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A review of the literature on post-operative pain in older cancer patients

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ABSTRACT

Post-operative pain in older people is a growing problem as the number of those undergoing surgical procedures for cancer continues to increase. Difficulties arise because of the complex nature of the pain itself and the variable manner in which older people can present and respond to treatment. Inadequately treated acute pain can result in significant consequences. Not all healthcare professionals have sufficient knowledge and training in this specific area. Management is also hindered by the limited kinds of pharmacological and non-pharmacological treatments actually available on a day-to-day basis. Nonetheless, much can still be done. Instead of being protocol driven, post-operative pain management should be tailored to the individual patient's requirements. This can be achieved through effective communication between healthcare team and patient, careful pre-operative planning and selective use of common analgesics based on knowledge of the different advantages and disadvantages of each.

1. Introduction

In 1999, a survey of all French hospitals on all age groups and American Society of Anaesthesiologists (ASA) classes reported a 196% increase in the number of anaesthetic procedures performed in patients aged over 60 between 1980 and 1996.[1] Today, older people undergoing surgery outnumber younger ones by a ratio of 4:1.[2]

The change in our population demographics is one reason for this trend. There is also a growing awareness that traditional mortality risk scores for surgery are heavily dependent on age without clear evidence. These are being revised.[3] Interestingly, in the abovementioned study, the ASA 3 cohort showed the greatest increase (268%) of all ASA classes.[1]

Add to that the fact that 64% of cancers are first diagnosed in people aged 65 and over,[4] and it comes as no surprise that the number of older people undergoing surgery for cancer is increasing as well. This is further encouraged by accumulating data suggesting comparable outcomes in older patients undergoing surgery for potentially curative surgery for colorectal, pancreatic and oesophageal cancer as well as liver resection for colorectal and hepatocellular cancer.[5]

Healthcare professionals have consequently had to learn to deal with a 'new' set of complications related to surgical procedures for older people in recent times. Of these, post-operative pain control numbers one of the more significant and important issues.

In 1997, the Audit Commission proposed a standard whereby less than 20% of patients should experience severe pain following surgery after 1997 and less than 5% by 2002.[6] In 2002 however, 1 in 5 patients still experienced severe pain, or poor or fair pain relief after surgery. Moderate or severe pain at rest or on movement was also common.[7]

This is still a problem. In a recent survey, 62% of 322 patients aged 65 and older undergoing open elective cardiac, thoracic, abdomino-pelvic and orthopaedic procedures

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reported experiencing post-operative pain. Only 87% of this subset were satisfied with treatment for it.[8]

2. Why is this important?

Cynics could say that the patient and the pain eventually 'go away'[9] so why worry? Not all post-operative pain 'goes away' however. Melzack and colleagues reported that pain could persist over a week for about one-third of post-operative patients. That group tended to be older and have more complex medical problems. Despite ongoing uncontrolled pain, they did not receive more potent or larger doses or analgesia but simply more of the same.[10]

It is vital to treat pain, regardless of how short-lived it might be. Simply 'waiting it out' may make matters worse as inadequately treated acute pain can turn into chronic pain. This results from the body's biphasic response to pain in the dorsal horns of the spinal cord. The first phase is usually immediate and well localised while the second tends to be duller and poorly localised. If the initial phase is terminated quickly enough, the 'windup' (hyperalgesia) or 'central sensitisation' phase that can cause long-term pain does not follow or is at least attenuated.[11]

Uncontrolled pain may lead to a variety of physiological complications (Table 1).[12,13] Higher post-operative pain intensity in older people is also related to decreased functional status two months after and poorer ambulation six months after.[14]

3. It is not just 'Another Pain Problem'

Post-operative pain in older people is often more complicated as it can be an amalgam of several conditions:

(a) *Chronic pain:*Patients may already have been suffering from pain prior to surgery. One in ten people in the United Kingdom (UK) suffers from some form of pain every day.[15] This figure increases with age.
A Scottish survey of the prevalence of chronic pain amongst patients registered to general practitioners found this to be a problem for 31.8% of those aged 25–34 years and 62% of those aged over 75 years. For the latter, chronic pain was most commonly due to arthritis, angina or back pain.[16] Two-thirds of the people with chronic pain believe that their current medications do not sufficiently control their pain all the time.[17]

