of use in patients with neuropathic pain, particularly in patients with intractable radicular pain or where systemic opioids have caused severe side effects. However, they may cause significant problems with bladder and bowel function. [31, 32] [Level 4]
* If unilateral pain below the shoulder and prognosis between three months and twelve months, consider referral for percutaneous cordotomy. [33, 34, 35] [Level 3]

28.3 STANDARDS

1. All patients with neuropathic pain should be monitored with a pain diary. [2, 23, 36] [Grade D]
2. Patients with poorly controlled neuropathic pain should have at least weekly follow up if an outpatient, and 48 hourly reassessment if an inpatient. [23] [Grade D]
3. If neuropathic pain is escalating, an Anaesthetic Pain Specialist should be contacted for advice within 48 hours. [11] [Grade D]

Table 28.1 Adjuvant oral analgesics used in the management of neuropathic pain				
Drug Name	**Initial dose**	**Titration**	**Side effects**	**Notes**
Amitriptyline [16] [Level 1+]	10mg-25mg at night. 10mg at night in the elderly. Median preferred dose of 75mg daily.	Increase every 3 days as tolerated.	Occur in 33% of patients. Include drowsiness and dry mouth.	Speed of onset 1-7 days. May get improved sleep pattern and mood. Use with caution in the following: cardiac disease; arrhythmias; epilepsy; concurrent use of SSRIs; angle closure glaucoma; history of urinary retention.
Capsaicin 0.075% cream [22] [Level 1-]	Apply topically three or four times daily.		Skin burning and redness.	May take up to 10 days to have an effect. Always wear gloves when applying.
Carbamazepine [37] [Level 1+]	200mg daily. 100mg daily in elderly.	Increase by 100mg-200mg every three days. Give in divided doses.	Nausea, drowsiness, confusion and ataxia.	Beware of drug interactions.
Clonazepam [38] [Level 3]	500 micrograms nocte.	Increase by 500microgrammes every third day. Maximum dose is 8 mg.	Sedation.	May be given subcutaneously via a syringe driver. May adsorb to PVC so use non PVC equipment for infusions. A CSCI containing clonazepam should only run for a maximum of 12 hours as stability of diluted clonazepam currently only confirmed for 12 hours.
Dexamethasone [21] [Level 1-]	8mg daily.	Give for 5 days. Discontinue if no response. Reduce to lowest dose to maintain effect (see *Guidelines on Corticosteroids*).		If good response then may benefit from radiotherapy. Monitor blood sugar levels. Consider gastric protection.
Gabapentin [17] [Level 1+]	300mg nocte. 100mg nocte if elderly.	Increase after 3 days to 300mg bd. Increase to 300mg tds after further 3 days. Maximum dose is 2400mg. Note: May need to use slower titration regimen e.g. start at 100mg od and increase by 100mg every two days.	Sedation, dizziness.	Reduce dose in renal failure/ impairment. Use with caution in patients with CCF. Diabetic patients may need to adjust hypoglycaemic treatment as weight gain may occur.
Lidocaine plaster [39] [Level 1-]	One strength. Apply for 12 hours daily over painful area and then remove.	Can use up to 3 patches at any one time	Skin reaction	Current evidence is for post herpetic neuropathic pain. May be useful for post thoracotomy pain.
Pregabalin [40] [Level 1-]	Day 1: 25mg od Day 2: 25mg bd Increase every two days by 25 mg bd.	150mg-600mg daily in two divided doses. Avoid tds dosing. Treatment costs increase with no benefit.	Sedation, dizziness.	Potential pharmacodynamic interactions with all opioids and sedatives. [42] Caution may be required in patients with chronic heart failure.[43] Diabetic patients may need to adjust hypoglycaemic treatment as weight gain may occur.
Sodium valproate [41] [Level 2-]	200mg at night.	Increase by 200mg every third day. Maximum dose is 1000mg daily.	Nausea, ataxia.	

NB. Choice of adjuvant analgesic will depend on clinician experience and the side effect profile of individual drugs.

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29. GUIDELINES FOR THE USE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN PALLIATIVE CARE

29.1 GENERAL PRINCIPLES

* Non-steroidal anti-inflammatory drugs (NSAIDs) consist of a heterogenous group of compounds that can be subdivided by virtue of their pharmacology: [1]
  - Non-selective NSAIDs inhibit both COX-1 and COX-2 receptors e.g. ibuprofen, naproxen.
  - COX-2 selective NSAIDs display some selectivity for COX-2 receptors but this diminishes as the dose increases e.g. etodolac, meloxicam.
  - COX-2 inhibitors specifically inhibit COX-2 receptors at therapeutic doses whilst being COX-1 sparing e.g. celecoxib, etoricoxib.
* All NSAIDs have significant cardiovascular and gastrointestinal toxicity. [2]
* Consider whether alternative treatment would be appropriate (e.g. topical NSAIDs, paracetamol, tramadol). [1]
* Prescribe the lowest effective dose of NSAID for the shortest time necessary. [3]

29.2 GUIDELINES

29.2.1 Cardiovascular risk and NSAID prescribing

* COX-2 inhibitors are contraindicated for use in patients with established ischaemic heart disease and / or cerebrovascular disease, and also in patients with peripheral arterial disease. [4] [Level 1]
* Despite conflicting evidence, non-selective NSAIDs and COX-2 selective NSAIDs are currently licensed for use in these groups of patients, although they should be used with caution. [1] [Level 4]

29.2.2 Renal dysfunction and NSAID prescribing

* Renal function should be assessed prior to the introduction of a NSAID and within 7 days of starting treatment or increasing the dose. [5, 6] [Level 4]
* Care is required when prescribing NSAIDs for patients with heart failure, ascites or impaired renal function, particularly those who are dehydrated or have a low effective circulating volume. [5, 6] [Level 4]

* Long term administration of NSAIDs has been linked to papillary necrosis and other renal injuries. Patients with impaired renal function, heart failure, liver dysfunction, the elderly and those taking diuretics and / or angiotensin-converting enzyme inhibitors are at greatest risk from this reaction. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state. [7] [Level 4]

* Use of NSAIDs in patients with advanced renal disease is not recommended due to a lack of safety data from controlled clinical studies. If NSAIDs are prescribed it is essential that renal function is monitored closely. [5, 6] [Level 4]

29.2.3 Gastrointestinal toxicity

* Patients at high risk of gastrointestinal side effects from NSAIDs include the following: [8, 9] [Level 4]
  - Elderly (age >65 years). The risk increases with age.
  - Previous upper gastroduodenal perforation, ulcers and bleeds.
  - Concurrent use of aspirin, warfarin, corticosteroids or selective serotonin reuptake inhibitors (SSRIs).
  - Patients receiving maximum doses of NSAIDs.

* Undesirable gastric side effects from celecoxib are significantly less than from non-selective NSAIDs although it is not clear whether this lower risk continues with long term use. [10] [Level 4]

* In patients taking clopidogrel, it is advisable to use an H_2 antagonist at a higher dose than usual e.g. ranitidine 300mg bd. [19] [Level 4]

29.2.4 Proton Pump Inhibitors

* A proton pump inhibitor (PPI) should be co-prescribed with a NSAID, regardless of which actual drug is chosen. [1] [Level 4] This is cost effective in the treatment of osteoarthritis, but the benefit of a PPI with a COX-2 inhibitor in other situations is unclear. [11] [Level 4]

* The relationship between H. pylori infection and NSAIDs in gastroduodenal pathology is complex. Eradication of H. pylori infection may prevent peptic ulcer disease in patients who are naïve users of NSAIDs. Patients receiving long term PPI treatment for prevention of NSAID ulcers should be tested for H. pylori. Eradication of H. pylori will reduce the risk of accelerated loss of specialised glands and atrophic gastritis. [12] [Level 4]

* Appropriate proton pump inhibitors and oral doses include: [15] [Level 4]
  - Esomeprazole 20mg od.
  - Lansoprazole 30mg od.
  - Omeprazole 20mg od.
  - Pantoprazole 40mg od.

* Misoprostol is a synthetic prostaglandin analogue with gastric anti-secretory and protective properties which can be used to protect against NSAID-induced gastrointestinal damage. It is more effective than PPIs but can be poorly tolerated. Side effects include colic and diarrhoea. A suggested starting dose is 200micrograms od, increasing by 200 micrograms every 1-2 days to a normal dose of 200micrgrams qds. [17, 18] [Level 1]

29.2.5 Choice of NSAID

* Before deciding which NSAID to use, the prescriber must first assess patient risk factors for cardiovascular and gastrointestinal toxicity (see Figure 29.1). [1, 2, 3] [Level 4]
* Table 29.1 lists NSAIDs currently recommended for use; Table 29.2 lists additional NSAIDs that may be considered second line options. [1] [Level 4]

29.2.6 Monitoring Effectiveness

* NSAIDs should be prescribed for at least 7 days before reviewing their clinical effectiveness. The analgesic effect of the drug becomes apparent within the first few days of treatment. The anti-inflammatory response may take at least 2 weeks to become evident. [8] [Level 4]
* It may be appropriate to use an alternative NSAID before concluding that NSAIDs are ineffective. [8] [Level 4]
* Due to the increased risk of renal and gastroduodenal toxicity, ketorolac should only be used for refractory pain (see Table 29.2). A PPI should always be co-prescribed with ketorolac unless the patient is in the dying phase. [8] [Level 4]

29.3 STANDARDS

1. COX-2 inhibitors are contra-indicated for use in patients with existing ischaemic heart disease, peripheral vascular disease or cerebrovascular disease. [4, 13] [Grade B]
2. In patients with existing cardiovascular disease, alternative analgesia should be considered before introducing a non-selective NSAID or a COX-2 selective NSAID (e.g. paracetamol, tramadol, topical NSAID). If NSAIDs are to be used, the lowest dose possible should be prescribed and the patient should be reviewed within 7 days.[3] [Grade D]
3. It may be appropriate to use an alternative NSAID before concluding that NSAIDs are ineffective. [8] [Grade D]
4. Patients with risk factors for gastrointestinal toxicity should be prescribed proton pump inhibitors or misoprostol for gastric protection. [14, 17, 18] [Grade B]
5. A PPI should be prescribed for all patients receiving subcutaneous NSAIDs, unless they are in the dying phase. [8] [Grade D]
6. Renal function should be assessed prior to the introduction of a NSAID and within 7 days of starting treatment or increasing the dose. [5, 6] [Grade D]

Table 29.1 NSAIDs currently recommended for use [1,] [Level 4]				
Class of NSAID	**Name of drug**	**Oral dose**	**CSCI over 24 hours**	**Additional notes**
Non selective	Naproxen	500mg bd	n/a	Suitable 1st line choice, together with PPI for patients with CV risk.
	Ibuprofen	400mg-800mg tds	n/a	Low dose ibuprofen (≤1200mg) suitable 1st line choice, together with PPI, for patients with CV risk. If low dose aspirin is co-prescribed, ibuprofen should be given at least 8 hours before or 30 minutes afterwards. Alternatively, change aspirin to clopidogrel.[1]
COX-2 inhibitor	Celecoxib	100mg-200mg bd	n/a	Suitable 1st line choice in patients at high risk of GI toxicity and low CV risk. PPI should be co-prescribed in high GI risk patients.

Table 29.2 Additional NSAIDs available for use [1, 8] [Level 4]				
Class of NSAID	**Name of drug**	**Oral dose**	**CSCI over 24 hours**	**Additional notes**
Non selective	Diclofenac sodium	50mg tds 75mg m/r bd	Painful. Dose 150mg daily	150mg daily via rectal route. Diclofenac is associated with similar thrombotic risk to COX-2 inhibitors.
	Nabumetone	500mg od-1g bd	n/a	Lowest GI risk of all non-selective NSAIDs. Some units may use first line.
	Ketorolac	n/a	30mg-90mg	Can give 10mg stat subcutaneous dose. Carries greater risk of renal and gastrointestinal toxicity compared to other NSAIDs. Due to the propensity for toxicity, the continued need for a CSCI of ketorolac should be reviewed on a weekly basis.
	Piroxicam melt	20mg od (sublingual)		Increased risk of GI toxicity and serious skin reactions. Not to be used for first line treatment.
COX- 2 selective	Etodolac	600mg m/r od		
COX-2 inhibitor	Etoricoxib	60mg-120mg od		NICE do not recommend etoricoxib for first line use in osteoarthritis. For this reason, consider as 2nd line choice.

Figure 29.1 – Flow Diagram of NSAID Choice [15] [Level 1]

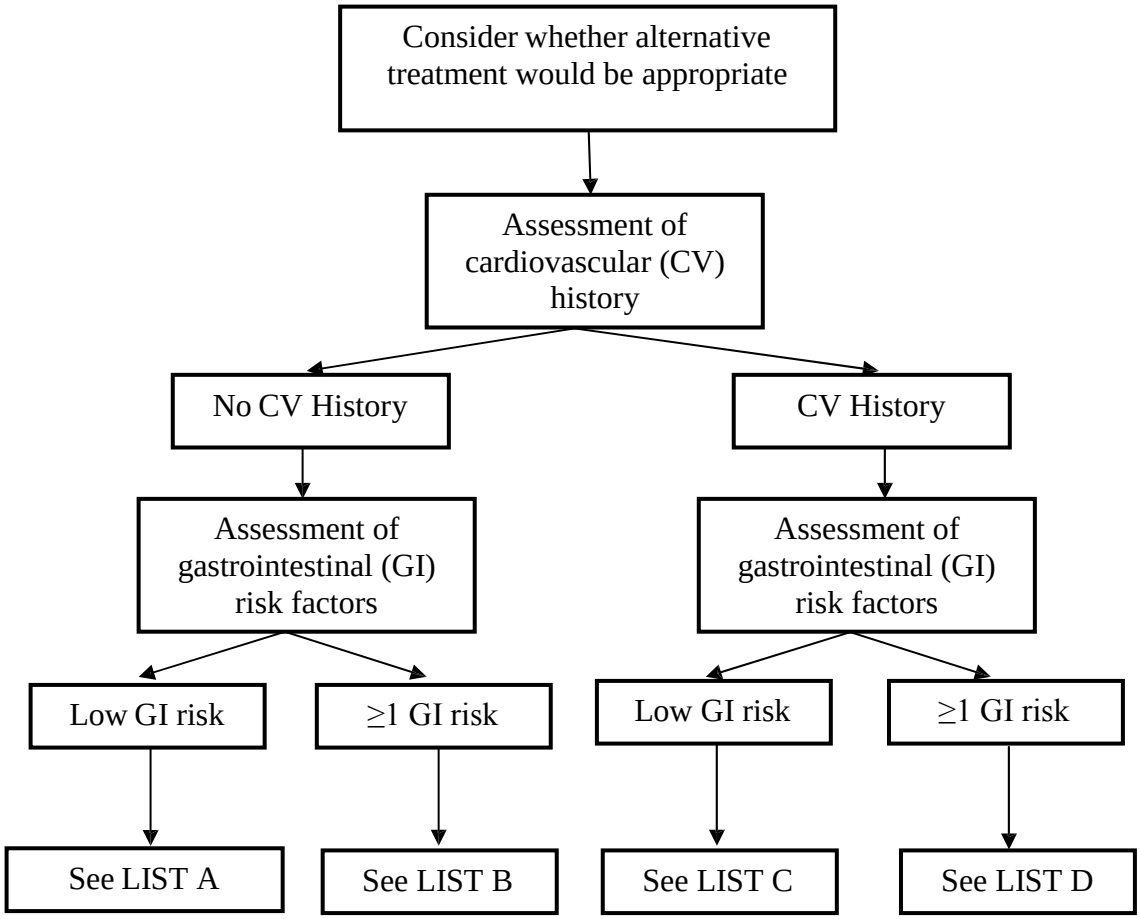

Table 29.3 Choice of NSAID available, according to cardiovascular history and gastrointestinal risk factors. [15] [Level 4]

Step	LIST A No CV history No GI risk	LIST B No CV history GI risk	LIST C CV history No GI risk	LIST D CV history GI risk
1	Alternative analgesia e.g. topical NSAID, paracetamol, tramadol.	Alternative analgesia e.g. topical NSAID, paracetamol, tramadol.	Alternative analgesia e.g. topical NSAID, paracetamol, tramadol.	Alternative analgesia e.g. topical NSAID, paracetamol, tramadol.
2	Low dose ibuprofen (≤1200mg/day) + PPI or nabumetone plus PPI	COX-2 Inhibitor e.g. celecoxib + PPI.	Low dose ibuprofen (≤1200mg/day) + PPI or naproxen +PPI	Low dose ibuprofen (≤1200mg/day) + PPI or naproxen +PPI
3	Non-selective NSAID e.g. diclofenac + PPI or naproxen +PPI	COX-2 Inhibitor e.g. etoricoxib + PPI.	Non selective NSAID e.g. nabumetone + PPI	Non selective NSAID e.g. nabumetone +PPI
4	COX-2 selective NSAID e.g. etodolac + PPI	Low dose ibuprofen (<1200mg/day) + PPI or nabumetone plus PPI		
5	COX-2 inhibitor e.g. celecoxib	COX-2 selective NSAID e.g. etodolac + PPI		

Note: Misoprostol can be considered as an alternative to a PPI

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30. GUIDELINES FOR STRONG OPIOID SUBSTITUITION IN PALLIATIVE CARE

30.1 GENERAL PRINCIPLES

* Morphine is the strong opioid of choice in palliative care. [1, 2]
* Options for opioid substitution include oxycodone, fentanyl, methadone, hydromorphone and alfentanil. [3]
* The intramuscular route for strong opioids is not recommended in palliative care patients. [1, 2]
* It is good practice to specify the brand when prescribing opioids e.g. Durogesic D-Trans,® MXL.® [24]

30.2 GUIDELINES

* Before considering opioid substitution, consider simple measures e.g.
  - Reduction in dose of strong opioid.
  - Use of appropriate rehydration.
  - Use of adjuvant medications to limit side effects e.g. haloperidol for hallucinations.
  - Checking for potential drug interactions.
  - Use of co-analgesics / interventional pain techniques appropriate to the pain syndrome. [1, 4, 5, 6, 7, 8] [Level 2+]
* Indications for choosing alternatives to morphine are as follows:
  - Intolerable neuropsychiatric side effects developing during continuous use (e.g. agitation, delirium, myoclonic jerks, hallucinations, hyperalgesia or allodynia), and which are unresponsive to simple measures such as dose reduction, or if the dose reduction leads to increased pain. [1, 4, 6, 7, 8] [Level 2+]
  - Dose-limiting side effects of morphine prohibit dose escalation, leading to inadequate pain relief. [1, 4, 5, 6, 9] [Level 2+]
  - In patients with malabsorption, dysphagia or poor compliance, substitution to a transdermal patch such as fentanyl should be considered, but **only** if analgesic requirements are **stable**. If pain is unstable, subcutaneous diamorphine / morphine are considered first line. [10, 11] [Level 2+]
  - For patients on morphine with moderate to severe constipation, despite adequate laxatives, substitution to transdermal fentanyl may be indicated. [10, 11] [Level 2+]
  - Patient acceptability. [10] [Level 4]
* Table 30.1A gives further details about possibilities for opioid substitution.

