Misconceptions of Opioids in Palliative and End of Life Care

Literature Review

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Abstract

Opioids are the most used medication in palliative or end-of-life care to manage patients' pain levels in different settings where these services are offered. Opioids are considered versatile pain medication because they are used for varying degrees of pain levels and are administered through different routes. Over the years, observations have been made regarding the many misconceptions held by patients and nurses about the use of opioids. These misconceptions led to poor pain management of patients since opioids were not administered as frequently or in the right doses as they should have been to alleviate patients' pain levels. For nurses especially, this element was detrimental as these misconceptions regarding opioid use allowed these views to be spread to patients which allowed most to oversee administering opioids as they saw fit.

The research aimed to describe the different misconceptions that patients and nurses had about opioid use in palliative or end-of-life care. The purpose of the research was to provide valid guidelines that dissipated misconceptions held by nurses and patients about opioid use in palliative or end-of-life care, so that poor pain management would be decreased. The method used was a literature review which used eight guidelines that came from PubMed, CINHAL, and Medline. Chosen data underwent content analysis and provided information from guidelines that could dispel any misconceptions about opioid use.

The main misconceptions held by nurses about opioid use in palliative or end-of-life care were addiction, side effects, legal ramifications, and euthanasia. When it came to the misconceptions about opioid use in palliative care or end-of-life care held by patients included side effects, fear that the opioids would mask their symptoms, and religious barriers. The findings provided vital information about how different side effects can be easily managed through non-pharmacological and pharmacological methods and how giving different opioids through different routes decreased side effects in many patients. This provided necessary information about how opioids do not cause euthanasia if they are given in correct doses and at the right times. The difference between sedation as a side effect and intentional palliative sedation was clearly emphasized, which showed that opioids do not play as great a role in palliative sedation as many individuals thought. The research recognized the limitations of this study and purposed that future research should focus more on opioid use specifically for patients in palliative or end-of-life care.

Keywords/tags (subjects)

Opioid use, pain management, dispelling opioid misconceptions, opioids in palliative care, end-of-life care

Miscellaneous (Confidential information)

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1 Introduction

The need for palliative and end-of-life care is a globally pressing issue that will continue to hold relevance in the medical field. This field requires professionals who are trained professionally in this field to educate their patients and the public regarding what occurs in palliative or end-of-life care (Goldwasser, Vinant, Aubry, Rochigneux, Beaussant, Huillard, & Morin, 2018). Opioid administration plays a crucial role in palliative and end-of-life care confirming that nurses, patients, and their families must use evidence-based material about opioids and their administration. The most important aspect of avoiding opioid misconceptions in palliative and end-of-life care is ensuring that awareness by nurses, patients, and their family members is achieved (Alwawi & İnkaya, 2023). These misconceptions regarding opioids should be circumvented by health professionals as it can influence the patients and public's view when opioids are used in palliative and end-of-life care. Nurses play a key role in this process as they have the most contact with patients and their families in palliative or end-of-life care, thus showing that it is crucial for nurses to not have misconceptions about the use of opioids, as there is a higher chance that these misconceptions will be transferred to patients and their family members (Cheung, Gorelik, Mehta, Mudannayake, Ramesh, Bharathan, & Goldenberg, 2019).

These misconceptions held by nurses result in occasions where opioids in palliative or end-of-life care are not administered as needed and can lead to poor pain management. This is a serious issue as the patients or family members who are taught these misconceptions will not choose medication that can aide their pain (Barnett, 2020). Having pain poorly managed during palliative or end-of-life care will cause a person great physical and psychological pain in the last few weeks or months of their life. These misconceptions have the possibility to harm the patient's family as they will see their loved ones in agonizing pain in their last weeks or months of life (Cox-Seignoret & Maharaj, 2020). As a nurse, it is crucial to be aware of the misconceptions regarding opioid use in palliative or end-of-life care that other nurses and patients believe as this will allow for credible information to be passed on to other nurses, patients, and their family members. Awareness of this issue allows nurses who do not possess opioid misconceptions to present evidence-based materials that might help to present more information to try to counter these misconceptions. This shows that misconceptions about opioids are apparent only due to the lack of information about opioids (Bailey, Williams, Woodby, Goode, Redden, Houston, & Burgio, 2014).

2 Palliative Care

The definition of palliative care is that it is a specialized field in the medical industry that seeks to support patients with terminal illnesses. Palliative care can last months and years, depending on patients' diseases (WHO, 2020). Palliative care is a term that can be further broken down into a smaller category (NHS, 2022). According to Hui, Nooruddin, Didwaniya, Dev, De La Cruz, Kim, Kwon, Hutchins, Liem, and Bruera (2014), palliative care can be further broken down into end-of-life care or EOL care. In simple terms, EOL care is caring for someone who has a terminal illness and will die in the near future, meaning that EOL care is only for a short amount of time and does not last as long as palliative care (Mauck, 2022).

In Central Eastern Europe, the life expectancy is increasing much closer to the life expectancy of the United States of America and other Western countries. Central Eastern European countries have more elderly people who require palliative care services, but these countries are unable to provide enough services that are established by the state (Luczak, Kluziak, & Hunter, 2002). Central Eastern European countries depend heavily on the support of family members of patients in palliative care as there are many instances where these individuals must play a role due to the healthcare institutions being overburdened (Jünger, Klose, Brearley, Hegedus, Payne, & Radbruch, 2015). Which means that if these family members are not supported in their tasks and are unable to care for their family members who need palliative care, palliative care patients end up suffering (Krakowiak, 2020).

According to Ferrell, Chung, Koczywas, Williams, Gallagher, Fischer, and Smith (2017), in palliative care it is vital that healthcare workers, and especially nurses, work to make a patient's palliative care experience as manageable as possible. Palliative care can occur in nursing homes, hospitals, and patient's homes (Thelen, Brearley, & Walshe, 2023). It is imperative that the patient’s quality of life is maintained as much as possible and that their suffering is alleviated as much as possible (U.S. Department of Health and Human Services, 2021).

Nurses and other health care professionals working in palliative care also seek to support family members of patients in palliative care. Although the family members are not the one who are sick, their support will help make a person’s palliative care experience easier and will also make it easier for the healthcare workers, like nurses, to care for the person (MacMahon, 2011). Family of

palliative care patients who do not feel like they are getting the support they need, will struggle to support their family member who is in palliative care (Hargreaves, Gardiner, Tod, & Darlison, 2023). Those who do not have supportive family members, or any family members, will then require extra support from healthcare workers, and their experience in palliative might not be as pleasant as those with supportive family (U.S. Department of Health and Human Services, 2021).

2.1 Rise of Palliative and End of Life Care

It is estimated that 56 million people in the world need palliative care every year. About 14% of people are getting the palliative care they need (WHO, 2020). This is due to many factors, such as insufficient money, not enough places for people to go to and be cared for, lack of understanding of palliative care, and lack of skilled nurses/health professionals to provide the type of care these individuals need (Nicholson, Combes, Mold, King, & Green, 2023). The number of individuals needing palliative care will increase due to many countries having an ageing population, with not enough young family members to care for their relatives, meaning individuals must look to the state or private hospitals or care places to care for them (Bain, 2015).

According to Connolly, Bell, Lawler, Timmins, and Ryder (2022), a person needs palliative care when they have a terminal illness that cannot be cured and these terminal illnesses might last for a long time, or they may last for a shorter time, thus requiring patients to seek EOL care. Kerr (2022), states that there are many types of illness that are terminal, and the person might suffer with them for many years but, will one day die of this disease in palliative terminal illnesses are continuously on the rise since individuals live longer than ever before and we have chemically filled food that is not as fresh as it used to be (U.S. National Library of Medicine, 2022). Noncommunicable diseases (NCD'S) also occur in many cities because of pollution and because people are leading extremely sedentary lifestyles (Manhanzva, Marara, Duxbury, Bobbins, Pearse, Hoel, Mzizi, & Srinivas, 2017). Additionally, many people smoke a lot and drink, which has been proven to cause noncommunicable diseases like kidney failure that cannot be reversed even with hemodialysis (Bertolin, 2016).

In lower income areas, there is an increase of NCD'S due to lifestyle choices which are mainly causing individuals to get high blood pressure and type 2 diabetes. Since individuals in developing countries do not have as much access to healthcare resources, they are not able to be taught how

to control their blood pressure levels or type 2 diabetes through medical means or lifestyle changes. So, this is why there is an increased number of individuals with many NCD'S caused by chronic high blood pressure and type 2 diabetes in developing/low-income countries (Munday, Kanth, Khristi, & Grant, 2019). Unmanaged type 2 diabetes and high blood pressure can lead to heart failure. Heart failure is a common chronic NCD that leads people to seek palliative care (Morken, Wathne, Karlsen, Storm, Nordfonn, Gjeilo, & Husebø, 2023). Another NCD that is on the rise, is cancer. Some cancers can be cured, but many cancers are chronic and will eventually require an individual to seek palliative care. Many cancers are caused due to lifestyle choices or environmental factors, but sometimes healthcare professionals are not sure why some individuals get cancer. Depending on what type of cancer an individual has, the palliative care that they will need to receive must be different, which is many times not possible because the palliative care systems are already overwhelmed (Rassouli & Sajjadi, 2016). Although heart failure and cancer are two of the most common NCD's that might require an individual to seek palliative care services, according to Matula (2019), NCD'S like chronic obstructive pulmonary disease (COPD), kidney diseases, lung diseases, AIDS, dementia, heart diseases, and degenerative diseases, like ALS, also might require an individual to seek palliative care services.

2.2 Pediatric Palliative Care

Palliative care is not only necessary for adults, but children as well. Children experience similar symptoms in palliative care that adults experience in palliative care as well as the side effects caused by opioids. Children are usually in palliative care due to cancer or genetic defects that they were born with and not due to diseases caused by lifestyle choices or old age (Nelson, Botkin, Kodish, & Levetown, 2000). Although the nursing interventions that must be done to children in palliative care are similar to the ones done to adults, when it comes to working with children who are dying, nurses must try to actively keep the children more entertained than they would adults. Nurses also must work more with the family or legal guardians of children in palliative care because they are not of legal age. Nurses emotional support of a child's family members is increased because it is extremely difficult to have a child in palliative care because they are so young and should have had their whole life in front of them (Vickers, Thompson, Collins, Childs, & Hain, 2007). When it comes to the use of opioids in children in palliative care, there is even a greater fear of administrating opioids than in adults because nurses fear that the children are too fragile or small to handle opioids for their pain. When administrating opioids to children in palliative care,

it is crucial that their weight is considered when calculating doses (Parikh, Amolenda, Rutledge, Szabova, & Chidambaran, 2019).

2.3 Nursing Interventions in End-of-Life Care

The role of nurses in supporting patients during end-of-life care (EOL care) is vital because nurses are the individuals who spend the most time with patients and are the ones who advocate on behalf of patients (Griffiths, Ewing, & Rogers, 2013). Nurses are the ones who report back to other healthcare professionals regarding the patient's palliative care experience is going and how different medications and procedures are aiding them in a more peaceful palliative care experience (Raphael, Waterworth, & Gott, 2014). If the patient is suffering or requires additional aides, it is nurses who support them and search for ways to alleviate their suffering and better their palliative care experience (Hagan, Lopez, & Bressler, 2018.)

If a patient is bed-bound, nurses try to make sure that the patient is as comfortable as possible by positioning them correctly and providing the correct things like a comfortable bed and pillows. According to Ferrell et al., (2017), if the patient is mobile, the nurses try to create an environment that allows the patient to move smoothly and be as independent as the patient's health condition allows them to be. Nurses also make sure that the wishes of the patients in EOL care are carried out as much as possible, for example, a DNR request (Stenman, Näppä, Rönngren, & Melin-Johansson, 2023). Before a patient enters EOL care, if their mental stability is intact after being evaluated by a doctor, they should be asked how they would like to be cared for and what interventions they would or would not want to receive (Robinson, Evans, Riley, Kowalchik, Adams, DeSanto, & Lucey, 2023).

Nurses not only support a patient in EOL care, but they also try to support the patients' family members as well (Scottish Nursing Guide, 2023). It can be painful to see a person that you love dying, so it is crucial that nurses realize this and try to support the loved ones of patients in EOL care to the best of their abilities or at least direct them to places where they can receive support (Moir, Roberts, Martz, Perry, & Tivis, 2015). This support not only helps the loved ones of patients, but it also allows them to better support their loved ones who are in EOL care, making it easier for EOL care patients to cope (Chan, 2021).