(b) *Cancer:*This can further complicate matters. Approximately, one in three people in the developed world will be diagnosed with cancer.[18] At the time of diagnosis, up to half of all patients with cancer already experience moderate to severe pain due to cancer. At least 80% of older patients will have significant pain when the disease is advanced.[19]
Cancer pain could arise directly from metastatic spread of the cancer and/or the activation of nociceptors by tumour-related mediators such as endothelin-1 (ET-1) and tumour necrosis factor alpha (TNF-α). This can contribute up to two-thirds of pain.[20] Treatment for cancer, even non-surgical modalities, may either alleviate or escalate this.[21] The vinca alkaloids for instance can cause abdominal pain, paraesthesias, dysthesias and allodynia.[22]
In general, cancer pain by itself is still poorly dealt with. It may be worse if one is female, part of a minority group and/or elderly – three conditions which are not mutually exclusive.[23]

Table 1 – Physiological consequences of unrelieved pain[12,13]

Domain	Stress response	Clinical manifestations
Endocrine/metabolic	Altered release of multiple hormones (e.g. ACTH, cortisol, catecholamines, insulin) with associated metabolic disturbances	Weight loss, fever, increased respiratory and heart rate, shock
Cardiovascular	Increased heart rate Increased vascular resistance Increased blood pressure Increased myocardial oxygen demand Hypercoagulation	Unstable angina Myocardial infarction Deep vein thrombosis
Respiratory	Decreased air flow due to involuntary (reflex muscle spasm) and voluntary ('splinting') mechanisms that inhibit respiratory effort	Atelectasis, pneumonia
Gastrointestinal	Decreased rate of gastric emptying, decreased intestinal mobility	Delayed gastric emptying constipation, anorexia, ileus
Musculoskeletal	Muscle spasm, impaired muscle mobility and function	Immobility Weakness Fatigue
Immune metastatic	Impaired immune function	Infection Impaired wound healing Increased susceptibility to spread of cancer
Genitourinary	Abnormal release of hormones	Decreased urine output Hypertension (fluid retention) Electrolyte disturbance

(c) *Surgery*:Logic dictates that there would be added discomfort after surgery in most cases. The length of operative time tends to correlate with severity of post-operative discomfort. Abdominal and thoracic procedures also appear to cause more pain.[24]

Post-operative pain control for older people undergoing surgery for cancer can therefore be a difficult problem. Nevertheless, much can still be done. Even better, in most cases, it is 'common sense' that is required, rather than an expensive new medication or technique – although the latter would not be remiss.

4. Post-operative pain management

This can be divided into three steps:

(a) prevention,
(b) recognising the problem,
(c) treating it.

Before discussing each in turn however, brief mention should be made of the age factor. One must be cautious in naming age as a risk factor here. It is physiological fitness rather than biological age that matters. Age is nonetheless important in that one needs to remember that older people can present in a myriad of ways. The majority are quite fit and well. However, a significant number still require caution in their management.

4.1. *Preventing post-operative pain*

Studies looking at the efficacy of pre-operative counselling in reducing pre-operative anxiety levels and subsequent post-operative pain have been unequivocal in their findings.[25] As for pre-emptive analgesia, it has not yet been shown to be at least as efficacious as routine post-operative analgesia.[26] Nonetheless, some still believe that this is due to differences in study design rather than failure of the concept – i.e. if the 'windup' phenomenon could be prevented, the resulting discomfort could be lessened.[27]

4.2. *Recognising pain*

We are not good at simply asking patients if they are in pain. Even when told, we do no better. Despite oft-repeated reminders that 'pain is whatever the patient says it is',[28] a significant number of healthcare professionals remain sceptical when patients complain of pain.

As mentioned before, patients, especially older ones, can present in many ways. They may also have a variety of attitudes towards pain, ranging from being stoical to highly sensitive. Up to 50% of older patients may have beliefs that inhibit the optimal diagnosis and management of pain.[29] Unfortunately, some misconceptions prevail (Table 2).

