Approach to CNS Symptoms in Palliative Oncology

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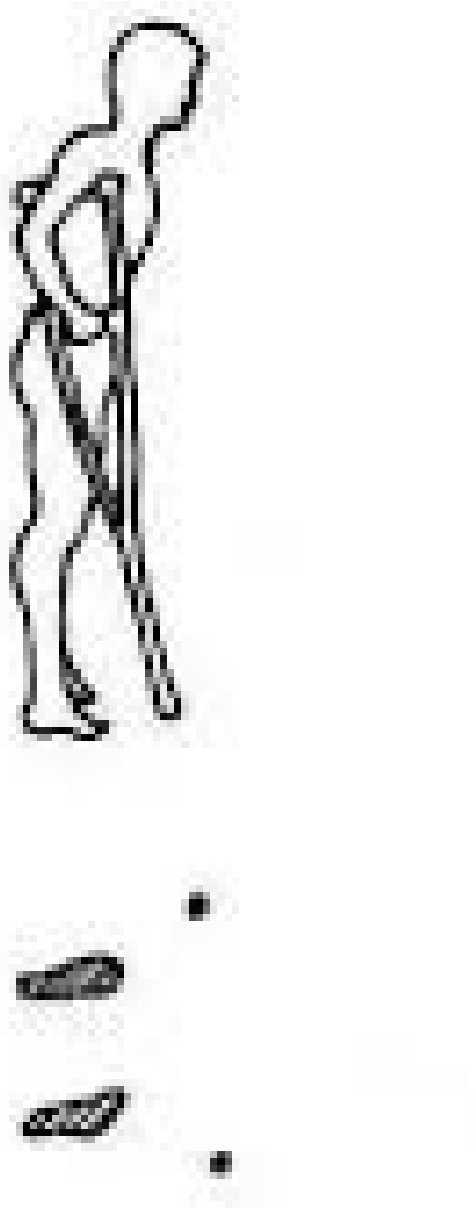
- **S**cience
  - Evidence informed treatment
  - Careful clinical assessment of symptom and pathophysiology
- **U**nderstanding (**Communication**)
  - Patient understands disease and treatment options
  - Doctor understands the communication gap and the patient’s expectations
- **E**thics
  - Do the benefits **(beneficence)** outweigh the harms (**maleficence)**
  - What impact does it have on family and society – **(justice)** equitable use of resources
  -