Nurses' role in EOL care is paramount and without nurses, EOL care would cease to exist. Nurses have many things that they must do in EOL care (Nacak & Erden, 2022). These tasks include physical support of EOL patients as well as emotional support of patients and their loved ones. In EOL care, nurses try their best to make sure that patients remain with as little pain as possible by using pain medication, like morphine, fentanyl, or oxycodone (Waller, Chan, S., Chan, C. W. H., Chow, Kim, Kang, Oldmeadow, & Sanson, 2020). Additionally, nurses confirm that all the care patients receive in EOL care follows evidence-based medical guidelines and that the patients do not undergo any interventions that do not provide any benefits to them. Nurses are also responsible for the basic hygiene of patients and positioning throughout the day (Hagan et al., 2018).

2.4 Symptoms in Palliative care

Patients in palliative care are given different medications, causing symptoms that arise from the side effects of the medication they are on. A person in palliative care will most likely have symptoms of constipation and nausea because these are common side effects of high doses of opioids, like morphine, that are given to alleviate pain (Henson, Maddocks, Evans, Davidson, Hicks & Higginson, 2020.) The individual might also experience pain during palliative care since they refuse strong pain medication like opioids because they are afraid of addiction or even if they take the opioids, they might be in such a severe condition that nothing can help them alleviate the pain (Pidgeon, Johnson, Currow, Yates, Banfield, Lester, Eagar, 2016). The individual might also experience, fatigue, delirium, and loss of appetite due to their comorbidities or deterioration of the body (Ryan, Ingleton, Gardiner, Parker, Gott, & Noble, 2013). Furthermore, the symptoms are not always physical, but can be physiological and emotional such as depression or loneliness due to the patient's fear of death or isolation (Kozlov, Niknejad, & Reid, 2018).

Symptoms in palliative care vary from individual to individual, depending on the type of terminal illness or noncommunicable diseases (NCD'S) that a person has. Cancer, chronic obstructive pulmonary disease (COPD), and heart failure are some of the most common NCD'S that require palliative care (Davis, Lagman, Parala, Patel, Sanford, lding, Brumbaugh, Gross, Rao, Majeed, Shinde, & Rybicki, 2017). For example, if a person needs palliative care because of heart failure they might experience the following symptoms: breathlessness after doing a simple task, feeling uncomfortable, continuous cough, inability to move a lot, exhaustion, peripheral edema, pain (if not given enough opioids) and cognitive impairment. Of course, these symptoms will vary in their severity

depending on how advanced the heart failure is (Strangl, Ischanow, Ullrich, Oechsle, Fluschnik, Magnussen, & Rybczynski, 2023).

Another common NCD that requires palliative care is cancer. Cancer symptoms might vary depending on the type of cancer an individual has, but some common symptoms include: loosing or gaining weight, an outgrowth of some sort on the body, exhaustion, continuous coughing, increase or decrease in bowel and bladder movements. Some individuals in palliative care might also consider receiving treatment for their cancer, like cytotoxic drugs, which can cause further symptoms like nausea, dizziness, and headaches (Pedersen, Forbes, Brain, Hvidberg, Wulff, Lagerlund, & Vedsted, 2018). A third NCD that commonly causes an individual to seek palliative care services is COPD. COPD patients might experience gasping for air, a feeling of their chest being tight, cough sputum that can vary in color, easily tired, frequent lung infections, and swelling of feet. Of course, these symptoms can worsen, and new symptoms can come depending on the stage of COPD that this individual is in (Rajnoveanu, Rajnoveanu, Todea, Man, Motoc, & Mosoiu, 2020).

2.5 Opioids in Pain Management

Opioids, especially morphine, are the most used analgesics for pain management during palliative care because they do not have a ceiling effect, which allows them to be continuously used if a patient has increasing pain levels (Menezes, Nair, Soumya, & Tarey, 2016). They are much stronger than other analgesics and are usually chosen for severe pain management. Opioids are agonists and bind to opioid receptor sites to stimulate them. By stimulating the opioid receptor sites, opioids act like endorphins. Endorphins are natural opiates that take part in the body's own pain relief system. Opioid receptor sites occur in the central nervous system and peripheral sites (Filizola & Devi, 2012). In case of an overdose, naloxone can be used to reverse the effects of opioids because it is an antagonist and binds to opioid receptor sites and does not stimulate them (Kim & Nelson, 2015).

Although Morphine is one of the most used opioids in palliative care, there are many other types of opioids available as well (Tayara & Ahmed, 2021). Opioids are divided into categories depending on their strength. There are weak opioids such as codeine and tramadol, semi-strong opioids like buprenorphine, and strong opioids like morphine, fentanyl, and oxycodone (Meyer, Schellack, &

Schellack, 2018). Codeine is a natural opiate given orally. It is also a pro-drug used as a cough depressant, and because it is suitable for mild pain, it does have the ability to be abused by an individual. Tramadol causes fewer side effects than other opioids if used in a normal dosage. It is also a pro-drug and increases levels of serotonin and noradrenalin (Voss, Ali, Singh, Rijnbeek, Schuemie, & Fife, 2022). Morphine is considered a drug that is used to compare the effectiveness and side effects of drugs considered analgesics and can be given through many routes (Iversen, 1996). Then buprenorphine is usually given sub dermally or sublingually because it is not effective if given orally and used in opioid replacement therapy. Finally, oxycodone has a better bioavailability than morphine when given orally, and fentanyl can only be given parentally and is stronger than morphine (Leppert & Nosek, 2019).

The side effects of opioids can be serious, but they vary between individuals, and it is vital to consider that the pain that a patient in palliative care would feel without opioids would be much more drastic than the side effects of opioids (Villanueva, 2017). In palliative care, it is important to weigh the costs and benefits of any medication that is being used. Opioids can cause respiratory depression as the number of opioids is increased and can also cause depression of cough and miosis (Dale, Moksnes, & Kaasa, 2011). The other common side effects of opioids are vomiting and nausea, and they seem to get worse if the patient moves around and possibly decreases if the patient is on the bed. Antiemetics are commonly also given with opioids to decrease nausea and vomiting (John Hopkins Medicine, 2023). Constipation is also a common side effect of opioid use, so patients are always given laxatives simultaneously. Tolerance, dependence, addiction, and itching also may occur in long-term usage. Not all the side effects of opioids are undesirable because some of the side effects of opioids are desirable like analgesia, euphoria, and sedation (Berde & Nurko, 2008).

Like with any other medication, the dosage of opioids given is important. According to Creedon and Regan (2010), the nurse must first ask the patient if they are in pain and their level of pain by using the pain scale. If they are not in pain, the doctor might prescribe an adult in palliative care morphine anyway as a pre-emptive way to prevent pain from occurring. There are many different routes and ways that morphine can be given to patients in palliative care. Specific countries vary in their guidelines when it comes to the administration of morphine in palliative care. According to

NHS (2019), 2.5-5 mg of morphine is given every two-four hours subcutaneously to prevent severe levels of pain from ever even occurring. In the case that the palliative patient says they are in pain, 2.5-5 mg subcutaneously is prescribed every two-four hours, and the medical abbreviation p.r.n is added close by meaning 'as needed' because the patient might require more frequent dosages if they have too much pain. If a patient needed two or more dosages on top of their regular dosage schedule in 24 hours, the health professionals might consider switching the patient to CSCI (continuous subcutaneous Infusion).

3 Fears and Misconceptions of Opioid Use in Pain Management

3.1 Nurses and other Health Care Professionals Views on Opioid Use

When it comes to anything in life and in any profession, there will always be misconceptions about how or why specific things are used. The same is true when it comes to misconceptions held by nurses and other health professionals regarding opioid use for medicinal purposes in palliative care (Ferreira, Verloo, Vieira, & Marques-Vidal, 2013). Regardless, of how many studies are done showing the importance of opioid use in palliative care and how opioids make palliative care less painful, there is still a lot of hesitancy among nurses and other health care professionals to administer morphine (Barnett, Mulvenon, Dalrymple, & Connelly, 2010).

Fearing Opioids Will Cause Addiction

One misconception that nurses and other health care professionals hold is that patients in palliative care who use opioids, which mostly include morphine, will become addicts (Chang, Yun, Park, Lee, Park, & Huh, 2005). The nurses fear that the patient will start to build a tolerance and get used to the morphine and will require higher doses of morphine to alleviate the same pain, leading to increased chances of side effects and possibly overdose (Porter & Jick, 1980). These patients in palliative care are dying, which means that the fear of addiction is not the biggest concern since the patient is dying and the main goal is to make them comfortable before their death (Shoqirat, Mahasneh, Al-Khawaldeh, & Singh, 2019). As time goes on, nurses fear that patients in palliative or end-of-life care will require more frequent doses of morphine because they are building a tolerance or addiction to the opioids and therefore give them less opioids as their body is deteriorating and they are having higher pain levels (Hajj, Halepian, Osta, Chahine, Kattan, & Rabbaa, 2017).

Nurses also fear that patients are over-exaggerating their pain levels to get more opioids. So, they rather leave patients in pain than give them opioids for over-exaggerated pain. Nurses fear that giving opioids to individuals for long periods of time, who are exaggerating their pain, will lead patients to become addicted (Miller, Eldredge, & Dalton, 2017). Nurses fear that opioids will cause addiction is so great, that they generally do not believe that how much pain a patient feels depends on what the patient reports. Some nurses lack the skills to investigate other ways, besides verbal conformation by a patient, to show a patient is in pain, so they decide to give the minimum amount of opioids prescribed by the doctor to alleviate their fears of patient addiction (Admass, Endalew, Tawuye, & Mersha, 2020). Many countries are facing an addiction crisis, and when nurses practicing in countries that have an addiction crisis or read about countries facing an addiction crisis, they immediately confuse the use of opioids in palliative and end-of-life care with addiction. Some of these nurses believe that the addiction crisis is increasing because of the increased use of opioids in palliative and end-of-life care, so they try to give as little opioids as possible (Clark, Salins, Daniel, Currow, Jones, Pearson, & Johnson, 2023).

Fear of Euthanasia

Another misconception that is held by some nurses and other healthcare professionals, is that by giving a patient opioid they are euthanizing the patient. Also, the instructions for how much opioids to give when a person is in palliative care versus when they are in severe pain, many times are not clear in certain countries, and this increases the fear of euthanasia held by nurses (Russo & Smallwood, 2022). The doses of morphine given in palliative and end-of-life- care is different because each country has their own dosing guidelines depending on the disease and if the patient is an adult or a child. This is another reason why nurses might fear that opioids are causing euthanasia because guidelines for dosing are many times not clear in each country and, depending on where a nurse did their training, they might be unsure about dosing of opioids in palliative care (Pappagallo, Dickerson, & Hulka, 2000). Nurses might also fear that administration of an opioid can cause euthanasia because opioids can cause respiratory depression by triggering opioid receptors that are in parts of the brain that control our breathing system (Baldo & Rose, 2022).

Palliative sedation is closely linked to nurses' fear of euthanasia because they are hesitant to partake in it because they feel that it is a form of euthanasia with a different name. Nurses are hesi-

tant to administer opioids as an analgesic during palliative sedation because they fear that the opioids are euthanizing a patient when they are in palliative sedation (Beng, Chin, Guan, Yee, Wu, Pathmawathi, & Meng, 2015). There are some nurses that feel a great burden when providing palliative sedation as they have the misconception that they have not done enough for a patient and are giving up on them. Nurses might also be hesitant to give opioids as an analgesic during palliative sedation, on top of other sedatives used to induce palliative sedation, because they fear that so many sedatives will hasten a patient's death (Morita, Miyashita, Kimura, Adachi, & Shima, 2004). Some nurses also find it difficult to take part in palliative sedation when it is for a patient who is suffering from non-physical symptoms. This is because they feel that palliative sedation could cause euthanasia, and they feel that the emotional distress felt by the patient might not warrant palliative sedation (Rietjens Hauser, van der Heide, & Emanuel, 2007).

Fear of Side Effects

Another concern that nurses have when it comes to the use of opioids in palliative or end-of-life-care are the side effects of opioids because, like all medications, opioids have side effects as well (Palliative Care Australia, 2021). It is possible for opioids to cause constipation, itching, decrease the effectiveness of the immune system, miosis, and delirium. Constipation is one of the most common side effects of opioid administration, like morphine. Constipation usually occurs because opioids decrease the rate that the stomach empties its contents. This causes more of the liquid to be absorbed and leaves less fluid for the stool to absorb in the intestine, making the stool hard as it leaves the body (Gonzales, Delmastro, Boyd, Sterling, Aube, & Glaser, 2016). Itching, medically know as pruritus, is another side effect that can be caused by opioids. Itching might occur because opioids prompt neurons that are involved in the itching sensation (Mercadante, Villari, & Fulfaro, 2001).