In addition, despite evidence to the contrary, many of us believe that we can actually 'tell' if a patient is truly in pain. Most healthcare professionals underestimate the severity of pain when using observation alone.[30] Changes in physiologic parameters such as blood pressure, respiratory rate and pulse rate are not sensitive for discriminating pain from other sources of distress.[31]

Table 2 – Common misconceptions about pain[12]

- Pain does not exist in the absence of physical or behavioural signs, or detectable tissue damage
- Physical or behavioural signs of pain (e.g. abnormal vital signs, grimacing, limping) are more reliable indicators of pain than patient self-report
- Pain without an obvious physical cause, or that is more severe than expected based on findings, is usually psychogenic
- Comparable stimuli produce the same kind of pain in all individuals
- Analgesics should be withheld until the cause of pain is found
- Patients who
  a) know a great deal about pain medications and/or
  b) attend emergency departments frequently and/or
  c) have been taking opioids for a long time are often assumed to be dependent on drugs

In older patients, communication problems due to visual, speech and hearing difficulties as well as the language barrier for a number of ethnic minorities may also become issues. Post-operative delirium is not uncommon.

Some pain assessment tools have therefore been introduced over the years to aid this process although no one tool has yet been found to be reliable and valid.[32] It mainly remains a matter of trial and error.

Melzack's verbal rating scale[33] is one of the most popular (Table 3). The Horizontal Visual Pain Scale[34] and the Faces Pain Scale[35] (Fig. 1) are unidimensional instruments recommended by the American Geriatrics Society. Gloth and colleagues's Functional Pain Scale is another useful one (Table 4).[36]

Cognitive impairment in a subset of people could be a problem. Nonetheless, some of them may still be able to complete self-assessment pain scales.[37] On the whole however, observational scales based on vocalisations, facial expressions and body language are recommended for this group. These include the assessment of discomfort in dementia protocol (ADD), Checklist of non-verbal pain indicators (CNPI)[38] (Table 5) and the Nursing Assistant-Administered Instrument to assess Pain in Demented Individuals (NOPPAIN).

Still, one must not presume that all patients will experience pain from any surgical procedure. One study has reported that up to 6% of patients undergoing elective orthopaedic surgery did not require any post-operative pain relief.[24]

There are socio-cultural differences as well. For example, Anglo-American men appear to tolerate deep pain, produced by mechanical pressure on the Achilles tendon, better than

Table 3 – Melzack's verbal rating scale[33]

How intense do you perceive your pain?
None
Mild
Discomforting
Distressing
Horrible
Excruciating

Fig. 1 – Adapted version of Biere's Faces Pain Scale.[35]

Table 4 – Functional pain scale[36]

0 = No pain
1 = Tolerable. Pain does not prevent any activities
2 = Tolerable. Pain prevents some activities
3 = Intolerable but still able to use telephone, view television, or read
4 = Intolerable. Pain prevents use of telephone, television or reading
5 = Intolerable. Pain prevents verbal communication

African-Americans. The latter in turn do better than Asian-Americans.[39] The literature on pain with regards to gender differences remains unclear.[40]

4.3. *Treating the pain*

4.3.1. *Timing*

Post-operative pain may only surface or worsen at certain times, for instance, when turning or standing up. Advising patients to ask for 'PRN' analgesia before they start to do things they know will cause pain may help. It is crucial then that pain relief is actually administered immediately thereafter.

4.3.2. *Patient factors*

Inter-individual variability prevents us from prescribing a standard 'one-size fits all' pain relief measure for all our patients. Genetics plays a role in responses to some analgesia. For example, the gene coding for the neuronal cytochrome P450IID6 enzyme involved in converting codeine to morphine by O-methylation is absent in 7–10% of Caucasians.[41,42]

Other co-morbidities can interfere with treatment. Older patients have a greater likelihood of multiple side-effects and interactions from pre-existing medications and post-operative analgesia. Physiological changes related to ageing can have a number of implications (Table 6).

(a) *Choice of analgesia*

There are a greater range of treatment options today (Table 6). Nevertheless, our actual day-to-day choices remain limited. Few hospitals can provide much in the non-pharmacological class apart from physical therapy. As for medication, morphine, codeine phosphate and paracetamol as well as non-steroidal anti-inflammatories (NSAIDs) remain the most commonly available.

Most pain control protocols are based on the 1996 World Health Organisation (WHO) pain ladder (Fig. 2). This is not fail-safe however. Take Step 2, for instance. It suggests that all weak opioids are superior to full doses of NSAIDs, whilst other studies have shown otherwise.[44] It has also been criticised for ignoring non-drug modalities.[45,46]

In addition, one cannot always follow this sequence of steps. Some patients need to start 'at the top' simply because the pain is so severe. One would never dream of only giving paracetamol to a patient who has just sustained a Colles fracture and a hip fracture as well as multiple rib fractures.