* Care should be taken when calculating conversion doses, as variation in bioavailability and genetically determined receptor affinities can influence drug effect. When switching opioids due to symptoms of opioid toxicity, even in the presence of uncontrolled pain, consider a dose reduction of 25-50% (to adjust for incomplete cross tolerance). [4, 6, 12, 13] [Level 3]

* Tables 30.2 A and 30.2 B feature equianalgesic tables for the strong opioids currently in common usage. Responsibility for prescribing the correct dose of a strong opioid remains with the prescriber.

30.3 STANDARDS

1. Morphine is the oral strong opioid of choice. [1, 2] [Grade C]
2. Morphine or diamorphine are the parenteral strong opioids of choice. [1, 2] [Grade C]
3. The reason for a change of opioid should be documented in the case notes. [27] [Grade D]
4. Transdermal fentanyl should only be used if analgesic requirements are stable. [1, 9] [Grade C]
5. The drug brand name should be used when prescribing strong opioids. [24] [Grade D]

Table 30.1A Options for Strong Opioid Substitution [1, 3, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 28]		[Levels of evidence in brackets]	
Name of strong opioid	**Indication**	**Formulations available**	**Notes**
Alfentanil	First choice parenteral opioid in renal impairment. (see *Guidelines for Analgesic Prescribing in Renal Failure*).	Alfentanil injection: - 500microgams / ml: 2ml, 10ml ampoules - 5mg/ml: 1 ml ampoules	Alfentanil has a relatively quick onset and short duration of action making it suitable for pain of short duration e.g. incident pain. Rescue doses are independent of background opioid requirements, so initial doses should start low and be titrated e.g. 0.5-1mg PRN. [Level 3]
Diamorphine hydrochloride	First line opioid for parenteral use (if available). Morphine is an alternative.	Tablets: 10mg Injection: 5mg, 10mg, 30mg, 100mg, 500mg ampoules	Highly soluble. May be used to reduce the volume in a CSCI.
Fentanyl (transdermal)	Patient has **stable pain** but: − unable to swallow / malabsorption. − moderate to severe constipation despite laxatives. − intolerable side effects with morphine. − for consideration in renal failure. [Level 2+]	Patch strength(all micrograms/hour) 12mcg (matrix type only), 25mcg, 50mcg, 75mcg, 100mcg/hour	Patch should be changed every 72 hours. It should be continued in the dying phase even if additional additional analgesia is required vi a CSCI. There are reservoir and matrix patches available. Patches should not be cut or divided. 12microgram patch appears not to be licensed as a starting dose therefore suggest should start with 25microgram and use 12microgram patch as part of titration regimen.
Fentanyl (transmucosal)	For breakthrough pain when background pain control is achieved and titration of opioid complete.	Lozenges (Actiq®) 200mcg, 400mcg, 600mcg, 800 mcg, 1.2mg, 1.6mg Buccal tablet (Effentora®) 100mcg, 200mcg, 400mcg, 600mcg, 800mcg Sublingual tablet (Abstral®) 100mcg, 200mcg 300mcg, 400mcg, 600mcg, 800mcg tablets Intranasal spray (Instanyl®) 50mcg, 100mcg, 200mcg	Starting dose should be lowest available dose irrespective of background analgesic use and adjusted according to the intensity of breakthrough pain and dose response. Consult individual drug SPC for further details. Note that Abstral® Effentora ®and Actiq® can not be prescribed by non- medical prescribers Abstral®/ Effentora® / Instanyl® / Actiq® **only to be used for patients on 60mg oral morphine daily (or equivalent).** [25, 26]
Hydromorphone	Intolerable side effects limiting dose escalation of morphine. [Level 1-]. Possible benefit in pruritis. [Level 2-] For consideration in renal failure (see *Guidelines for Analgesic Prescribing in Renal Failure*).	Hydromorphone IR (immediate release) capsules: 1.3mg or 2.6mg Hydromorphone SR (slow release) capsules: 2mg, 4mg, 8mg, 16mg, 24mg	Capsule form only. Parenteral preparation available on an individual basis and is currently unlicensed in the UK.

30.1A Options for Strong Opioid Substitution [1, 3, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 28]		[Levels of evidence in brackets]	
Name of strong opioid	**Indication**	**Formulations available**	**Notes**
Methadone	Partially opioid responsive pain especially neuropathic pain. Intolerable side effects limiting dose escalation of other strong opioids. Methadone should not be considered a first line alternative to morphine (see *Guidelines for Conversion from Strong Opioid to Methadone*).	Methadone tablets: 5mg Methadone solutions: 1mg/ml, 10mg/ml, 20mg/ml Methadone for injection 10mg/ml: 1ml, 2ml and 3.5ml ampoules NB: The 2mg/5ml linctus is only used for the management of intractable cough	Effects may be unpredictable. [Level 3] Dose titration should be carried out in a specialist unit following the established guidelines. [Level 4] No guidelines exist for conversion back to other strong opioids. [Level 3] Parenteral form should only be used with caution due to site reaction.
Morphine	First choice oral opioid. First choice parenteral opioid. Diamorphine is an alternative	Oramorph® solutions: 10mg/5ml or 20mg/ml or 100mg/5ml Sevredol® solutions 10mg/5ml or 100mg/5ml Sevredol® tablets: 10, 20, 50mg MXL® capsules: 30, 60, 90, 120, 150, 200mg MST® tablets: 5, 10, 15, 30, 60, 100, 200mg MST® sachets: 20, 30, 60, 100, 200mg Zomorph® capsules: 10, 30, 60, 100, 200mg Rectal preparations (immediate release) Morphine sulphate amps for injection:10mg/ml, 15mg/ml, 30mg/ml. 1ml or 2 ml ampoules	Avoid in patients with severe renal impairment i.e. (eGFR < 30ml/min). *See Guidelines for Analgesic Prescribing in Renal Failure.*
Oxycodone hydrochloride	Intolerable side effects limiting dose escalation of morphine. [Level 1+] For consideration in renal failure (see *Guidelines on Analgesic Prescribing in Renal Failure*).	Oxynorm® solutions: 5mg/5ml or 10mg/ml Oxynorm® capsules : 5, 10, 20mg Oxycontin® tablets: 5, 10, 20, 40, 80mg Oxycodone hydrochloride for injection: 10mg/ml: 1 ml or 2ml ampoules;50mg/ml ampoule	

Table 30.2A Equianalgesic Table for Strong Opioids [23] [Level 2]

These tables serve as a guide only. The prescriber is ultimately responsible for his/her own actions. Equianalgesic doses are difficult to ascertain due to wide inter-patient variations, drug interactions and non-interchangeability of products. Initial dose conversions should be conservative; it is preferable to under-dose the patient and use rescue medication for any shortfalls.

Morphine PO 4 hourly	Morphine SR PO BD	Morphine SR PO 24 hourly	Oxycodone PO 4 hourly	Oxycodone SR PO BD	Hydromorphone PO 4 hourly	Hydromorphone SR PO BD	Transdermal Fentanyl 72 hrly
2.5mg	10mg	-	1.25mg	5-10mg	-	-	-
5mg	15mg	30mg	2.5mg	10mg	1.3mg	2mg	12mcg
10mg	30mg	60mg	5mg	20mg	1.3 mg	4 mg	25 mcg
20mg	60mg	120mg	10-15mg	40mg	2.6 mg	8 mg	50 mcg
30mg	90mg	180mg	20mg	60mg	3.9 mg	12 mg	75 mcg
40mg	120mg	240mg	25mg	80mg	5.2 mg	16 mg	100 mcg
50mg	150mg	300mg	30-35mg	100mg	6.5 mg	20 mg	125 mcg
60mg	180mg	360mg	40mg	120mg	7.8 mg	24 mg	150 mcg
65-70mg	200mg	400mg	40-45mg	130mg	9.1 mg	28 mg	162–175 mcg
80mg	240mg	480mg	50-55mg	160mg	10.4 mg	32 mg	200 mcg
85-90mg	260mg	520mg	55mg	170mg	11.7 mg	36 mg	225 mcg
100mg	300mg	600mg	65mg	200mg	13 mg	40 mg	250 mcg
110mg	330mg	660mg	70-75mg	220mg	14.3 mg	44 mg	275 mcg
120mg	360mg	720mg	80mg	240mg	15.6 mg	48 mg	300 mcg
140mg	420mg	840mg	90-95mg	280mg	18.2 mg	56 mg	¥
160mg	480mg	960mg	105mg	320mg	20.8 mg	64 mg	¥
180mg	540mg	1080mg	120mg	360mg	23.4 mg	72 mg	¥

¥ Manufacturer recommends that above doses of 300 microgram/hour, alternative or additional methods of analgesia should be used

Due to the non-uniformity with equianalgesic ratios in the literature with oxycodone, use the table below to convert between routes

Oxycodone SR PO BD	Oxycodone SC PRN	Oxycodone CSCI in 24 hrs
5mg	2.5mg	5-10mg
10mg	2.5-5mg	10-15mg
20mg	5mg	25-30mg
40mg	10mg	50-55mg
60mg	15mg	80mg
80mg	20mg	105-110mg
100mg	20-25mg	130-135mg
120mg	25-30mg	160mg
130mg	30mg	170-175mg
160mg	35mg	210-215mg
170mg	40mg	225-230mg
200mg	45mg	265-270mg
220mg	50mg	290-295mg
240mg	55mg	320mg
280mg	60mg	370-375mg
320mg	70mg	425-430mg
360mg	80mg	480mg

General Guidance

- **Prescribe *all* strong opioid preparations by brand where applicable to ensure continuity of therapy.**
- Leave transdermal patches *in situ* when the patient can no longer tolerate oral medication and use subcutaneous injections to deliver breakthrough medication and a syringe driver to deliver the increasing analgesia requirements.
- Doses shown here are approximated to the most practical, based on current formulations.
- The tables have been generated using values based on expert consensus which may differ from manufacturers' recommendations:-
  - Oral *morphine* 3mg = oral *oxycodone* 2mg (oxycodone is more potent than morphine when given by mouth; NB – manufacturer states 2:1).
  - Oral *morphine* 3mg = parenteral *morphine* 1.5mg = parenteral *diamorphine* 1mg.
  - Oral *oxycodone* 3mg = parenteral *oxycodone* 2mg (manufacturer states 2:1).
  - Parenteral *morphine* 1.5mg = parenteral *oxycodone* 1.5mg = parenteral *diamorphine* 1mg (morphine and oxycodone are considered equivalent when given parenterally).

Table 30.2B Equianalgesic Table for Strong Opioids [23] [Level 2]

These tables serve as a guide only. The prescriber is ultimately responsible for his/her own actions. Equianalgesic doses are difficult to ascertain due to wide inter-patient variations, drug interactions and non-interchangeability of products. Initial dose conversions should be conservative; it is preferable to under-dose the patient and use rescue medication for any shortfalls.

Morphine SC PRN	Morphine CSCI in 24hrs	Diamorphine SC 4hrly	Diamorphine CSCI in 24hrs	Alfentanil SC PRN	Alfentanil CSCI in 24hrs	Oxycodone SC PRN	Oxycodone CSCI in 24 hrs
2.5mg	10mg	2.5mg	5-10 mg	0.25mg	0.5-1mg	2.5mg	10mg
2.5mg	15mg	2.5mg	10 mg	0.25mg	1mg	2.5mg	15mg
5mg	30mg	5mg	20 mg	0.5mg	2mg	5mg	30mg
10mg	60mg	5-10mg	40 mg	0.5-1mg	4mg	10mg	60mg
15mg	90mg	10mg	60 mg	1mg	6mg	15mg	90mg
20mg	120mg	15mg	80 mg	1.5mg	8mg	20mg	120mg
25mg	150mg	15-20mg	100 mg	1.5-2mg	10mg	25mg	150mg
30mg	180mg	20mg	120 mg	2mg	12mg	30mg	180mg
30-35mg	200mg	20mg	130 mg	2mg	13mg	30-35mg	200mg
40mg	240mg	25-30mg	160 mg	2-3mg	16mg	40mg	240mg
40-45mg	260mg	25-30mg	170 mg	3mg	17mg	40-45mg	260mg
50mg	300mg	30-35mg	200 mg	3-3.5mg	20mg	50mg	300mg
55mg	330mg	35-40mg	220 mg	3.5-4mg	22mg	55mg	330mg
60mg	360mg	40mg	240 mg	4mg	24mg	60mg	360mg
70mg	420mg	45-50mg	280 mg	4.5-5mg	28mg	70mg	420mg
80mg	480mg	50-55mg	320 mg	5.5mg	32mg	80mg	480mg
90mg	540mg	60mg	360mg	6mg	36mg	90mg	540mg

Transtec® Patch 96 hourly	Morphine PO 4 hourly	Morphine SR PO BD	BuTrans® Patch weekly
-	2.5-5mg	10-20mg	10 mcg
-	5-10mg	20-30mg	20mcg
35 mcg	10-15mg	30-50mg	-
52.5 mcg	15-25mg	50-75mg	-
70 mcg	20-30mg	60-100mg	-
105 mcg	30-50mg	100-150mg	-
140 mcg (max)	40-60mg	120-190mg	-
Buprenorphine equianalgesia with PO morphine varies in the literature from 75:1 to 115:1. The values in the table reflect this.			

General Guidance

- **Prescribe *all* strong opioid preparations by brand where applicable to ensure continuity of therapy.**
- Leave transdermal patches *in situ* when the patient can no longer tolerate oral medication and use subcutaneous injections to deliver breakthrough medication and a syringe driver to deliver the increasing analgesia requirements.
- Doses shown here are approximated to the most practical, based on current formulations.
- The tables have been generated using values based on expert consensus which may differ from manufacturers' recommendations:-
  - Oral *morphine* 3mg = oral *oxycodone* 2mg (oxycodone is more potent than morphine when given by mouth; NB – manufacturer states 2:1).
  - Oral *morphine* 3mg = parenteral *morphine* 1.5mg = parenteral *diamorphine* 1mg.
  - Oral *oxycodone* 3mg = parenteral *oxycodone* 2mg (manufacturer states 2:1).
  - Parenteral *morphine* 1.5mg = parenteral *oxycodone* 1.5mg = parenteral *diamorphine* 1mg (morphine and oxycodone are considered equivalent when given parenterally).

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31. GUIDELINES FOR ORAL CARE IN ADVANCED CANCER

31.1 GENERAL PRINCIPLES

* A healthy mouth is highly relevant to the care of all patients in terms of quality of life. In patients with cancer, the maintenance of oral health is integral to care. [1]
* Patients with advanced cancer are at high risk of developing oral problems. These may have a great physical, psychological and social impact on their quality of life. [2]
* A patient information leaflet is a useful aid when giving advice on oral care.

