

The use of essential oils in relieving symptoms specific to brain malignancies: A systematic review

M Durr



orcid.org/0000-0002-8037-4664

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Supervisor: Prof AJ Blignaut

Co-supervisor: Prof CS Minnie

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Student number: 22744754



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DECLARATION

I, Mari-Louise Durr, M.Cur student 22744754, solemnly declare that the following study is my own work regarding the study with title: *The use of essential oils in relieving symptoms specific to brain malignancies: A systematic review*. No plagiarism or intention to steal was committed of my knowing, whenever literature was needed to support or strengthen my argument. I have completely referred to the author's whose work I have used. Full credit was provided to the authors as cited in the bibliography and in the text.



Mari-Louise Durr

20/11/2017

ABSTRACT

Background

Brain-malignancy incidence is on the rise globally. Traditional treatment options for brain-malignancies such as surgery, radiation or chemotherapy bring about side-effects that may add to the already distressing symptoms of the malignancies. Essential oils have been proven to be effective in assisting in the relief of symptoms, yet no summary of the best available evidence for the use of brain-malignancy related symptoms with essential oils is available.

Aim

The main aim of this study was to provide a summary of the best available evidence regarding the use of essential oils to relieve specific brain malignancy-related symptoms (such as headaches, seizures, increased intra-cranial pressure, vomiting/nausea, depression and anxiety) and to design a patient information leaflet with the findings of the study.

Method

A systematic review was conducted and the following databases were utilised : Medline, eJournal, CAB abstracts, Health source, Academic Search Premier, CINAHL, Pubmed, Cochrane, Web of Science, Scopus, ScienceDirect, SAePublications, AHFS Consumer Medication information, SocINDEX and Masterfile. Applicable academic literature was identified following a predetermined search strategy. The reference lists of secondary sources were searched to determine and include the primary sources. Inclusion and exclusion criteria were predetermined and all studies were critically appraised by validated critical appraisal tools.

Results

24 studies were included in the final report. Essential oils proved to assist in relieving brain-malignancy related symptoms of headaches, vomiting/nausea, depression and anxiety. No symptomatic treatments results were found for the treatment of seizures and increased Intracranial pressure. The essential oils found to assist in the relief of these symptoms were Lavender, Basil, Spearmint, Peppermint, Bergamot, Roman

Chamomile, Sandalwood, Frankincense, Spikenard, Rose, Juniper, Geranium and Jasmine. Different routes of administration were used such as oral intake, topical application, inhalation and aromatherapy massage.

Conclusion

Essential oils are effective in relieving specific brain malignancy-related symptoms (such as headaches, vomiting/nausea, depression and anxiety). A patient information leaflet created from the information gathered during the study presents an essential oils guide for easy reference of treatment of symptoms in patients with brain malignancies.

Keywords

Essential oils, brain malignancy, cancer, headaches, vomiting/nausea, depression, anxiety, symptoms.

OPSOMMING

Agtergrond

Die insidensie van brein maligneiteite wêreldwyd is aan die toeneem. Die tradisionele behandelingsopsies vir breinmaligneiteite, soos sjirurgie, bestraling en chemoterapie ontketen almal hulle eie nuwe-effekte wat die pasiënt belas met simptome bykomend tot dié van die reeds-bestaande simptome van die breinmaligniteit. Essensiële olies is bewys om te help verligting bring van simptome. Tog is daar geen opsomming van die beskikbare navorsing rakende die behandeling van simptome verwant aan 'n breinmaligniteit met essentiële olies nie.

Doel

Die hoofdoel van hierdie studie was om 'n opsomming te skep wat handel oor beskikbare navorsing aangaande die gebruik van essentiële olies om simptome (soos hoofpyne, epileptiese aanvalle, verhoogde intrakraniale druk, naarheid/braking, depressie en angstigheid) verwant aan breinmaligniteit te help verlig, asook om 'n inligtingsvoubiljet vir pasiënte saam te stel uit die bevindinge van die studie.

Metode

'n Sistematiese oorsig is onderneem en die volgende databasisse is geraadpleeg: Medline, eJournal, CAB Abstracts, Health source, Academic Search Premier, CINAHL, Pubmed, Cochrane, Web of Science, Scopus, ScienceDirect, SAEpublications, AHFS Consumer Medication information, SocINDEX en Masterfile. Toepaslike literatuur is op grond van 'n voorafbepaalde soekstrategie geïdentifiseer. Die bronnelyste van die sekondêre bronne is deursoek om die primêre studies te vind en in te sluit. Die kriteria vir die insluit of uitsluiting van al die bronne is vooraf bepaal en elke bron is geëvalueer op grond van die gevalideerde kritiese evalueringinstrumente.

Resultate

'n Totaal van 24 studies is in die finale verslag ingesluit. Die bevinding was dat essentiële olies effektief is die verligting vir simptome van hoofpyne, naarheid/braking, depressie en angstigheid soos verwant aan breinmaligneiteite. Geen resultate is gevind vir simptomebehandeling van epileptiese aanvalle of verhoogde intrakraniale druk nie.

Die essensiële olies wat gehelp het vir die verligting van die bogenoemde simptome is Laventel, Basieliekruid, Kruisement, Peperment, Bergamot, Romeinse Kamille, Sandelhout, Wierook, Nardus, Roos, Jenewer, Malva en Jasmyn. Verskillende toedieningsroetes is gebruik; soos orale inname, topikale aanwending, inhalasie en aromaterapeutiese masserings.

Gevolgtrekking

Essensiële olies is effektief om simptome (soos hoofpyne, naarheid/braking, depressie en angstigheid) verwant aan breinmaligniteite te verlig. 'n Inligtingsvoubiljet vir pasiënte is saamgestel as riglyn vir die behandeling van simptome in pasiënte met breinmaligniteite.

Sleutelwoorde

Essensiële olies, breinmaligniteite, kanker, hoofpyne, naarheid/braking, depressie, angstigheid, simptome.

LIST OF ABBREVIATIONS

BPI-K	The Korean version of Brief Pain Inventory
CANSA	Cancer Association of South Africa
CASP	Critical Appraisal Skills Programme
CES-D	Center for Epidemiological Studies Depression
CRD	Centre for reviews and dissemination
EORTC	European Organisation for Research and Treatment of Cancer
Eppi	Evidence for Policy and Practice Information-reviewer
HADS	Hospital Anxiety and Depression Scale
HREC	Health Research Ethics Committee
ICP	Intracranial pressure
INSINQ	Quality in Nursing and Midwifery
JB	The Joanna Briggs Institute
MYMOP	Measure Yourself Medical Outcome Profile
NCI	National Cancer Institute
PICO	Patient, Intervention, Comparison and Outcome
POMS	Profile of Mood States
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International prospective register of Systematic Reviews
RN	Registered Nurse
RSCL	Rotterdam Symptom Checklist
SA	South Africa
SAI	State Anxiety Inventor
SCID	Structured Clinical Interview
SPHERE	Somatic and Psychological Health Report
SR	Systematic review
TAI	Trait Anxiety Inventory
VAS	Visual Analogue Scale
VSH	Verran and Snyder-Halpern
WHO	World Health Organization

CHAPTER 1 STUDY OVERVIEW

1.1 Introduction and background

One in every two people will develop a **malignancy** once or more in their lifetimes (Ahmad *et al.*, 2015:943). In 2012 an estimated 14 million people were newly-diagnosed with cancer for the first time, while eight million people died of cancer (Forman & Ferlay, 2014:16). An estimated 60% of cancer sufferers reside in Africa, Asia, Central America and South America with 70% of reported cancer deaths ascribed to these countries (Forman & Ferlay, 2014:16). For South Africa the numbers were just as alarming in 2012 with an estimated 82 900 people being newly-diagnosed with cancer and 51 000 people dying of cancer in 2012 (American Cancer Society, 2015:3). The Cancer Association of South Africa (CANSA) further explains that according to statistics of 2012 the risk for South Africans to develop cancer in their lifetime was one in every eight for women and one in every seven for males (CANSA , 2012).