There are comparison tables available today. However, it is not useful to apply the number Needed to Treat approach[47] or league tables[48] to older patients either as the original data is often derived from younger populations. One would therefore do better by trying to remember the 'worst' or 'best' of each drug class (Table 7).

4.3.3. *Opioids*

Opioids that are both agonist and antagonist should be avoided as they often cause more delirium.[52] Other reasons include the following:

(1) Normeperidine, the renally excreted metabolite of meperidine, can cause central nervous excitation, tremors and seizures.
(2) Methadone, with its long half-life and risk of accumulation, should be avoided in older adults.[51]
(3) Buprenorphine should not be used in a patient already on morphine as it is a partial agonist and will replace morphine at the receptor site. This could increase pain, or precipitate symptoms of withdrawal from morphine. If a patient is on buprenorphine and morphine is added, the effect of morphine will be delayed.[53]

Immediate-release opioids such as morphine hydromorphone and oxycodone have extensive first-pass metabolism. It can therefore take up to 30 min for their analgesic effects to set in. More rapid-onset opiods such as oral transmucosal fentanyl citrate can work within 5–15 min and thus could be considered for breakthrough pain.[54]

Table 5 – Checklist of non-verbal pain indicators (CNPI)[38]

	With movement	Rest
1. Vocal complaints (non-verbal)	–	–
2. Facial grimaces	–	–
3. Bracing	–	–
4. Restlessness	–	–
5. Rubbing	–	–
Subtotal score (In addition, also record verbal complaints)	–	–
6. Vocal complaints	–	–
Total score	–	–

Score 0 if behaviour not observed, 1 if behaviour observed.

Table 6 – Physiological changes due to ageing and their implications for post-operative pain control[2]

Physiologic changes	Implications
Cardiovascular function	
Decline in arterial compliance and cardiac output. Reduced preload	Hypovolaemia or decreased sympathetic response following epidural anaesthesia
Decreased myocardial responsiveness to catecholamines and diminished heart rate response	Reduced clearance of morphine
Decreased muscle mass leading to reduced systemic arteriovenous oxygen difference	Higher peak arterial concentrations after intravenous administration of morphine
Peripheral and central nervous system	
Change in all forms of sensory perception	May complicate communication
Decrease in neuronal and neurotransmitter density and activity and in the number of neurotransmitter receptor sites	Anaesthetic techniques such as spinal or epidural anaesthesia that induce a rapid loss of sympathetic activity are more likely to cause hypotension
Neuronal loss in autonomic nervous system associated with impaired cardiovascular reflexes	
Pulmonary system	
Decreased sensitivity of respiratory centres to hypoxia and hypercapnia	Increased risk of hypoxaemia
Increased periodic breathing or apneic periods during sleep	Higher likelihood of post-operative apnea and airway obstruction
Ossification of costal cartilages, loss of vertebral disc space, increased anteroposterior diameter, calcification of rib articulatory surfaces	Increased risk of atelectasis, pneumonia Greater difficulty in performing regional anaesthesia
Altered pharyngeal function and diminished cough	Increased risk of false passage
Renal function	
Decreased glomerular filtration rate, tubular excreation, tubular excretion, tubular reabsorption	Reduced renal metabolism and clearance of morphine and NSAIDs
Kidney more sensitive, less flexible and slower to respond to maintain homeostasis	
Gastrointestinal and hepatic system	
Decreased gastric prostaglandin synthesis, bicarbonate and non-parietal fluid secretion	Greater risk of NSAID-induced mucosal damage
Reduced liver size, liver blood flow and liver perfusion	Reduced hepatic metabolism of drugs with high hepatic extraction ratio: opiods and lidocaine

Hydrophilic drugs such as morphine usually have a higher serum concentration and lower redistribution. On the other hand, lipophilic ones, such as pethidine, morphine and fentanyl, tend to be more widely distributed, accumulated, and subsequently delayed in their release.[55,56]