31.2 GUIDELINES

31.2.1 Basic oral care

* Good oral hygiene is essential in the prophylaxis and treatment of oral conditions. All patients should have an oral assessment at initial consultation. [3] [Level 4]
* Risk factors for oral problems (see Table 31.1) should be identified and documented in the case notes.[1] [Level 4]
* A good light source, tongue depressor and gloves should be used when examining the mouth. [1] [Level 4]
* Basic oral care includes assessment; cleaning of natural teeth / dentures; maintenance of oral hydration and cleaning of the oral mucosa with either a soft or electric toothbrush. Natural teeth and the tongue should be brushed twice daily using fluoride toothpaste and a small-headed soft toothbrush. [4] [Level 4]
* Dentures should be cleaned prior to each insertion and after every meal. They should be removed at night and soaked in a proprietary cleaner. Dentures should be cleaned with fluoride toothpaste using a small-headed soft toothbrush. [1] [Level 4]
* In-patients should have their oral mucosa cleaned on a daily basis using gauze or foam sticks. Antiseptic mouthwashes may also be used twice daily. [2] [Level 4]
* Oral hydration may be maintained using water, saliva stimulants or saliva substitutes. [3] [Level 4]

Table 31.1 Risk factors for oral problems in patients with advanced cancer [1] [Level 4]

Alcohol	Mouth breathing
Concurrent disease	Old or misfitting dentures
Debility (anorexia, malnutrition, poor oral intake)	Oxygen delivery via a mask
Iatrogenic e.g. drugs, head and neck radiotherapy, chemotherapy	Smoking
Malignant disease e.g. local / distant	Sugary dietary supplements
	Reduction in conscious level / dying phase

31.2.2 Xerostomia

* Xerostomia is a subjective sensation of oral dryness. [5] [Level 3]
* All patients should be asked about the presence of a dry mouth as part of their initial assessment. [6] [Level 4]
* The majority of palliative care patients complain of xerostomia. If present, it is important to ask whether a patient is also suffering from oral discomfort, altered taste, difficulty swallowing or difficulty speaking. [5] [Level 3]
* The mouth should be examined for buccal and mucosal dryness and inspected for the presence of candida, ulceration and erythema. [3] [Level 4]
* The most commonly used drugs known to cause xerostomia are listed in Table 31.2. [5] [Level 4]
* Treatment should be based on the minimisation of risk factors and the maintenance of excellent oral hygiene. [5] [Level 3]
* Patient preference for the different treatment options should be taken into consideration to improve compliance. [6] [Level 4]
* Table 31.3 lists various management options for xerostomia. It is important to try various options in a structured and systematic way in order to ascertain which is the most effective / suitable for an individual patient. [5] [Level 3]
* If there is residual production of saliva, a saliva stimulant should be used (see Table 31.3). [7] [Level 2]
* Carboxymethylcellulose based products such as Glandosane® are acidic and should be avoided in dentate patients. Saliva Orthana® is a porcine gastric mucin spray. It may therefore not be suitable for patients from certain cultural backgrounds. [7] [Level 2]

Table 31.2 Drugs which may cause xerostomia [5] [Level 4]

Anticholinergics	Diuretics
Antidepressants	NSAIDs
Antipsychotics	Opioids
Benzodiazepines	Oxygen
Beta blockers	Proton pump inhibitors
Corticosteroids	

Table 31.3 Treatment options for xerostomia [5] [Level 3]		
Agent	**Dose / Administration**	**Comments**
General		
Water [6] [Level 4]	As required.	No limit to use; preference of many patients.
Ice chips [6] [Level 4]	As required.	May ease a painful mouth. Risk of mucosal soreness in head and neck malignancies.
Vaseline [6] [Level 4]	Apply sparingly to lips.	Do not use with oxygen.
Saliva Stimulants		
Chewing gum [8] [Level 2]	Sugar free gum. Use as required.	Often well tolerated. Marked increase in salivary flow.
Pilocarpine [7, 11] [Level 2]	5mg tablets tds orally **or** 3 -5 drops of 2% eye-drops in water as a mouthwash bd-tds.	Can cause cholinergic side effects. Poorly tolerated at higher doses.
Bethanechol [21][Level 4]	10mgs tds orally with meals increasing to 25mgs tds after 48 hours if response poor.	Similar side effect profile to pilocarpine, but less severe.
Acupuncture [9, 10] [Level 3]	Twice weekly for at least five weeks.	Mechanism unclear.
Saliva substitutes		
Carboxymethyl-cellulose e.g. Glandosane® [7][Level 2]	As required.	Avoid in dentate patients as acidic. Short-acting.
Mucin-based, e.g. Saliva Orthana® [7] [Level 2]	As required.	Short-acting. Contains fluoride.
Others		
Biotene® and Oral Balance® products [11] [Level 3]	As required. Gel, mouthwash, chewing gum.	Standard toothpaste renders ineffective, therefore do not use at the same time.
Gelclair® [11] [Level 3]	Use before meals. Give other topical therapies prior to Gelclair as it forms a barrier.	Particularly useful in oral ulceration and mucositis.
Xerotin® [Level 4]	Spray	pH neutral No animal derivatives

31.2.3 Oral candidosis

* Oral yeast carriage is common in patients with advanced cancer. [13] [Level 4]
* Predisposing factors for oral candidosis include advanced disease, immunosuppressive medication, antibiotics, dry mouth and continuous wearing of dentures. [13] [Level 4]
* Candidosis may cause significant symptoms such as altered taste, sore mouth, hoarse voice and difficulties with eating, chewing and swallowing. [13] [Level 4]
* Candidal infection can present in a variety of ways. Table 31.4 gives a clinical classification. Oral swabs may clarify an atypical presentation. [13, 14] [Level 3]
* Good oral hygiene is essential to minimise the risk of oral candidosis. [3] [Level 4]
* Inpatients should be re-examined on a daily basis. [4] [Level 4]
* Prophylactic antifungal medication should be avoided to minimise the risk of resistance developing. [15] [Level 3]
* When treating candidosis, a short course of an appropriate dose of antifungal medication should be used. It may be necessary to use repeated courses. [15] [Level 3]
* The use of nystatin and chlorhexidine-containing mouthwashes should be separated by one hour to guarantee effectiveness of the two drugs. [2] [Level 4]
* Medications commonly used for the treatment of oral candidosis are listed in Table 31.5. [16, 17] [Level 4]

Table 31.4 Clinical classification of oral candidosis [13] [Level 4]

Classification	Appearance	Comments
Pseudomembranous	White membranes that scrape off	Classical appearance
Erythematous	Red raw appearance	Often denture related
Hyperplastic	Raised red and white patches	Candidal leukoplakia
Angular cheilitis	Sore corners of mouth (cracked / red)	Often combined with bacterial infection especially staphylococcal

31.2.4 Stomatitis

* Stomatitis may be defined as diffuse inflammatory, erosive or ulcerative conditions that affect the mucous membranes of the mouth. [18] [Level 3]
* Causes of stomatitis include: dry mouth; medications such as corticosteroids or antibiotics; infections such as candida or bacteria; mucositis due to radiotherapy or chemotherapy; malnutrition caused by hypovitaminosis or protein deficiency. [3] [Level 4]
* Good oral hygiene is essential in the prophylaxis and treatment of stomatitis. [18] [Level 4]
* There are no universally accepted treatment protocols for the management of stomatitis. [18] [Level 4]
* At clinical assessment, the stomatitis should be graded using the World Health Organisation (WHO) scale (see Table 31.6). [19] [Level 4]
* Spicy foods, alcohol and smoking should be avoided. [18] [Level 4]

Table 31.5 Commonly used anti-candidal medications [16, 17] [Level 4]			
Name	**Preparation**	**Dose**	**Comment**
Nystatin (Nystan®)	Oral suspension	100,000 units (1ml) qds usually for 7 days. Continue for at least 48 hours after lesions resolved.	After food. Beware resistance.
Nystatin (Nystan®)	Pastilles	100,000 units (1 pastille) qds usually for 7 days. Continued for at least 48 hours after lesions resolved.	After food. Avoid concurrent use with chlorhexidine or separate administration by at least one hour. Beware resistance.
Fluconazole (Diflucan®)	Capsules	50mg-100mg od for 7 to 14 days.	Watch for significant drug interactions.
Fluconazole (Diflucan®)	Oral suspension 50mg/5ml	50mg-100mg od for 7 to 14 days.	Watch for significant drug interactions.
Amphotericin (Fungilin®)	Lozenges	10mg qds for 10-14 days or at least until 48 hours after lesions resolved.	After food.
Itraconazole (Sporanox®)	Capsules	100mg od for 7 to 14 days.	Watch for significant drug interactions.
Itraconazole (Sporanox®)	Oral liquid 10mg/ml	10ml od for 7 to 14 days.	After food. Watch for significant drug interactions.
Miconazole (Daktarin®)	Gel 24mg/ml	5ml-10ml qds. Continued for 48 hours after lesions resolved.	After food. Watch for significant drug interactions.

* Concurrent infections such as candidosis or bacterial infections should be treated.[13] [Level 3]
* Systemic analgesia should be optimised. This may include NSAIDs and strong opioids. In severe cases, it may be necessary to administer medication via the parenteral route. [18] [Level 4]
* Topical pharmacological options for the treatment of stomatitis are listed in Table 31.7. [20] [Level 4]

Table 31.6 WHO Stomatitis Scale [19] [Level 4]	
Grade	**Clinical Features**
0	None.
1	Soreness + /- erythema.
2	Erythema and ulcers. Able to eat solid food.
3	Ulcers with extensive erythema. Unable to swallow solid food. Liquid diet only.
4	Oral intake not possible.

31.3 STANDARDS

1. All patients should have an oral assessment at the initial consultation. This should include examining for the presence of xerostomia, candidosis and stomatitis. [3] [Grade D]
2. All inpatients should receive basic oral care on a daily basis.[3] [Grade D]
3. All natural teeth should be cleaned twice daily. [4] [Grade D]
4. Dentures should be cleaned prior to each insertion, after every meal and after removal at night. [1] [Grade D]
5. Patients with xerostomia should receive a saliva stimulant if there is residual saliva production present. [7] [Grade D]
6. Patients with oral candidosis should receive an adequate course of antifungal medication where clinically appropriate.[15] [Grade D]
7. If oral candidosis is present, dentures should be removed and treated separately. [14] [Grade D]
8. All patients should be re-assessed at the end of a treatment course. [3] [Grade D]

Table 31.7 Management options for stomatitis [20] [Level 4]			
Name	**Preparation**	**Dose / usage**	**Comments**
Mouth washes			
Benzdyamine 0.15% (Difflam®)	Oral rinse	15ml as required 1.5-3 hourly for up to 7 days.	Good for pain. If full strength, mouthwash may sting so can dilute with water.
Chlorhexidine gluconate 0.2% (Corsodyl®)	Mouthwash	10ml held in mouth for one minute twice a day. Spit out after use.	Useful in management of multiple apthous ulcers. Chronic use may cause brown staining of teeth. Avoid concurrent use with nystatin or separate administration by at least one hour
Morphine Sulphate liquid	10mg/5ml solution	5ml every four hours.	Use as mouthwash then swallow. OxyNorm® liquid is alcohol free and may be preferred.
Sucralfate	1g/5ml suspension	5ml qds.	Is beneficial in less severe stomatitis. Should be swallowed.
Pastes / Gels			
Carmellose sodium (Orabase®, Adcortyl in Orabase®, Orahesive®)	Protective paste / powder	Apply to sore area in thin layers after meals and as required.	Adcortyl contains a corticosteroid.
Choline salicylate (Bonjela®)	Oral gel	Apply to affected area, up to 3 hourly.	
Gelclair®	Oral gel	Apply to affected areas as required.	Use prior to meals. Apply other topical therapies prior to using Gelclair as it will form a barrier.
Lidocaine gel 2% (Instillagel®)	Gel	Apply to affected area as required.	Local anaesthetic. Should not be swallowed.
Morphine Sulphate ampoules	Injectable form	This may be added to an oral gel and used topically as required.	
Mu Gard®	Mucoadhesive oral rinse	Prevention and treatment of mucositis	
Pastilles/Lozenges			
Flurbiprofen	Lozenge	8.75mg up to 4 hourly as required.	Useful for sore throat.
Hydrocortisone (Corlan®)	Pellets	2.5mg qds applied locally to ulcers.	Useful for recurrent attacks of apthous ulcers.

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32. GUIDELINES FOR THE PREVENTION OF PATHOLOGICAL FRACTURES IN PALLIATIVE CARE

THIS GUIDELINE HAS BEEN UPDATED
PLEASE SEE A-Z SECTION FOR UPDATED GUIDELINE

32.1 GENERAL PRINCIPLES

* Bone is one of the commonest sites of metastatic disease. The most likely primary tumours to spread to bone are breast, bronchus, kidney, thyroid and prostate. The axial skeleton (skull, ribs, spine and pelvis) is more likely to develop metastatic disease than the appendicular skeleton. [1]
* Bone metastases may be described as osteolytic, osteoblastic or mixed in nature. [2]
* The major associated morbidities of bone metastases include pain (the most common symptom occurring in 70% of patients), pathological fractures (occurring in 8-30% of patients) and hypercalcaemia. [2, 3]
* Bone pain may be due to structural damage, periosteal irritation, nerve entrapment or secretion of chemical mediators causing osteolysis e.g. prostaglandins and cytokines. These mediators activate both osteoclasts and nociceptors. [2]
* The most frequent clinical symptoms of bone metastases includes pain. This may be described as a dull ache to a deep intense pain; pain at rest; pain exacerbated by weight bearing and importantly, pain which is worse at night. [2] Patients should be encouraged to report skeletal symptoms promptly. [4]
* Advances in hormonal treatments, use of bisphosphonates and chemotherapy treatments have meant that the prognosis of patients with bone metastases, without visceral metastatic disease, has greatly improved. [4]
* Clinical features of impending pathological fracture include pain on movement, persistent pain and increasing pain. Pain in an area which has already been treated with radiotherapy, but has not responded, may also be considered as a clinical indicator of possible impending fracture. [6, 7]
* Prediction of pathological fractures before the event is a relevant clinical problem. Prophylactic fixation of long bone metastases is generally easier for the surgeon and less traumatic for the patient. Therefore, prophylactic fixation of long bones prior to radiotherapy should be considered. Stabilisation of impending pathological fractures is likely to result in shorter hospital stays, with patients more likely to be discharged to their own homes. [8]
* Radiotherapy has a major role in the treatment of bone metastases. 70% of patients will achieve pain relief with palliative external beam radiotherapy. It may also prevent additional bone destruction, help to maintain function, prevent neurological compromise and maintain quality of life. [5]
* The prevention and management of pathological fractures should be within the context of a multi-disciplinary team. [4, 9]

32.2 GUIDELINES

32.2.1 Investigation of bone pain

* Reports of bone pain should be investigated following the British Association of Surgical Oncology (BASO) Guidelines (see Table 32.1). [9] [Level 4]

Table 32.1 BASO guidelines for the investigation of bone pain [9] [Level 4]

Level of clinical suspicion of metastatic disease	Clinical features	Action
Minimal	Known cause for pain. Resolves well usually 2-3 weeks from onset.	Normal outpatient review. Return to GP if resolution not complete.
Low	Probable cause known. Good resolution over 4-6 weeks.	Plain radiograph. If negative: no action. If positive: follow advice regarding the need for orthopaedic assessment.
Moderate	No clear cause for pain which is persistent but not progressive.	Plain radiographs, serum calcium and bone scan within 10 working days. Review one week later. If all negative, review in 8 weeks if symptomatic. If one or more tests positive, follow advice regarding the need for orthopaedic assessment.
High	No identified cause for pain. Night pain, severe and / or progressive pain. Neurological symptoms and signs.	Plain radiographs, serum calcium and bone scan within 10 working days. Review one week later. If all negative but suspicion high, review in 1 week (appendicular skeleton). If pain in spine, then arrange MRI. If one or more tests positive, then follow advice regarding need for orthopaedic assessment.

* Plain radiographs should be of the entire bone, including the joint above and below the site of pain. Specific radiographs should be centralised over the painful area in an AP and lateral view. [4] [Level 4]

* Areas of increased uptake in any long bones on an isotope bone scan should be followed up by plain radiographs of the whole bone in two planes at 90° to each other, to assess for size and cortical involvement. [9] [Level 4]

* Any plain radiograph report that details the presence of a lytic lesion in a long bone should be questioned regarding its size and degree of cortical involvement, if not already stated. [6, 7, 9] [Level 4]

* Patients with symptomatic bone metastases should be referred urgently to an orthopaedic clinic or be discussed at a site-specific multidisciplinary team meeting if they have any of the following:
  - Structurally significant bone destruction.
  - Uncertainty whether the destruction is significant.
  - Pain of sudden onset (or change in character) that is exacerbated by movement. [9] [Level 4]

32.2.2 Prediction of pathological fracture

* The risk of a pathological fracture occurring, and therefore the need to consider prophylactic fixation, may be assessed using either Mirels scoring system or Hartington's classic definitions. These are detailed below (see Table 32.2). [6] [Level 2-]
* The maximum possible score is 12. If a lesion scores 8 or above, then prophylactic fixation is recommended ***prior*** to radiotherapy.

Table 32.2 Mirels scoring system for the prediction of pathological fractures [6] [Level 2-]

Score **Clinical features**	**1**	**2**	**3**
Site	Upper limb	Lower limb	Peritrochanteric
Pain severity	Mild	Moderate	Functional
Type of lesion	Blastic	Mixed	Lytic
Size (Maximum destruction of cortex in any view as seen on plain x-ray)	<1/3	1/3-2/3	>2/3

* Any one of Harrington's classic definitions indicates a high risk of pathological fracture (see Table 32.3). [7] [Level 3].

Table 32.3 Harrington's classic definitions. Risk of a pathological fracture [7] [Level 3]

1. ≥ 50% of circumferential cortical bone has been destroyed.
2. Where pain with weight bearing stresses persists, increases or recurs, despite adequate local irradiation.
3. Lesions in the proximal femur in excess of 2.5cm in any dimension.
4. Lesions in the proximal femur associated with avulsion of the lesser trochanter.