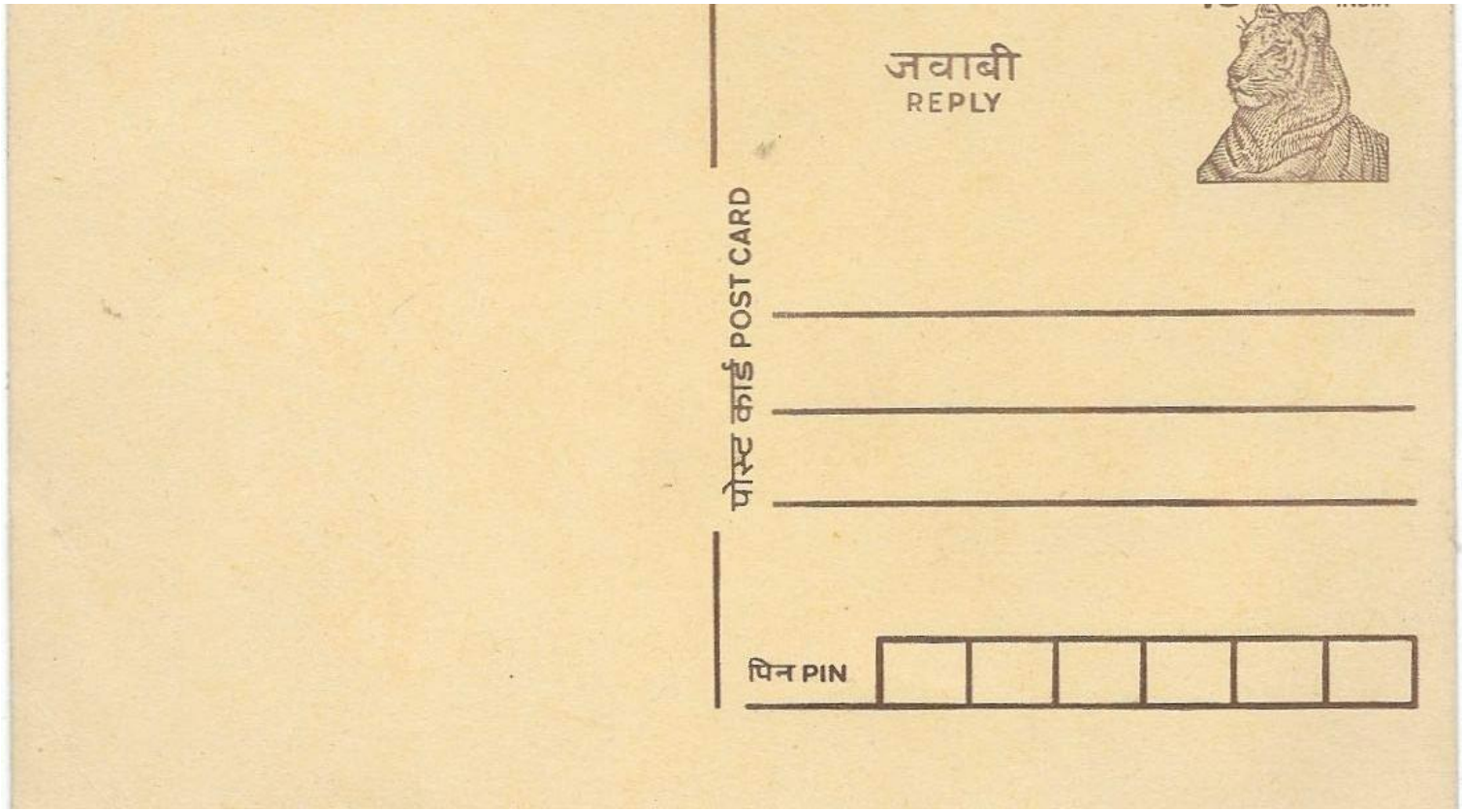
A patient I met when I was doing my MD in Rad Onc in Delhi in the early 1990s

Osteosarcoma, post amputation, with small lung secondaries

On palliative chemotherapy



Postcards to family…please come soon



Murr Gaya’

Across the world desperate families still leave—or lose— homes and livelihoods seeking treatment for incurable disease. My medical history has begun to include the questions

George R, ***Indian Journal of Medical Ethics, 2022***

Understanding... Expectations and Background

“Where is your home?”

“What were you hoping for when you came this far?”

“Who has come with you?”

“What is your profession?”

“How are you raising money for this treatment?”

“How old is your youngest child?”

George R, **Indian Journal of Medical Ethics, 2022**

Such questions frame the therapeutic chessboard, in the hope that the pieces will not fall off the table because of treatment recommendations

George R, ***Indian Journal of Medical Ethics, 2022***

Cochrane Database of Systematic reviews | Review - Intervention

Interventions for the treatment of metastatic extradural spinal cord compression in adults

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Authors' declarations of interest