Opioids can also cause miosis. Miosis is when pupils become constricted. Opioids bind to opioid receptors in the parasympathetic part of the autonomic nervous system and cause the pupils to shrink in size because the iris sphincter muscle contracts (Rollins, Feiner, Lee, Shah, & Larson, 2014). Delirium can also be caused by using morphine or other opioids. This may cause the patient to not know where they are or cause them to speak incoherently. Opioids block many types of neurotransmitters in the brain, and one of the neurotransmitters that they block is acetylcholine. Acetylcholine deals with learning and our ability to focus, so blocking it would cause delirium

symptoms (Swart, van der Zanden, Spies, de Rooij, & van Munster, 2017). Opioids can also cause a decrease in a person's immunity by attacking natural and adaptive immunity. Opioids affect the immune system by decreasing the growth of lymphocytes which are essential during the body's immune response (Sacerdote, 2006).

Fear of Legal Ramifications

Nurses try to give as little opioids as possible during palliative or end-of-life care because they fear legal ramifications. They feel that if they give a lot of opioids and a patient dies, they will be blamed for the death of the patient and face legal ramifications (Allmark & Tod,2009). Although most nurses are never blamed when a patient dies in palliative or end-of-life care, many nurses are afraid that they will lose their jobs or be charged criminally if they were the ones who administered the opioids before a patient died. Some nurses acknowledge that many times opioids are withheld from a patient because nurses are terrified that they will be blamed by the family or country for the death of the patient and that their career or reputation in nursing could be demolished (Willmott, White, Yates, Mitchell, Currow, Gerber & Piper, 2020). Many nurses fear that a dose of opioids for one patient in palliative or end-of-life care might help one patient with pain management but might kill another, so they rather just give the bare minimum of opioids because they fear they will be faced with legal issues. Many patients receive palliative or end-of-life care at home because the hospitals lack space, and in many countries, there are issues with the regulation of opioids, so many nurses do not give patients enough opioids because they are not able to deal with the legal ramifications (Luna-Meza, Godoy-Casasbuenas, Calvache, Díaz-Amado, Gempeler Rueda, Morales, & de Vries, 2021).

3.2 Patient and Family Member's Concerns about Opioid Use in Palliative Care

Fear of Side Effects

Patients and family members also have concerns about opioid use in palliative care or end-of-life care, one concern is the side effects of opioids because, like all medications, opioids have side effects as well (Palliative Care Australia, 2021). Opioids can cause nausea and vomiting, sedation, and tolerance. Nausea and vomiting might also occur after morphine administration because opioids interfere with the chemoreceptor zone in the brain. Also, since opioids decrease gastric movement, food remains longer in the stomach and does not correctly move through the body, so

this causes an individual to feel nausea and want to vomit (Raffaeli, Marconi, Fanelli, Taddei, Borghi, & Casati, 2006). Opioids can also cause sedation by attaching themselves to certain opioid receptors and stimulating these receptors that have to do with sedation (Shin Wei Sim, Shirlynn Ho, & Lalit Kumar, 2014). Patients also fear that they will build a tolerance to opioids. Tolerance can occur when a person becomes used to a specific opioid dose and requires more opioids to feel the effect that they did previously with a lesser dose (Baker Rogers, J., & Higa, 2022).

Fear of Masking Symptoms

According to Glose and Rowan (2021), another concern that patients and family members have about the use of opioids in palliative care, is that opioids will make it impossible for the nurses or doctors to correctly evaluate how their disease or their loved one's disease is progressing. Just because they might not necessarily feel that their disease is progressing, although the patient might still be able to tell even with the use of opioids, the nurses and doctors will be able to tell (Meghani, Wool, Yeager, Mao, & Barg, 2020). The patients and family members might also fear that the morphine will cause palliative sedation. They might think healthcare professionals might not be aware of palliative sedation because it is not necessarily a thing that they are focused on (Seymour, Bellamy, Gott, Ahmedzai, & Clark, 2002).

Religious and Cultural Barriers

Patients or family members might be hesitant about the use of opioids during palliative or end-of-life care because of religious or cultural beliefs. This is especially true when it comes to older patients because they tend to be more religious and skeptical about opioids. The patients or family members might also feel that the pain will soon pass, and they do not think it is relevant to burden the healthcare system with their concerns about their pain levels, so they rather not ask for opioids because that is how they were raised in their culture (Yao, Kibu, Asahngwa, Ngo, Ngwa, Jasmin, & Foretia, 2023). In many cultures or religions, pain is believed to be a part of a disease, and if an individual complains about their pain and asks for opioids to relieve their pain, they are showing that they are weak. Many times, not requesting opioids when an individual is in pain makes a person feel honorable because they are able to deal with the pain without complaining. Some cultures fear death a lot, and they believe that pain is a sign that a person is dying, so they rather not talk about their pain at all (Zuccaro, Vellucci, Sarzi-Puttini, Cherubino, Labianca, & Fornasari,

2012). Some religions believe that opioids hasten death, so patients might refuse to take opioids if they have any feeling that it could quicken their death. Also, some religions see suffering as a punishment for sins and feel that a person must refuse opioids and suffer with their pain to atone for their sins (Al-Shahri, 2016).

3.3 Consequences of Misconceptions

When nurses and other health professionals have misconceptions about the use of morphine in palliative care, it can lead to consequences because patients in palliative care and their families trust the opinions of nurses and other healthcare professionals (Fine, 2007). Patients in palliative care will not want to use morphine for pain management if they hear misconceptions from their nurses and other healthcare professionals who surround them (Coyne, Mulvenon, & Paice, 2018). Misconceptions about the use of morphine during palliative care will cause the patients to only tell their nurses and doctors about their pain when it has reached an unbearable level. Or they might voice their concerns about their pain levels but will refuse to use morphine until their pain levels have become extremely high (Martin & Barkley, 2016). This will also make it more difficult for the nurses and doctors to help these patients in palliative care who wait to take morphine until they have unbearable pain because it is more difficult to control pain levels once they have become chronic (Mao, Gold, Backonja, Mao, Gold, & Backonja, 2011). According to Klein, Lang, Bükki, Sittl, and Ostgathe (2011), correct pain management with the use of morphine or other opioids in palliative care will increase the quality of life of patients.

When speaking about pain management, one must also consider the ethical perspective on this topic. It is not ethical to allow any person to suffer in pain, just because this individual is misinformed or does not have the right information about morphine (Fine, 2007). Pain does not only hurt the body physically, but also causes psychological and emotional distress. In palliative care, poor pain management will disrupt the patient's sleep schedule and decrease their movement, which will cause further issues, like pressure ulcers (Kizza & Maritz, 2019). In palliative care, it is important that the patient's pain is well managed so that they will not have to feel their body deteriorating so much. In EOL care, poor pain management will cause patients to die painfully (Chi & Demiris, 2017).

Ethically, every individual should be given the resources and knowledge to be able to make well-informed healthcare decisions about the use of morphine, so they do not end up having poorly managed pain (Chaturvedi, 2008). Some individuals have a lack of pain management in palliative care because their country is not able to get enough morphine transported to them. Ethically speaking, no one should have to die in pain just because their country is a developing country and is not able to have as much access to morphine as developed countries (Dehghan, Ramakrishnan, Ahmed, & Harding, 2010). Also, it is not ethical that an individual cannot have correct pain management in palliative care just because they are not able to afford to pay for the morphine because the country, they are living in, has high prices for morphine (Qanungo, Calvo-Schimmel, McGue, Singh, Roy, Bhattacharjee, & Cartmell ,2021).

4 Aim and Purpose

The aim of this literature review is to explore the misconceptions and misinformation about opioid use in palliative and end-of-life care. Looking at the misconceptions that patients and nurses have concerning opioid administration.

The purpose of this literature review is to provide evidence-based information, that dispels these misconceptions surrounding opioid use in palliative and end-of-life care; to prevent the negative outcomes of poor pain management.

Research question: what are the evidence based guidelines that dispel misconceptions in opioid use and administration during palliative and end-of-life care?

5 Methods

5.1 Literature Review

A literature review is a research method summarizing already existing information and seeks to better or uncover issues that exist, for example, in the healthcare sector (Mongan-Rallis, 2006). A literature review also seeks to educate individuals about a specific topic by using current information and providing additional insights or possibly critiquing the lack of information on a specific

topic (Ratto, Davis, & Shaughnessy, 2018). A literature review compiles various systematic research that was done previously in a concise manner. It does this by integrating relevant findings from different research articles, allowing the research question to be answered from different avenues of thought and data (Snyder, 2019). A literature review thoroughly researches a chosen topic or subject by using peer-reviewed articles from reliable sources. Ensuring that the results are accurately reported without any personal bias included, is a vital part of the literature review process (Webster & Watson, 2002).

In the context of healthcare, a literature review betters the nursing profession by giving already-known information and possibly finding out new things. A literature review desires to further develop a part of nursing by providing evidence-based information that can be used in various sectors of nursing or in a specific field of nursing (Grace, 2011). A literature review can provide a summary of relevant information that can be quickly accessed by nurses and can answer their questions. A systematic literature review that is done properly clearly states why it is being carried out and how it will better the lives of patients and the overall healthcare system (Smith & Noble, 2016). Having a clear inclusion criterion and simultaneously being aware of what information to exclude, ensures that a literature review stays on track. Clear criteria in a literature review make sure that the necessary articles can be found, ensuring the research question is answered and no unnecessary information is reported (Twizeyimana & Andersson, 2019).

This literature review provided evidence-based medical guidelines that dispelled misconceptions about opioid use in palliative and end-of-life care (Matney, 2018). This study analyzed guidelines and presented the conclusions that have been achieved in these guidelines in a concise manner that can then be used by other healthcare professionals (Baker, 2016). This literature review also presented additional commentary and knowledge about opioids and outlined in the background section what are the misconceptions held by nurses and patients about opioids in palliative and end-of-life care. A literature review was the method chosen by the author because there are enough guidelines about opioid use in palliative care and end-of-life care that can be used to critically analyze why there are many misconceptions surrounding this topic and to further analyze why this is leading to poor pain management (Denney & Tewksbury, 2013).

5.2 Literature Search

Carrying out a literature search in any literature review is paramount in the nursing profession because it allows nurses to build on their existing foundation of knowledge that they already possess on a wide range of different medical topics. It allows nurses to broaden their expertise on topics that are essential to helping them provide the best care to their patients in an ever-shifting patient-centred healthcare system. A literature search allows nurses to see the information that is already available to them and to observe any gaps in the healthcare market that must be addressed when it comes to accessible material on specific topics (Oermann, Wrigley, Nicoll, Ledbetter, Carter-Templeton, & Edie, 2021). The literature search for this literature review was carried out in connection with the research question and it was ensured that only relevant search terms were created to guarantee that the inclusion and exclusion structures were closely followed. The researcher who carried out this study carried out the literature search in such a such a way that relevant guidelines became easily accessible. Preventing research bias was a great concern for the researcher, so it was paramount for them that the literature search used all the reported search terms and that the inclusion and exclusion criteria were clearly highlighted throughout the whole process.

At the start of the literature search, any duplicates that were found were eliminated from being eligible for this literature review, ensuring that guidelines that had relevant titles were put aside to undergo further in-depth screening. The guidelines that were put aside to undergo further screening, were further accessed to guarantee that they met the inclusion criteria that was created. In relation to the research question, the researcher meticulously created a list of inclusion criteria that would be set in each database before search terms were inserted to make sure that the chances of errors or research bias were reduced as much as possible. The electronic storages on each database were utilized to make certain that all guidelines that fulfilled the inclusion criteria were accurately stored and easily accessible for future analyzing and use.

During this literature review, strict search criteria and eligibility were created to guarantee that everything was carried out in the correct manner and that only relevant information was gathered. In Table 1, the PICOS terms utilized in this literature review can be clearly seen, followed by a paragraph outlining the search terms that were used to carry out the literature search. The inclusion and exclusion criteria can be seen in Table 2, followed by the Prisma chart in Figure 1. Three

databases and an open search were the digital resources that were chosen to facilitate the literature search. The three databases were CINHAL, Medline, and PubMed. CINHAL was the database that housed most of the chosen guidelines because, although PubMed had a greater selection of guidelines or articles, many of the articles or guidelines in PubMed were not as relevant to the research question as the guidelines that CINHAL had. Medline had a similar number of guidelines to CINHAL once search terms were inserted and criteria were set, but not as many guidelines were picked from Medline as CINHAL because Medline was lacking in substantive guidelines. All the databases were used in a way that followed the inclusion and exclusion criteria outlined in Table 2.