32.2.3 Role of orthopaedic surgeon

* A lead orthopaedic surgeon for appendicular metastatic bone disease should be identified in each local NHS trust. [4] [Level 4]
* Referral to an orthopaedic surgeon is appropriate in the following situations:
  - Prophylactic fixation of metastatic deposits when there is a high risk of fracture i.e.
  - Mirels score equal or greater than 8 (see Table 32.2).
  - Presence of any one of Harrington's classic definitions (see Table 32.3).
  - Stabilisation or reconstruction after pathological fracture.
  - Decompression of the spinal cord and nerve roots and / or stabilisation for spinal instability. [4] [Level 4]

32.2.4 Radiotherapy

* Following nailing of a bone, radiotherapy should be considered by appropriate specialists within the context of the multidisciplinary team. [4, 10, 11] [Level 2-]

32.2.5 Other treatment modalities

* Bisphosphonates should be considered, where clinically appropriate, for the prevention of skeletal related events and treatment of malignant bone pain in patients with bone metastases from breast cancer or hormone refractory prostate cancer, and also patients with multiple myeloma.[12] [Level 1+] Decisions to treat should be based on an assessment of their general medical condition and expected survival time (see *Guidelines on the Use of Bisphosphonates in the Management of Malignant Bone Disease*). [13] [Level 4].
* Radiofrequency ablation of bone metastases is an emerging alternative therapy for the management of bony metastatic disease. Referral to an appropriate specialist may be beneficial for effective pain palliation and local control of disease. [14] [Level 3]
* Percutaneous cementoplasty is indicated for patients with painful vertebral metastases. It is a minimally invasive technique involving injection of polymethylmethacrylate to strengthen a vertebra. It may provide fast pain relief for patients when traditional surgical options are considered to be too invasive. [15, 16] [Level 3]

32.3 STANDARDS

1. Reports of bone pain should be promptly and appropriately investigated following British Association of Surgical Oncology (BASO) Guidelines. [9] [Grade D]
2. Patients presenting with a lesion due to metastatic bone disease must be discussed with an oncologist for consideration of further therapy (e.g. hormonal manipulation, bisphosphonates, chemotherapy, radiotherapy) regardless of orthopaedic intervention. [9] [Grade C]
3. If there is evidence of significant risk of a pathological fracture, orthopaedic review should be urgently sought and the patient seen within one week. [4, 9] [Grade D]
4. When a fracture is likely to occur, prophylactic fixation, appropriate to the site of the lesion, should be performed prior to treatment with radiotherapy. [6] [Grade D]
5. Following any orthopaedic intervention (prophylactic stabilisation or fracture management) a patient must be discussed with an oncologist regarding the possibility of further therapy. [9] [Grade D]

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33. GUIDELINES FOR THE MANAGEMENT OF PLEURAL EFFUSIONS IN ADVANCED CANCER

PLEASE REFER TO BTS NATIONAL GUIDANCE
SEE A-Z LIST ON WEBSITE FOR LINK

33.1 GENERAL PRINCIPLES

* Pleural effusions can occur in all types of advanced cancer, but approximately 65% of all malignant effusions are related to carcinoma of the lung and breast. [1]
* The aetiology of the process in malignant effusions may be mixed, but usually involves the direct effect of the cancer on the pleura resulting in reduced pleural fluid outflow, lymphatic obstruction and increased vascular permeability.[2]
* The presenting symptoms of a patient who suffers from a pleural effusion may be dyspnoea, cough or chest pain. A pleural effusion may be found incidentally during examination or investigation. [1, 2]
* Pleural effusions may have a malignant or non-malignant cause. The management of the patient should be determined by the symptoms and performance status of the patient. Pleural aspiration may not be the most appropriate management option. [3]
* The median survival of a patient who suffers from a malignant pleural effusion is 3-12 months. Patients with lung cancer generally have the shortest prognosis. [1]

Table 33.1 Common causes of pleural effusions [3]

Malignant	**Non Malignant**		
Breast carcinoma Lung carcinoma Lymphoma Ovarian carcinoma	Cardiac Failure Connective Tissue Disorders Hypoproteinaemia Liver Failure	Nephrotic Syndrome Pancreatitis Pneumonia Post Myocardial Infarction	Pulmonary Embolus Rheumatoid Arthritis Systemic Lupus Erythematous Tuberculosis Uraemia

33.2 GUIDELINES

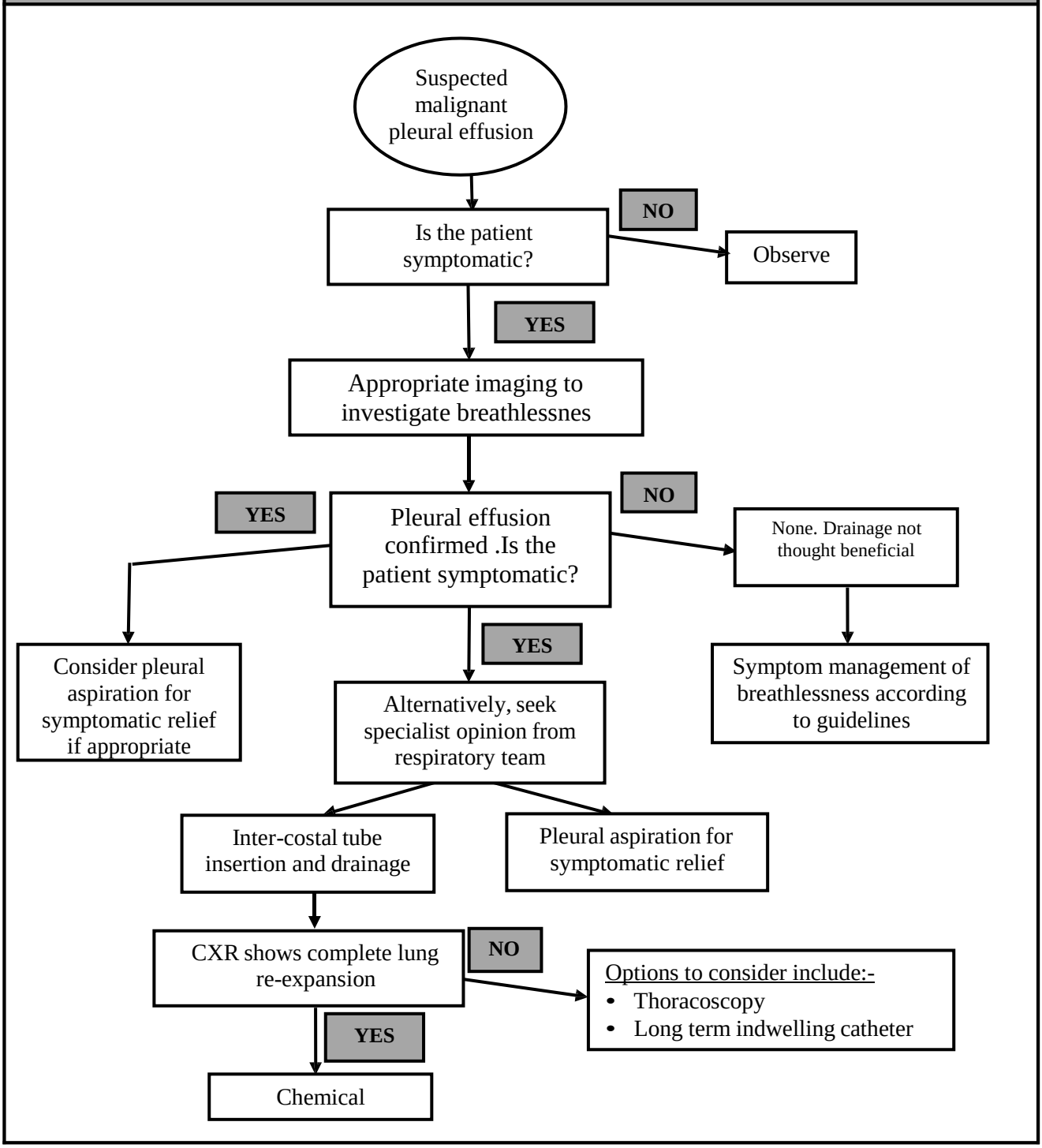
* Figure 33.1 is an algorithm outlining the suggested management of a malignant pleural effusion in palliative care.
* Patients with symptomatic malignant pleural effusions should ideally have therapeutic intervention, if appropriate, within 48 hrs. [4][Level 4]
* For pleural aspirations, the maximum volume drained at a single aspiration should be 1500ml. [5, 6] [Level 4]
* Post aspiration chest x-ray (CXR) is indicated if air is aspirated or increased breathlessness occurs post-procedure. [4] [Level 4]
* Aspiration of simple pleural effusions may be considered in the hospice setting, depending on local unit guidelines / protocols. [4] [Level 4]

* Patients with proven or suspected mesothelioma should be discussed with the oncologist regarding radiotherapy to the pleural aspiration / drain site, as this may prevent malignant seeding. The benefit of radiotherapy will be dependent on prognosis and / or performance status. If the prognosis is < 3months or the performance status is > 2, then radiotherapy may be of limited benefit. [7, 8] [Level 3]

* The specialist respiratory team should be consulted regarding management of recurrent symptomatic pleural effusions. [1] [Level 4]

* Dyspnoea should be managed according to guidelines for the management of breathlessness (see *Guidelines on the Management of Intractable Breathlessness*). [4] [Level 4]

Figure 33.1 Algorithm for suggested management of malignant pleural effusions in palliative care [Level 4] Adapted from Antunes et al.[1]



33.3 STANDARDS

1. Individual units should have a policy regarding performing pleural aspiration in the hospice setting. [4] [Grade D]
2. Appropriate imaging should be performed before the first interventional procedure. [1] [Grade D]

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34. GUIDELINES FOR THE MANAGEMENT OF PRURITUS IN PALLIATIVE CARE

34.1 GENERAL PRINCIPLES

* Pruritus may be defined as: "an intense cutaneous discomfort occurring with pathological change in the skin or body and eliciting vigorous scratching". [1]
* Mild to moderate pruritus is a common problem which increases with age in the general population. [2]
* Pruritus in the absence of skin disease may have a systemic cause. Diagnosis of a systemic cause is made by the history, clinical examination and use of appropriate investigations. [1]
* Pruritus is distressing for patients and a challenge for clinicians to manage effectively. It is incompletely understood and is difficult to treat in many circumstances. [1, 2, 3]
* Pruritus may be primary or secondary. Table 34.1 lists the causes of pruritus. [4] In advanced malignancy, cholestatic jaundice is probably the most frequent cause.

Table 34.1 Causes of pruritus [4]

Idiopathic	Skin diseases associated with pruritus	Systemic diseases associated with pruritus
Often limited in extent This is a diagnosis of exclusion	Asteatosis (dry skin) Dermatitis / eczema Dermatitis herpetiformis Folliculitis Lichen planus Pruritus ani and vulvae Psoriasis Scabies Urticaria	Biliary and hepatic disease Haematological disorders e.g. lymphoma Infectious diseases e.g. HIV Iron deficiency Malignancy Medications e.g.opioids Neurological diseases Thyroid disease Uraemia

* Drugs used to treat pruritus should be selected according to the underlying mechanism causing the pruritus. There is no broad spectrum anti-pruritic agent. Antihistamines are not effective in treating chronic pruritus as histamine is not the causative agent. Any benefit in non-histamine mediated itch is associated with the sedative effect of the drug. [1]
* Low sedative H_1 antihistamines are indicated in histamine-mediated itch.[1] This includes insect bite reactions, drug rashes, most forms of urticaria and cutaneous mastocytosis.

* Iron deficiency, with or without anaemia may cause pruritus. This can respond to iron therapy which should be continued until iron stores are replaced. [2] Serum iron is the most reliable investigation as haemoglobin levels are poor indicators of iron deficiency.

* Serotonin is thought to produce itch by both peripheral and central mechanisms. The central mechanism is thought to involve the opioid neurotransmitter system. [1] These theories provide the rationale for the use of opioid antagonists or selective serotonin reuptake inhibitors (SSRIs) in certain types of pruritus. [5]

34.2 GUIDELINES

* Skin disorders should be diagnosed and treated appropriately. [2] [Level 4]

* It is important to exclude drugs as a cause of pruritus. [2] [Level 4]

* Table 34.2 illustrates a step approach to the management of pruritus. Emollients should be used as a soap substitute and as a moisturiser. Calamine lotion should be avoided as it is extremely drying and can exacerbate pruritus, especially in the elderly or those with dry skin. [1] [Level 4]

Table 34.2 Management of pruritus [1] [Level 4]	
Step 1	Treat underlying cause if possible
Step 2	Use general measures (see Table 34.3)
Step 3	Consider topical agents (see Table 34.4)
Step 4	Consider drug treatments (see Table 34.5)

* The effectiveness of any treatment should be reviewed on a regular basis. [2] [Level 4]

* Failure of one treatment should lead to the selection of an alternative anti-pruritic agent appropriate to the cause. [2] [Level 4]

Table 34.3 General measures used in the management of pruritus [1] [Level 4]	
Avoid alcohol / spicy foods	Tepid showers
Avoid vigorous scratching	Use an emollient as soap substitute and a moisturiser
Keep nails short	Ultraviolet phototherapy. e.g. uraemia / AIDS / malignant skin infiltrations

Table 34.4 Topical agents used in the management of pruritus [1, 6] [Level 4]		
Topical agent	**Dose**	**Comments**
Emollient e.g. Oilatum®	Use as required	Soap substitute and moisturiser.
Lauromacrogols - bath oil - cream	Use as required.	Available as Balneum® Plus. Specific anti-pruritic agent useful for dry itchy skin or dermatoses.
Menthol	Add to aqueous cream to make a 1-2% compound. Apply several times daily.	Acts as skin cooling agent.
Corticosteroids (topical)	Apply sparingly.	Useful in dermatitis / eczema. Short term use recommended.
Doxepin cream 5%	Apply bd-qds.	May cause transient stinging and drowsiness. Limit to small localized areas of dermatitis.
Local anaesthetics - Lidocaine - Benzocaine	Apply as required (see comments).	Benzocaine may cause contact dermatitis. Absorption is variable. There is a risk of cardiac arrhythmias if high absorption. Restrict use to small local areas of pruritus for a short period.
Capsaicin cream	0.025% or 0.075% applied three times daily.	May cause burning on initial use. Settles after a few days. Useful for pruritus secondary to uraemia. Also useful for neuropathic pain.

Table 34.5 Systemic drugs used in the management of pruritus				
Class of drug	**Name of drug**	**Indications for use**	**Dose (oral unless otherwise stated)**	**Comments**
H_1 receptor antagonist [1] (Level 4)	**Non sedative** Levocetirizine Desloratidine Fexofenadine **Sedative** Chlorpheniramine Hydroxyzine Promethazine Trimeprazine / Alimemazine	Histamine induced itch	Consult BNF for individual doses	Non-sedating drugs can be used during daytime.
H_2 receptor antagonist [1] [Level 4]	Ranitidine	Urticaria / Hodgkins lymphoma / Polycythaemia Rubra Vera	300mg daily in divided doses	Enhances effect of H_1 receptor antagonists in urticaria.
Combined H_1 and H_2 receptor antagonists [1, 2] [Level 4]	Doxepin	Chronic urticaria not responding to H_1 antihistamines	10mg-75mg od	Beware drug interactions.
$5HT_3$ antagonists [8, 9, 10] [Level 1]	Ondansetron	Itch secondary to spinal opioids	4mg-8mg intravenously daily. Can be given orally.	No clinical trials but likely to be class effect.
SSRI* [8, 11] [Level 3]	Paroxetine	Unknown cause. Paraneoplastic itch	5mg-10mg od	Anti-pruritic effect wears off after 4-6 weeks. Some evidence for higher doses e.g.30mg.
NaSSA** [1] [Level 4]	Mirtazapine	Malignant homeostasis / Lymphoma / Uraemia	7.5mg-30mg od	Sedative at low doses.
Anion-exchange resins [1, 12] [Level 3]	Colestyramine	Cholestatic disorders	4g bd or tds	Not effective if complete biliary tract obstruction.
Rifamycin [13] [Level 1]	Rifampicin	Intrahepatic cholestasis	Starting dose 75mg od. Maximum dose 150mg bd	May cause bloating, constipation. Beware drug interactions.
Immuno-modulator [14] [Level 1]	Thalidomide	Uraemia	Seek specialist advice before use	Avoid in fertile women.
Androgens [2] [Level 4]	Danazol	Cholestasis	200mg od Maximum dose 200mg tds	No clinical reports to support use as yet. Beware liver toxicity.
Corticosteroids [1] [Level 4]	Prednisolone Dexamethasone	Hodgkins lymphoma	30mg-60mg od 4mg-8mg od	

* Selective serotonin reuptake inhibitor.

** Noradrenergic and specific serotoninergic antidepressant.

34.3 STANDARDS

1. All patients should be asked about the presence of pruritus at assessment and the results documented in the case notes. [7] [Grade D]
2. Reversible causes of pruritus should be treated where appropriate. [7] [Grade D]
3. General and topical measures should always be considered first. [7] [Grade D]
4. The efficacy of any medication used should be reviewed every one / two weeks. [7] [Grade D]
5. Drug treatment should be selected according to the most likely underlying aetiology. [7] [Grade D]

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35. GUIDELINES FOR THE DEVELOPMENT OF PSYCHOLOGICAL SERVICES IN PALLIATIVE CARE

35.1 GENERAL PRINCIPLES

* Psychological distress is defined as "a multifactorial unpleasant experience of a psychological (cognitive, behavioural, emotional), social and/or spiritual nature that may interfere with the ability to cope effectively with cancer." [1]

* Psychological distress is commonly experienced in cancer and palliative care patients. [2-5] The prevalence of conditions such as anxiety and depression are significantly higher in cancer (10-30%) and palliative care patients (45-58%) [2-5] than in the general population. Various types of cancer (e.g. head & neck) and differing stages of disease process (e.g. diagnosis or advanced disease) predispose patients to experience greater distress. [6]

* Psychological distress has been shown to have a significant impact on quality of life, degree of pain, physical functioning and families.[7] Research indicates that the identification, assessment and treatment of distress is far from optimal.[8] Evidence suggests that lack of rigour in the assessment of psychological distress is further compounded by difficulties in accessing treatment and intervention. [5]

* It is suggested that regardless of severity, patients with psychological distress will benefit from appropriate professional support. [9] At least 10-15% of these patients will warrant specialist psychological or psychiatric intervention. [10] However in order to access such support, appropriate identification, assessment and referral systems for psychological distress are required.

* There are various professional and voluntary services available to assist patients experiencing psychological distress. Currently there remains a lack of co-ordination and integration of specialised psychological support services with palliative care providers e.g. counselling, clinical psychology, liaison psychiatry. [10]

35.2 GUIDELINES

35.2.1 Service provision

* The National Institute for Health and Clinical Excellence (NICE) Guidance suggests that palliative care service providers in each Integrated Care Network (ICN) should look to develop services in line with a four level model.[10] For further details of this model see Figure 35.1. [Level 4]

* There should be support available for all staff who offer psychological support. [10] [Level 4]

* There should be access to formal clinical supervision for staff utilising psychological approaches who are working at Levels 3 and 4. [10] [Level 4]

35.2.2 Education and training

* Specialist palliative care units should provide access to education programmes in psychological care. These programmes should be open to all clinical staff working with palliative care patients and their families. Programmes should include the assessment and management of Level 1 and Level 2 situations (see Figure 35.1). [10] [Level 4]

* Training in communication skills is essential for all clinical staff. [10] [Level 4]

* Training programmes should be developed in accordance with the evidence base and in collaboration with psychological specialists. This training should be updated on a regular basis.[10] [Level 4]

Figure 35.1 Suggested four level model for the provision of psychological support [10]

Level	Professionals	Assessment	Interventions
1	All health and social care professionals	Recognition of psychological needs	Information giving and general psychological support
2	Health and social care professionals with additional/advanced training e.g. clinical nurse specialists	Screening for psychological distress	Psychological techniques e.g. problem solving
3	Trained and accredited professionals	Assessment of psychological distress and ability to diagnose some forms of psychopathology	Counselling and specific psychological interventions e.g. anxiety management, solution-focused therapy
4	Mental health specialists e.g. clinical psychologists and psychiatrists	Diagnosis of psychopathology	Specialist psychological and psychiatric interventions e.g. psychotherapy, cognitive behavioural therapy

35.2.3 Service delivery

* Appropriate facilities/environment for psychological assessment and intervention should be available/identified, providing privacy and comfort for patients and their carers. [10] [Level 4]

* Each palliative care service provider should establish written criteria for the identification and assessment of psychological distress, together with referral criteria to the appropriate professionals providing psychological assessment and intervention at Levels 3 and 4.[10] [Level 4]

35.3 STANDARDS

1. Each palliative care service provider should have written referral criteria to guide access to professionals working at Levels 3 and 4. [10] [Grade D]
2. All clinical staff providing palliative care must have access to the referral criteria. [10] [Grade D]
3. There should be a named lead psychiatrist and psychologist identified at Cancer Network level to advise on the provision of specialist care at Levels 3 and 4, including access to emergency psychiatric support. [10] [Grade D]
4. Clinical staff practising at Levels 3 and 4 should have regular clinical supervision. [10] [Grade D]
5. All clinical staff working in specialist palliative care should have had accredited communication skills training and receive regular updates. [10] [Grade D]
6. Managers of staff involved in providing palliative care must ensure that there are procedures in place to provide appropriate support for all staff and that staff are aware of the procedures. [10] [Grade D]

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36. GUIDELINES FOR THE USE OF PSYCHOSTIMULANTS IN PALLIATIVE CARE

36.1 GENERAL PRINCIPLES

* Current research evidence supports the use of psychostimulants in palliative care in four areas: depression; [1, 2] opioid induced sedation; [3, 4] hypoactive delirium [5] and cancer-related fatigue.[6] They are not appropriate for use as day time stimulants in the palliative care setting.[7]

* A psychostimulants may be the drug of choice for treating depression in patients with a prognosis of < 3 months because they may not live long enough to achieve maximum benefit from a conventional antidepressant. However they are not as effective as conventional antidepressants which should be considered in patients with a prognosis of > 3 months.[1, 2, 8]

* The most commonly used psychostimulant in palliative care is methylphenidate hydrochloride. It has been shown to be effective in the management of cancer related fatigue [6]. Dexamfetamine (Dexedrine®) and modafinil (Provigil®) are alternatives.[9, 10, 11]

* Psychostimulants (with the exception of modafinil) are Schedule 2 drugs, and therefore are subject to the regulations for controlled drugs. Prescriptions must comply with controlled drug requirements.[7] The UK product licences do not currently cover the use of these psychostimulants in palliative care.