Although advances in the treatment of malignancies have been prevalent in recent years, cancer remains one of the most dreaded diagnoses (Ahmad *et al.*, 2015:943). A malignancy could be caused by a number of factors, such as lifestyle or behavioural factors, occupational factors, diseases, or the physical environment. (Danaei *et al.*, 2005:1785, 1791). The estimated 21.7 million forecast cases of cancer in the world for 2030 might even be an underestimation, according to the American Cancer Society (2015:1), because more people are adopting the western lifestyle which approves the use of tobacco, improper diets, a decline in physical activities, and giving birth to fewer children, which all raises one's chances of developing cancer.

In this study the focus will be on **brain malignancies**. Brain malignancies are invasive masses of cells in the skull of a person (Mosby's Dictionary of medicine, nursing and health professions, 2006:250). There are many types of brain malignancies of which many are already at a World Health Organisation (WHO) stage rating of stage three or four on diagnosis (Figaji, 2015). Stage four is the last stage before a person receives a terminal diagnosis (Kleihues *et al.*, 2014:514-518). Brain malignancies cause a significant number of deaths annually, and in adults 20-40% of cancers from other parts of the body will metastasise to the brain at some stage (Schmieder *et al.*, 2016:415). In children, brain cancer is the second most prevalent cancer found in South Africa (SA) (Figaji, 2015). Brain malignancies and central nervous system malignancies are

categorised together in the statistics of the Cancer Association of South Africa (CANSA, 2012). This is important to note as no definite number regarding brain malignancies are available in South Africa and thus the increase or decrease in incidence of brain malignancies cannot be properly traced.

The pressure maintained inside the skull is called **Intracranial pressure (ICP)** (Rodríguez-Boto *et al.*, 2015:18). The Intracranial pressure is determined by the relationship between the brain, cerebral spinal fluid and also the cerebral blood (Rodríguez-Boto *et al.*, 2015:18). Symptoms of brain malignancies are usually caused by the increase of pressure in the skull and include headaches, vomiting/nausea, tiredness, papilledema (swelling of the optic disk of the eye), and behavioural changes (Mosby's medical dictionary of medicine, nursing and health professions, 2006:250; The Merck manual, 2011:622). The specific signs and symptoms depend largely on where the brain malignancy is located inside the skull (Kleihues *et al.*, 2014:514). According to Kleihues *et al.* (2014:514) brain tumours can cause an increase in pressure in the skull that could lead to the loss of consciousness and respiratory arrest, resulting in death.

One of the main problems with brain malignancies is that, as soon as the fontanelles in the skull have closed, there is no way for expansion if the volume of the contents in the skull would suddenly increase (Rodríguez-Boto *et al.*, 2015:17). According to the **Monro-Kellie doctrine** the inside of the skull is divided into three compartments which have to stay in equilibrium and if one of the three constituents develops pathology the other two constituents will also be influenced (Rodríguez-Boto *et al.*, 2015:18). If sudden pressure arises in the skull homeostasis is maintained through the movement of the cerebrospinal fluid, but this leads to a decrease in the cerebral blood flow (which also then leads to a reduction in the perfusion of the brain) and later, in chronic situations, the body will lose some neurons and glial cells and will be unable to keep on compensating effectively (Rodríguez-Boto *et al.*, 2015:17). Thus, when a malignancy develops in the skull this would then lead to the decrease in space for the other compartments and a negative effect on their functioning (Rodríguez-Boto *et al.*, 2015:18). The meninges are stretched due to a brain malignancy and the malignancy could also cause an increase in intracellular pressure (Greenman & Stern, 2009:627).

The effect of a malignancy inside a person's skull can also cause **herniation**, which is when segments of the brain are pushed out of their original places and pressed into a different space (Partington & Farmery, 2014:190). Herniation can be fatal if the part of

the brain presses on another important part such as the respiratory centre in the brain stem (Partington & Farmery, 2014:190).

Apart from brain **malignancy-related symptoms** being influenced by the location thereof and the increased Intracranial pressure (Greenman & Stern, 2009:627) the age of the person can also influence the symptoms (Wilne & Waller, 2014:121). Furthermore the growing of the brain malignancy, oedema associated with it (Longo & Slater, 2014:9), the effect of the mass on the brain, or the effect of hormones being secreted (Tagoe *et al.*, 2015:181) will usually add to the signs and symptoms in the patient.

Krüger and Engelbrecht (2013:480) categorise brain malignancy-related symptoms as physical, emotional or neuro-cognitive. Further categorisation will be used in the following section to allow for a better understanding of the signs and symptoms seen in people with a brain malignancy. In the physical category there will be looked at the gastro-intestinal system, and general signs and symptoms. For the emotional category there will be looked at the psychological signs and symptoms and under the neuro-cognitive category the neurological and hormonal signs and symptoms will be explored, lastly treatment related signs and symptoms will be discussed.

One example of **physical symptoms** is headache. Headaches could be due to raised Intracranial pressure, the mere presence of the malignancy, hydrocephalus or progression of the malignancy (Raphael *et al.*, 2010:756-757). The brain malignancy could also start to bleed which would lead to a sudden increase in the intracellular pressure, extreme headaches and sudden changes in vision (Greenman & Stern, 2009:627). On the psychological side of a headache it can also be caused by depression and anxiety (Raphael *et al.*, 2010:757). Due to the wide array of factors leading to headaches childhood brain malignancies are difficult to diagnose as the symptoms of a brain malignancy usually are attributed to a less serious viral condition commonly found in children which then delays diagnosis (Paul *et al.*, 2014:32). To reduce the delay in diagnosis, a programme called HeadSmart have listed numerous signs and symptoms as signs of brain malignancies in babies, children and teenagers (HeadSmart, 2017).

In the category of physical signs and symptoms, gastro-intestinal symptoms in children and adults include vomiting (HeadSmart, 2017; Tagoe *et al.*, 2015:183; Wilne & Waller 2014:123) and nausea (Jones, 2012:14; Tagoe *et al.*, 2015:183). This could be due to

raised Intracranial pressure in the skull (James & Varelas, 2011:412; Lv *et al.*, 2015:1203; Paul *et al.*, 2014:32-33) or side-effects from treatment such as chemotherapy and radiation (Jones, 2012:16). Eating problems due to raised Intracranial pressure could also arise in people with brain malignancies (Paul *et al.*, 2014:32-33). According to Mahalakshmi and Vanisree (2015:583) constipation and diarrhoea are signs and symptoms not often seen as the presenting signs and symptoms of a brain malignancy. When the brain malignancy causes pressure on the brainstem the person can experience difficulty in swallowing (Wilne & Waller, 2014:122).

To conclude the physical category, general signs and symptoms will be explored. Specific to children under the age of two years, a growing head circumference could be an indication of a brain malignancy (HeadSmart, 2017; Wilne & Waller, 2014:123). Tagoe *et al.* (2015:183) found the following general symptoms in patients presenting with brain tumours from children to adults: swelling in the neck and retraction of the eyelids. Signs and symptoms specifically caused by raised Intracranial pressure on the other hand are listed as: a bulging anterior fontanel in babies, babies crying with a high pitch, Cushing's triad (observed in acutely ill patients as an abnormal respiration rate, slow heartbeat, and high blood pressure), and pains in different parts of the body (Paul *et al.*, 2014:32-33).