5.3 Article Selection Process

At this stage of the thesis writing, the literature review method started using the research question that was created previously and which was based on the title of this thesis. In the PICOS table, (Problem, Interest, Context, and Study) the research question ``What are the evidence-based guidelines that dispel misconceptions in opioid use and administration during palliative and end-of-life care?" was thoughtfully broken down to fit the various aspects of the PICOS table. The problem that needs to be addressed is the misconception that nurses and patients have about opioid use in palliative or end-of-life care. The intervention for this literature review includes guidelines or articles on opioid use in palliative care and end-of-life care. These guidelines or articles must provide information about how opioids can be administered safely in different healthcare settings where palliative or end-of-life services are provided. The outcome is to improve the pain management of patients in palliative or end-of-life care by dispelling misinformation held by healthcare professionals and patients surrounding opioid use in this context. Ultimately, a PICOS table makes sure that when searching for articles, only relevant information is gathered (Methley, Campbell, Chew-Graham, McNally, & Cheraghi-Sohi, 2014). PICOS is shown in Table 1.

Table 1. PICOS Table

P (Problem)	Misconceptions of opioid use in palliative care and end-life-care

I (Intervention)	Guidelines on opioid use in palliative care and end-life-care
C (Context)	Palliative and end-of-life care healthcare settings
S (Studies)	Peer reviewed, full text guidelines, guidelines published from 2012-2024, written in English, and answered the research question

Three databases and open search were used to find research guidelines for this literature review. The three databases used were as follows: CINAHL, Medline, and PubMed, as well as an open search was conducted. By using three different databases, the author is given the ability to choose from a substantial number of different guidelines; the open web search yielded non-article format information that answered the research question. The first database, CINAHL, used many keywords. In the first line, the keywords used were ’opioids or opiates or pain medication’. The first and second lines were connected by the Boolean operator ’and’. The second line used the keywords ’palliative care or end-of-life’. The second and third lines were connected by the Boolean operator ’and’. The third line used the keywords ’guideline or protocols or practice guidelines’. The second database that was used, Medline, used all the same search terms and Boolean operators as CINAHL. The last database, PubMed, did not have three lines for search terms like the other databases; so, all the keywords ’opioids, palliative and end of life care, guidelines’ were just put in a row and no Boolean operators were used. Lastly, an open search was made by using the search phrase ‘opioid guidelines in palliative or end-of-life care’.

5.4 Inclusion and Exclusion Criteria

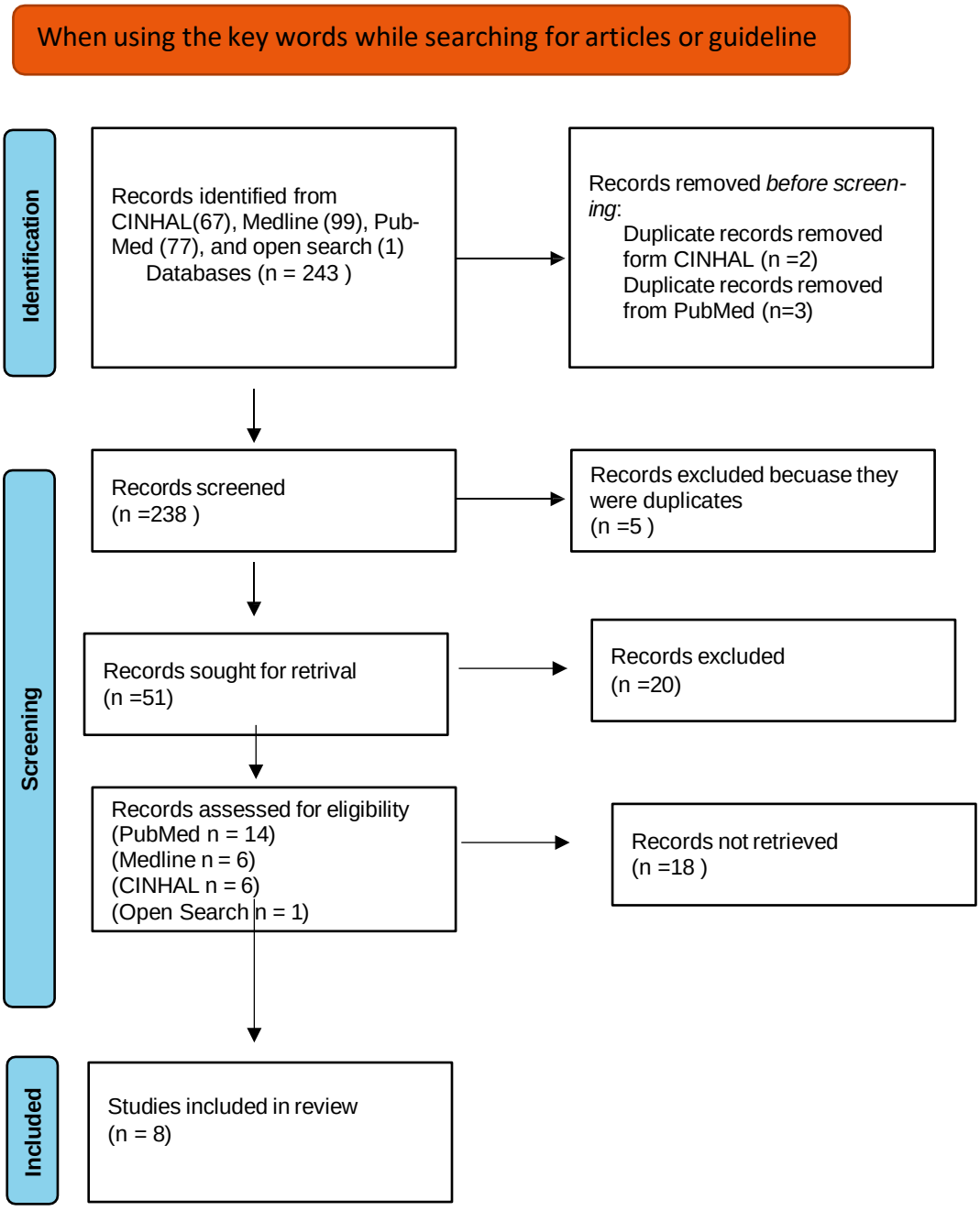
In the process of selecting guidelines, keywords were used that correlated to the research question and used to find the articles needed. The inclusion criteria that were used in this literature review were the same for all three databases that were used. The inclusion criteria stated that all

articles or guidelines that might be chosen to be part of this literature review can only be chosen if they adhere to the following inclusion criteria. The inclusion criteria are as follows: all articles or guidelines chosen should be written in the English language, peer-reviewed, full text should be available to the author, year limitation 2012-2024, and are relevant to the research question. The inclusion and exclusion criteria are also outlined in Table 2.

Table 2. Inclusion and Exclusion Criteria

Inclusion Criteria	**Exclusion Criteria**
• Guidelines in English • Peer-reviewed • Full Text • Guidelines within years 2012-2024 • Relevant to research question	• Guidelines that did not answer the research question • Guidelines published before 2012 • Guidelines repeated in different databases

Figure 1. Prisma Chart



A Prisma chart (shown in Figure 1) shows how the search was done by using the three different databases. When using the keywords outlined previously, while searching for articles or guidelines in the CINHAL database, 67 articles were found. At least 2 of them were duplicates, so there were only 65 original articles and databases found. When using the keywords outlined previously while searching for articles or guidelines in the Medline database, 99 articles were found, and two of those articles were the same as two articles found in the CINAHL database. Then when a search was carried out in the PubMed database, 77 articles and guidelines were found, and at least three

of them were duplicates, so there were only 74 articles or guidelines found. Lastly, an open search was conducted, with one guideline selected according to inclusion/exclusion criteria.

A total of 238 articles or guidelines were identified after visible duplicates were removed. All the titles and abstracts of the 238 guidelines or articles were read, and 51 of them were deemed appropriate to be part of a deeper analysis. A summary of all chosen guidelines can be seen in appendix 2. The researcher screened and chose the publications in a way that ensured that they all answered the research question and were appropriate for this literature review. After a deep analysis of many guidelines, eight guidelines were chosen. The publications that were not picked were not chosen because they did not fully answer the research question or remained out of the research scope. The eight guidelines deemed relevant for this literature review were published in these subsequent years: 2012 (1), 2016 (1), 2018 (1), 2019 (2), 2020 (1), 2023 (1), 2024 (1). The chosen guidelines were published in the following areas: Germany (2), America (3), England (1), India (1), and South Korea (1).

5.5 Method of Analysis

Data analysis takes various information from different sources and changes this data into relevant content that can be useful in a literature review. There are many types of methods that data analysis can use to ensure that relevant data and themes can be found while simultaneously ensuring that conclusions can be taken from all this information (Pandey & Pandey, 2016). Data analysis wants to ensure that all intricate data collected is turned into data that can be understood and accessed by ordinary individuals. The data analysis process seeks to first identify what topic must be accessed, allowing the researcher to understand what is the main purpose that data analysis seeks to answer (Bhatia, 2017).

In this literature review, content analysis was the method used by the author to categorize all articles or guidelines chosen for this thesis. This allows the researcher to take concepts or topics found in the articles or guidelines that were found using keywords based on the topic of this thesis and based on the research question (Elo, Kääriäinen, Kanste, Pölkki, Utriainen, & Kyngäs, 2014). While searching for different articles or guidelines by looking at different databases, the research question ensured that the research stayed on track and that only relevant search terms and articles or guidelines were picked. Any information that stood out was coded and then this allowed

the author to create categories and subcategories based on the coding. This method of analysis allows the researcher to put topics or keywords that have to do with this thesis into categories and subcategories. This makes it clearer to the reader because it summarizes key points while also allowing the possibility for the steps in this method of analysis to be easily traceable (Serafini & Reid, 2023).

When data was being collected, the researcher guaranteed that all articles or guidelines picked were searched for in the appropriate manner and were thoroughly screened. The chosen articles or guidelines used in this literature review were analyzed in depth and were only chosen if they proved pertinent to the study. This type of in-depth data analysis is crucial because it confirms that only data that answers the research question is used and that no information that is relevant gets left unnoticed. A summary of all chosen articles can be seen in Appendix 2.

The analysis of the chosen guidelines involved creating categories and concepts. It started out by identifying any guidelines that taught healthcare professionals how to safely prescribe, administer, and manage side effect of opioids in palliative or end-of-life care. This was carried out because clear guidelines from reputable sources needed to be extracted. Following this, key words that fit in similar contexts were added to subcategories. These subcategories were further developed, depending on how many themes arose from the chosen guidelines. The categories and subcategories can be seen in Table 3.

6 Results

The result section concentrated on guidelines that focused on how to safely administer opioids to patients in palliative or end-of-life care. The result section intended to dispel misconceptions about opioid use in palliative or end-of-life care by providing evidence-based material extracted from reputable medical guidelines. The three core categories that were identified through the literature search were: (1) opioid administration, (2) opioid side effects, and (3) palliative sedation. All categories and subcategories that came from the data analysis process can be seen in a clearer version in table 3. The section after this goes into more detail of all the results found in the chosen guidelines.

Table 3. Categories and Subcategories

Categories	Subcategories
Opioid Administration	• Dosage • Opioid Switching • Breakthrough Pain • Follow-up • Types of Opioids • Opioid Prescription
Opioid Side Effects	• Constipation • Nausea and Vomiting • Pruritus • Delirium • Sedation • Respiratory Depression • Addiction
Palliative Sedation	• Opioid Role

6.1 Opioid Administration

6.1.1 Dosage

How severe and type of pain a patient has in palliative care or end-of-life care help doctors choose what type of opioids to prescribe. It is recommended that patients suffering with cancer pain get regular dosage of opioids throughout the day. Individuals starting out on opioid therapy, should always start with the lowest morphine oral opioid dosage which is instant relief (IR) 5 mg every 4 hours (Thota, Ramanjulu, Ahmed, Jain, Salins, Bhatnagar, & Bhattacharya, 2020). The WHO pain relief levels should be followed, and mu-opioid receptors, like morphine, can be started at 20-30 mg for moderate pain because cancer pain is so extreme. The dose for scheduled opioids must be increased whenever there is more pain because this ensures that the patients are not left in severe pain (Schneider, Voltz, & Gaertner, 2012). The lowest effective opioid dosage is the amount that all patients should start out with. Doctors can start with the dosage recommended on the

medication label and can decide how much should be prescribed by considering each patient's kidney or liver function or the use of other concurrent medications that effect that effect the central nervous system. A dose of 20–30 MME is the dose recommended for one day when starting out. Dosage of opioids should only be increased if absolutely necessary and should be done slowly and the costs and benefits of an increase in dosage should always be considered. It is not advisable to raise doses above the point when the advantages are not expected to balance the hazards (Kim, Park, Kim, Kim, Kim, Park, Choi, & Choi, 2024).