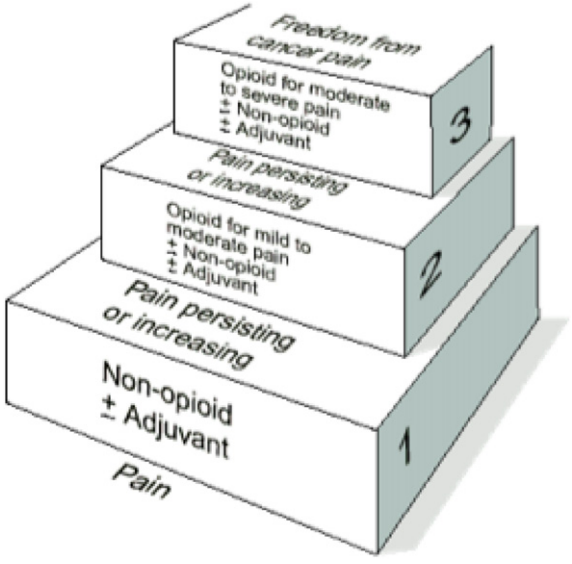

Fig. 2 – WHO Pain Ladder.

Most analgesics can now be administered via a variety of routes (Table 8).[49–51]

Keeping in mind inter-individual variability in responses to analgesia, failure of one patient to respond to one opioid should prompt a trial of another. A higher dose of the same drug might not relieve pain any better and could potentially cause more adverse effects.[10]

Table 7 – Methods of relieving acute pain[43]

Non-pharmacological
Cognitive-behavioural therapy
Physical therapy
Transcutaneous nerve stimulation (TENS)
Acupuncture
Music therapy
Aromatherapy
Relaxation therapy
Massage
Heat or cold
Pharmacological
Opioids
NSAIDs
Local anaesthetics
Paracetamol
Adjuvants

Table 8 – 'Better' choices of opioids[48–50]

Common side-effects of opioids	Drugs with a lesser degree of these problems compared to morphine
Confusion	Oxycodone Fentanyl
Respiratory depression	Tramadol Fentanyl
Accumulation in renal impairment	Hydromorphone
Constipation	Fentanyl
Myoclonus	Hydromorphone

'Multi-modal' therapy offers additive beneficial effects whilst reducing drug side-effects. Tramadol with paracetamol, or tramadol with morphine and an NSAID make effective combinations.[12,14,54–57] (see Table 9).

4.3.4. *Non-steroidal anti-inflammatories (NSAIDs) and cyclo-oxygenase II inhibitors (COX-II inhibitors)*

Although these have morphine-sparing effects, they are often inadequate if used alone post-operatively. Other analgesics still need to be added to the regime.

Traditional side-effects remain a worry for both classes. COX-II inhibitors are not significantly safer with regards to gastro-protection when compared to a combination of a proton-sparing inhibitor to a non-selective NSAID. Non-selective NSAIDs also carry the risk of cardiovascular events.[58,59]

Interestingly, non-selective NSAIDs have also been reported to inhibit bone fusion and fracture healing. COX-II inhibitors affect bone formation as well.[51]

4.3.5. *Paracetamol*

The usefulness of paracetamol should not be under-estimated. It is widely available and very cheap (1 g costs 3.1 p). It can spare the dose of morphine by at least 20% after major surgery.[60]

Paracetamol (as Perfalgan) is now available intravenously as well. Apart from providing lighter pain relief for patients who cannot take oral medication, Perfalgan may be more efficacious than other paracetamol formulations.[61] Current costs (£1.50 per 1 g) unfortunately prohibit its wider usage.

More recently, another oral formulation, nitroxyparacetamol, has been found. It has additional anti-inflammatory properties as well as the added advantages of fewer hepatic side-effects at equimolar doses of paracetamol.[43] This is not yet available for routine use.

Table 9 – Pros and Cons of different routes used for opioids[54,11,13,53–56]