Pain experienced by a person can be caused by the malignancy, the treatment, weakness in a part of the body, or other comorbidities (Raphael *et al.*, 2010:743). Managing of pain for a patient with a malignancy is usually very difficult and might require more than just pharmacological therapies, even more so when it is a brain malignancy causing pressure or infiltrating the brain meninges, nerves, the spinal cord or other parts in the skull (Raphael *et al.*, 2010:744). Another important symptom experienced by people with a brain malignancy is fatigue. According to Tse and Babu (2011:81) fatigue is one of the most common symptoms for people experiencing recurrence of their glioblastoma multiforme malignancy. The exact pathophysiology of fatigue related to malignancies has not been established completely (Wang, 2008:11). However according to Wang (2008:12) various factors have been identified which could lead to fatigue, such as the treatment received by a patient, malnutrition, infections or failure or dysfunction of organs. A malignancy could also cause abnormalities in the body's energy metabolism which leads to cachexia (an unexplained decrease in muscle

and body mass), and this in turn also leads to further fatigue (Wang, 2008:12). Psychosocial factors such as depression, anxiety, stress and struggling to cope with the diagnosis could also further lead to fatigue (Wang, 2008:12).

Under the category of emotional factors the **psychological signs and symptoms** will be discussed. Emotional and psychological signs and symptoms seen in patients are stress, anxiety, anger outbursts, blame, fear, social isolation, resentment (Longo & Slater, 2014:9), tiredness, depression, and anxiety (Krüger & Engelbrecht, 2013:480). Wang (2008:13) states that depression could be due to fatigue or also due to the changes in inflammatory pathways seen in patients with brain malignancies. According to Jones (2012:14) people with brain malignancies can experience shock, anxiety and stress along the course of their life after diagnosis. Psychological signs and symptoms of raised Intracranial pressure are further listed as irritability and sluggishness (Paul *et al.*, 2014:32-33).

Psychological factors attributed to the chronic pain experience are fear, depression, anxiety and not enough sleep (Raphael *et al.*, 2010:752). Conversely, pain experienced with a malignancy can worsen when a person becomes psychologically distressed (Raphael *et al.*, 2010:743). This can be worsened by side-effects of certain treatment regimes, which also lead to emotional distress or depression in a person (Raphael *et al.*, 2010:752,759).

Lastly, the **neurological and hormonal signs and symptoms** will be discussed, categorized as neuro-cognitive signs and symptoms. First a look will be taken at the neurological signs and symptoms. HeadSmart (2017) listed headaches, problems with walking or balance, abnormal eye movements, distorted vision, changes in behaviour, fits or seizures and abnormal tilting of the head as signs and symptoms seen in children. Wilne and Waller (2014:123) agree with these signs and symptoms of HeadSmart and add that the fits or seizures are without the presence of a fever. Signs and symptoms are the following for all ages: paralysis or a decrease in sensory abilities of one side of the body (Longo & Slater, 2014:9; Saria *et al.*, 2015:476; Tagoe *et al.*, 2015:183), changes in a person's mood and character (Longo & Slater, 2014:9; Tagoe *et al.*, 2015:183), stroke (Longo & Slater, 2014:9) seizures (Jones, 2012:14; Longo & Slater, 2014:9; Tagoe *et al.*, 2015:183), olfactory abnormalities (Jones, 2012:14) or a loss of the sense of smell (Tagoe *et al.*, 2015:183), headaches (Krüger & Engelbrecht, 2013:480; Longo & Slater, 2014:9; Saria, *et al.*, 2015:476; Tagoe *et al.*, 2015:183),

problems remembering (Krüger & Engelbrecht, 2013:480; Longo & Slater, 2014:9; Tagoe *et al.*, 2015:183), attention span challenges, uncertainty, a difficulty to communicate (Krüger & Engelbrecht, 2013:480), and numerous eye and sight problems, constant buzzing in the ears, and loss of motor functioning (Tagoe *et al.*, 2015:183). Arber *et al.* (2010:24-25) describe another cognitive symptom as struggling to make decisions and elaborates on hemiparesis (paralysis of one side of the body) as this further leads to an increase fall-risk and reduced mobility.

Seizures in persons with a brain malignancy are quite common and the seizures could be one of the symptoms before / leading to diagnosis of the brain malignancy or develop later (Schaller & Rüegg, 2003:1223-1224; Shamji *et al.*, 2009:275-276). According to Shamji *et al.* (2009:276) slow-growing tumours cause seizures more commonly. The epileptic attacks could be due to the progression or even shrinking of the brain malignancy (Schaller & Rüegg, 2003:1223-1224). Causes of the epileptic attacks could be due to pathophysiological aspects including abnormal movement of neurons, changes in synaptic vesicles, loss of neurons, abnormal synaptic activity due to the secretions of the brain malignancies such as calcium, the brain malignancy can over-activate specific receptors, alterations in the pH levels of the head, changes caused in the brain by bleeding from the brain malignancy, changes in amino acids, and changes in the communication between cells (Schaller & Rüegg, 2003:1224-1227). The treatment of these attacks with standard anti-epileptic medication is not always successful due to different causative pathophysiologies or malignancy sites (James & Varelas, 2011:412; Schaller & Rüegg, 2003:1223-1224). Furthermore controlling seizures can be difficult due to the effect of the seizure medication on the other treatment such as chemotherapy and surgery received by the patient and also the side-effects of the seizure medication (James & Varelas, 2011:411).

Now the **hormonal signs and symptoms** will be discussed. The following symptoms in patients presenting with brain tumours from children to adults were listed: abnormal menstruation, milky discharge from nipples not related to breastfeeding, hoarse voice (Tagoe *et al.*, 2015:183) and puberty problems (HeadSmart, 2017; Wilne and Waller 2014:123). In the case of a malignancy on the pituitary gland that suddenly starts to bleed it could lead to sudden hypopituitarism (Greenman & Stern, 2009:627). When the brain malignancy causes pressure on the pituitary gland and this leads to hypopituitarism the following symptoms can be seen: abnormal physical weakness, impotence, a

decrease in the person's libido and also changes in a woman's menstruation cycle (Greenman & Stern, 2009:627). The hypopituitarism is usually caused by the brain malignancy putting pressure on the vessels and the infundibulum (connecting the hypothalamus and the pituitary gland) which causes a blockage in the flow of the hormones travelling from the hypothalamus to the pituitary gland (Greenman & Stern, 2009:627).

Under **treatment-related signs and symptoms** we will explore side-effects of chemotherapy, radiation, surgery and also Corticosteroids. Another treatment with side-effects to keep in mind is that of pharmacological treatments for pain, such as constipation (Raphael *et al.*, 2010:743). James and Varelas (2011:411), Jones (2012:16), and Khalili (2007:5) state that a patient can experience signs and symptoms from the treatment which the patient would also have to endure in combination with the other symptoms of the brain malignancy itself. These signs and symptoms could be seen as follows: deep vein thrombosis, confusion, fits and loss of independence (Khalili, 2007:5). Further pharmacological side-effects found by Mahalakshmi and Vanisree (2015:583) are less common and include hair loss and skin itching.

There are a few common procedures followed as a first-line treatment plan, such as surgery, chemotherapy and radiation (Alberts, 2012:61-64), and corticosteroids are commonly used to assist in treating brain malignancy-related symptoms (Lin *et al.*, 2016:94). Mosby's medical dictionary of medicine, nursing and health professions (2006:250) agrees that surgery is seen as one of the first treatment options for patients with brain-malignancies.