* Methylphenidate hydrochloride increases dopamine signalling by several mechanisms including blocking the dopamine re-uptake transporter, and modulates catecholamine tone. [12]

* Methylphenidate hydrochloride is available in both short acting and long acting formulations. The long acting formulations should be avoided for palliative care use. Tablets may be dispersed in water (allow 2-5 minutes) and dispersed tablets may be administered via a PEG tube. [13]

* Methylphenidate hydrochloride is rapidly and completely absorbed after oral administration, reaching peak blood levels in 1-3 hours.[7]

* A test dose of 5mg methylphenidate hydrochloride should always be tried before commencing any treatment regimen. In the frail or elderly a starting dose of 2.5mg may be more appropriate.[5, 14]

* Care should be taken when prescribing psychostimulants in patients with marked anxiety, agitation, hypertension or epilepsy. They should be discontinued if seizures occur, there is a rise in blood pressure or an increase in anxiety or agitation. [13]

* Methylphenidate hydrochloride is generally well tolerated in the palliative care population.[6, 10] Serious side effects such as aggression or psychosis have been reported in 2-4 % of patients following a test dose of psychostimulants.[4] A past history of aggression or psychosis was a common feature in many of these patients. Stopping the psychostimulants and use of haloperidol is often helpful.

* The most commonly reported side effects are insomnia, anorexia, irritability, weight loss, abdominal pain and headaches.[13] Psychostimulants may also cause tachycardia and hypertension.[7] Stimulant side effects tend to be dose-dependent. Despite the potential negative

impact on appetite, anxiety and insomnia, when used in the palliative care population the increased arousal and improved mood often negates these effects or even reverses them. [15]

* Absolute contraindications to the use of psychostimulants include hyperthyroidism, angina, severe hypertension, glaucoma, schizophrenia and cardiac arrhythmias. Relative contraindications are mild hypertension, Tourette's syndrome, motor tics, drug abuse, alcohol abuse, porphyria and epilepsy. [7, 15]

* Psychostimulants have several potentially important drug interactions. (see Table 36.1)

Table 36.1 Important drug interactions of methylphenidate hydrochloride [7]

Drug(s)	Effect
Phenytoin Phenobarbital Primidone	Increase plasma levels of anticonvulsants.
Carbamazepine	Effectiveness of methylphenidate may be reduced. Monitor effect.
All antihypertensives	Antagonises hypotensive effects.
MAOI* Moclobemide* Alcohol	Increases hypertension and CNS excitation. * There is a risk of a hypertensive crisis and psychostimulants should not be used either with, or within 14 days, of administering MAOIs.
Warfarin Tricycyclic antidepressants SSRIs	Use with caution with drugs that are predominantly metabolised by CYP2D6 e.g. warfarin, as a degree of competitive inhibition may develop.

* Serious adverse events have been reported with clonidine, but a causal relationship has not been established.[8]

* Concurrent use of anti-dopaminergic agents such as haloperidol, levomepromazine and metoclopramide may reduce the clinical response to psychostimulants with the exception of modafinil. [7, 8]

36.2 GUIDELINES

* Table 36.2 describes the clinical use of psychostimulants in palliative care.

36.3 STANDARDS

1. All patients should receive a test dose of the psychostimulant before commencing a treatment regimen. [14] [Grade D]
2. Pulse rate and blood pressure should be monitored on a daily basis during the titration phase. [7] [Grade D]
3. The clinical response to psychostimulants should be closely monitored and recorded in the case notes. [2] [Grade D]
4. If a patient is discharged on psychostimulants, a copy of the discharge letter should be sent to the GP and other health professionals involved in their care.[2] [Grade D]

Table 36.2 Clinical use of methylphenidate hydrochloride, dexamfetamine and modafinil [7, 8] [Level 3]			
Indication	**Dosing regimen**	**Response**	**Long term use**
1. Diagnosis of depression and/or adjustment disorder using ICD 10 or DSM IV (see *Guidelines on Depression*). 2. Where a rapid response is required (prognosis less than 3 months) and/or other antidepressants are contraindicated or not tolerated.	**Methylphenidate hydrochloride** Initial test dose of 5mg methylphenidate hydrochloride. Monitor closely for any adverse reactions. In the frail or elderly it may be more appropriate to use a starting dose of 2.5mg methylphenidate hydrochloride. Following test dose, use methylphenidate hydrochloride 5mg bd. Do not give second dose later than 2pm as may result in sleep disturbance. Titrate upwards as necessary by 2.5mg-5mg every 48-72 hours. During the titration phase, BP and pulse should be monitored on a daily basis. Recommended maximum dose of methylphenidate hydrochloride is 40mg/day.[5] If no response and treatment is still indicated, consider changing to dexamfetamine sulphate. **Dexamfetamine** Can be given once daily 2.5mg-5mg od as starting dose. Can increase every few days to 20mg od depending on response. Monitor as above. **Modafinil dose** 100mg (elderly)-200mg (adult) per day orally as single morning dose. Adjust according to response to a maximum of 400mg daily. Monitor as above.	A response occurs within 48 hours in 75% of patients. The response rate may be less in those with a shorter prognosis.	Long term use (up to 12 months) has been observed. Stopping treatment may lead to withdrawal symptoms and a reducing regimen is recommended. Depression may recur once treatment is discontinued.
Cancer-related fatigue.	As above.	Important to monitor.	
Opioid induced sedation.	As above.	Important to monitor.	Tolerance to methylphenidate hydrochloride is more likely to develop if used for > 4 weeks. [8, 13]

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37. GUIDELINES FOR PRESCRIBING IN RENAL FAILURE

37.1 GENERAL PRINCIPLES

* Renal impairment constitutes a major source of morbidity and mortality in patients with malignancy. [1, 2]
* Acute renal failure is defined as a sudden decrease in the glomerular filtration rate (GFR) associated with a rise in serum urea and/or creatinine. There is usually, but not always, a reduction in urine output. [3, 4]
* Acute renal failure is often reversible if diagnosed and treated promptly. [3]
* The causes of acute renal failure in cancer patients may be multifactorial (see Table 37.1).

Table 37.1 Causes of acute renal failure in cancer patients [1, 2]

Causes	Comments
Drugs	NSAIDs, mitomycin-C, platinum compounds, methotrexate, ifosfamide, ACE inhibitors, diuretics
Extracellular fluid depletion	Poor oral intake, vomiting or diarrhoea
Hypercalcaemia	
Hyperuricaemia	
Sepsis	Following chemotherapy
Tumour infiltration	
Tumour lysis syndrome	Renal vein or ureter
Urinary tract obstruction	Following chemotherapy

* Chronic renal failure is a long-term condition in which there is reduction in glomerular function. It is often progressive and irreversible. [5]
* Drugs or drug metabolites may accumulate in renal failure, leading to toxicity. Prescribing in renal failure should be approached with caution and should be in accordance with the estimated GFR. [6]
* Evidence suggests that some opioids are safer to use than others. However all patients with renal impairment are at risk of drug toxicity and therefore should be monitored on a regular basis. Signs of opioid toxicity may include visual hallucinations, myoclonus, drowsiness or confusion.[7]
* Long acting opioid preparations should be avoided (e.g. MST®/MXL®) as the metabolites accumulate in renal failure. An exception to this rule is transdermal fentanyl as renal failure does not affect the pharmacokinetics of the drug. [6, 7, 8]

37.2 GUIDELINES

37.2.1 Assessment of acute renal failure

* If acute renal failure is diagnosed, an assessment of the cause should be carried out where appropriate (see Table 37.2).

Table 37.2 Assessment of acute renal failure [3] [Level 2]
Assessment of fluid status
Review of medication. Discontinue nephrotoxic drugs
Baseline bloods e.g. FBC, urea and electrolytes, urate, Ca^{2+}(corr)
Septic screen: including MSSU and blood cultures
Dipstick urine/ measure urine output
Urinary catheterisation
Renal ultrasound

37.2.2 Calculating the degree of renal impairment [5, 9, 10] [Level 1]

* When diagnosing renal failure the serum creatinine may be misleading as it is significantly influenced by muscle mass, age and sex. [5]
* The estimated Glomerular Filtration Rate (eGFR) should be calculated using one of the formulae in Table 37.3. The result may then be used to estimate the degree of renal impairment and the stage of chronic kidney disease (see Table 37.4). Alternatively, on line calculations may be done at www.renal.org/eGFRcalc/GFR.pl
* Clinical biochemistry laboratories can report the eGFR if requested. An estimated GFR should not be used for acute renal failure or in patients on dialysis.

Table 37.3 Formulae for calculations of eGFR [5, 9, 10] [Level 1]	
Modification of Diet in Renal Disease-abbreviated (MDRD) [11]	eGFR (ml/min) = 186 x $(Creat/88.4)^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.210 if black)
Cockcroft and Gault Equation [12] (males)	eGFR(ml/min) = (140 - age) x weight (kg) x 1.23 divided by Serum creatinine (micromols/l)
Cockcroft and Gault Equation [12] (females)	eGFR(ml/min) = (140 - age) x weight (kg) x 1.04 divided by Serum creatinine (micromols/l)

Table 37.4 Stages of chronic kidney disease (CKD) [5, 13]			
Stage	**GFR (mls/min)**	**Description**	**Complications**
1	>90	Normal renal function	
2	60-89	Mildly reduced renal function	Early hyperparathyroidism
3a 3b	45-60 30-45	Moderately reduced renal function	Renal anaemia, altered bone metabolism
4	15-29	Severely reduced renal function	Acidosis, hyperkalaemia, accumulation of drug metabolites
5	<15	Very severe or end stage renal failure	Anorexia, vomiting, pruritus, sodium retention

37.2.3 Analgesic prescribing in renal failure

* If the GFR is below 30mls/min (Stage 4 or 5 CKD), there is an increased risk of toxic side-effects with all opioids due to drug and metabolite accumulation. Opioids should therefore be used with caution. [7] [Level 2+]
* NSAIDs should be avoided if possible, unless a patient is already on dialysis. If a NSAID must be prescribed, the lowest effective dose should be used and the renal function should be rechecked within five to seven days of starting the drug. [5] [Level 4]
* Table 37.5 suggests guidelines for analgesic use according to the World Health Organisation (WHO) analgesic ladder in patients with severe renal failure (stage 4 and 5) who are able to swallow medication. [14] [Level 2-]
* When prescribing oral strong opioids, the immediate release forms are preferred. [7, 14] [Level 4]
* Once a patient is established on a regular dose of strong opioid, conversion to transdermal fentanyl may be better tolerated as the metabolites are inactive. [7, 14] [Level 4]
* If a patient requires more than three stat subcutaneous doses of a strong opioid, consider starting a continuous subcutaneous infusion. [7, 14] [Level 4]
* Alfentanil is pharmacokinetically the safest analgesic to use in renal failure. The metabolites are non toxic and only 1% is excreted unchanged by the kidneys. The limitations are that it can only be given parenterally and it has a very short half life. Fentanyl is an alternative strong opioid.[15, 16, 17, 18] [Level 3]

Table 37.5 Guidelines for the use of analgesia in patients with renal failure (CKD Stages 4 and 5) [7,14, 15, 16, 17, 18, 26] [Level 3 / 4]

WHO ladder	Name of drug	Dose	Notes
Step 1	Paracetamol	Maximum daily dose 4g orally	Reduce to maximum of 3g if additional liver impairment. Avoid effervescent tablets because of high sodium content.
Adjuvants	NSAIDs	Lowest effective dose	Use is not recommended due to lack of safety data from controlled clinical studies. If prescribed need to monitor renal function closely.
Step 2	Cocodamol 8/500 or 30/500	4 tablets in 24 hours	Use with caution. Accumulation of metabolites may cause profound narcosis and respiratory depression.
	Codeine Phosphate 30mg	120mg in 24hrs (orally)	Use with caution.
	Dihydrocodeine 30mg	120mg in 24hrs (orally)	Use with caution.
	Tramadol	50mg-100mg 6-8 hourly (orally)	Only use immediate release preparation. Start at 50mg and titrate upwards. If creatinine clearance is ≤ 30ml/min give 12 hourly. May be poorly tolerated in Stage 5 CKD.
Step 3	Morphine	Oral Titrate with low starting dose e.g. 2.5mg-5mg 6-8hrly Parenteral Titrate with low starting dose e.g. 2.5mg as required	Use with caution. Accumulation of parent drug and metabolites reported to cause profound respiratory depression and narcosis.
	Hydromorphone	Oral Titrate with low dose e.g. 1.3mg 6-8hrly	Use with caution as limited data. Evidence suggests pharmacokinetic properties safer than morphine. Parenteral preparation available as unlicensed special order
	Oxycodone Hydrochloride	Oral Titrate with low starting dose e.g. 2.5mg-5mg 6-8hrly Parenteral Titrate with low starting dose e.g. 2.5mg subcutaneously as required	Use with caution as limited data. Evidence suggests pharmacokinetic properties safer than morphine, however 10% of parent drug excreted renally therefore toxicity may occur.
	Methadone	Reduce by 50-75% of normal starting dose	Use with caution as limited data. Evidence suggests pharmacokinetic properties safer than morphine.
	Diamorphine	Titrate with low starting dose e.g. 2.5mg-5mg subcutaneously as required	Use with caution. Accumulation of parent drug and metabolites reported to cause profound respiratory depression and narcosis.
	Fentanyl	Transdermal patch for stable pain only	Recommended. Liver metabolism mainly. No toxic metabolites. 10% parent drug excreted renally so may get some accumulation in renal failure. Use may be limited by size of patches and difficulties in titration. Can be given subcutaneously.
	Alfentanil	$1/10^{th}$ dose of diamorphine Use in CSCI only	Recommended. Not excreted renally. Liver metabolism. No toxic metabolites.Do not use rescue doses of alfentanil to titrate the background dose because of its short half life.
	Buprenorphine	Normal dose and interval	Not excreted renally, however very limited evidence for safe use in humans.

37.2.4 Dialysis and opioids [7] [Level 3]

* The role of dialysis and how it affects the clearance of a drug is very complex and depends on many factors including the properties of the parent drug and its metabolites. The technical aspects of the dialysis procedure are also important. [7]
* If a drug is cleared by dialysis, it should be administered after the dialysis procedure. [7]
* Table 37.6 illustrates the effect of dialysis on different strong opioids.

Table 37.6 Effect of dialysis on opioids [7] [Level 3]

Drug	Effect of Dialysis
Codeine	Little evidence. Metabolites not cleared well.
Tramadol	Little evidence. Only slowly removed by dialysis.
Morphine/Diamorphine	45% cleared by haemodialysis. Metabolites cleared less well.
Oxycodone	Little evidence. Properties suggest cleared significantly by dialysis.
Hydromorphone	Little evidence. Properties suggest cleared significantly by dialysis.
Fentanyl	Not cleared by dialysis.
Alfentanil	Little evidence. Properties suggest not cleared by dialysis.
Methadone	Not cleared by dialysis. Wide inter-patient variation.

37.2.5 Other drugs used in palliative care

Gabapentin / pregabalin [6, 27, 28] [Level 3]

* Dosage adjustment is recommended in patients with compromised renal function (see Table 37.7) and/or those undergoing haemodialysis. Gabapentin 100mg capsules can be used to follow dosing recommendations for patients with renal insufficiency.

Table 37.7 Dosage of gabapentin in adults based on renal function [27] [Level 3]

Creatinine Clearance(ml/min)	Total Daily Dose [a] (mg/day)
≥ 80	900-3600
50-79	600-1800
30-49	300-900
15-29	150-600 [b]
<15 [c]	150-300 [b]

a *Total daily dose should be administered as three divided doses. Reduced dosages are for patients with renal impairment (creatinine clearance < 79 ml/min).*

b *To be administered as 300 mg every other day.*

c *For patients with creatinine clearance <15 ml/min, the daily dose should be reduced in proportion to creatinine clearance (e.g., patients with a creatinine clearance of 7.5 ml/min should receive one-half the daily dose that patients with a creatinine clearance of 15 ml/min receive).*

* Pregabalin is eliminated from the systemic circulation primarily by renal excretion as an unchanged drug. As pregabalin clearance is directly proportional to creatinine clearance, dosage reduction in patients with compromised renal function must be individualised according to creatinine clearance as indicated in Table 37.8.