The dose for scheduled opioids must be increased whenever there is more pain because this ensures that the patients are not left in severe pain. It is advised to give patients with severe and progressing illness either regular oral sustained-release or oral immediate-release morphine (patient can choose) when initiating heavy opioid therapy (Schneider et al., 2012). There were no positive effects on pain, function, or quality of life, according to a comparison study comparing retaining existing dosages as a threshold and liberally increasing dosage based on patients' ratings of pain severity. No dose-response impact was seen for pain alleviation or functional recovery in a meta-regression of moderately rated trials evaluating various opioid dosages (Kim et al., 2024). If the patient is on the 2nd level of the WHO analgesic ladder, 10 mg of morphine is recommended. Consensus is that for patients taking morphine a double dosage at bedtime is advised, so as not to be awakened by pain at night. It is advised to take opioid treatment ATC (around-the-clock) in cancer patients who are continuously struggling. A consistent 4-hourly dosage of oral IR morphine should be administered until pain is stabilized. When the amount of morphine needed in 24 hours is decided, the patient can have a 12-hourly sustained-release (SR) formulation which is equal to a 24-hour intravenous morphine dose (Thota et al., 2020)

A dosage of 20–30 mg of oral morphine for patients without kidney or renal issues with 5 mg of oral immediate-release morphine for rescue doses throughout the titration period. Ensure that there is a decent balance between tolerable pain management and side effects by making sure right dosage amount is given. Give patients regular dosage adjustment, especially during the titration stage therapy (Schneider et al., 2012). It does not seem like doses above 50 MME/day improve a patient's quality of life that much. On the other hand, individuals administered dosages of 50–90 MME/day had a significantly higher risk of unfavourable opioid treatment outcomes while this risk is comparatively modest for patients prescribed less than 50 MME/day. So, the risks and

benefits should always be considered before prescribing opioid doses greater than 50 milligrams per day (Kim et al., 2024).

6.1.2 Opioid Switching

Opioid rotation refers to switching from a first-line opioid to a second-line opioid because to unacceptable side effects associated with appropriate pain management when the opioid dose is raised due to insufficient pain treatment, analgesia or worsening adverse effects. All the trials showed that pain was controlled for 14 days after each change and, except for methadone, they all required increasing more of the amount of the new medication then was originally calculated as an adequate dose for pain management (Thota et al., 2020). Experts in palliative care should be consulted before a cancer patient gets switched to methadone. Methadone is also many times desirable for patients with kidney damage in some countries, but it has a long half-life and can cause heart issues (Schneider et al., 2012).

Transdermal fentanyl is the most widely used opioid substitute in India and after it comes transdermal buprenorphine. Fentanyl transdermal opioid route does not produce such a quick analgesic effect during the switch. The patch must be administered at the time of the last SR opioid medication dosage. Transdermal fentanyl and SR morphine were compared in a comprehensive review, showing equal effectiveness in pain management, but reduced constipation and laxative intake. Therefore, oral opioids should be taken every four hours for 12 hours after patch is put on patient. (Thota et al., 2020). Transdermal patch formulations should not be regularly used as the first-line maintenance treatment if oral drugs work for them. Transdermal patches are the first line of therapy if oral opioids are not appropriate. After optimizing first-line maintenance therapy, if pain is still not well managed, consider different opioids. If pain management doesn't improve after therapy optimization, you might want to consult a professional (NICE, 2016). According to Schneider et al. (2012), oral and transdermal slow-release opioids are the routes that are recommended to try before opting for other routes.

The duration of any side effects and the analgesic impact of ER/LA opioids may be prolonged due to their extended half-lives. ER/LA opioids have a higher chance of causing an overdose when compared to IR opioids, particularly during the first two weeks of treatment. Therefore, when treating non-cancer pain, IR opioids should be used initially rather than ER/LA opioids. However,

patients who have built a tolerance to opioids and have received a daily IR opioid at a prescribed dose for at least a week should be the only ones to get ER/LA opioids (Kim et al. ,2024). Patients with severe pain and degenerative diseases should be treated with oral sustained-release morphine as their first-line maintenance medication (Nice, 2016). Oral oxycodone and oral naloxone have been used together as well for cancer pain in the last few years because oral naloxone is metabolized completely by the liver but does not interfere with the analgesic effects of oral oxycodone. It also decreases constipation caused by opioids as well (Schneider et al., 2012). The side effects caused by opioids did not reduce that much during rotation, but the patients enjoyed the rotation. It wasn't determined which opioid medication was most appropriate (Thota et al., 2020).

It is also important to note that everyone responds to different opioids differently, and so far, there is not one opioid that works for all individuals. It is recommended that doctors continually give different opioids to patients and continually monitor their effects (Schneider et al., 2012). Patients in palliative or end-of-life care should be offered the chance to take opioids parenterally if they are not able to take oral opioids due to various reasons (Thota et al, 2020). Opioids administered intramuscularly do not seem to cause any benefit and cause pain, while opioids given rectally are not considered a good choice. Sustained and immediate-release opioids can be used together because the European Association of Palliative Care recommends this for patients with breast cancer and bone metastases (Schneider et al., 2012). European recommendations stress that the selection of IR vs ER/LA opioids should be made depending on the unique circumstances of each patient. It is advised not to use extended-release/long-acting (ER/LA) opioids for the first prescription of opioids for non-cancer pain. Instead, use immediate-release (IR) opioids. When it comes to immediate pain alleviation and functional improvement, we did not find any indication that ER/LA opioids are superior. ER/LA opioids may be preferred to IR opioids in certain situations like when a patient is experiencing pain during rest and not when they are moving (Kim et al., 2024).

The effects of analgesia or side effects that a patient has from opioids will vary depending on patients. As a result, switching from one type of opioid to another, may improve pain management and lessen side effects. Opioid switching might be considered if there are unbearable negative effects, if they do not manage the pain well enough even after increasing the dose, if the patient

gets new health issues, or if the route of administration needs to be changed (Kim et al., 2024). According to Bemand-Qureshi, Gishen, and Tookman (2019), another issue that may arise is determining the strength of different opioids due to tolerance. As a result, while switching opioids, use caution as the new opioid being given may powerful than expected. Hence, while titrating medications, dose decrease is advised, and frequent follow-up is crucial.

Switching between opioids is a typical procedure when analgesia is insufficient and/or concerning adverse effects surpass advantages. The EAPC was able to issue a flimsy recommendation for this technique based on data from previous research, thought that long-term opioid usage in certain people may lead to drug tolerance, which would reduce the effects of the opioid. The total quantity of the opioid being used and the MME dosage of the opioid that must be replaced should be determined when doing opioid rotation (Bemand-Qureshi, Gishen, & Tookman, 2019). To accommodate for partial opioid cross-tolerance, the new medication should be administered at 50%–75% of the estimated dose at the beginning. Likewise, to minimize the possibility of partial tolerance, the dose should be lowered when converting from an IR opioid to an ER/LA opioid. Doctors should evaluate the new drug's analgesic properties and side effects before titrating the dosage (Kim et al., 2024).

6.1.3 Breakthrough Pain

Breakthrough pain means when a patient experiences pain situations, even though they are most of the time without any pain. Patients with severe pain using long-acting opioids remain pain-free when not doing anything, but when they must move and do daily tasks, that is when they experience breakthrough pain (Schneider et al., 2012). For breakthrough pain (BTP), oral morphine is most commonly given. Slow onset of work lead to inefficient or slowed analgesia and issues with pain management. Buccal soluble film, sublingual and intranasal spray, buccal soluble tablet, oral, and transmucosal buccal tablet, all coming from fentanyl have been able to quickly manage pain. Transmucosal fentanyl citrate (OTFC) is the most common pharmacological way that has been studied to help BTP. OTFC is offered in a 200-mcg formulation in India. A patient should roll it against their cheek until they feel their pain is relieved enough. When it comes to the use of morphine for BTP, IR morphine is recommended and can be raised in sets of 5–10 mg if necessary. IR and SR doses must be made to work together to benefit the patient as much as possible (Thota et al., 2020).

A short-acting opioids used when pain reaches the breakthrough point should be changed regularly to ensure that they still have the same effect. Rapid-onset fentanyl is recommended to be used when patients with cancer or bone metastasis have to do some sort of activity because it lasts for 30-60 minutes, which is enough for them to complete their tasks. Doses of oral immediate-release morphine should always be available for breakthrough pain. (Schneider et al., 2012). Subcutaneous opioid route is used for patients who can take oral opioids but are experiencing breakthrough pain. For patients on maintenance oral morphine therapy, provide oral immediate-release morphine as the first-line rescue drug for breakthrough pain. Fast-acting fentanyl shouldn't be used as the first-choice rescue drug (NICE, 2016). Thota et al. (2020), said that the generally recognized ratio of the breakthrough dose to the anatomical therapeutic chemical (ATC) drug is 1:6, or equal to the 4 hourly opioid doses, but if there is kidney damage doses of 1/12 in a 24 hour cycle might be considered.

6.1.4 Follow-up

Kim et al. (2024) stated that for patients with non-cancer pain, one-week follow-ups are advised following the first prescription of opioids and for dosage titration; however, the schedule can be customized based on specific clinical circumstances. It is critical to identify opioid therapy responders and non-responders during the initial follow-up sessions to prevent unintentional adverse effects and unsuccessful long-term therapies. They said before choosing long-term opioid treatment, different standards recommend different lengths of time for opioid trials: one month in the USA guidelines from 2022, one to three months in the European guidelines from 2021, and six months in the Canadian guidelines from 2017. Consequently, we advise that the choice to continue using a specific opioid medication be made in the the first month of treatment. Based on the degree of pain relief received, the patient's function, and their overall quality of life, the choice to continue opioid medication should be made (Kim et al., 2024).

According to Kim et al. (2024), studies evaluating the impact of certain monitoring intervals on the risk of overdose and opioid use disorder were not found. It was observed that prolonged use of opioids for acute pain increases the chance that long-term opioid use is necessary. Furthermore, it was demonstrated by placebo-controlled trials that the benefits of opioid medication on pain management and function were greater after 1-3 months as opposed to 3-6 months. More than three months of opioid therapy was found to be a significant risk factor for opioid use disorder in

observational research. They said data from a different study showed that the first three months following the start of opioid medication were a high-risk period for overdoses, opening the door for risk-mitigation techniques. These findings suggest that the benefits for patients receiving opioid therapy for non-cancer pain could change at any moment, so they should be continuously monitored We advise monitoring patients on long-term opioid therapy at intervals of no more than three months to reevaluate the advantages and disadvantages of the medication. Patients who require higher doses of opioids (≥ 50 MME/day) or at risk of opioid use disorder, should be monitored more often. Any times doses of opioids are increased or decreased, the patient should be accessed by a doctor in 1 or 2 weeks after (Kim et al., 2024).

6.1.5 Types of Opioids

According to Bemand-Qureshi, Gishen, and Tookman (2019), morphine sulphate is the opioid that all other opioids are compared to because of its accessibility, familiarity, and price as opposed to demonstrated superiority. It is possible to provide morphine as an immediate-release formulation (tablets and liquid) every one to four hours regularly or as needed, waiting for at least one hour between administrating a new dose. Subcutaneous morphine has replaced diamorphine as the preferred subcutaneous opioid in the past, mostly due to the latter's more restricted supply. They say that in the voice of 2012 EAPC recommendations, there seems to be no difference between morphine, oxycodone, hydromorphone, when it comes to analgesic properties and any of them can be used for severe cancer pain. Both immediate-release (including liquid) and modified-release formulations of oxycodone are accessible. It has around 1.5–2 times the potency of morphine when taken orally. Because it is believed to have less clinically significant active metabolites, oxycodone is used for individuals who cannot stand morphine. Some health places use oxycodone instead of morphine if a patient has kidney problems and a dosage modification may be necessary (Bemand-Qureshi at al., 2019).

Bemand-Qureshi et al. (2019) expresses that a transdermal fentanyl patch that is replaced every 72 hours can be used. This is especially helpful for people who have trouble swallowing, have issues with GI absorption, or have low drug compliance. It is a helpful medication for those with kidney problems. Additionally, fentanyl comes in nasal spray, sublingual pill, and lozenge form. Buprenorphine functions as a partial antagonist of morphine and a mild agonist of opioids. It functions as a step 3 opioid at larger dosages and as a step 2 opioid at lower levels. In addition to

being available as a sublingual formulation, it is typically used as a transdermal patch. Different buprenorphine patches come with varying dosage instructions. It might be used in non-malignant pain (Bemand-Qureshi et al., 2019).