Surgery usually has side-effects, some of which can last for a number of years. According to Visser (2006:74) an example of a common but under-stated long-term side-effect is chronic post-surgical pain. This pain is a condition in which a person's amount of pain post-surgery does not correlate with the type of surgery he/she had. It is affected by the extent of tissue and nerve damage incurred during the surgery. This then leaves the patient in pain for years after the surgery - even long after the surgical wounds and disease treated by surgery have healed (Visser, 2006:74). Furthermore, the study of Visser (2006:74) also provides significant findings regarding complications that patients have had to deal with after their surgery; of which 11% to 24% of patients indicated major complications. Another side-effect from surgery which also has a

psychological impact is the scar left by any operations and weakness of the body (or parts of the body) (Jones, 2012:16).

Patients receiving chemotherapy or radiation usually experience side-effects in accordance with the location of their tumour where the treatment is concentrated. Common side-effects include diarrhoea, vomiting, pain, swelling, taste disturbances, eating problems (Pedersen *et al.*, 2013:715), decreased fertility and immunity, hair loss, tiredness, short-term memory loss, nausea and vomiting (Jones, 2012:16).. Other side-effects of radiotherapy are tiredness, skin reactions such as dry and flaky skin as well as itchiness, and loss of appetite (Alberts, 2012:78). For chemotherapy side-effects can furthermore include mouth and throat problems such as blisters and painful areas, increased risk of infections, anaemia, muscle pain, changes in the colour of the person's urine, swelling of body parts, and flu-like symptoms (Alberts, 2012:94-98). According to Alberts (2012:93) the side-effects experienced by patients vary greatly and can start within a few hours after the treatment starts and last for even some time after a patient has completed the treatment course until the body has regained its health.

Corticosteroids such as Dexamethasone are used to help relieve the brain oedema caused by the brain malignancy (Lin *et al.*, 2016:94) and thus lower the raised Intracranial pressure (Raphael *et al.*, 2010:757) but this medication can also cause side-effects in the person (Khalili, 2007:5; McNamara, 2012:43-45). According to McNamara, (2012:43-45) the side-effects listed for corticosteroid usage differ from the brain-malignancy related symptoms already mentioned and include stomach problems, hyperglycaemia, a weakened immune system, sleeplessness, fluid retention, high blood pressure, and changes in the person's body image. Khalili (2007:5,8) adds weakness of the legs as another of these symptoms.

To summarize the above-mentioned, brain malignancies can cause signs and symptoms in the physical, emotional or neuro-cognitive areas of the patient (Krüger & Engelbrecht, 2013:480). These signs and symptoms of brain malignancies are usually caused by the following:

- Increase in the size of the brain malignancy and the pressure thereof on the surrounding area of the brain (Greenman & Stern, 2009:626; Longo & Slater, 2014:9; Tagoe, *et al.*, 2015:181);

- Oedema or raised Intracranial pressure or obstruction of the flow of the intracranial fluid (Longo & Slater, 2014:9; Tagoe *et al.*, 2015:181; Wilne & Waller, 2014:122);
- Abnormal secretions of hormones caused by the presence of the brain malignancy in the skull and then the hormones cause certain symptoms in the body of the person (Greenman & Stern, 2009:625; Tagoe *et al.*, 2015:181);
- The brain malignancy could move into certain parts of the brain such as the brain stem which would then influence the respiratory and cardiovascular system leading to specific symptoms (Paul *et al.*, 2014:33); and
- The treatment received by the person with the brain malignancy such as chemotherapy, radiotherapy, surgery or corticosteroid usage (Jones, 2012:16; Khalili, 2007:5,8; Lin *et al.*, 2016:94; McNamara, 2012:43-45; Saria *et al.*, 2015:476).

Recently, patients started to shy away from treatments such as surgery and chemotherapy as first-line medical treatment due to the side-effects of these treatments sometimes being worse than the disease itself according to the patients. They then tend to search for **alternative treatment options**. These treatments often have their origin in the earliest philosophies and religious practices (Cross & Berry, 2010:7). Alternative treatment options can be divided into the following categories as presented by Alberts (2012:300-320). Examples of each category are provided:

- Psychological, spiritual and bodily therapies such as art therapy, aromatherapy (essential oils), dance therapy;
- Physical touch therapies are such as acupuncture, chiropractic treatments, hydrotherapy, hyperbaric oxygen therapy;
- Herbs, vitamins and mineral therapies consumed by patients for example aloe vera, arnica root, calcium, camomile, chlorella, cloves, ginger, liquorice root, milk thistle, turmeric;
- Diet and eating programmes consist of the intake of probiotics, broccoli, mushrooms, garlic and other food for treatment regimens. Also following certain eating programmes such as Gerson therapy, grape diet, juicing, macrobiotic diet, Gonzales treatment, Kelley's treatment; and
- Pharmacological and biological therapies are for example antineoplaston therapy, cell therapy, chelation therapy, enzyme therapy, hydrazine sulphate, insulin potentiation therapy and urotherapy.

Essential oils are part of the category of psychological, spiritual and bodily therapies and could even be incorporated into physical touch therapies where aromatherapy massage is used. Aromatherapy is when essential oils are administered for medicinal purposes (Mosby's dictionary of medicine, nursing and health professions, 2006:138). Besides the side-effects of the treatments, another difficulty in treating patients with brain-malignancies involves the blood-brain barrier. Not all treatment methods such as medication can cross the blood-brain barrier to reach the brain malignancy, which makes the treatment options more limited (The Merck manual, 2011:3177). Yet essential oils have the ability to cross the blood-brain barrier (Rogers, 2015:31; Stewart, 2012:26-27). This makes essential oils even more advisable for the relief of brain malignancy-related symptoms.

Essential oils are extracts from plants with the essence of the plant still in it. This essence is seen as the life of the plants (Stewart, 2012:xv-xvi). Essential oils are extracted from the plants through hydrodiffusion, steam distillation or pressure (Manion & Widder, 2017:154). Essential oils can be considered part of psychological, spiritual and bodily therapies when it is used as aromatherapy, but could also fall under physical touch therapies if used in massage therapy, or herbs, vitamins and mineral therapies if it is taken orally by the patient. The essential oils can be administered through a massage, applied to the skin of the patient, put into a bath, be given to the patient to inhale, a douche, or in the form of a hot or cold compress. It is usually applied to help the patient to relax and calm down but also for relief of pain and to promote a patient's comfort (Mosby's medical dictionary of medicine, nursing and health professions, 2006:138). According to Halm (2008:160), when essential oils are applied topically it can be in the patient's blood stream within 10-30 minutes after application. It is important for the medical profession to take note of alternative treatment options as it was found by Bega (2017:305) that patients with chronic neurological conditions are searching for alternative treatment options more and more. On the other hand nurses often have to deal with the symptoms of their patients and to educate their patients on the treatment options of medication or alternative treatments (Johnson *et al.*, 2016:164).