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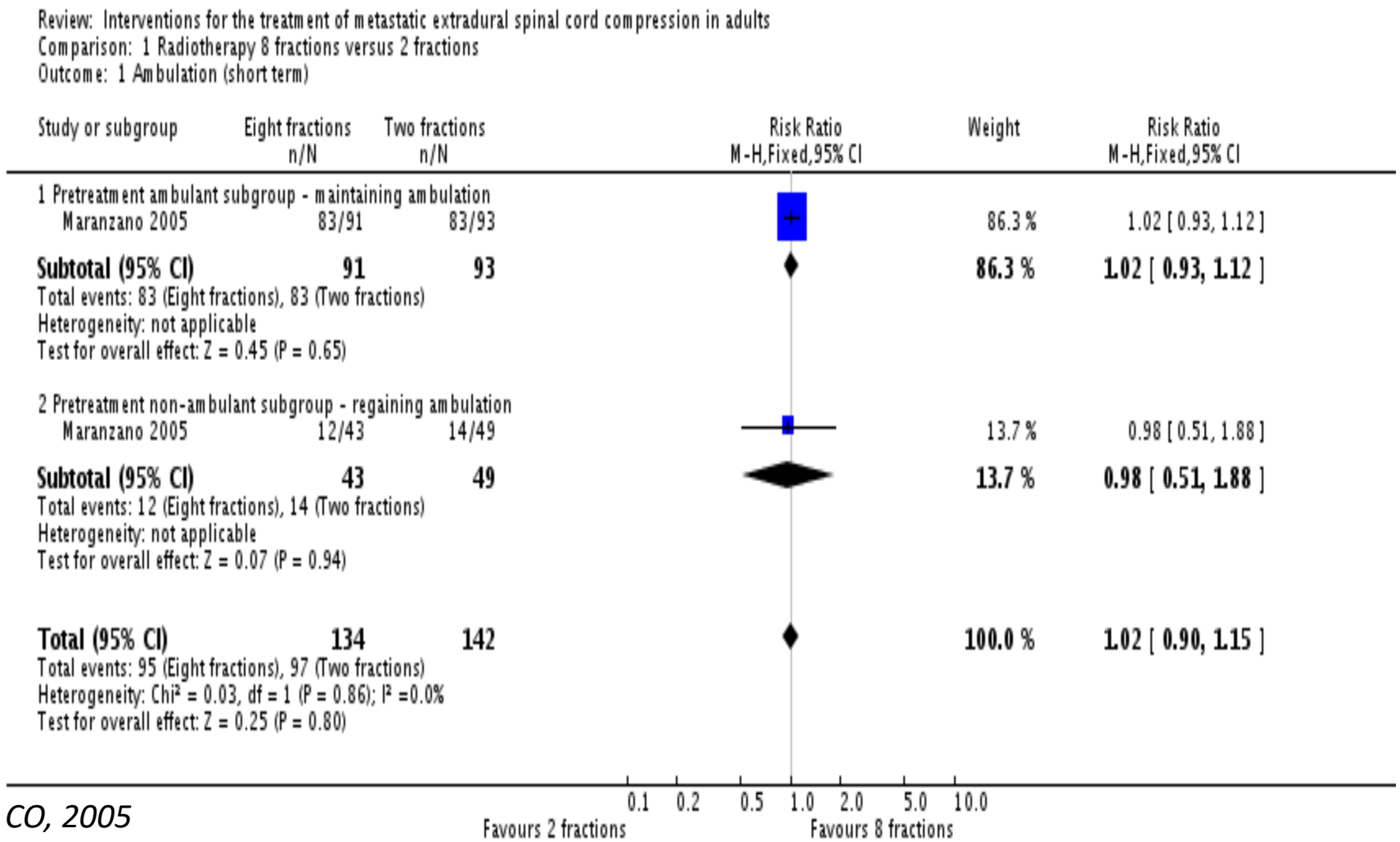
Abstract

Available in **English** | Español | فارسی | 简体中文

George et al, Cochrane Database of Systematic Reviews, 2015

Background

Metastatic extradural spinal cord compression (MESCC) is treated with radiotherapy, corticosteroids, and surgery, but there is uncertainty regarding their comparative effects. This is an updated version of the original Cochrane review published in the *Cochrane Database of Systematic Reviews* (Issue 4, 2008).



Maranzano et al, J CO, 2005

George at al, Cochrane Database of Systematic Reviews, 2015

Comparison 2: Patients with metastatic spinal cord compression - single fraction radiotherapy versus multiple (or short) fraction radiotherapy

Figure 6: Neurological and functional status: Ability to walk after treatment

Study or Subgroup	Single fraction Events	Total	Multiple fractions Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hoskin 2019	115	166	128	176	49.1%	0.95 [0.83, 1.09]
Lee 2018	28	36	24	37	9.4%	1.20 [0.89, 1.61]
Maranzano 2009	95	153	104	150	41.5%	0.90 [0.76, 1.05]
Total (95% CI)		**355**		**363**	**100.0%**	**0.95 [0.86, 1.05]**
Total events	238		256			

Heterogeneity: Chi² = 2.90, df = 2 (P = 0.23); I² = 31%
Test for overall effect: Z = 0.98 (P = 0.33)