Bemand-Qureshi et al. (2019) states that, although 7.5 times stronger than morphine, hydromorphone is comparable. The fact that it may also be obtained as a high-concentrate injection, which allows a large dose to be given in a short volume, is a noteworthy feature. This is not included in the BNF and can only be obtained by special order for certain patients. When substantial dosages are needed, hydromorphone can be used in syringe drivers in nations where diamorphine is not accessible. Methadone is a long-acting opioid with the potential to operate as an NMDA-receptor antagonist, which may contribute to neuropathic pain. Its roughly eighteen-hour half-life is uncertain, and frequent usage causes it to accumulate in tissues. Only after the medicine has been used in significant volumes may side effects like sedation manifest. The drug's clearance may take a while to occur after a dose change. As a result, only skilled practitioners ought to utilize it (Bemand-Qureshi et., 2019).

Bemand-Qureshi et al. (2019) insists, when other step 3 opioids are insufficient, it is more frequently utilized in practice to treat moderate to severe cancer pain. Step 3 opioid with central action, tapentadol possesses both noradrenaline reuptake inhibitory activity and mu-opioid receptor agonist action. Compared to morphine, it is about three times less powerful. Few research has compared it to more affordable powerful opioids; using them to treat acute pain is not advised. It could be beneficial for those with persistent, benign discomfort who do not be affected by morphine. Alfentanil is an injectable opioid called alfentanil is frequently used in syringe pumps and patients with severe renal impairment. Hepatic failure should be treated cautiously since it might worsen. Because it is thirty times more powerful than oral morphine, conversions must be handled carefully. Because there isn't an oral formulation and subcutaneous alfentanil acts quickly, breakthrough pain patients may benefit from immediate-release oxycodone, either ingested or applied subcutaneously (Bemand-Qureshi, 2019).

6.1.6 Opioid Prescription

In the words of Bemand-Qureshi et al. (2019), patients with advanced and progressive diseases experiencing acute pain need to be treated quickly. It was conventional knowledge that the most effective way to quickly titrate a dose to reduce discomfort was to use four-hourly immediate-release opioid doses, with a transition to a modified-release dosage after pain had subsided. Modified-release preparations might also be used as first-line medicines in cases where doctors feel comfortable doing so. Opioids used for long-term pain during cancer should ideally follow the above-mentioned steps for acute pain. Opioid use in palliative care for pain other than cancer can be contentious. Patients with advanced, progressing non-malignant illness who have a short prognosis may benefit from opioids. It is known that certain patients with chronic will be helped by opioid therapy. But there isn't much proof that opioids work well for managing persistent or chronic pain. It's crucial to consider the potential for long-term damage given the paucity of evidence showing beneficial impacts. If opioids are ineffective, they should be stopped, even in the absence of any other alternative treatments (Bemand-Qureshi, 2019).

6.2 Opioid Side Effects

6.2.1 Constipation

There are now more new medications for constipation than ever before, and this study sent out by the National Hospice and Palliative Care Organization to different hospice centers in America shows how many new options are available and how it is helping patients. This study shows that constipation should not be a major concern when dealing with opioid use in palliative or end-of-life care and that continuously new methods are being developed, so that patients can get the pain management that they need and not suffer from constipation side effects. Constipation is one of the most common side effects of opioid therapy suffered by patients with advanced cancer pain (Sera & McPherson, 2018). Constipation is one of the most common side effects of opioid therapy suffered by patients with advanced cancer pain. Combining naloxone and an opioid has proven to decrease OIC (opioid-induced constipation). Also, healthcare professionals might consider switching patients to fentanyl or methadone if they have chronic constipation. Laxatives should also be given when opioid therapy is started and throughout the duration of the opioid therapy to reduce the risks of constipation. Combining nonpharmacological interventions like fiber

and water intake with the use of laxatives and opioids might help some patients but does not address the underlying issue that causes OID (Thota et al., 2020).

The majority of the places providing palliative or end-of-life care services that responded said that about 90% of their patients are on a bowel regime the moment they are admitted and that this greatly reduces their chances of ever suffering from constipation. A bowel regime is a combination of medications that prevent constipation. The first-choice products included senna and docusate combined, then senna alone, docusate alone, PEG 3350, methylcellulose, lactulose, sorbitol, and enemas (Sera & McPherson, 2018). Senna or macrogol are examples of preventive regular laxatives that might be administered for constipation brought on by opiate usage. There is no proof to support the preference of one laxative over another. Combining laxatives with distinct mechanisms of action may be necessary for certain people (Bemand-Qureshi et al., 2019). NICE (2016) emphasized that before considering an opioid transition, laxatives should be optimized. Peripherally selective opioid antagonists may be taken into consideration in cases when maximally tolerated dosages of oral laxatives are ineffective. They work specifically on the intestine without interfering with the central analgesic action of opioids, hence reducing their constipating impact. NICE observed that while these mu-opioid receptor antagonists are useful, their usefulness in a palliative care context is not well-established, particularly when contrasted with optimal laxative treatment. Sera an McPherson (2018), said some newer products on the market like methylnaltrexone, lubiprostone, linaclotide, and naloxegol, were not considered as popular and were considered third-line agents. The preparations that were used the most in the hospice for the treatment of constipation caused by opioids by the centers that responded included senna plus docusate, senna alone, docusate alone, bisacodyl, PEG 3350, and lactulose in the following order. Intestinal propulsive movements are enhanced, and fluid secretion into the intestinal lumen is encouraged by stimulant laxatives, which include senna and bisacodyl. By functioning as a surfactant and helping water to be absorbed into the feces, docusate softens it.

Healthcare professionals must tell patients that the majority of them will most likely suffer from constipation when taking strong opioids. Provide patients starting powerful opioids with a prescription for laxative therapy, to be taken on a regular basis at an effective dose. Remind patients that commitment to medication is crucial and that constipation takes time to resolve. Before

thinking about upgrading to a stronger painkiller, make the most out of laxative therapy for constipation management (NICE, 2016). Senna plus docusate was used for constipation for about 50% of patients in 80% of responding hospice organizations, and senna and docusate on their own or together were used to treat constipation caused by opioids in at least 50% of patients in 60.7% and 35.5% of responding organizations as follows. Although there are so many new medications on the market to treat constipation caused by opioids, 75% of hospice places said they had never used linaclotide, lubiprostone, naloxegol, or methylnaltrexone. The hospice facilities stated that their constipation management methods had remained constant, regardless of the changes in the market. If a new drug was used for constipation caused by opioids, methylnaltrexone was the one most picked because it is cheaper and easier to administer, especially in subcutaneous form. Methylnaltrexone, a peripherally acting μ-opioid receptor antagonists (PAMORA), is given subcutaneously and licensed for the treatment of constipation caused by patients receiving palliative or end-of-life care. Since they do not pass across the blood-brain barrier, methylnaltrexone and other PAMORAs do not reverse analgesia; instead, they work by reversing the effects of opioids in the stomach (Sera & McPherson, 2018).

6.2.2 Nausea and Vomitting

Thota et al. (2020), pronounced Nausea and vomiting can occur in individuals in palliative or end-of-life care for many reasons, including being caused by opioid use. In the treatment of nausea and vomiting in patients in palliative or end-of-life care, antiemetics like olanzapine, levomepromazine, and haloperidol have never gone through randomized control trial and are only used because case studies and comprehensive reviews support their use. Olanzapine seemed to decrease nausea and vomiting that were extreme, according to a case study. A randomized clinical study that observed the use of metoclopramide and dexamethasone for nausea and vomiting was unable to prove their definite efficacy. Nausea and vomiting caused by opioids can occur for many reasons, so choosing the right antiemetic sometimes requires trial and error. It also must be stated that many patients build a tolerance to nausea and vomiting, 5-10 days after getting opioids, indicating that medicine might not have to even be used at all for this side effect (Thota et al., 2020).

Healthcare professionals should inform patients that nausea is likely to be temporary and that it may happen when beginning a powerful opioid medication or when the dosage is increased. Before thinking about upgrading to a stronger opioid, prescribe and maximize antiemetic medication

if nausea continues (NICE, 2016). It is possible to prescribe frequent antiemetics as a preventative measure for nausea and vomiting, however this is not essential. Nonetheless, it is helpful to prescribe when it is needed. Cyclizine can be given three times a day at a dose of 50mg each time, or metoclopramide three times a day at 10 mg each time are appropriate anti-emetics for nausea caused by opioid (Bemand-Qureshi et al., 2019).

6.2.3 Pruritus

Thota et al. (2020), declares that itching, or pruritus, is a rare adverse effect of opioid usage that is more frequently observed when morphine is administered intrathecally or epidurally. It is possible to utilize antihistamines like cetirizine and diphenhydramine. Diphenhydramine's sedative properties might be helpful in reducing itching. Ondansetron, a serotonin antagonist, has been examined and shown to be beneficial. For symptom alleviation, a μ-opioid receptor antagonist, such as naloxone, might be taken and given slowly. There are no randomized studies that show how to manage this side effect (Thota et al., 2020).

6.2.4 Delirium

Thota et al. (2020), says it is difficult to say if delirium is caused by opioids because delirium can occur due to many reasons in patients who are in palliative or end-of-life care. Furthermore, Patients with liver or kidney problems are more vulnerable to have delirium caused by opioids. They are dehydrated, have some form of mental impairment, or are taking multiple drugs simultaneously. Four opioids influenced delirium and hallucinations of less than 5%, according to a Cochrane analysis (Thota et al., 2020).

According to Bemand-Qureshi et al. (2019), when using opioids for the first time, patients may suffer slight sleepiness or attention problems, although these side effects normally go away on their own. Once on a steady dose for longer than a week, there no elevated risk associated with chronic opioid usage; nonetheless, breakthrough amounts may result in temporary impairment. Clinicians may think about reducing the dosage or switching to an opioid if CNS adverse effects are still present. In these situations, the EAPC recommendations offer a flimsy recommendation for the use of methylphenidate as a psychostimulant. It is uncommon to apply this in clinical practice, though. If

patients experience delirium or bothersome hallucinations, it may be necessary to contemplate dose decrease or switching to another opioid (Bemand-Qureshi et al., 2019).

6.2.5 Sedation

Thota et al. (2020), states that education for patients when starting using opioids or increasing opioid doses must be carried out. It is critical to differenciate sedation brought on by opioids and exhaustion brought on by cancer and to understand how different drugs used in palliative or end-of-life care interact with each other. It is possible to think about lowering the opioid dosage and adding adjuvants to lower the dosage to decrease the chances of opioid- induced sedation. There are not enough studies that can show if stimulants would at all. Individuals with disturbed sleep-wake cycles and inadequate pain management that interferes with sleep require analgesic medication adjustments and education (Thota et al., 2020).

6.2.6 Respiratory Depression

According to Thota et al. (2020), voices that opioids that are taken orally or given slowly they have a very low chance of causing respiratory depression in palliative or end-of-life care. If respiratory depression develops in these circumstances, multiple medication causing drug interactions, or some other reason could be causing this and not the use of opioids. Careful monitoring of the state of awareness is a stronger signal for the early detection of respiratory depression when quickly titrating or increasing the dose of opioids. Naloxone should be gradually increased if respiratory depression is detected. While doing this, the patient should be monitored for increased pain levels and if this occurs, they should be given a different type of analgesic until they are stable. Nine milliliters of regular saline are added to one ampoule of naloxone (1 ml = 0.4 mg/40 mcg) every 60 seconds, 1-2 ml (0.04-0.08 mg) until risk for respiratory depression is alleviated. The effect of naloxone should be monitored closely, and its dosage should be increased as needed. After taking 1 mg of naloxone in if there is still no improvement, one must consider that the respiratory depression is being caused by something other than opioids (Thota et al., 2020).

6.2.7 Addiction

Pharmacological pain management is still considered one of the best methods for pain management in cancer patients. Opioid use in pain management is extremely useful, but like with any

drug, opioids have the potential to cause addiction or abuse with a higher chance when it comes to long-term cancer pain. Healthcare professionals must understand what addiction means, and they must realize that addiction has a lot to do with genetics and that addiction can cause tolerance or physical dependence. drug abuse must be clearly explained because drug abuse means using drugs for non-medical reasons. That is why all health professionals should ask patients about their history with drugs (legal or not) before they are prescribed opioids to find out how they should be monitored during opioid use (Schneider et al., 2012). To prevent addiction in palliative or end-of-life care facilities, holistic strategy is needed to address opioid use disorders in patients who are more susceptible to such things. Healthcare workers must be taught how to use screening instruments, and methods to maintain patient safety while addressing pain. The healthcare workers must also receive comprehensive education about opioid misuse. Psychosocial evaluations that hospice workers conducted were not standardised, that they were very wide, and that they failed to account for possible diversion, so that is why individuals working in hospice work should provide services that are tailored to their level of training about SUDs, risk factors, and warning signals when they meet patients (Gabbard, Jordan, Mitchell, Corbett, White, and Childers, 2019).