Aromatherapy using essential oils can be used to calm a patient and has a good effect on stress, depression and pain (Alberts, 2012:300). According to Dyer *et al.* (2014:203) aroma sticks (inhaler sticks with added essential oils), have been used with great success for nausea. Sixty-eight per cent of users reported relief of their nausea in one

survey and in another survey 81% of users reported that the use of an aroma stick did also help to alleviate their specific symptoms. Aroma sticks relieved symptoms for 80% of people using it for anxiety, 82% of people using it for nausea, and 71% of people using it for sleep disorders (Dyer *et al.*, 2014:2013; Stringer & Donald, 2011:118). Halm, (2008:161) also states that essential oils helped to improve symptoms of anxiety, stress, restlessness, and pain management. Peppermint, spearmint, cardamom, ginger and tarragon essential oils have also been used successfully to help people improve nausea after surgery (Dyer *et al.*, 2014:203-204). Anxiety has been reduced in several people inhaling lavender, calendula, and/or orange essential oil (Dyer *et al.*, 2014:204). For depression citrus fragrances have been used to help improve the condition of the patient (Dyer *et al.*, 2014:204).

According to Halm, (2008:163) aromatherapy is seen as part of holistic care in nursing in the United States and nurses use it mainly for symptom relief in patients suffering from pain, sleeplessness and for relaxation and comfort, improving anxiety and the overall well-being of a patient. The essential oils do not necessarily only work to relieve the specific symptom but patients have reported that using the aromas have increased their overall wellbeing and that the essential oils used for one symptom sometimes also alleviates other problems (Stringer & Donald, 2011:118-119). Thus, essential oils could be applied to treat symptoms associated with brain malignancies such as vomiting/nausea, headaches/migraines, increased Intracranial pressure, depression, anxiety and seizures.

Just as with conventional cancer treatment, **side-effects** can also occur with the use of plants and plant extracts, also due to interactions of the plants and plant extracts with conventional drugs (Arslan *et al.*, 2013:1468). The most common side-effects of essential oils are usually allergic reactions while other effects are phototoxicity, necrosis, sedative effects, kidney or liver damage and the promotion of cancer. These effects are usually caused by the misuse of essential oils which would have otherwise been without any side-effects (Schilcher, 1985:217). A lack of knowledge contributes to a patient's incorrect use of plants and plant extracts as alternative malignancy therapy and can contribute to the occurrence of side-effects experienced by the patient. This can be seen in an example of Andersen *et al.* (2012:116-117) who noted that side-effects such as an increased risk of bleeding with or after surgery for women with ovarian malignancy were experienced after taking herbal supplements. These women

used the herbal supplements as alternative malignancy treatments without knowing the increased risk for bleeding caused by the herbs in the supplement. Side-effects can furthermore occur due to the wrong dosage of a certain plant as treatment being used (Duke, 2008:xi). These side-effects are either unknown to the patient or poorly defined, proving the need for knowledge dissemination and further research in this regard. This necessitates medical personnel and especially nursing professionals who give patient education to have knowledge with regards to the usage of essential oils to promote the safety of the patient.

Thus this study will aim to provide a summary of the best available evidence regarding the use of essential oils to relieve specific brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety) and to design a patient information leaflet with the findings of the study. This summary of information could help a patient to make more informed decisions.

1.2 Problem statement

The use of alternative therapies such as essential oils as cancer-related symptom treatment is on the increase (Duke, 2008:ix). Although research regarding the efficacy of essential oils in relieving brain malignancy-related symptoms exists, no summary of the best evidence is available regarding the use of essential oils in the treatment of brain malignancy-related symptoms. Dyer *et al.* (2014:203), Halm (2008:161) and Stringer and Donald (2011:118) defend the efficacy of essential oils in relieving brain malignancy-related symptoms, while Andersen *et al.* (2012:116-117) and Arslan *et al.* (2013:1468) caution that incorrect usage of essential oils could lead to negative patient outcomes.

The need for alternative therapies in symptoms-relief in brain malignancies is evident as malignancy statistics estimate that currently half of the population will have a malignancy during their lifespan (Ahmad *et al.*, 2015:943) and 20-40% of cancers will metastasise to the brain (Schmieder *et al.*, 2016:415). Symptoms of brain malignancies, such as headaches, vomiting/nausea, tiredness, papilledema and behavioural changes could be debilitating and often traditional treatment options do not relieve these symptoms adequately, or even present added side-effects for the patient to suffer (Alberts, 2012:61-64). The American Cancer Society (2015:3) and Forman and Ferlay (2014:16) support the alarming statistics of cancer incidence, while Kleihues *et al.*

(2014:514) confirm the severity of related symptoms. Furthermore, Pedersen *et al.* (2013:715) and Visser (2006:74) endorse the notion of traditional treatments causing serious side-effects.

Literature presents a sound base for the advocacy of essential oil usage to relieve brain malignancy-related symptoms (Alberts, 2012:300; Andersen *et al.*, 2012:116-117; Dyer *et al.*, 2014:203-204; Halm, 2008:161 & Stringer & Donald, 2011:118), yet studies done on the subject are diverse and often focussed on either only one essential oil, or limited symptoms that respond to the treatment. For this reason, a synthesis of the best-practice usage of essential oils in the treatment of brain malignancy-related symptoms is required.

1.3 Research question

The abovementioned problem statement led to this research question: What is the best available evidence regarding the use of essential oils in the relief of specific brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety)?

1.4 Aim and objectives

The main aim of this study was to provide a summary of the best available evidence regarding the use of essential oils to relieve specific brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety). In order to attain this aim, the following objectives were set:

- To review the evidence regarding which essential oils can be used and the route of administration of these oils to relief specific brain malignancy-related symptoms such as headaches, seizures, increased Intracranial pressure, vomiting / nausea, depression and anxiety.
- To design a patient information leaflet from the findings of the study.

1.5 Research design

For the outline of this study the systematic review was done in accordance with the PRISMA criteria checklist for all the necessary aspects which have to be included (see Addendum H). A systematic review design will be used to answer the research question, as a systematic review aims to include applicable academic literature of good

quality and to combine the findings hereafter. A systematic review is helpful in formulating conclusions on large numbers of academic literature answering the same questions. Systematic reviews can help in showing the best evidence-based practices (Brink *et al.*, 2012:114). However, as prerequisites, Hemingway and Brereton (2009:1) describe the following components as important for a good-quality systematic review:

- In a systematic review the goal is to search for as much as possible academic literature applicable to the study;
- Academic literature is sifted and only the applicable literature included;
- Each academic literature document is evaluated regarding its quality;
- The findings are combined while trying to keep bias at a minimum; and
- In the end a summary of the findings is made and any errors in the literature is kept in mind as well.

With the above-mentioned in mind, a systematic review for this study is the most appropriate design. This study seeks to find answers regarding the possibility of using essential oils for relief of specific brain malignancy-related symptoms. To accomplish this, academic literature will have to be sifted through to decide which will be included and which not with regards to the academic literature leading to answers to the research question. At the end the findings will be combined to lead to a summary and an answer for the research question. A systematic review design was able to accomplish all of these requirements and thus was chosen.

1.6 Theoretical framework

The research cycle in patient safety as presented by Bates (2013:2) and depicted in Figure 1.1 will be applied as a theoretical basis for this study.