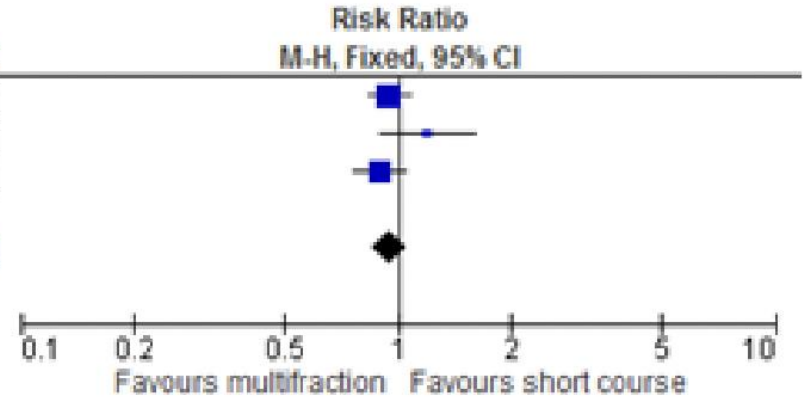
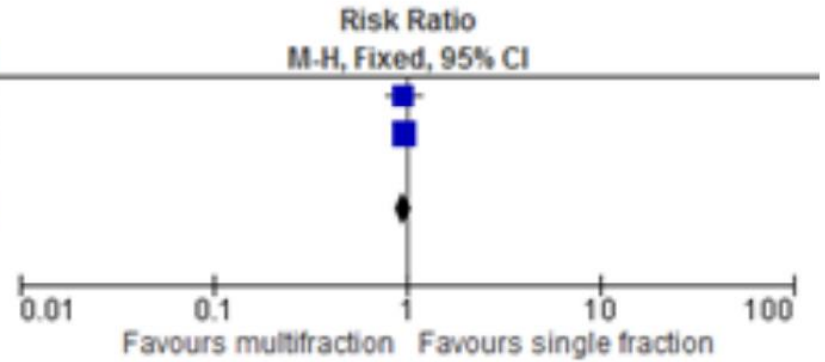


Figure 7: Neurological and functional status: Normal bowel function after treatment

Study or Subgroup	Single fraction Events	Total	Mulitple fraction Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hoskin 2019	112	315	118	322	46.9%	0.97 [0.79, 1.19]
Maranzano 2009	130	153	131	150	53.1%	0.97 [0.89, 1.06]
Total (95% CI)		**468**		**472**	**100.0%**	**0.97 [0.87, 1.08]**
Total events	242		249			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.52 (P = 0.60)



https://www.nice.org.uk/guidance/ng234/evidence/

- Single fraction verses multiple fraction radiotherapy There was moderate to high quality evidence of no important difference between single fraction radiotherapy and multiple fractions in terms of neurological and functional status, quality of life, pain, overall survival and treatment toxicity..

https://www.nice.org.uk/guidance/ng234/evidence/

NICE Guidelines 2023

- Use 8 Gy single fraction radiotherapy for people with MSCC having radiotherapy unless they are at high risk of side effects. **[2023]**
- Consider multiple fraction radiotherapy for people at high risk of side effects from radiation, for example, if they have:
  - disease requiring a large treatment field or fields
  - had previous radiotherapy treatments. **[2023]**