Table 37. 8 Pregabalin dosage adjustment based on renal function [28] [Level 3]			
Creatinine Clearance (ml/min)	**Total daily dose of pregabalin**		**Dose regimen**
	Starting dose(mg/day)	**Maximum dose (mg/day)**	
≥ 60	150	600	bd or tds
≥30 < 60	75	300	bd or tds
≥15 < 30	25-50	150	once daily or bd
< 15	25	75	once daily

Metoclopramide [30] [Level 3]

* Clearance reduced by 50% in renal failure. Increased risk of extra-pyramidal side effects. May want to consider lower initial doses. Titrate as necessary. Patient should be monitored closely.

Haloperidol [29] [Level 4]

* Haloperidol is the drug of choice for uraemia induced nausea.

Bisphosphonates

(See Guidelines on the User of Bisphosphonates in the Management of Malignant Bone Disease for further details)

* To avoid renal toxicity with bisphosphonates, serum creatinine should be checked and hydration status clinically assessed prior to each treatment. The serum calcium should also be checked prior to every infusion. [20, 21] [Level 4]
* The risk of renal failure is directly related to drug infusion time and dosage. High dose zoledronic acid with a short infusion time is especially nephrotoxic. [22, 26] [Level 4]
* Treatment with zoledronic acid and disodium pamidronate should not be initiated in patients with severe renal impairment (Cr Cl < 30mls/min) unless in cases of life threatening hypercalcaemia where the benefits are judged to outweigh the risks. If there is a marked deterioration in renal function following initiation of therapy then treatment should be stopped. It should only be restarted when the serum creatinine has returned to within 10% of the baseline. [23, 24, 25] [Level 4]
* If using bisphosphonates for bone pain it may be clinically appropriate to consider dose reduction or use of a longer infusion time rather than stopping treatment. [20] [Level 4]
* There is a growing body of evidence showing that ibandronic acid is better tolerated in renal failure compared to other bisphosphonates. [24] [Level 2+] However monitoring, dose reduction and longer infusion times are still required if there is severe renal impairment.[20] [Level 4]

Midazolam [29] [Level 4]

* Midazolam metabolites accumulate in renal failure. Patients may be more sensitive to midazolam. The lowest effective dose should be used.

Glycopyrronium [31] [Level 4]

* Glycopyrronium accumulates in renal failure and a dosage reduction will be necessary

37.2.6 Management of other symptoms in the dying phase [26] [Level 4]

* Uraemia may cause or contribute to agitation in the dying phase.
* Consider the use of haloperidol if the patient is suffering from delirium rather than agitation/anxiety.
* The renal LCP guidelines give useful information on managing symptoms during the dying phase for patients with renal failure.

37.3 STANDARDS

1. Estimated GFR (e GFR) should be used to determine renal function. [12, 14] [Grade B]
2. In severe renal impairment, drug doses should be reduced and/or dosing intervals increased as appropriate. [15] [Grade C]
3. All patients should be closely monitored for evidence of drug toxicity or drug induced renal impairment. [9, 15] [Grade C]
4. If a non-dialysis patient is started on an NSAID, the renal function should be rechecked within 5-7 days. [6] [Grade D)]
5. In patients with severe renal impairment, alfentanil or fentanyl are the strong opioids of choice for use in a CSCI. [4, 5] [Grade D]

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38. GUIDELINES FOR SEXUAL HEALTH ASSESSMENT IN PALLIATIVE CARE

38.1 GENERAL PRINCIPLES

* Sexuality is: "an integral part of personality which is developed over time through a mixture of physical, psychological, social, cultural and spiritual beliefs." [1]
* Sexual health is as important as physical, psychological and social well-being. [2]
* An assessment of sexuality and sexual health should be part of every assessment. Sexual health issues matter to all patients, not just those with sexually related cancers. [3] Over two thirds of respondents in a recent cancer survey said that cancer had affected their sexual relationship with their partner. [4]
* Sexual health assessment may be a challenging area of patient care. Health care professionals need to recognise their own personal and professional limitations. [5]

38.2 GUIDELINES

* A sexual health assessment should be part of the initial patient assessment (where appropriate) and it should be documented in the medical records. [6] [Level 4]
* It is important that the environment for assessment is appropriate e.g. need to ensure privacy and confidentiality. [2] [Level 4]
* Use open-ended questions to encourage exploration of sexual health issues. [7] [Level 4].

  Examples of appropriate questions include:

  - Do you currently have a partner/close relationship?
  - Has your illness/treatment affected how you feel about yourself?
  - Has the illness affected your relationship in any way?
* The PLISSIT model may be useful in sexual health assessment. An outline of this model can be seen in Table 38.1. [8] [Level 3]
* Health care professionals should be prepared to seek further help and advice if necessary. Useful contacts are listed in Table 38.2. [9] [Level 4]

Table 38.1 Outline of P-LI-SS-IT model [8] [Level 3]

Level 1: Permission (P)

- Health care professionals need to create a comfortable environment that gives patients permission to discuss concerns and problems related to their sexuality and sexual health.
- Ensure a comfortable and private physical environment.
- Use of open questions, reflection and paraphrasing.
- Use of cue questions to allow the patient the opportunity to raise sexual health concerns.
- Give reassurance that patient's current sexual practices are appropriate and healthy or that experimentation is appropriate.
- Have a range of information available that is educational and non-personal.
- Be aware of where to get further information and the routes for specialist referral if required.
- Acknowledge the needs of sexual partners. Spouses and partners of people with dementia, or partners of homosexuals or lesbians, may welcome specific supportive measures.
- Acknowledge the sexuality and sexual health needs of patients in relation to their cultural background.
- It should be remembered that patients may not wish to discuss intimate information with a health care professional.

Level 2: Limited Information (LI)

- Health care professionals may provide limited information e.g.
  - Pelvic radiotherapy may cause vaginal dryness and potential problems with future fertility.
  - Prostatectomy may result in retrograde ejaculation and cloudy urine.

Level 3: Specific Suggestions (SS)

- To be able to give specific support and help with sexual health issues, health care professionals will need further training e.g.
  - Advice for patients with COPD on how to minimise dyspnoea during sexual intercourse.
  - Advice on comfortable positions for sexual intercourse for patients with chronic arthritis or disability.
  - Advice on pharmacological interventions and mechanical aids. [10]
- If a patient requires this level of help they may need specialist referral.

Level 4: Intensive Therapy (IT)

- This involves interpersonal and psychological issues and is used with patients who have specific sexual problems e.g. erectile dysfunction. This level also includes relationship counselling.
- Providing this level of care will require further training or referring the patient to an appropriate specialist.

Table 38.2 Useful addresses / contacts	
For a full range of reading material	www.relate.org.uk
For a full list of recognised therapists contact	British Association for Counselling and Psychotherapy www.BACP.co.uk
Sex and Disability Helpline Helpline open 11am-7pm	Dr Tuppy Owens BCM Box Lovely London WC1N 3XX Tel: 0707 4993527 sexdis@outsiders.org.uk.
Outsiders Club	The Outsiders 4S Levoy House 435 Essex Road London N1 3QP Tel: 02073548291 www.outsiders.org.uk
Counselling service for Merseyside	Dr Helen Wilkins Psychosexual Counsellor for Wirral St Catherine's Hospital Birkenhead Tel: 0151 652 2901. Will need written referral
Psychosexual advice for women in Merseyside	Woman's Health Directorate Central Abacus Ground and First Floor 40-46 Dale Street Liverpool LL2 5SK Tel: 0151 284 2500 NB: Written referral is essential.

38.3 STANDARDS

1. All patients should have a sexual health assessment as part of their general assessment. [6] [Grade D]
2. The sexual health assessment should be documented in the medical records. [6] [Grade D]

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39. GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF MALIGNANT SPINAL CORD COMPRESSION IN PALLIATIVE CARE

SEE A-Z LIST FOR LINKS TO ACUTE ONCOLOGY GUIDANCE AND PRIMARY/COMMUNITY CARE GUIDANCE

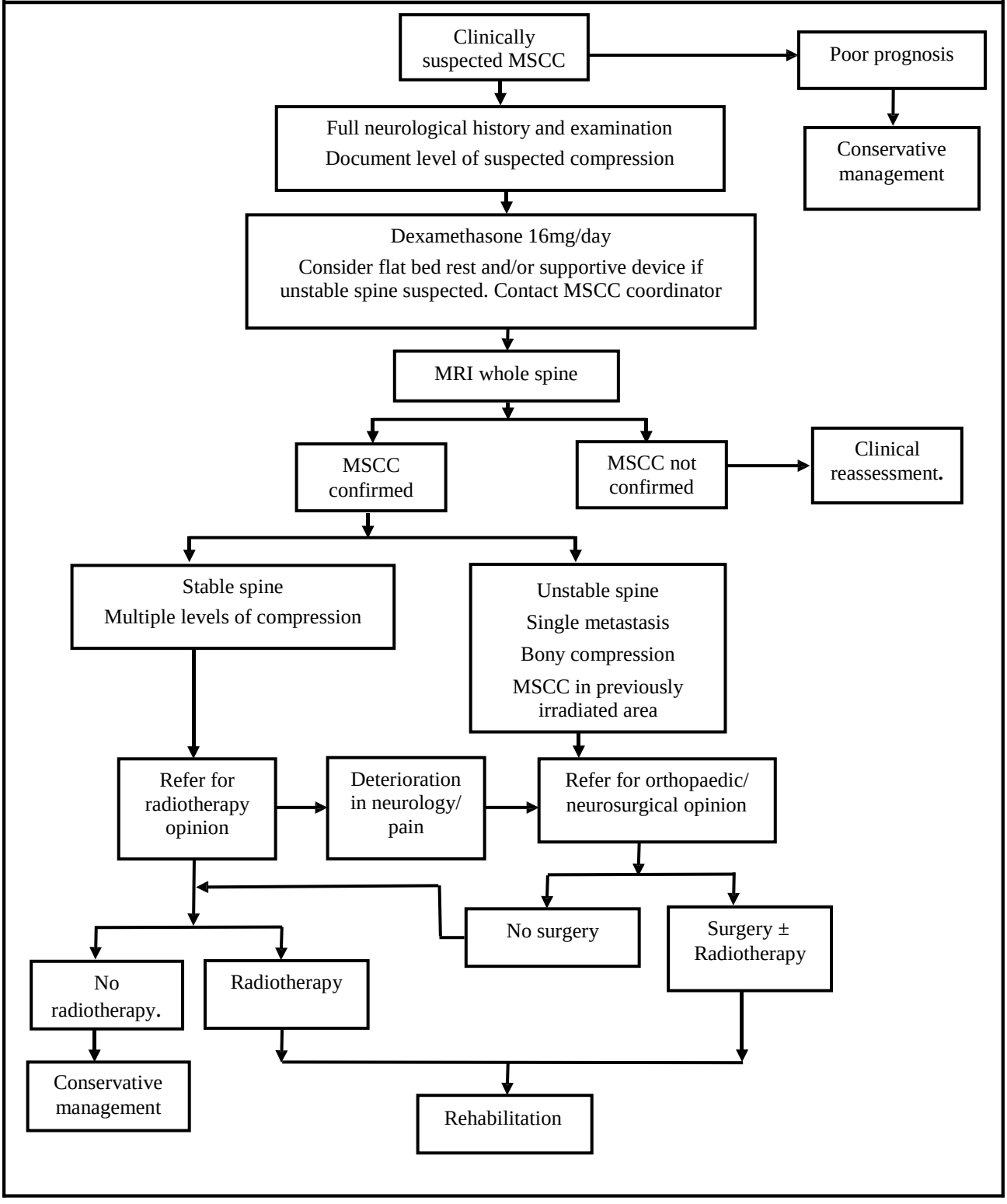
39.1 GENERAL PRINCIPLES

* Malignant spinal cord compression (MSCC) is one of the commonest neurological complications in cancer patients, occurring in around 5% of patients. [1]
* MSCC usually involves epidural sites but intradural and intramedullary sites may also be affected. MSCC most commonly occurs in the thoracic spine but multiple levels of compression are often present. [2]
* Continuous spread of tumour into the epidural canal is the commonest mechanism for MSCC, followed by malignant bone destruction. [2]
* The most common malignancies to be associated with MSCC are prostate, lung and breast cancer. [3]
* Pain, particularly in a nerve root distribution, is the commonest symptom of MSCC. Motor weakness, sensory dysfunction and autonomic disturbances such as impotence, urinary incontinence/urinary retention or faecal incontinence may also occur. The distribution of symptoms does not necessarily correlate to the level of compression. [4]
* Magnetic resonance imaging (MRI) of the whole spine is considered the gold standard for diagnosing MSCC. [5] Plain X-rays are of no benefit in the assessment of MSCC. [5]
* Commonly used treatments include corticosteroids and radiotherapy. In well selected cases surgery may be an option. The choice of treatment depends on the general status of the patient. The optimal treatment for MSCC remains unclear due to a lack of conclusive evidence. [3]
* The neurological function before treatment will often determine the functional outcome following treatment. Ambulant patients and patients without bladder symptoms before treatment have the best chance to maintain function after treatment. [6]
* Quality of life is improved in patients with a greater performance status at diagnosis. [7]

39.2 GUIDELINES

* A flowchart illustrating the diagnosis and management of MSCC is shown in Figure 39.1.
* The symptoms of MSCC may be subtle and therefore careful history taking and examination are essential. [4] [Level 3]
* Always consider the overall condition of the patient before investigation and treatment are commenced, as maintaining quality of life should be the main aim of care. [7] [Level 3]

Figure 39.1 Diagnosis and management of malignant spinal cord compression [5] [Level 4]



* If a cancer patient with known back pain experiences changes in pain severity and/or presence of root pain, MSCC should be considered as a possible diagnosis. [4] [Level 3]

* In patients with back pain but no cancer history, the diagnosis of MSCC may be delayed. This delay may be minimised by focusing on the history / examination and considering associated features which may suggest an underlying cancer diagnosis e.g. weight loss, general performance status or older age. [6] [Level 3]

* Cancer patients with known bone metastases or who are at high risk of developing spinal metastases should be given an information leaflet detailing symptoms of MSCC and who to contact in an emergency. [5] [Level 4]

* Cancer patients who develop clinical features of spinal metastases should have an MRI of the whole spine performed within one week. [5] [Level 4]

* If MSCC is suspected and patients are considered fit for investigation, an urgent MRI of the whole spine should be performed within 24 hours. [5, 9] [Level 2-]

* If an unstable spine or MSCC is suspected clinically or radiologically, consider immobilising the patient with flat bed rest until definitive treatment can be arranged. [5] [Level 4]

* If MSCC is suspected dexamethasone is the corticosteroid of choice. [3] [Level 2+]

* Dexamethasone should be given in a daily dose of 16mg as soon as MSCC is suspected. If dexamethasone is not given or given in a lower dose, the reason for this should be documented. The dose of dexamethasone may have to be higher in patients receiving phenytoin or carbamazepine (see *Guidelines on Antiepileptics and Corticosteroids*). [3, 5] [Level 2+]

* The basic care of patients with confirmed malignant spinal cord compression will include use of appropriate analgesia; pressure area care and bowel/bladder care. [1, 5] [Level 4]

* Appropriate patients should be referred for surgery/radiotherapy immediately after diagnosis. [8] There is some evidence that clinical outcomes are better with surgery than radiotherapy. [10] [Level 3]

* Consider referral for a surgical opinion if the patient has a life expectancy of greater than 3 months and has not been paraplegic for more than 24 hours. Patients who may be suitable include:

  - No prior history of cancer.
  - Single metastasis.
  - Spinal instability.
  - Bony compression of the spinal canal.
  - Progression of symptoms during radiotherapy.
  - Bone compression of MSCC in a previously irradiated area. [7, 5] [Level 3]

* All teams should be aware of the local guidelines for referral of patients with suspected MSCC. [5] [Level 4]

39.3 STANDARDS

1. All patients with suspected MSCC should be asked about the presence or absence of back pain, nerve root pain, motor, sensory and bladder symptoms and the results documented in the case notes. [4] [Grade D]
2. Dexamethasone should be given as soon as MSCC is suspected in a total daily dose of 16mg. If dexamethasone is not given or given in a lower dose the reason for this should be documented.[3, 5] [Grade D]
3. If a patient with MSCC is considered fit for investigation and treatment an MRI is the investigation of choice. [5, 9] [Grade D]
4. If MSCC is confirmed, transfer for definitive treatment to oncology/surgery should be completed within 24 hours. [8] [Grade D]

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40. GUIDELINES FOR SPIRITUAL CARE IN PALLIATIVE CARE

THIS GUIDELINE HAS BEEN UPDATED

PLEASE SEE A-Z SECTION FOR UPDATED GUIDELINES

40.1 GENERAL PRINCIPLES

* Every individual has a spiritual dimension relating to the meaning of life for them, which may or may not be expressed in terms of a faith or belief system. [1]
* Palliative care aims to deal holistically with physical, social, psychological and spiritual needs. [2]
* There is no one agreed definition of spirituality although it is suggested that this lack of definition may be strength, rather than a weakness. [3]
* Spiritual care and religious care are different and very individual although the differences are not always clearly understood. They should neither be artificially separated nor assumed to be interchangeable. Spiritual care is not necessarily religious but religious care at its best should always be spiritual. [1]
* Patients and families state that they want to be treated individually and holistically with respect, dignity and kindness in a pleasing environment by all personnel involved in their care. [4]
* The diagnosis of life threatening illness has a profound effect on people who are ill and on their family and friends. It often provokes questions relating to identity and self worth as patients seek to find an ultimate meaning to their lives. [5]
* Health and social care professionals need to be able to acknowledge spiritual issues among patients and carers, and to respond in a flexible, non-judgmental and non-imposing way. [5]
* Accurate and timely evaluation of spiritual issues should be facilitated through a form of assessment, based on recognition that spiritual needs are likely to change with time and circumstances. [5]
* Assessment of spiritual needs does not have to be structured, nor require the use of an assessment tool, but would need to include care elements such as:[5]
  - Exploring how people make sense of what happens to them.
  - Identifying sources of strength they can draw on.
  - Exploring whether these are felt to be helpful to them at this point in their life.
* Patients and their carers should have access to different forms of spiritual support appropriate to their needs. [5]
* Medical professionals working in palliative care often feel that they have had little preparation or training for responding to patients who are struggling to find meaning in life. As a consequence, meeting the emotional and spiritual demands of patients and their families can be significant stressors for hospice nurses. [6]
* Awareness raising procedures and specific simple educational programmes have been shown to improve the documentation of spiritual and religious needs and the care given. [7]

* In the spiritual care policy produced by Merseyside and Cheshire Cancer Network the following points are highlighted: [8]
  - Recognition of the uniqueness of each individual and their needs; the value of skilled and sensitive listeners; the need to take account of ethnic and religious diversity, the spiritual needs of individuals who have no religious affiliation.
  - Encouragement for each community/trust/organisation to develop and implement a local spiritual care plan within the healthcare institutions and out in the community which reflects the spiritual and religious needs of the community served.
  - The need to ensure that compassionate human support is available for all; that appropriate services where practicable are easily accessible and sensitive to religious, spiritual and human needs; that information about spiritual care services is widely available.
  - Commitment to support patients in their choice of spiritual care (formal, informal or relatives) and to support and develop staff and spiritual care givers by facilitating appropriate education and training.