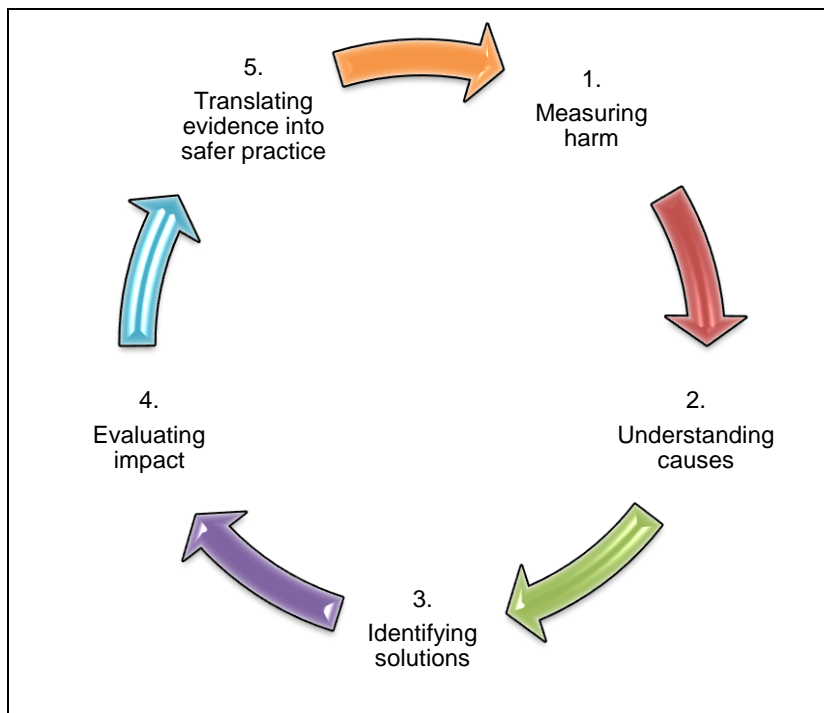


Figure 1.1: The research cycle in patient safety (Bates, 2013:2)

The first phase in this cycle includes measuring harm. In the context of this study, harm refers to the effect of malignancy on the patient. Therefore, the symptoms of brain malignancies were thoroughly investigated through the literature review.

The second phase in this cycle, namely understanding causes, addresses both causes of malignancies and causes of the symptoms caused by the malignancies. These causes were previously described in that the malignancy itself and different treatments were seen as causing brain malignancy-related symptoms.

Phase 3 states the identifying of solutions which consists of the identification of alternative solutions consisting of essential oils for the relief of brain malignancy-related specific symptoms. This phase will be the main focus within this study. A search was done to gather information regarding essential oils which have been effectively used to relieve specific brain malignancy-related symptoms and the findings will be summarized in a patient-information leaflet.

Phase 4 (evaluating impact) builds on the previous phase of the research cycle, as the impact of the usage of essential oils as treatment option for specific brain malignancy-related symptoms were broadly explored and described in this study. As the focus of this study was to determine the essential oils that have been effectively used to relieve

specific brain malignancy-related symptoms. The side effects found in the studies used was included in the information leaflet.

Lastly, phase 5 (translating evidence into safer practice) is addressed by this study in that it will lead to results showing evidence of the usage of essential oils to treat specific brain malignancy-related symptoms. This will lead to safer practice in the usage of essential oils as treatment option for specific brain malignancy-related symptoms. The translation of evidence was addressed in the formulation of an information leaflet regarding the use of essential oils in the treatment of these symptoms.

1.6.1 Concept clarification

Chemotherapy – the usage of medicinal compounds to treat malignancies which kills malignant cells (Alberts, 2012:82).

Complementary and alternative treatments – are treatments which are not acknowledged as conservative treatments (Karal *et al.*, 2012:335). In this study, the use of essential oils treatment option for brain malignancy-related symptoms is seen as a complementary and alternative treatment.

Depression – a mood disturbance where the person experiences extreme sadness, worthlessness, hopelessness and more feelings of despair. There are a number of causes usually such as a certain illness or trauma (Mosby's dictionary of medicine, nursing and health professions, 2006:537).

Essential oils – in this study essential oils includes concentrated extracted oils from plants with the fundamental nature of the plant still in it. Essential oils are used for flavouring of food, body sprays, and medicines (Mosby's dictionary of medicine, nursing and health professions, 2006:678).

Malignancy/tumour - normal cells in the body turning to abnormal behaviour by dividing uncontrollably and thus causing organ and tissue damage (National Cancer Institute (NCI), 2015).

Radiation – is the therapeutic usage of x-rays to cause death of malignant cells and thus treat the malignancy location specifically (Alberts, 2012:66).

1.7 Meta-theoretical assumptions

1.7.1 View of the world

God created the world and all that is on it. Everything was placed under the stewardship of man at the beginning of time. When the Garden of Eden was created plants especially played a big role in the survival of the current population living there (Genesis 2:15-16). To this day people are using plants and plant extracts to sustain their bodily functions and also to focus on promoting health (Duke, 2008:2). The world in this study will include the environment wherein plants and plant extracts are used for people's physical well-being. In this world, pharmaceutical products are often seen as primary treatment while plants and plant extracts take second place, whereas in earlier times plants and plant extracts were the first line of defence as medication (Duke, 2008:2-4). Thus this presupposes an environment in which knowledge is needed to use plants and plant extracts safely and effectively alone or in combination with pharmaceutical products.

1.7.2 View of man

Man is seen as a person consisting of mind, body and soul (Cross & *Berry*, 2010:7). Man's intellect and will to live play a big part in his or her use of plant extracts as a treatment option and is thus considered an important aspect. Knowledge is seen as power and a lack of knowledge as a danger to man's existence. Thus man needs to empower himself with knowledge to promote his intellect and through doing this he is showing a will to live (Alberts, 2012:V). Man will be mostly referred to as patients and medical personnel.

1.7.3 View of health

Health is seen as the golden thread keeping man functioning. Without health or well-being in any of the areas described of man's being, man cannot function optimally. The World Health Organization summarises this in their statement of " ... health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1948:100). Health influences every area of man and of man's world around him.

1.7.4 View of nursing

Nursing is seen as an art. It is the art of doing medical interventions but without compromising humanity in any way and to promote the empowering of the patient to promote his or her own health (Michalis, 2004). Nursing has to focus on the person as a whole and not leave out any part. Also, important components of nursing are seen as to do no harm and provide accurate and relevant information to patients in advocating for their health.

1.8 Research method

The research method is now presented. This includes the protocol and registration of the review, eligibility criteria related to articles considered for inclusion, the search strategy utilized, study selection, an overview of the data collection process, data items extracted from the literature, measures used in the synthesis of results, and additional analysis performed on included literature.

1.8.1 Protocol and registration

The review protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) database in order to ensure that the review would not duplicate a study already undertaken (registration number CRD42018080791). This registration with PROSPERO is also necessary for this review to comply with the PRISMA checklist. According to the PRISMA checklist (Addendum H) the systematic review has to be registered and a web address has to be provided if available. The web address for PROSPERO is: <https://www.crd.york.ac.uk/prospero/>.

1.8.2 Eligibility criteria

The review included quantitative, qualitative, non-research and mixed method literature. The included non-research academic literature is book chapters and journal-published literature. The PICO (Patient, Intervention, Comparison intervention and Outcome) acronym was used to formulate the key elements (Botma *et al.*, 2010:241-242):

Population – People with brain malignancies.

Intervention – Use of essential oils for the relief of specific symptoms (such as headaches, seizures, increased intra cranial pressure,

vomiting/nausea, depression and anxiety) associated with brain malignancies.

Comparator – Other modalities used to relieve specific brain-malignancy related symptoms.

Outcome – Relief brought by essential oils for brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting / nausea, depression and anxiety).

PICO leads to the formulation of the following review question: 'In patients with brain malignancy, what is the best available evidence about the ability of essential oils to relieve associated symptoms?'

1.8.3 Search strategy

Specific search words were selected based on the PICO with the help of the subject librarian to ensure that the search results represent all applicable academic literature. The search words were as follow: brain malignancy or brain tumour or brain tumour or brain mass or brain cancer; essential oils or essential oil or aromatherapy; headaches or migraines; vomiting or nausea or emesis; Intracranial pressure or ICP; depression or anxiety; seizures or fits or stroke or epilepsy or seizure activity. All symptoms were searched individually to better the result outcomes. No restriction as to date was used as essential oils have been used for an indefinite time period.