NICE guideline number NG234, 2023

- Nineteen studies were included in this review reporting results from 13 randomised controlled trials (Hoskin 2019 [SCORAD-III trial], Howell 2013 [RTOG 97-14 trial], Lee 2018 [ICORG 05-03 trial], Majumder 2012, Maranzano 2005, Maranzano 2009, Patchell 2005, Rades 2016 [SCORE-2 trial], Rades 2018 [SCORE-2 trial], Rades 2019 [SCORE-2 trial], Roos 2005 [TROG 96-05 trial], Sahgal 2021, Sprave 2018 – a, b, c [IRON-1 trial], Sprave 2018 d, e, f [NCT- 02358720], Steenland 1999 [Dutch bone metastasis trial]). The included studies are summarised in Table 2. Four randomised controlled trials (Howell 2013 [RTOG 97-14], Majumder 2012, Roos 2005 [TROG 96-05], Steenland 1999 [Dutch Bone Metastasis trial]) compared single fraction radiotherapy to multiple fraction radiotherapy in patients with spinal metastases (without evidence of cord compression). Three randomised controlled trials (Hoskin 2019 [SCORAD-III trial]), Lee 2018 [ICORG 05-03 trial], Maranzano 2009), compared single fraction radiotherapy to multiple fraction or splitcourse radiotherapy in patients with metastatic spinal cord compression. One randomised controlled trial (Sprave 2018 a, b, c [IRON-1 trial]) compared image guided intensity modulated radiotherapy (IMRT) to conventional radiotherapy (CRT) in patients with spinal metastases (without evidence of cord compression). Two randomised controlled trials (Sahgal 2021, Sprave 2018 d, e, f [NCT- 02358720]) compared stereotactic ablative body radiotherapy (SABR) to CRT in patients with spinal metastases (without evidence of cord compression). Two randomised controlled trials compared different regimens of radiotherapy (Maranzano 2005, Rades 2016 [SCORE-2 trial], Rades 2018, Rades 2019 [SCORE-2 trial]) in patients with metastatic spinal cord compression; and 1 randomised controlled trial compared surgery + radiotherapy to radiotherapy alone (Patchell 2005) in patients with metastatic spinal cord compression

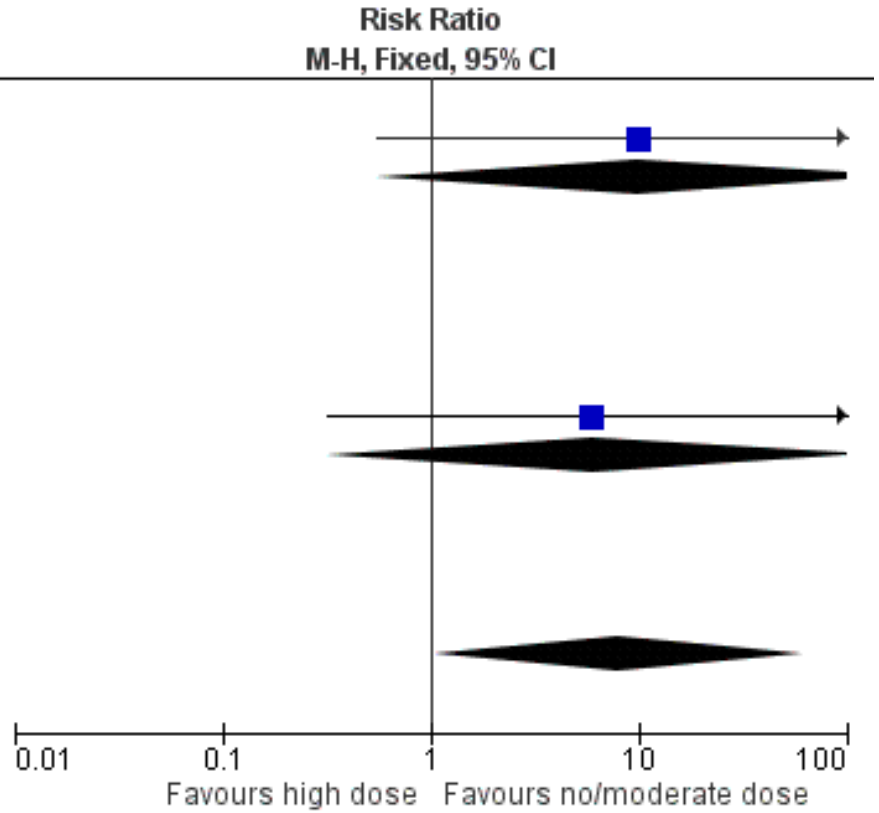
NICE guideline number NG234, 2023

https://www.nice.org.uk/guidance/ng234/chapter/Recommendations

- Commence steroids (dexamethasone 8 mg twice a day).
- Offer gastroprotection
- blood glucose monitoring
- pain management
- bowel management
- urinary catheter