Red flags for medication abuse should be identified by healthcare workers, such as early medication runout, misplaced or stolen drugs, and recurrent requests for medication escalation in the absence of a change in the patient's clinical condition Fellowship programs have to include instruction on substance abuse. Hospice personnel and trainees should get training on addiction, drug abuse, and diversion in addition to how to interact with patients and families in the event of opioid usage. Additionally, considering the frequency of these patients, all healthcare professionals (oncologists, primary care physicians, etc.) must get training about substance use disorders (Gabbard et al., 2019). This concern for addiction is not so great during end-of-life care when the cancer is at the later stages because there is then no hope for a cure, and the patient will soon die. During palliative care, the patient can continue to live for many years, so there should be more caution when prescribing opioids for a long amount of time or when prescribing opioids that start quickly. Usually, mu-opioid receptor agonists are used to manage cancer pain, but morphine still tends to be the most chosen opioid because it is cheaper and more readily available, even though it can cause a lot of harm to patients who have kidney issues (Schneider et al., 2012).

According to Gabbard et al. (2019), to identify patients who may be at risk of substance abuse, screening methods might be useful. While there are several screening instruments available, none have been approved for use in hospice care. The opioid use assessment instruments used were created in an outpatient context for patients with chronic non-malignant pain. Family and psychological risk variables are included in the Opioid Risk Tool (ORT), which is based on risk factors. Because the ORT asks simple questions on alcohol, mental problems, and family history without requiring patients to fill out a form, we strongly advise utilizing it. Due to limited resources and availability of addiction specialists to visit hospice patients at home or facilities, hospices need to integrate aspects of substance use treatment into their practices for patients who have active SUDs (Gabbard et al., 2019). An individualized care plan for pain management should be initiated between the patient and the hospice agency. We recommend a pain management agreement between the provider and the patient. Compared to other opioids, buprenorphine is safer for people suffering from pain and addiction since it is a partial agonist and has a ceiling effect. The use of buprenorphine as the main medication for patients with a life-limiting disease is not well documented in the literature, but as more healthcare professionals feel comfortable prescribing it, it is expected to rise. An additional alternative for people with life-limiting conditions is methadone. It is affordable and available in many forms, which is beneficial for people who are nearing the end of their lives and may not be able to swallow (Gabbard et al., 2019).

Palliative Sedation

6.2.8 Opioid Role

According to Klein, Voss, Ostgathe, Schildmann, & SEDPALL study group (2023), an individual might undergo palliative sedation if they have a disease that limits their life or will kill them soon, and they also usually have a DNR request. Palliative sedation might also be carried out when a patient has tractable delirium, dyspnea, or extreme pain. Palliative sedation is also many times only carried out as a temporary solution when a patient is in extreme pain and needs some time to rest before being brought back. Midazolam, levomepromazine, and propofol are the drugs most recommended for palliative sedation, so opioids are not responsible for any adverse effects. These guidelines also brought up the point that specific types of drugs should be chosen for palliative sedation depending on what symptoms a patient has and not just since palliative sedation is needed. Opioids can cause sedation as well and are still many times used to induce sedation, but they

should not be used for sedation purposes but should instead be used for pain management (Klien et al., 2023).

Klein et al. (2023), voices that many healthcare professionals do not want to use opioids at the same time as other drugs that have induced sedation, but opioids should still be used for pain management during sedation because patients are still in pain. During sedation, the patient should be monitored on how deep their sedation is and if the sedation is helping relieve their symptoms. the Richmond Agitation Sedation Scale – Palliative Version (RASS-PAL) can be used to carry out the necessary observation and monitoring of patients undergoing palliative care sedation. Depending on how deep the palliative sedation is, some of the guidelines recommend that patients should also have their respiratory rate, oxygen saturation, respiratory movement, and other vital signs monitored (Klien et al., 2023). All side effects of medications should be monitored as well. There are different degrees of palliative sedation, and depending on what type of suffering the patient is facing, that is the degree of palliative sedation they will receive. Palliative sedation is not what causes death or a patient's condition to worsen but is carried out when these things are already happening. There is still a lot of discussion among health professionals if existential distress should be a reason to induce sedation because it is considered psychological suffering and physiological suffering (Klein et al., 2023).

7 Discussion

7.1 Main Findings

Multiple misconceptions held by nurses or patients about the use of opioids in palliative or end-of-life care were easily refuted as various related guidelines were analyzed that showed how any concerns that individuals might have about opioids could easily be managed by multiple methods or other medications. All the guidelines clearly showed how the benefits of opioid use for pain management in palliative or end-of-life care outweigh any potential harm that they might cause. Many misconceptions about the use of opioids were irrelevant in the context of palliative or end-of-life care because patients all have chronic illnesses and are deteriorating. Any issues possibly caused using opioids in palliative or end-of-life care do not pose as much of a threat as leaving patients in pain throughout their last days on this earth.

Firstly, when it comes to the use of opioids in palliative or end-of-life care, ensuring that the risk of addiction is carefully mitigated. Firstly, healthcare professionals must learn to differentiate between addiction and tolerance (Schneider et al., 2012; Gabbard et al., 2019). Addiction is when patients are not able to stop using an opioid while, tolerance is a normal process that causes a person to become used to using a specific opioid and requiring larger or more frequent doses of a specific opioid. Nurses can ask patients about any personal history concerning addiction and can also use different screening tools to see how at-risk patients are for opioid addiction (Schneider et al., 2012). It is important to note that, when it comes to palliative or end-of-life care, addiction should not be a major concern because patients are close to the end of their life. Usually, morphine is the opioid chosen for pain management but, if addiction is a great concern, buprenorphine might be considered the opioid of choice (Gabbard et al., 2019).

Following this, constipation is also a side effect of opioids and is the most common side effect caused by opioids, but it can be easily managed and should not cause much concern. This is especially true when it come cancer pain because patients require larger doses of opioids due to the severe suffering that they are enduring (Bemand-Qureshi et al., 2019). Currently, so many different types of medication to deal with constipation are being released on the market every day. Although there are so many different medications and non-pharmacological methods to treat opioid induced constipation, laxatives are still the most frequently chosen medication. Non-pharmacological methods can be used in combination with a laxative when treating opioid-induced constipation but are not recommended to be used on their own because non-pharmacological methods are not strong enough on their own for this type of constipation (Thota et al., 2020).

Other common feared side effects caused using opioids in palliative or end-of-life care include nausea and/or vomiting. Nausea and vomiting usually lessen as time passes on and are at their worst at the start of opioid therapy. Nausea and vomiting can also be possibly caused by other diseases that individuals have in palliative or end-of-life care, and not because of the administered opioids (NICE, 2016). Opioid-induced nausea and vomiting can occur for many reasons, so many times health professionals must try different types of antiemetics or other medications to see what works best for each patient because every patient responds differently. Also, it seems like many patients might even become tolerant of opioids, so medication might not even be needed (Thota et al., 2020).

Unlike nausea and vomiting, respiratory depression is a rare side effect caused by opioid use that can be fatal. It seems that when opioids are administered orally or at a slowed pace, they rarely cause respiratory depression in palliative or end-of-life care (NICE, 2019). If respiratory depression is experienced by a patient, it is possible that it is due to their other illnesses or because of some medication interaction and has nothing to do with opioids. Patients should be closely observed when having their opioid dose increased or given a different type of opioid to observe if they are experiencing any respiratory discomfort/depression and can be given naloxone as needed. Usually, the only reason respiratory depression occurs due to opioid use is because the opioid dose is too large or given too rapidly (Thota et al., 2020).

Other rare side effects caused by opioid use, are pruritus and delirium. Pruritus occurs less often than delirium, and usually only occurs when morphine is not given orally or intravenously. Antihistamines might be considered beneficial or naloxone, but there are not many studies or information regarding pruritus caused by opioid use (Thota et al., 2020). Delirium is another side effect that might be caused by opioid use or because of another illness that the patient is suffering from. Many palliative or end-of-life patients take multiple medications, have some organ failing, or are dehydrated which are all conditions that can increase the chances of delirium in a patient. It is common that delirium occurs when opioid use is first initiated, but most of the time it will disappear as the patient becomes accustomed to using this opioid. It is recommended that if delirium persists, a patient changes the type of opioid they are being given or the route of the given opioid is changed if possible (Bemand-Qureshi et al., 2019).

A few other guidelines that were inspected also pointed out that opioid switching, changing the route of administration, or the dosage of a specific opioid could potentially decrease side effects caused by opioids in certain patients. Changing the opioid is also done when a specific opioid does not provide enough pain management for a patient. Opioid switching can be vital in many cases and should be practiced as much as possible because each patient is an individual and to promote holistic care each patient should be given a specific opioid administration care plan that fits best with their needs. Opioid dosage will depend on what type of opioid is, the level of pain a patient is in, and the patient's history of taking pain medication because this will determine their level of tolerance and how their body reacts to opioids. The dosage should also be determined according to

how active a patient is, and larger dosages should be given before any strenuous activity to decrease pain (Thota et al. 2020; Kim et al. 2024; Schneider et al. 2012).

Education among healthcare providers plays a vital role in decreasing misconceptions about opioid use in palliative or end-of-life care held by patients, family members, and even other health professionals. These healthcare professionals are given the job of educating patients about any side effects that might be caused by opioids and ways that healthcare professionals can help them decrease the side effects caused by opioids. All the healthcare professionals in the care team are tasked with ensuring that patients are getting correct pain management, so it is essential that they are correctly educated about the role of opioids in palliative or end-of-life care and are clear about how opioids are different in the context of this type of health service (Kim et al. 2024; Thota et al. 2020). Follow-up care is also crucial because it shows the patients how healthcare workers are aware of any side effects that they might be facing and are able to help them ensure that they get adequate pain management for opioids. Talking and educating patients about the benefits of opioids in pain management will decrease any misconceptions they might have because of the respect that they hold for healthcare professionals (Bemand-Qureshi et al. 2019; Kim et al. 2024).

Another clear confusion related to misconceptions about opioid use in palliative or end-of-life is when it comes to considering sedation and palliative care as the same thing. Sedation is a possible side effect caused by using opioids and is usually caused when an opioid dose is increased rapidly. It is crucial to consider that sedation might not be caused by opioids but could be caused by diseases that the patient might be facing. Stimulants might be considered appropriate to help in this situation but have not proved very effective (Thota et al., 2020). On the other hand, palliative sedation is a conscious act that is carried out when a patient is in extreme pain and is going to die soon. Palliative sedation must not be confused with euthanasia because palliative sedation does not hasten death or kill a patient but instead decreases their level of consciousness until the diseases they are suffering from will kill them. It is important to note that sometimes opioids might be used to cause palliative sedation, but this has been proven to be incorrect, and they should only be administered to help ensure the patient is not in severe pain (Klien et al., 2023).

7.2 Validity and Reliability

In Finland, the Ministry of Education and Culture established the 'The Finnish National Board on Research Integrity (TENK)' to ensure that all research carried out follows the same rules and scientific practices. The Finnish Advisory Board has not only provided guidelines on how researchers must act and report their scientific discoveries when carrying out their research, but they have also set up institutions that deal with and investigate any scientific discrepancies that have been reported or involving any issues concerning how specific research was carried out (Räsänen & Moore, 2016). These guidelines must also be followed by all JAMK students while they write their theses. The Finnish Advisory Board has clearly stated that it is up to the researcher to guarantee that any results they report in their thesis are accurately reported and that none of the results are interpreted to serve a specific bias. The researcher is also accountable for verifying that all results came from reputable evidence-based guidelines that they retrieved from the databases that JAMK University acquires or the use of all students.

The Finnish Advisory Board states that all researchers are responsible for following all ethical practices which include validity and reliability. Validity shows how well a study can measure or accurately reflect on the activity that it was examining and by doing this the study can prove that anything that was found or reported was important and without bias (Roberts & Priest, 2006). When it comes to reliability, this means how well and dependable the examiners felt about the way a study was carried out and any findings found in the study. Reliability in any research or study is a must because it allows anyone to observe how well any results found during research can be viewed as durable, replicable, and honest (Babu & Kohli, 2023). Only when both validity and reliability are carried out, can any research accurately follow any ethical guidelines laid out. Having both components gives confidence to the public that the carried-out research or the reporting of the results gained from the research can be accurately used and valuable in any further research.