Route	Advantages	Disadvantages
PATIENT CONTROLLED ANALGESIA (PCA) *Opioids*	Most ideal Avoids risk of over- or under-dosing	Patient needs to understand the concept Requires the ability to 'press button' Expensive Administration of drug ceases when the patient is asleep unless background infusion is prescribed
ORAL *All classes*	More options available Inexpensive	Patient must be able to swallow
INTRAVENOUS *Opioids and NSAIDs*	Works fast	Duration of action shorter
INTRAMUSCULAR *Opioids and NSAIDs*	Can be used if patient cannot swallow or if there is no intravenous access available	Painful Can cause tissue necrosis Unreliable drug absorption Tendency for rapid fall-off in drug levels
SUBCUTANEOUS *Opioids and NSAIDs*	As for intramuscular route Effect lasts a bit longer than the above route	Less painful Unreliable drug absorption
EPIDURAL *Opioids*	Can reduce dosage of oral analgesia, especially if used in conjunction with local anaesthesia	Variable onset of analgesia and duration of action depending on whether hydrophilic or lipophilic drug used Hypotension Epidural abscess Haematoma
TRANSDERMAL *Opioids*	'Painless' and 'effortless'	Slow onset of action, although may reach similar final plasma concentration as in younger patients Could cause skin irritation
RECTAL *Opioids and NSAIDs*	Useful if oral or intravenous route not possible	Potentially uncomfortable Variable drug absorption Limited data
INHALED *Opioids*	Possibly useful alternate route	Limited data

4.3.6. *Nefopam*

This little-used drug is another option. It is a centrally - acting non-opiod which probably works by inhibiting serotonin and noradrenaline reuptake. It spares the use of morphine and does not affect platelet aggregation.

However, its sympathomimetic action calls for caution when used in patients with limited coronary reserve, renal failure, prostatitis and glaucoma. Patients (15–30%) still report side-effects such as nausea, vomiting, sedation and sweating.[51]

It is generally suggested that one starts with 25–50% of the recommended dose for adults when prescribing analgesia for older patients. Similarly small increments should be made until the patient reports satisfactory pain relief. The same small steps downwards may be considered if the patient develops side-effects.[14]

Older patients may accumulate drugs over time due to changes in their overall body composition, physiology and metabolism.[14,2] As mentioned before, there can be a huge variability here. Thus, regardless of the route chosen, doses of any new medications should be reviewed within a few days of their commencement. Ideally, pain should be reassessed:

(1) within 30 min of parenteral drug administration;
(2) within 1 h of oral drug administration;
(3) with each report of new or changed pain.[62]

Table 10 – Suggested protocol

Pre-operative preparation
Meet with patient prior to procedure
Discuss fears, anxieties and anticipated discomfort
Aim to control any pre-existing pain problems
Negotiate method of reporting post-operative pain, e.g. Faces Scale
Negotiate choice of analgesia and mode of administration (consider co-morbidities and potential drug interactions/side-effects)
Aim to offer medications orally where possible
Paracetamol should be used as starting point
Ideally, construct a multi-modal combination of analgesia
Tailor choice, route and dose of drug to type and severity of pain
Anticipate possible side-effects of analgesia
e.g. offer anti-emetic and/or laxative with opioid medications
On the day of procedure
Ensure that the ward and team are apprised of plan for analgesia
Ensure that the drugs of choice are available on ward
Include a pain control level in 'early warning score' for are urgent review
Attach a copy of the plan on drug chart and in case-notes
Post-operative period
Ensure that the means to call for assistance is easily available to the patient, e.g. call button at hand
Record pain control levels routinely with other observations for blood pressure, temperature, oxygen saturations
Provide analgesia as soon as required and review response to it
Review pain control levels on daily basis and adjust as needed
Ask for help from Acute Pain Team if no better

4.4. *A practical approach*

Table 10 illustrates one approach to the problem. Communication is key here to ensure that the 'right' expectations are met and that the 'wrong' assumptions are not made. The whole healthcare team and the patient as well as the patients' close ones need to be able to talk to each other easily and honestly throughout the whole process. A close interaction is recommended with surgeons and anaesthesiologist with a view to offering tailored management.[63]

Healthcare resources will always be limited and thus it is more important to be familiar with what is available locally so that whatever is obtainable is utilised most efficiently and effectively. Quite often, it is the 'little things' such as ensuring that the patient in pain receives an adequate dose of an appropriate analgesia at the right time (i.e. without delay) that makes all of the difference, rather than a new drug.

Summary of key points:

- Post-operative pain control in older patients remains a significant problem because of various reasons
- This could be improved with better training of healthcare providers
- Although we have more choices in terms of pain control methods today, those that are actually available for use are few in number
- Nonetheless, with careful thought and planning, much can still be done

'Pain may be unavoidable, but suffering is optional'[64]

Conflict of interest statement

There is no conflict of interest to declare.

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