Corticosteroids

Study or Subgroup	High dose steroids Events	Total	No / mod dose steroids Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 High dose versus no corticosteroids						
Sorensen 1994	4	27	0	30	51.1%	9.96 [0.56, 176.92]
Subtotal (95% CI)		**27**		**30**	**51.1%**	**9.96 [0.56, 176.92]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.57 (P = 0.12)						
1.2.2 High dose versus moderate dose corticosteroids						
Graham 2006	2	9	0	11	48.9%	6.00 [0.32, 111.04]
Subtotal (95% CI)		**9**		**11**	**48.9%**	**6.00 [0.32, 111.04]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						
Total (95% CI)		**36**		**41**	**100.0%**	**8.02 [1.03, 62.37]**
Total events	6		0			
Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%						
Test for overall effect: Z = 1.99 (P = 0.05)						
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%						



George et al, Cochrane Database of Systematic Reviews, 2015

- For people **with neurological symptoms or si**gns of MSCC:
- Offer 16 mg of oral dexamethasone (or equivalent parenteral dose) as soon as possible with gastroprotection.
- After the initial dose, continue 16 mg of oral dexamethasone (or equivalent parenteral dose) daily for people awaiting surgery or radiotherapy.
- After surgery or at the start of radiotherapy, reduce the dose gradually until stopped.
    - *https://www.nice.org.uk/guidance/ng234/chapter/Recommendations*

Suspected Raised ICT

- For patients with cancer, raised ICP may be caused by the cancer or a bleed into or around the tumour

    - Consider a trial of corticosteroids with gastroprotection (usually proton pump inhibitor),
    - †Dexamethasone 8mg to 16mg orally (or IV) immediately and subsequently †Dexamethasone 4mg to 8mg twice daily orally (second dose before 2pm if possible). Discontinue promptly if no benefit and reduce gradually in responders.

    - Symptom relief with analgesia and anti-emetics (†ondansetron 4mg twice a day can be effective in patients with raised ICP)

- *https://rightdecisions.scot.nhs.uk/scottish-palliative-care-guidelines/palliative-emergencies/raised-intracranial-pressure-icp/*

Proven Raised ICT Corticosteroids: Raised ICT

- Mild symptoms: 4-8 mg
- Moderate to severe symptoms -16 mg stat , 8 mg bd 8 am and 2 pm
- Taper over 2-4 weeks if possible, in patients who were on less than 4 mg for less than 4 weeks
- Others needs slower tapering, some may need indefinite maintenance at lower dose

Symptoms in palliative oncology

- Caused by cancer
- Caused by treatment
- Caused by debility/immobility
- Caused by unrelated causes
- May be multifactorial

Twycross, Introducing Palliative Care,2003

Scientific Assessment of Symptoms

- Extent of cancer, comorbidities, drug chart
- Probability
- Pattern recognition- narrowing down history and exam
- Confirming examination, targeted investigations

Twycross, Introducing Palliative Care,2003

History of ‘Not speaking properly’

Man in his 50s, treatment refractory squamous cell lung cancer, no co-morbidities

- **Probability**: Primary known to be prone to brain metastases
- **Pattern recognition**- narrowing down history and exam
- Confirming targeted investigations

SCC Lung ‘Not speaking properly’: Scenario 1

Recent onset of	On examination	Fundus:
• Headache • Vomiting • **Slurred *articulation*** of words	• Conscious, in pain, oriented,	• **Papilloedema**

Sq Cell Ca Lung ‘Not Speaking Properly’: Scenario 2 a.

Talks irrelevantly, unable to give a proper history
Irritable
Drowsy
Not recognizing relatives
Seeing insects on the roof- **hallucinations**
Better in the afternoon
Worse again at night
Tongue very dry ? Probable cause ?

Delirium: Salient features

Acute or subacute onset
Reduced attention span
Often diurnal variation and fluctuation
Incoherent content of speech
Hallucinations may be present-plucking at bed clothes or ceiling
Short term memory impairment
Hypoactive/hyperactive

Twycross et al, Introducing Palliative Care, 2023

Delirium

- Caused by
    - Cancer?
    - Treatment?
    - Debility?
    - Unrelated?

Can be multifactorial…

Twycross, Introducing Palliative Care, 2003

Delirium: Squamous Cell Ca Lung: Scenario 2 a.