40.2 GUIDELINES

* Spiritual needs should be included as part of the initial holistic assessment and ongoing care for every patient who has contact with a palliative care professional. [5] [Level 4]
* Spiritual care should provide support to make sense of difficult life events. This may be achieved through exploration of spiritual and existential issues, fostering of realistic hope and the promotion of wellbeing. [5] [Level 4]
* All palliative care professionals should be aware of spiritual issues for patients and families and be able and feel confident to respond in a flexible, non imposing and non judgmental manner. This will include support in living with unanswered questions without necessarily requiring an onward referral. [5] [Level 4]
* Palliative care professionals should be able to facilitate access to different forms of spiritual support, religious or otherwise, sought by patients and families and have a current awareness of local community resources in their area. [5] [Level 4]
* Recognising the spiritual needs of staff, palliative care services should facilitate the support and education of their own staff members in the work they do in this area. Palliative care services should encourage the process of spiritual caring which requires constant reflection, assessment and review. [5] [Level 4]

40.3 STANDARDS

1. Every patient record should demonstrate documentation of an initial spiritual care assessment.[5] [Grade D]
2. Every patient record should demonstrate a record of the patient's faith tradition (religious affiliation or belief system) or its absence. There should also be a record of the significance for the patient. [5] [Grade D]
3. Every patient record should demonstrate evidence of ongoing spiritual assessment and care. [5] [Grade D]
4. All palliative care staff should be able to demonstrate attendance at training in spiritual awareness at least on induction and/or as part of their continuing professional development. [5] [Grade D]
5. All palliative care staff should be able to demonstrate that they undertake assessment of spiritual needs. [5] [Grade D]

6. All palliative care staff should be able to demonstrate that they provide or arrange provision of ongoing spiritual care. [5] [Grade D]
7. All palliative care staff should have access to suitably qualified, authorised and appointed spiritual care givers. [5] [Grade D]
8. All palliative care staff should have access to a current directory of local community spiritual care resources (religious and other). [5] [Grade D]
9. Each Integrated Clinical Network should have a nominated person to be responsible for liaising with local faith leaders and other spiritual resources. [5] [Grade D]
10. Each Integrated Clinical Network should have inpatient and day facilities with dedicated and accessible multifaith quiet space and equipment. [5] [Grade D]
11. Each Integrated Clinical Network should have palliative care services whose policies and procedures reflect recognition of the spiritual needs, support and education of their own staff members. [5] [Grade D]
12. There should be an agreed Network Spiritual Care Policy. [9] [Grade D]

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41. GUIDELINES FOR THE MANAGEMENT OF PALLIATIVE CARE PATIENTS WITH A HISTORY OF SUBSTANCE MISUSE

41.1 GENERAL PRINCIPLES

* The ICD 10 diagnostic criteria for dependency syndrome are listed in Table 41.1 below.

Table 41.1 ICD 10 Diagnostic criteria for dependence syndrome [1]
A diagnosis of dependence can only be made when 3 or more of the following have been present at some time in the past year: − A strong desire or compulsion to take the substance − Difficulty in controlling substance taking behaviour − Physiological withdrawal − Evidence of tolerance − Progressive neglect of alternative pleasures or interests − Persisting with substance use despite clear evidence of overtly harmful consequences

* The General Medical Council has stated "The investigations and treatments you provide must be based on the assessment you and the patient make of their needs. You must not refuse or delay treatment because you believe that a patient's actions have contributed to their condition. You must treat your patients with respect whatever their life choices and beliefs." [2]
* Drug misusers have the same entitlement as other patients to the services provided by the NHS.[2] It is the responsibility of General Practitioners to provide general medical services for drug misusers. [2]
* The structure of drug dependency services varies according to local population needs. [2]
* Ongoing management of dependence at the end of life can improve quality of life for the patient and reduce stress and frustration in the family. [4]
* The management of drug misuse may involve several health and social care teams. Ongoing good communication between these agencies is essential. [2]
* All patients known to drug dependency services will have a key worker. Their role includes developing and agreeing the treatment plan and providing ongoing advice and support. The key worker may be the GP, a doctor, nurse or voluntary sector drugs worker.[2]
* Patients with a history of opioid addiction may have a low tolerance to pain due to neuroplastic changes in pain perception. [3]
* Patients on long term methadone may develop hyperalgesia with increasing doses of opioids. They may display allodynia on examination. [3]
* Treatment should include both psychosocial and pharmacological measures. [2]

* Pharmacological management of opioid maintenance includes methadone, buprenorphine or Suboxone® (buprenorphine: naloxone 4:1) (see Table 41.2). [2]

* Supervised consumption is used to decrease adverse events at commencement of treatment and to aid compliance. The use of a single prescriber and close liaison with a named pharmacist can help to avoid overuse and diversion of drugs. [2]

Table 41.2. Drugs used in the management of opioid dependence [2, 9, 10]

Drug	Preparations	Key Points
Methadone	Oral solution 1mg / ml	Opioid agonist Single daily dose Long half life (13-50 hours) Analgesic effect is 4-8 hours Suppression of opioid withdrawal is 24-48 hours
Buprenorphine (Subutex®)	Sublingual tablets 400microgrammes, 2mg, 8mg.	Opioid partial agonist Only partially reversed by naloxone Single daily dose, maximum 32 mg daily Can be crushed and injected by drug misusers
Buprenorphine/ naloxone (Suboxone®)	Sublingual tablets 2mg / 500microgrammes 8mg / 2mg	Buprenorphine and naloxone (opioid antagonist) Naloxone has poor bioavailability orally. However this increases when tablets are crushed and injected. Thus Suboxone® is used to discourage misuse.

41.2 GUIDELINES

41.2.1 General Management

* The patient's pain and substance misuse should be managed concurrently as two separate issues.[4] [Level 3]

* The assessment of a patient with substance misuse should include assessment of drug and alcohol use, general health issues, social functioning and criminal involvement. [2] [Level 4]

* The patient should be involved in the development of their treatment plan including a strategy for responding to non-compliance. An individual opioid agreement for both the maintenance opioid and the analgesic opioid may aid this process. This may take the form of a verbal or written contract (see Table 41.3*).* [2, 5, 6] [Level 3]

Table 41.3 Key elements of an opioid agreement
Explain the expectations of the patient − Use clear and concise language − Write flexibly and avoid ultimatums Explain the role of the physician e.g. − Medications will be provided by a single provider − Medications will be prescribed on a regular basis − Lost or stolen medication will not be replaced List risks and benefits of the proposed therapy Designate a single pharmacy Provide a rationale for your policies Get consent for treatment and testing

* If known to drug dependency services, the patient's key worker should be included in the development of the treatment plan and informed of all changes. [2] [Level 4]
* The patient's community pharmacist should be informed if a patient is admitted to or discharged from a hospital or hospice. [2] [Level 4]
* If on opioid maintenance therapy, a single prescriber should be responsible for the prescribing of their opioid maintenance. This is likely to be the GP or the Substance Misuse Doctor. [2] [Level 4]
* The analgesia should be prescribed by a single named prescriber. This is likely to be the GP with guidance from the Palliative Care Team. This will avoid duplicate prescribing. [2] [Level 4]
* There should be separate monitoring procedures for substance misuse and symptom control, except during the terminal phase. [7] [Level 4]

41.2.2 Pain Management

* Discontinuation of long-term methadone therapy can lead to an increase in pain, even when other opioids are added. [3, 8] [Level 3]
* The principles of analgesic practice in substance misusers are fundamentally no different from those for other adult patients needing palliative care. [7] [Level 4]
* Titration of opioid, non-opioid and adjuvant analgesics should be regulated against analgesic response in the usual way. Distinctions between symptoms of poor analgesic response and withdrawal should be recognised. [7] [Level 4]
* Disease related pain should be managed according to the WHO analgesic ladder. Where strong opioids are required for pain management, oral morphine remains the strong opioid of choice. [6, 7] [Level 3]
* Where a patient is on dialysis, fentanyl or methadone should be considered for pain management as these drugs will not be removed by dialysis. [12] [Level 4]

* If a patient is on buprenorphine or Suboxone® opioid maintenance and requires a strong opioid for pain management then switching the buprenorphine / Suboxone® to methadone should be considered. A switch should only be made in conjunction with the drug dependency team. [3] [Level 4]

41.2.3 Management of the Dying Phase

* If a patient is on methadone maintenance therapy and a second opioid for pain, then both the methadone and the second opioid should be administered separately via continuous subcutaneous infusions when the patient is no longer able to take oral medication. This is to avoid the symptoms of opioid withdrawal in the dying phase.[11] [Level 4]

41.3 STANDARDS

1. All patients who are known to both palliative care and drug dependency services should have the name and contact number of their drug dependency key worker documented in their palliative care notes. [11] [Grade D]
2. All patients on opioid replacement therapy should have the name and contact number of their community pharmacist documented in their palliative care notes. [11] [Grade D]
3. The key worker and community pharmacist should be informed of changes to medication.[11] [Grade D]
4. Disease related pain should be managed according to the WHO analgesic ladder. [7] [Grade D]
5. If a strong opioid is required for pain management, morphine should be the opioid of choice. [6, 7] [Grade D]
6. A single named prescriber should be responsible for opioid maintenance therapy. A separate single named prescriber should be responsible for opioids used for symptom control. [2] [Grade D]
7. Any changes in the opioids used for these patients e.g. type or dose should be communicated clearly to all health care professionals involved with the patient. [11] [Grade D]
8. Each palliative care service should have the contact details for their local drug dependency team. [11] [Grade D]

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42. GUIDELINES FOR THE USE OF SYRINGE DRIVER/ PUMPS IN PALLIATIVE CARE

42.1 GENERAL PRINCIPLES

* The syringe driver / pump is a portable battery operated device that can be used to deliver a continuous subcutaneous infusion of medication when the oral route is not feasible. [5]
* There are 3 models of syringe driver / pump in general use:
  - Graseby MS26: delivers liquid at a rate set in mm per 24 hours.
  - Micrel MP Daily: delivery is based on mm per 24 hours.
  - McKinley T34: delivers volume over 24 hours.
  - Other models include. Graseby MS16 (mm per hour) and Alaris AD (ml / hour)
* Adequate competency based training, relating to the model used in their workplace, should be available for all staff.
* Patients discharged home with a syringe driver/pump in situ should be given a contact number to use in the event of queries or problems. Patients/families should be shown how to check the following:
  - That the syringe driver/pump is working.
  - The presence of site reactions.
  - Clarity of syringe solutions.

42.2 GUIDELINES

42.2.1 Equipment

* A Luer lok® syringe is recommended. This ensures a fixed connection between line and syringe removing the risk of disconnection during ambulation or high pressure states. A 20ml syringe is the recommended minimum size, as this allows for a larger volume of diluent. [5] [Level 4]
* The use of extension lines should be avoided as they produce an increase in "dead space," which can lead to a decrease in the amount of drug delivered to the patient. [5] [Level 4]
* If a patient requires repeated administration of subcutaneous breakthrough medication, a subcutaneous butterfly should be used. This will avoid the need for repeated injections. The line of the butterfly should be flushed with a volume of diluent equal to that of the tubing after each dose of medication. [5] [Level 4]
* If a fault occurs with the equipment, staff should refer to the operating manual for the model that is in use.[5] [Level 4]

42.2.2 Set-up and Use of a Syringe Driver/Pump

* All syringes should have labels. The label should be attached in such a way that the contents and the volume of the syringe are clearly visible. The label should contain the following information:
  - Name of patient.
  - Name(s) of drug(s) in syringe.
  - Dose(s) of each drug.
  - Name of diluent (if used).
  - Length of total fluid in syringe at time syringe diver / pump commenced.
  - Date and time syringe driver / pump commenced. [5] [Level 4]
* If the machine has a boost button this should not be used for delivering additional analgesia.[5] [Level 4]
* For a Graseby MS26/ Micrel MP Daily, the **length** of fluid in the syringe should be measured **AFTER** the line has been primed. The rate is based on length of liquid and not volume. [5] [Level 4]
* The rate set should be checked every time the syringe in the driver is changed. [5] [Level 4]
* The following checks should be made on any syringe driver / pump in use: [5] [Level 4]
  - Presence or absence of site reactions.
  - Length of fluid remaining in the syringe.
  - Clarity of solution in syringe.
  - Battery check.
* The above checks should be documented every 4 hours for inpatients and at least daily for patients in the community. [5] [Level 4]
* Syringe driver/pump sites should be changed at least every three days. [5, 6] [Level 4]
* Figure 42.1 illustrates the suggested management of site reactions. [1, 5, 6] [Level 4]

42.2.3 Drugs

* It is suggested that most drugs should be diluted in sodium chloride 0.9% when making up a syringe driver. Most injections are isotonic and diluting with saline does not change this.

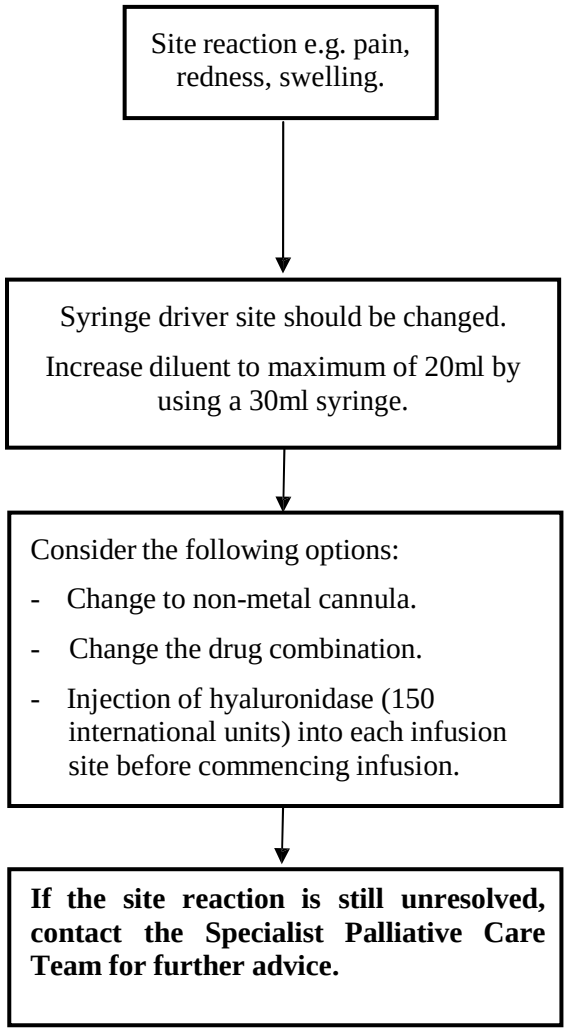
  Use of water has the potential to make the solution more dilute and more likely to cause a site reaction. At the present this is suggested practice based purely on theory. Appropriate studies are awaited.

  Water for injection should be used for cyclizine and diamorphine > 40mg/ml. [5] [Level 4]
* The following drugs should be used in a syringe driver/pump as **single** agents unless otherwise advised by a specialist:[5] [Level 4]
  - Dexamethasone.
  - Diclofenac.
  - Ketorolac.
  - Phenobarbital.

* If more than one drug is delivered via the same continuous subcutaneous infusion, always ensure there is stability/compatibility data to support the combination. If a combination of 4 or more drugs is considered, then contact the specialist palliative care team for further advice. [5, 2, 7] [Level 4]

* Avoid using the combination of cyclizine plus hyoscine butylbromide in a syringe driver as there is a risk of crystallisation. If crystallisation or cloudiness does occur, the infusion should be discontinued and the contents of the syringe discarded. The drug combination should then be reviewed. [5, 2, 7] [Level 4]

Figure 42.1 Management of syringe driver site reactions



42.2.4 Use of Syringe Drivers/Pumps and Epidural Infusions [8] [Level 4]

* Separate machines should be used for administering medication via the epidural route. Using different machine types and different colour tubing helps to avoid confusion with subcutaneous syringe pumps.

* Avoid the use of the MS26 or MS16 models for delivering an epidural infusion.

* Prescriptions for an epidural infusion should be on a separate chart from prescriptions for a CSCI.

* Appropriate training in the care of patients with epidural infusions should be delivered to all staff.
* Each unit should have written guidelines for the management of epidural infusions.

42.3 STANDARDS

1. All syringes should have labels containing the following information:

   Name of patient.

   Name(s) of drug(s) in syringe.

   Dose(s) of each drug.

   Name of diluent (if used).

   Length of total fluid in syringe at time syringe driver/pump commenced.