While choosing the guidelines used in this literature review, the researcher confirmed that all guidelines met the reliability and validity standards thereby ensuring that ethical guidelines were followed. By clearly explaining in detail how this literature review was carried out, it established the possibility of anyone interested to be able to replicate the process and find the same results each time (Ciubotariu & Bosch, 2022). This literature review proved its reliability by picking only guidelines that followed the research inclusion criteria (guidelines in English, peer-reviewed, full-

text guidelines within years 2012-2024, relevant to the research question). The researcher who carried out this literature review has extensive experience working with palliative or end-of-life care patients in various nursing practices that they attended, allowing them to provide beneficial insights about the importance of pain management and how misconceptions about opioids lead to poor pain management. Carrying out this literature review allowed the researcher to learn more about opioids and equipped with valuable knowledge about how to use opioids to manage patients' pain in the best possible way.

7.3 Ethical Considerations and Study Limitations

When finding guidelines or research papers for a literature review study, it is crucial to follow specific rules when it comes to data collection and investigation. Ethical considerations and ethical guidelines are created and published by different ethical committees to ensure that all participants are participating voluntarily and that everything that is being carried out meets acceptable research ethical standards. All researchers must provide information that their research is conducted in a manner that is acceptable to ethical guidelines. When it comes to a literature review, asking for consent and ensuring the privacy of patients is not carried out by the researcher because it has already been done by the individuals who carried out the research studies used in a literature review (Reid, Brown, Smith, Cope, & Jamieson, 2018). Nevertheless, it is still expected that general ethical guidelines must be kept throughout the research regardless of the type of research that is being carried out. According to the Finnish National Board on Research Integrity, it is paramount that the researcher tries to avoid any personal bias when reporting results and must clearly show how they came to each conclusion during each step of the way. Credit must be given to the researchers whose articles were used correctly to meet ethical guidelines and give credit where credit is due. Correct citations ensure that researchers get their credit and allow anyone who encounters a literature review the ability to quickly confirm that the reported results are backed by evidence-based information. When it comes to limitations involving this literature review, there are some key points. Firstly, there is a limited number of countries providing research about how opioids are used in palliative or end-of-life care in their own countries. Following this, there is also a limited sample size because it is unclear in many of the guidelines in this literature review how many individuals were studied when it comes to the way they reacted to opioids and how their side effects were managed in palliative or end-of-life care and also how long these studies were carried out.

8 Conclusion

In conclusion, any misconceptions that nurses or patients might have about opioid use in palliative or end-of-life care can be easily alleviated by providing guidelines as chosen in this literature review. Any side effects potentially caused by opioids can be easily managed by using different medications, non-pharmacological methods, or a combination of both medication and non-pharmacological methods. Many times, side effects will lessen or go away on their own after a patient continues to use a specific opioid. How many side effects and for how long a patient will suffer from these side effects will vary substantially because each patient is an individual. Patients who have a history of taking opioids might experience fewer side effects caused by opioids. Also, the side effects might vary depending on the opioid or the route of administration. Constipation, nausea, and vomiting are the most common side effects caused by opioid use. Laxatives are usually given for constipation, and for nausea and vomiting, antiemetics can be administered. Side effects caused when using any opioid in any form do not pose as great an issue as a patient being in pain. Poor pain management is harder to deal with than any side effects caused by opioid use, so a patient must be given as many opioids as they need. When it comes to addiction to opioids, it is not much of a concern in palliative or end-of-life care because the patient is at the end of their life, so it does not pose an issue. Still, different screening methods and history taking of a patient can be carried out to see if addiction might have a higher chance of occurring in a specific patient. Addiction and other side effects caused by opioids will also depend on how long a person is in palliative or end-of-life care and requires the use of opioids.

Opioid switching is often used in palliative or end-of-life care to prevent specific side effects or decrease the duration of side effects. Using different opioids or administrating opioids through different opioids might lessen or prevent side effects in certain patients. Some patients with liver or kidney diseases might deal better and have fewer side effects when given weaker opioids that are administered more frequently. Decreasing the dose of a specific opioid and increasing the frequency might reduce the amount of side effects or the duration of the side effects. One must also consider if long-lasting or rapid-release opioids should be given while also considering if an IV bolus would be the most beneficial way to administer a drip. The route and type of opioid administered will also depend on how much pain a patient is doing and how much movement a patient is doing. Each patient is an individual, so to be able to provide holistic care, a patient must be continually evaluated to see the type of opioid, route of administration, and dosage that works best for a

specific patient. Decreasing the dosages but increasing the frequency of dosing will also prevent respiratory depression from occurring, which is a great fear held by nurses and patients. Patients should be continuously told about the importance of opioid use in palliative or end-of-life care and how it will better their experience by providing adequate pain management.

While writing this literature review, there lacked certain information about opioid use in palliative or end-of-life care that that could be further explored in future studies. It would be beneficial if future research focused more on opioid use specifically in palliative or end-of-life care and not only on opioids as a form of pain management in other sectors where the patients are not actively dying. This is because opioid use in palliative or end-of-life care is different from opioid use in other situations where patients have many years left ahead of them. It would be helpful to have more research carried out that did not focus so heavily on the side effects of opioids but focused more on all its benefits when it comes to pain management in palliative or end-of-life care. In up-coming studies, it would be crucial to highlight how side effects can be easily managed, and that poor pain management in palliative or end-of-life care is much worse than any side effect caused by opioids. Information focusing more on how to alleviate misconceptions held by patients and nurses fearing opioid-induced addiction would better pain management in health sectors like palliative or end-of-life care where addiction should not be a major concern.

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Appendices

Appendix 1. Critical Appraisal of all Articles

Author	1.Abstract/Title	2. Introduction and Aims	3.Methods and Data	4.Sampling	5.Data Analysis	6.Ethics and Bias	7. Results	8.Transferability or generalizability	9. Implications and Usefulness	Total
Schneider, G., Voltz, R., & Gaertner, J.	4	3	4	3	4	4	4	4	4	34
Klein, C., Voss, R., Ostgathe, C., Schildmann, J. A., & SEDPALL study group	3	4	4	3	4	3	4	4	4	33

Thota, R., Ramanjulu, R., Ahmed, A., Jain, P., Salins, N., Bhatnagar, S., & Bhattacharya, D.	4	4	4	3	4	4	4	4	4	34
Gabbard, J., Jordan, A., Mitchell, J., Corbett, M., White, P., & Childers, J.	4	4	4	4	4	4	4	4	4	36
Kim, M., Park, S. K., Kim, W. M., Kim, E., Kim, H., Park, J. M., Choi, S. S., & Choi, E. J.	4	4	4	3	4	3	4	4	4	34
NICE Clinical Guidelines	4	4	4	4	4	4	4	4	4	36
Sera, L., & McPherson, M. L.	4	4	4	4	4	3	4	3	4	34
Bemand-Qureshi, L., Gishen, F., &	4	4	4	4	4	4	4	4	4	36

Tookman, A. (2019).										

Appendix 2. Summary of Reviewed Articles

Author, year, and country	Purpose and Aims of the Study	Research Methods or Instrument	Sample (*n*)	Main results	Critical appraisal (Hawker et. al 2002)
Schneider, G., Voltz, R., & Gaertner, J. (2012). Germany	Different methods of pain management that can be offered to patients with breast cancer and bone metastases in order to better their pain management.	Explaining about different pain management methods, and especially focusing on opioid use.	Using different guidelines that have to do with pain management in individuals with breast cancer and bone metastases	If taking opioids orally is not feasible, transdermal opioids represent a valuable alternative. Only individuals with severe pain syndromes should be prescribed methadone due to its complicated pharmacology. One encouraging breakthrough for the reduction of opioid-induced constipation is the availability of a set mix of oxycodone and naloxone. Breakthrough pain episodes are frequently caused by metastases, particularly bone metastases.	34

				Therefore, in addition to routine opioid therapy, the administration of an on-demand opioid is required. Recently, because of their quick onset and shorter duration of effect, rapid onset fentanyl's have been highly recommended for breakthrough cancer pain.	
Klein, C., Voss, R., Ostgathe, C., Schildmann, J. A., & SEDPALL study group. (2023). Germany	In palliative care, the proper use of sedation as a last option to relieve pain is handled differently in real-world situations. This article aims to provide a practical summary of pertinent information included in treatment guidelines and recommendations.	In addition to a manual web search, a comprehensive literature search was performed in the PubMed, Scopus, and Google Scholar databases.	29 publications (11 journal articles, 18 other)	In patients with a maximum two-week life expectancy, intractable delirium, dyspnea, and discomfort are the usual reasons for sedation. A contentious sign is existential suffering. Midazolam is the first-choice medication. Opioids shouldn't be used as sedatives since it's difficult to forecast when people will get drowsy. Sedation can cause respiratory and circulatory depression, loss of control, autonomy, and capacity to communicate. Monitoring the patient's level of sedation and the severity of their symptoms is typically	33

				advised; depending on the circumstances, several publications also propose clinical and technically supported monitoring.	
Thota, R., Ramanjulu, R., Ahmed, A., Jain, P., Salins, N., Bhatnagar, S., & Bhattacharya, D. (2020). India	The guidelines provided by the Cancer Pain Special Interest Group (SIG) of the Indian Society for Study of Pain (ISSP) on the pharmacological management of adult cancer pain offer a methodical and structured approach that can enhance the treatment of cancer pain and offer patients a minimum level of acceptable quality of life.	A literature search was conducted utilizing the OVID Search engine, Google Scholar, MEDLINE, PubMed, and Cochrane Database. Studies that were published in English up until November 2018 were included in the search. A questionnaire was distributed during the via email to all ISSP and Indian Association of Palliative Care (IAPC) members.	All the ISSP and Indian Association of Palliative Care (IAPC) members.	It was proposed that the World Health Organization's three-step analgesic ladder, which is suitable for the level of pain, be followed when prescribing analgesics for cancer pain management. Weak opioids like codeine, tapentadol, and tramadol can be used with nonopioid analgesics to treat mild to moderate pain. For moderate-to-severe cancer pain, morphine is the first-choice opioid that we advise. Following the establishment of the effective 24-hour dosage with immediate-release morphine, sustained-release formulations can be begun 12 hours a day. Consider switching to another opioid or rotating them if the adverse	34

				effects become unbearable or the analgesia is insufficient. One μ receptor antagonist that should be used immediately for opioid-induced respiratory depression is naloxone.	
Gabbard, J., Jordan, A., Mitchell, J., Corbett, M., White, P., & Childers, J. (2019). America	To examine the research on the subject and provide recommendations for managing pain in patients with SUD who are currently receiving hospice care or who are at risk of acquiring SUD.	Providing guidelines on how to screen for substance use disorders in patients receiving opioids during hospice care	Individuals in hospice care	There are different ways that individuals can be screened for SUD in hospice care. Healthcare professionals should be taught how to screen for SUD and should use the opioid risk table.	36
Kim, M., Park, S. K., Kim, W. M., Kim, E., Kim, H., Park, J. M., Choi, S. S., & Choi, E. J. (2024). South Korea	To help doctors administer opioids safely and efficiently for chronic non-cancer pain, guidelines for opioid prescriptions have been developed.	Updated the previous KPS recommendations after expert talks with the KPS Committee on Hospice and Palliative Care, and a thorough evaluation of the literature and consensus-building processes.	Different Experts	Doses of opioids to prescribe, how to carry out opioid switching, and how to follow up on opioid administration.	34
NICE Clinical Guidelines. (2016). England	Guidelines for use of strong opioids for pain	Different articles	Different articles	Took a look at strong opioids and how to administer and use	36

	relief for adults in palliative care				
Sera, L., & McPherson, M. L. (2018). America	To find out what medication regimens hospice programs now employ to treat and prevent OIC, if those regimens have changed in response to the availability of newer medications and evidence against the use of docusate, and whether hospice organizations are standardizing the care of OIC	The National Hospice and Palliative Care Organization sent an online survey consisting of ten questions. The demographics, first-, second-, and third-line pharmaceutical treatments covered by bowel protocols, changes in prescription patterns over the previous five years, and the proportion of patients using certain constipation medications were also questioned.	131 Hospice Facilities	A bowel regimen was recommended to at least 90% of patients upon admission to hospice, according to most organizations. The most often utilized preparations for OIC therapy for patients receiving hospice care included bisacodyl, polyethylene glycol 3350, lactulose, senna with docusate, senna alone, and docusate alone. More than 75% of hospice groups stated they have never utilized naloxegol, lubiprostone, linaclotide, or methylnaltrexone. In summary, this study sheds light on the latest methods used by hospice groups to care for older adults. The administration of OIC will probably keep changing as additional agents hit the market.	34

Bemand-Qureshi, L., Gishen, F., & Tookman, A. (2019). America	Help healthcare professionals correctly use opioid in palliative care	Different guidelines from different sources	Different guidelines from different articles	How to prescribe opioids, the different opioids that can be used, opioid switching, and how to manage some opioid side effects.	36