Hypercalcemia

Metabolic causes of delirium are common-

- Hypercalcemia
- Hyponatremia including SIADH

Delirium: Squamous Cell Ca Lung with Cord Compression on RT : Scenario 2c

- Talks irrelevantly, unable to give a proper history
- Drowsy
- Not recognizing relatives

- **Pulse rate 130/min, RR 30/m, SpO2 85, blood pressure 80/50**

On steroids for cord compression

A pneumonia or a UTI may not show obvious fever

Tachycardia, tachypnoea, hypotension and delirium may be the manifestations of infection/sepsis

Delirium: Squamous Cell Ca Lung with cord compression on RT : Scenario 2d

- Talks irrelevantly, unable to give a proper history
- Drowsy
- Not recognizing relatives
- Seeing insects on the roof- hallucinations
- **Pin point pupils, myoclonic jerks**

Had been on morphine for bone pain

Pain has come down with steroids and radiotherapy

Opioid dose is now higher than needed for pain

Drugs are a common cause of delirium, especially when renal function deteriorates

Delirium: Squamous Cell Ca Lung with cord compression on RT : Scenario 2e

- Agitated
- Sweating
- Blood pressure increased
- **Suprapubic mass**

Delirium due to debility

- Constipation
- Faecal impaction
- Spurious diarrhoea
- Urinary retention
- Hypertension, sweating, autonomic dysreflexia

Management

- Correct correctable causes where appropriate and feasible
- Non drug measures
  - Speak calmly, do not argue, explain to relatives that delirium is not madness
  - Clock, calendar for orientation
- Pharmacologic measures
- Caregiver education

Pharmacologic measures

? Antipschychotics for the disordered cognition and hallucinations

e.g. haloperidol

e.g- risperidone

Benzodiazepines. e.g lorazepam may worsen the confusion but may have a role in agitated delirium

From ‘SUE’ to ‘USE-Team’

Understanding (Communication)	Science	Ethics	**Team**
Patient understands disease and treatment options Doctor understands the patient’s context and expectations	Evidence changes. Assess it critically Explore the pathophysiology of the symptom	Do the benefits **(beneficence)** outweigh the harms (**maleficence)** What impact does it have on family and society – **(justice)** equitable use of resources **?**	**What can others in the team do to maximize benefits and justice**

Caregiver Education and Rehab

Caregiver support: Oncology+ Nursing

- Medicines to give sos for pain and other symptoms
- Transfers
- Pressure sore prevention
- Catheter care at home
- Administering suppositories, manual evacuation
- Mouth care

Raised ICT and vomiting

- In hospital was on
  - Injectable dexamethasone 8 mg
  - ondansetron
- At home, no injections, is vomiting out Tab dexamethasone and ondansetron
- What can we do ?

The subcutaneous route can be taught even to illiterate caregivers

- Like teaching insulin administration
- Insulin needle or 23 G insyte or scalp vein
- If the steroids and the anti-emetics are given subcutaneously, the patient may be able to tolerate the analgesics orally