   Date and time syringe driver/ pump commenced. [5] [Grade D]

2. Syringe pump checks should be documented every 4 hours for inpatients and at least daily for patients in the community. [5] [Grade D]
3. Patients in the community and / or their families, should be shown how to check the following:
   - That the syringe driver/pump is working.
   - The presence of site reactions.
   - Clarity of syringe solutions. [5] [Grade D]
4. All patients/families in the community should be given a contact number to use in the event of queries or problems. [5] [Grade D]
5. Any syringe pump with evidence of precipitation (e.g. crystallisation or cloudiness) should be discontinued and the contents of the syringe discarded. The drug combination should then be reviewed. [2, 5, 7] [Grade D]
6. On a Graseby **MS26**, the boost button should not be used to administer breakthrough medication. [5] [Grade D]
7. Drug administration using a syringe driver/pump should meet compatibility guidelines. [2, 5, 7] [Grade D]

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43. GUIDELINES FOR THE MANAGEMENT OF URINARY INCONTINENCE IN THE PALLIATIVE CARE SETTING

43.1 GENERAL PRINCIPLES

* Urinary continence can be defined as "the ability to store urine in the bladder and to excrete voluntarily where and when it is socially acceptable." [1]
* Urinary incontinence has a significant impact upon an individual's dignity and self-esteem, thus a sensitive approach to assessment is required. [2]
* Urinary incontinence has a significant impact on the patient-carer relationship and is one of the main reasons for admission to residential care. Carers should be involved in assessment where appropriate. [3, 4]
* Symptoms of urinary incontinence can be improved with basic nursing interventions in up to 70% of patients. [3, 4, 5]
* Constipation, urinary tract infections and urinary retention are the most common reversible causes of urinary incontinence. The symptoms of urinary incontinence may not be related to the palliative diagnosis and may be longstanding. [2]
* Social stigma, embarrassment and lack of knowledge of health care professionals can all be barriers to recognising and treating urinary incontinence. [3, 5]
* Urethral catheters can be a useful containment measure but both the risks and benefits need to be considered when they are used (see Table 43.1). [6]

Table 43.1. Considerations when using a urinary catheter.[6]

Blockage / bypass	Dignity
Bladder spasms	Impact on independence
Confidence	Source of infection

43.2 GUIDELINES

43.2.1 Assessment

* All patients should be asked about the presence of urinary symptoms on initial assessment and any findings should be documented. [3, 7] [Level 3]
* Assessment of urinary incontinence should focus on identifying reversible causes such as constipation, infection and urinary retention. See Figure 43.1 for further details. [3, 8, 9] [Level 3]
* Medications which may be contributing to incontinence should be reviewed. [3] [Level 4]
* The verbal history from the patient can be confirmed by use of a bladder frequency chart completed for a minimum of 3 days (see Table 43.2). [8] [Level 4]
* If the patient is too unwell or declines a further continence assessment this should be documented in the notes.[3, 7] [Level 4]

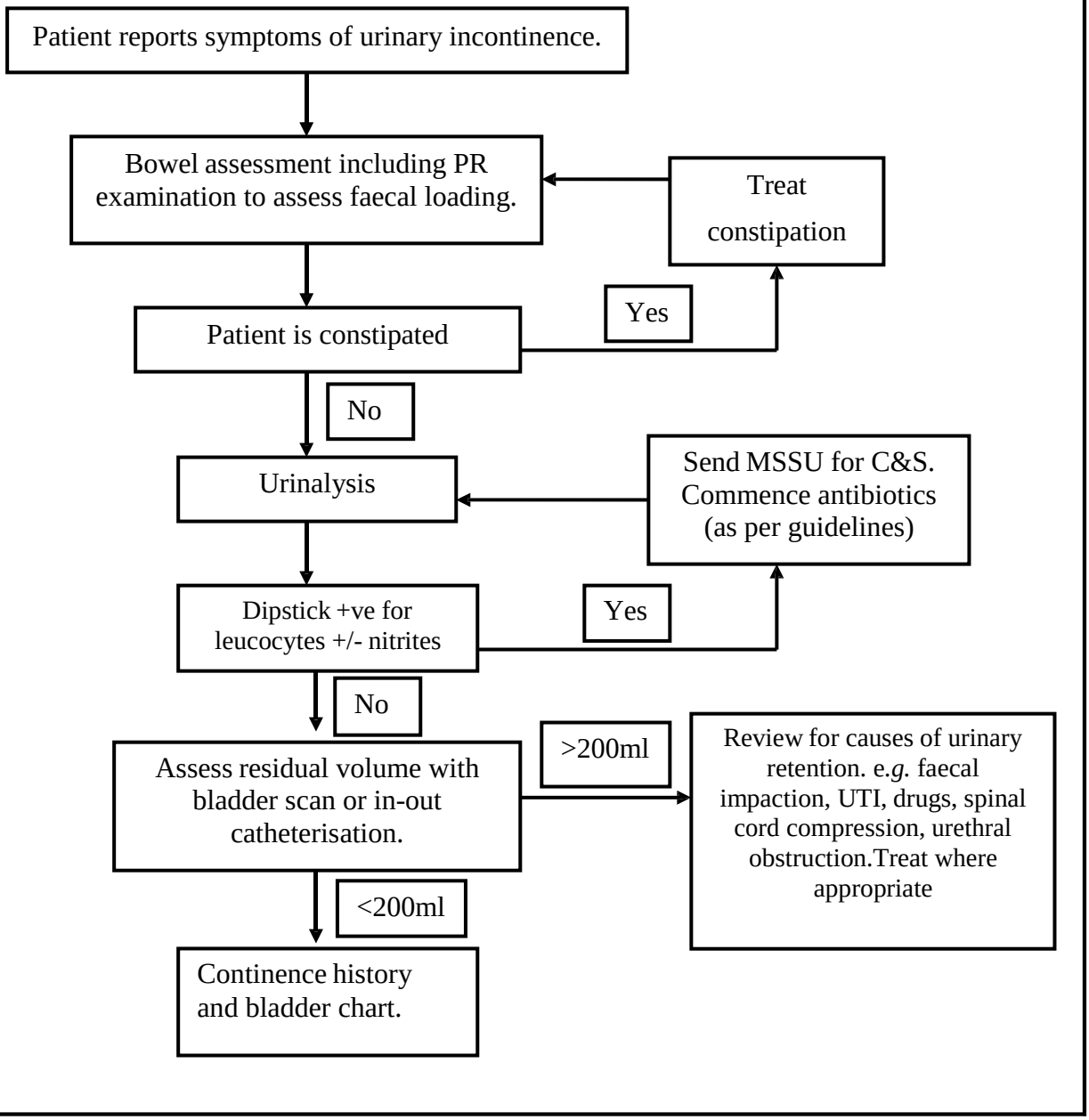
Table 43.2. Continence history	
Duration	Leakage
Changes in severity	Nocturia / nocturnal enuresis
Dysuria	Poor stream
Frequency	Straining
Haematuria	Urgency
Hesitancy	

43.2.2 Management

* When discussing the management of urinary incontinence with the patient and their carer, realistic goals should be set and included in their care plan. [10] [Level 1-]
* Reversible causes should be treated e.g. constipation, urinary tract infection, urinary retention. [3, 8, 9] [Level 3]
* Where there is impaired mobility, manual dexterity or cognition consider referral to a physiotherapist and occupational therapist.[3] [Level 4]
* For patients with a good performance status, consider referral to specialist continence services following initial assessment and management. They may provide pelvic floor exercise training and advice on referral for urodynamics. [3] [Level 4]
* Where there is no evidence of infection, constipation or urinary retention, or where there is intractable incontinence, containment products should be used. These include pads, male and female urinals, bed-pans, conveens and catheters. Referral to the district nursing team or community continence assessment team may be required to ensure a supply of containment measures. [3] [Level 4]
* The use of catheters should be documented in the case notes, and the care plan communicated when the patient is admitted, transferred or discharged. Table 43.3 lists the documentation required. [3, 11] [Level 4]

Table 43.3. Documentation required at catheterisation.[3, 11] [Level 4]
Date, time, location and name of professional performing procedure
Reason for catheterisation
Consent
Type and size of catheter
Residual volume
Date for reassessment
Date for renewal

Figure 43.1 The assessment of urinary incontinence.[3, 7-9, 12] [Level 4]



43.3 STANDARDS

1. A basic knowledge of continence is required to perform a continence assessment. All units should have a continence link nurse who will attend continence study days and cascade training to the team. [3, 4] [Grade D]
2. All patients should be asked about the presence of symptoms of urinary incontinence at initial assessment. This should be documented in the case notes. [3, 4, 7, 9] [Grade D]
3. All patients with urinary incontinence should be assessed for constipation and urinary tract infection excluded. [3, 11] [Grade D]
4. All patients with urinary incontinence should be offered a basic continence assessment. This should be documented in the case notes. [3, 7, 12] [Grade D]
5. The use of catheters should be documented in the case notes, and the care plan communicated when the patient is admitted, transferred or discharged (see Table 43.3). [3, 11, 12] [Grade D]

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APPENDIX A

ABSTRACTS AND PUBLICATIONS

ABSTRACTS (POSTERS AND PRESENTATIONS)

2009

Bellieu J, McKenna E, Hugel H, Sharma M, Goebels A. Percutaneous cordotomy for unilateral cancer pain - does it work? *Marie Curie Cancer Care Research Conference,* London, 2009.

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APPENDIX B

LEVELS OF EVIDENCE AND THE DEVELOPMENT OF CLINICAL GUIDELINES

Introduction to Evidence-based Medicine

Palliative care patients have the right to receive the optimum and most appropriate care in the last weeks, days and hours of life. [1] With the continued expansion of palliative care and integration into mainstream healthcare there is an increasing need for evidence that interventions produce high quality outcomes for patients and their families. [2] This approach is known as evidence-based medicine and is defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." [2] High quality research will help to produce the evidence on which clinical decisions are made. [3]

Definitions and Objectives of Clinical Guidelines

Guidelines result from a review of the evidence and are defined as: "systematically designed statements to assist practitioner and patient decisions about appropriate health care for particular clinical circumstances." [4]

They were initially developed to encourage the use of evidence in delivering patient care and have four main objectives:

1. To translate research into clinical practice.
2. To encourage the setting and monitoring of standards.
3. To promote clinical excellence resulting in high standards of patient care and the improvement of outcomes.
4. To aid in eliminating wide variation in medical practice.

Quality of Guidelines/ Clinical Application

It is important that all clinical guidelines are interpreted with care. They are not a substitute for clinical judgment but can assist health care professionals in making decisions about appropriate and effective patient care by providing evidence of effective practice. [6] Ultimate decisions about the management of an individual patient will depend on the clinical situation, the wishes of the patient and the judgment of the multi-professional team. [7]

Guidelines with a wide variety of styles and formats have been shown to be effective in changing practice. However, all guidelines and recommendations should ensure validity, reliability, clarity and flexibility. They should be applicable to the clinical setting and result from a multidisciplinary process, be well documented and undergo regular scheduled review. [4, 8]

Drawbacks of Guidelines

There has been criticism about the increasing focus on evidence-based medicine. It is important to remember that medical decision making does not only rely on evidence from clinical trials, but will also take into account other factors e.g. the wishes of an individual; social, psychological and educational influences; ethical considerations and cost implications. [5] Ignoring these factors means that the complexity of healthcare is not taken into consideration. There can also be problems with interpretation of the evidence because of problems with meta-analyses and the different characteristics of patients randomised into clinical trials.

National Guidelines Groups

The past decade has seen the development of national groups with a focus on the production of guidelines for various healthcare topics. The Scottish Intercollegiate Guidelines Network (SIGN) was formed in 1993 by the Academy of Royal Colleges and their Faculties in Scotland and produces evidence based guidelines for the National Health Services in Scotland. [6] The National Institute for Health and Clinical Excellence is a separate organisation which produces guidance on health technologies and clinical practice for the NHS in England and Wales. [9] These two organisations co-operate in the Guidelines International Network. This is a major international initiative involving organisations from around the world. The aim is to improve the quality of health care by promoting the systematic development of clinical guidelines and their application in clinical practice**.** [10]

Levels of Evidence and Grades of Recommendation

Prior to 2000 the system for grading guidelines and recommendations used by SIGN was based on the work of the US Agency for Health Care Research and Quality. [8] 2003 saw the development of a revised system. [6, 11] Table 1 illustrates the new grading system for recommendations in evidence based guidelines. [11]

There needs to be increasing attention on how guidelines are developed in order to adequately address potential biases and to ensure that recommendations are valid. It is important to strengthen the link between the recommendations and the scientific evidence in a way that is clearly visible.

Merseyside and Cheshire Palliative Care Network Audit Group

The standards and guidelines in this book have been developed by the Merseyside and Cheshire Palliative Care Network Audit Group. The guidelines are formulated following a review of the literature, presentation of the results of local and regional clinical audit, multi-professional discussion and review. All of the guidelines are reviewed by external experts prior to dissemination.

The fourth edition of this book is now comprehensively referenced, and has levels of evidence and grades of recommendation for the standards and guidelines in all 43 chapters. [12] The grades of recommendation are based on the strength of supporting evidence, but also take into account the judgment of the lead contributors and external reviewers for each chapter.

The reader will note that the levels and grades of evidence are often low and this reflects the difficulty in performing randomized controlled trials in palliative care. However it is important to emphasise that the grade of recommendation relates to the strength of the supporting evidence rather than its importance and so equal attention should be given to both low and high grade recommendations. [6]

Future Developments

The standards and guidelines will continue to be reviewed and updated every three years as recommended. [13] The fifth edition is due to be published in 2012 and will continue the increasingly structured approach to systematic reviews of the literature and a commitment to relevant high quality audit work.

Table 1 Levels of evidence and grading of recommendations [11]	
Levels of evidence/ Description of the evidence	
1+++	High quality meta analyses, systematic reviews of RCTs or RCTs with very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias.
2++	High quality systematic reviews of case-control or cohort studies with a low risk of confounding, bias or chance and a high probability that the relationship is causal.
2+	Well conducted case control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal.
2-	Case control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.
3	Non-analytic studies e.g. case reports, case series.
4	Expert opinion.
Grades of recommendation	
A	At least one meta-analysis, systematic review or RCT rated as 1++ and directly applicable to the target population, **or** A systematic review of RCTs, or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results, **or** Extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, **or** Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4, **or** Extrapolated evidence from studies rated as 2+.

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APPENDIX C

Merseyside and Cheshire Palliative Care Network Audit Group

Audit Programme 2000-2009

Audit Topic	Dates of Local Audit(s)	Dates of Regional Audit(s)	Reviews by Lead Contributor	Reviews by External Expert
Agitation	April 1995 March 2002	July 2008	July 2006 January 2009	July 2006 January 2009
Antibiotics	October 1998 July 2007		July 2006 January 2009	July 2006 January 2009
Anticoagulation	April 2002		July 2006 January 2009	July 2006 January 2009
Anticonvulsants	October 2004		July 2006 January 2009	July 2006 January 2009
Ascites	June 1995	July 2005	July 2006 January 2009	July 2006 January 2009
Bereavement	October 2003		July 2006 January 2009	July 2006 January 2009
Bisphosphonates	February 2000	November 2008	July 2006 January 2009	July 2006 January 2009
Blood Transfusion	February 1996 June 2000	September 2007	July 2006 January 2009	July 2006 January 2009
Bowel Obstruction	February 1997 April 1998	February 2006	July 2006 January 2009	July 2006 January 2009
Breathlessness	February 1998 January 2003		July 2006 January 2009	July 2006 January 2009
Constipation	October 1996 December 1999	March 2008 (S)	July 2006 January 2009	July 2006 January 2009
Corticosteroids	June 2001	March 2009 (S)	July 2006 January 2009	July 2006 January 2009
CPR	December 2002	October 2009	July 2006 January 2009	July 2006 January 2009
Delirium	April 1995 March 2002	July 2008	July 2006 January 2009	July 2006 January 2009
Depression	June 1996 February 2001		July 2006 January 2009	July 2006 January 2009
Diabetes	December 2000	January 2008	July 2006 January 2009	July 2006 January 2009
Drugs used at the End of Life	September 2006		January 2009	January 2009
Fatigue	April 2001	July 2009	July 2006 January 2009	July 2006 January 2009
Fentanyl in the Dying Patient	June 2001		July 2006 January 2009	July 2006 January 2009
Genograms	March 2003		July 2006 January 2009	July 2006 January 2009

(S) Denotes a Supraregional Audit

Audit Topic	Dates of Local Audit(s)	Dates of Regional Audit(s)	Reviews by Lead Contributor	Reviews by External Expert
Hydration in the Dying Patient	June 1999	July 2006	July 2006 January 2009	July 2006 January 2009
Hypercalcaemia	October 1995 December 1998	February 2004	July 2006 January 2009	July 2006 January 2009
Insomnia	September 2002		July 2006 January 2009	July 2006 January 2009
Interventional Pain Techniques	October 2008		January 2009	January 2009
Major Haemorrhage	November 2007		January 2009	January 2009
Methadone	2001		July 2006 January 2009	July 2006 January 2009
Nausea and Vomiting	August 1996	July 2003	July 2006 January 2009	July 2006 January 2009
Neuropathic Pain	June 1997 April 1999	July 2004	July 2006 January 2009	July 2006 January 2009
NSAIDs	October 1997	December 2005	July 2006 January 2009	July 2006 January 2009
Opioid Substitution	February 1995 December 1997	July 2007	July 2006 January 2009	July 2006 January 2009
Oral Care	May 2000	February 2005	July 2006 January 2009	July 2006 January 2009
Pathological Fractures	April 2005		July 2006 January 2009	July 2006 January 2009
Pleural Effusions	August 1995	March 2007	July 2006 January 2009	July 2006 January 2009
Pruritus	December 2003		July 2006 January 2009	July 2006 January 2009
Psychostimulants	September 2001		July 2006 January 2009	July 2006 January 2009
Psychological Support Services	December 2004		July 2006 January 2009	July 2006 January 2009
Renal Failure	October 1999	September 2005	July 2006 January 2009	July 2006 January 2009
Sexual Health	December 2001	Due December 2009	July 2006 January 2009	July 2006 January 2009
Spiritual Care	April 2006		July 2006 January 2009	July 2006 January 2009
Spinal Cord Compression	March 2004		July 2006 January 2009	July 2006 January 2009
Substance Misuse	January 2009		January 2009	January 2009
Syringe Drivers	April 1996 July 2002		July 2006 January 2009	July 2006 January 2009
Urinary Incontinence	November 2006		January 2009	January 2009

(S) Denotes a Supraregional Audit

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