The Evidence for Policy and Practice Information-reviewer (EPPI-reviewer) 4 software for systematic reviews was used to select literature and manage the review process with regards to compiling a list of all the academic literature found by the search and then removal of all the duplicate academic literature. The EPPI-reviewer 4 software can be used for all types of literature reviews and is a web-based programme used for data analysis (EPPI-Centre, 2008:1). More information regarding EPPI-reviewer 4 can be found in Addendum I.

The following data-bases were searched for academic literature and grey literature: Medline, eJournal, CAB abstracts, Health source, Academic search premier, CINAHL, Pubmed, Cochrane, Web of Science, Scopus, ScienceDirect, SAEpublications, AHFS Consumer Medication information, SocINDEX and Masterfile. The reference lists of

academic literature with secondary sources to be included were searched by hand to make sure that all academic literature got the necessary attention to determine their inclusion. All academic literature with secondary information was only used to find the primary sources. Effort was made to find difficult-to-trace academic literature and grey literature as applicable by contacting the researchers directly through e-mail and also using interlibrary loans to acquire the academic literature from other institutions.

Care was taken to include all relevant academic literature using inclusion and exclusion criteria.

The following inclusion criteria were applied:

- Academic literature containing information on essential oils and the above mentioned symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting / nausea, depression and anxiety);
- Academic literature addressing any route of administration of the essential oils;
- Academic literature pertaining to human participants and
- Academic literature or at least its abstracts are available in English.

The exclusion criteria were:

- Academic literature focussing on essential oils tested in vitro or on any other live organisms other than humans,
- Academic literature on essential oils chemical extracts.

All academic literature was sifted according to the above-mentioned criteria (Joanna Briggs Institute [JBI], 2013:24). The academic literature was first examined for the appropriate information in the title and abstracts and if it was still unclear if the academic literature had to be included or excluded, the full text was searched to make a decision. For academic literature in which it was not clear if the criteria were met, the researcher contacted the authors. If potential useful academic literature were published in another language than English with no English abstract available, effort was made to find the academic literature in English.

1.8.4 Study selection

Critical appraisal was done to ensure that only high quality academic literature was included. All academic literature was assessed through the use of the following tools:

The Critical Appraisal Skills Programme (CASP) appraisal tools were used for Randomised Controlled Trials (Addendum C), Systematic Reviews (Addendum D), Cohort Studies (Addendum E), and Qualitative Studies (Addendum F). For mixed-method literature and for other designs that do not have a specific CASP tool, the Johns Hopkins Research Evidence Appraisal Tool (Addendum A) was used, while the Johns Hopkins Non-Research Evidence Appraisal Tool (Addendum B) was used for non-research literature such as book chapters and journal-published academic literature. Scores of 70% or above as attained on these tools allowed for inclusion of academic literature for further analysis. If literature scored below 70% it was excluded. All information regarding the critical appraisal was entered into a table (Please see Chapter 3, table 3.2) and the calculation of the critical appraisal score is documented in Addendum K to indicate that all academic literature received adequate critical appraisal.

1.8.5 Data collection process

The following data-extraction sheet was designed for the process of data collection to help with the organising of all the findings needed to answer the review question. In this spread sheet all findings were summarised under specific headings. All included academic literature information were collected and listed under the following titles in table format.

Table 1.1 Data extraction

Authors and date	Title	Essential oil route, type and indication	Relevant findings

1.8.6 Data items

All included data consisted of the usage of any essential oils used on human participants to relief symptoms of headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety. The route of administration of the oils and the type of essential oils and the effect it had on the participants were noted.

1.8.7 Synthesis of results

Data synthesis is the process of combining and intertwining all the information gained from the included academic literature into a whole (Centre for Reviews and Dissemination [CRD], 2009:45). Thematic analysis and data-synthesis was used. Thematic analysis is a process for analysing qualitative data (Braun & Clarke, 2006:87). According to Thomas and Harden (2008:45) thematic analysis consists of the following three steps: coding of the text, developing explanatory themes and lastly to develop analytical themes. By following this analysis method data specific to essential oils, the symptoms which were relieved by essential oils and the route of administration was noted. Data synthesis was conducted by taking all the relevant data that have been generated and incorporating it into a whole to lead to a conclusion answering the research question (Botma *et al.*, 2010:245).

1.8.8 Additional analysis

After the research question had been answered in the format of a systematic review study, a patient information leaflet was compiled. The leaflet provides information on the essential oils determined to have a positive impact on brain malignancy-related symptoms, specifically the name of the essential oil and the method of administration.

The patient information leaflet is easy to read as some South Africans are illiterate (Joubert & Githinji, 2014:354) and many readers complain about long and unclear text on patient information leaflets (Maat & Lentz, 2010:118). Furthermore the guidelines proposed by Joubert and Githinji (2014:357) were used in regards to the structure of a leaflet with an A5 size, with a white background and black print, necessary details regarding the producer of the flyer and also information organised into columns with headings. The columns with appropriate headings will aim to help users find the information they are searching for as quickly as possible, as struggling to do so could result in the reader not continuing to read the information (Maat & Lentz, 2010: 116).

1.9 Summary measures

Data of the following was included in the data extraction table: authors and date, title of the academic literature, sample, methodology, route of administration of essential oils (list oils used), conclusion (findings), critical appraisal score, strengths and limitations.

1.10 Rigour

The same rigour is expected of a systematic review than any other study because a systematic review is seen as a scientific study which will have an influence on the health care system. A subject librarian was involved to help ensure that the search strategy was as effective as possible to include all the relevant academic literature needed for it to be comprehensive. The reference lists of academic literature using secondary sources to be included were searched by hand to make sure that all academic literature got the necessary attention to determine their inclusion. An effort was made to find difficult-to-trace academic literature. The systematic review was done according to a set process to improve rigour. It is important to put strategies in place to minimize bias throughout the study (Hemingway & Brereton, 2009:4-5). Bias is described by Brink *et al.* (2012:208) as anything that can influence the results of the study so that it is not truthful anymore and thus leads to the data favouring the outcome of the study. Bias can either be exhibited towards individual studies, or across studies in reporting results. These biases will now be addressed in more detail. During the process of data synthesis it is important for the researcher to also note similarities, differences and the strength of the evidence collected to ensure that the right conclusions are reached (CRD, 2009:45). In this study the researcher looked at different literature to see if the same essential oils brought relief for the same symptoms and which route of administration was used.

1.10.1 Risk of bias in individual studies

Conflict of interest or any funding should be assessed for bias in all literature (Haddaway *et al.*, 2017:357). In this systematic review the researcher took care not to be biased towards any findings in individual academic literature sources. The process of data synthesis as well as the data extraction process was done by more than one person as Botma *et al.* (2010:244-245) and Milner (2015:90) agree that more than one person conducting these steps help to lessen any human errors and bias. Reviewer bias was further lessened by conducting the systematic review in such a manner that it ensured duplicability and thus rigour to conclude with the same results (Botma *et al.*, 2010:241). Academic literature and grey literature were included in accordance to the inclusion criteria which have been established beforehand to further reduce bias that could develop as the researcher reads through the literature (Joanna Briggs Institute, 2000:3).