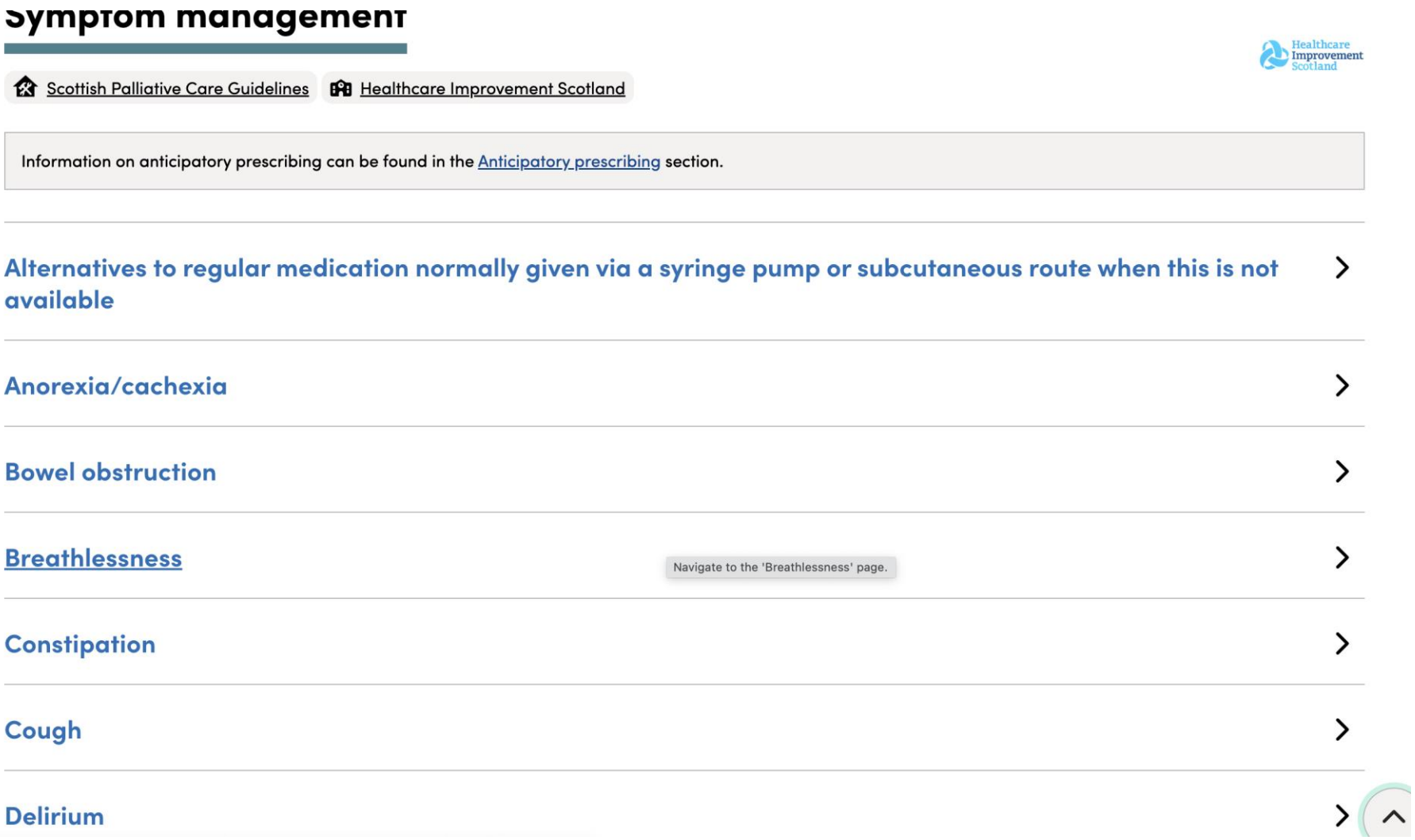
In the patient with raised ICT on dexamthasone which analgesic/s will you avoid?

- NSAIDs (Step1)
- Paracetamol (Step 1)
- Buprenorphine (Step 2)
- Tramadol (Step 2)
- T Morphine CR 10 mg bd (Step 3 used as Step 2 in low dose)
- Tab Morphine IR 5 mg q4h and sos (Step 3)

In the patient with raised ICT on Dexamthasone which analgesic/s will you avoid?

- NSAIDs: Increased risk of GI bleeds along with steroids
- Paracetamol (Step 1)
- Buprenorphine (Step 2)
- Tramadol (Step 2): May reduce seizure threshold in brain mets
- T Morphine CR 10 mg bd (Step 3 used as Step 2 in low dose)
- Tab Morphine IR 5 mg q4h and sos (Step 3)

https://rightdecisions.scot.nhs.uk/scottish-palliative-care-guidelines/symptom-management/



Oncology + Physiotherapy

- Prognosis directed goals for physical rehabilitation and caregiver education in cord compression
    - New prostate cancer vs end stage lung cancer

Social Work Plus Oncology

- Financial prognosis vs financial toxicity
- Fundraising for curative treatments
- Fundraising for family’s economic rehab

IMPORTANT

You have done something worthwhile when your patient survives a curable cancer.

You have done something worthwhile when the bereaved family survives the ravages of an incurable cancer

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Thank you for your attention