Critical appraisal was done to ensure that only good quality academic literature were included in the review. The critical appraisal conducted in this review specifically focussed on the following to promote rigour of the review: the review question, how did the researcher search for the literature incorporated into the academic literature, how were academic literature included or excluded, critical appraisal of the academic literature which were included, can the findings of the academic literature be combined through data synthesis procedures, did the researcher explain all methods used in the study, and lastly is there a proper summary in the study (Joanna Briggs Institution, 2000:1-2).

1.10.2 Risk of bias across studies

A variety of literature sources were used. Only reputable databases were used and this was defended by the authority and search ability of the database to ensure all relevant literature to be included (Adams *et al.*, 2016:10). Furthermore, the reference lists of the included academic literature from the initial search were also sought through for identification of further academic literature that merited inclusion.

In this review grey literature was included. Grey literature was defined in October 1999 at an international conference about grey literature that was held in Washington as follows: “That which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers” (The New York Academy of Medicine, 1999). According to Ward-Smith, (2016:253) the inclusion of grey literature can help to reduce bias which might be seen in the published literature in a literature review. Grey literature was included because there are several organisations focused on cancer and essential oils with valuable publications that can address the aim of this study. However, grey literature included was limited to chapters from books and non-research literature published in academic literature in order to maintain the quality of included literature through support of the peer review process. Adequate records of the included grey literature were kept in order to promote rigour in the usage of grey literature (Adams *et al.*, 2016:8). This was done to promote the credibility of the review by showing that only reputable sources were used for grey literature, and it also promotes the study’s ability to be replicated.

In order to further promote the rigour of the study, the academic literatures to be included have been reviewed by two reviewers. Title-sifting, abstract-sifting, full-text

assessments and critical appraisal of literature considered for inclusion was co-reviewed by a second reviewer, namely the study supervisor. All data relevant to the research question was collected, both in favour of and against essential oils, to further ensure that no reporting bias was present.

1.11 Ethical considerations

Usually the use of animal and human participants is of greatest concern in ethical considerations. In a systematic review where no informed consent is needed from human participants, there are still areas of ethical consideration that are extremely important (Weingarten *et al.*, 2004:1013).

In this study the academic literature used was read thoroughly to see whether ethical scientific rigour could be ascribed to it in the following respects:

- The academic literature was examined for ethical clearance or by using personal judgement to decide whether the research had been conducted in an ethical manner. All academic literature sources have to comply with ethical considerations. The ethical considerations, however, can be different for different academic literature depending on the year in which it was conducted as ethical considerations have changed dramatically over time (Weingarten *et al.*, 2004:1013).
- Further considerations include authorship of included literature. Only people who really worked on the document can be named as authors and also in the order of how much they contributed to the work.
- In this study the researcher was cautious of plagiarism. Plagiarism is an ethical issue involving the use of someone else's work and presenting it as one's own without the proper acknowledgement to the person who wrote/invented it first (Wager & Wiffen, 2011:132).
- Lastly, accuracy of information provided is an ethical consideration. It is important that the researcher do not try to force the information obtained into a set idea to fit the researcher's theory (Wager & Wiffen, 2011:130-133).

To make sure that the ethical considerations are in place the systematic review has to be reviewed by an ethics committee (Weingarten *et al.*, 2004:1014). The researcher has also undergone ethical training in the year 2017 (Addendum G). The researcher did the study in an unbiased manner so as to improve the outcome of the study. The

researcher ensured unbiasedness through the following strategies: using the established inclusion and exclusion criteria as mentioned, following the search strategy as determined with the help of the subject librarian, following the criteria for the critical appraisal and making use of a second reviewer to ensure the academic literature included and thus the results have been concluded to in an unbiased manner.

Any conflict of interest was stated and also any funding received for the study as this could lead to bias (Haddaway *et al.*, 2017:357). There is no conflict of interest with the researcher in this study and also the only funding received by the researcher was that of the North-West University which had no special interest regarding the subject of the study.

In this systematic review precautions were taken so as to conduct this study in an ethically correct manner and all precautions mentioned above were implemented. The study was reviewed by the scientific committee of the INSINQ Research Focus Area and the Health Research Ethics Committee (HREC) of the Faculty of Health Sciences of the North-West University to ensure that the study was ethically correct. Thus ethical clearance was received for the proposal before furthering this study (Ethical number NWU-00113-17-S1). The ethical clearance certificate is attached as Addendum J.

1.12 Outline of chapters

Chapter 1 – Study overview

Chapter 2 – Research methodology

Chapter 3 – Review findings

Chapter 4 – Conclusions, limitations and recommendations

1.13 Conclusion

Brain malignancies are the second most prevalent cancer in children (Figaji, 2015) and 20-40% of cancers from other parts of the body affecting adults will metastasise to the brain (Schmieder *et al.*, 2016:415). There are three main traditional treatment options for malignancies, namely surgery, radiation and chemotherapy. These traditional treatments come with side-effects for the patient to bear (Alberts, 2012:61-64). The brain malignancy itself also has numerous symptoms affecting the patient (Mosby's

medical dictionary of medicine, nursing and health professions, 2006:250). An introduction to the systematic review done to formulate a summary on the best evidence available regarding the use of essential oils to relieve brain malignancy-related symptoms have been provided in this chapter. A research question has been developed with use of PICO and the inclusion and exclusion criteria stated. An overview of the search strategy and analysis methods has been discussed. In Chapter two the systematic review process will be discussed in more detail.

CHAPTER 2 RESEARCH METHODOLOGY

2.1 Introduction

In this section the systematic review process followed will be described. Furthermore a summary of the signs and symptoms of brain malignancies will be presented in order to justify the search terms for the systematic review.

In this chapter the methodology foundation of this study will be described. A systematic review process will be discussed as consisting of four phases (conceptual phase, search strategy, data-collection process and data synthesis), each comprising different steps. All of these steps as pertaining to relevant phases will be discussed.

2.2 The systematic review method

Systematic reviews are being done more and more and to accompany this growing tendency certain steps to follow have been proposed to ensure that the systematic reviews are of good quality (Milner, 2015:89). The growing need for systematic reviews arose from the increased research-focus of the global community and the internet's role in wide-spread data-dissemination that led to vast amounts of information available (Hemingway & Brereton, 2009:2). Although the increase in research is very valuable, it is seemingly impossible to digest it all; thus doing a systematic review is of great value to combine all the available evidence and to derive summative conclusions, all in one study (Hemingway & Brereton, 2009:2 and Joanna Briggs institute, 2000:1). A systematic review is described by Botma *et al.* (2010:241) as a combination or a summary of numerous items of literature or trials that are reviewed to answer a specific research question posed by the researcher. Clark (2011:64) agrees on this definition and adds that a systematic review is a very precise summary of the primary research and is as such seen as secondary research. The Joanna Briggs Institute (2000:1) elaborates that a systematic review helps to inform researchers on where there are gaps and research needed for the future (Joanna Briggs Institute, 2000:1). With this in mind this review is in line with the requirements for a systematic review. According to the PRISMA criteria checklist (addendum H) the title has to indicate that it is a systematic review.

Although the need of systematic reviews is evident, Botma *et al.* (2010:241) warn that it is important that the systematic review be carried out in such a manner that the review can be duplicated if someone followed the exact same steps, thus reducing reviewer bias and providing the reader with a concise and well-rounded opinion on the specific subject. This possibility of systematic reviews to be duplicated with the added scientific merit of being peer-reviewed sets a systematic review apart from other literature reviews (Hemingway & Brereton, 2009:2). This review has been properly described so that duplication could be done when following the exact steps as described.

Further adding to the scientific merit of systematic reviews, Khalid *et al.* (2003:118) emphasize that a systematic review has to have a valuable question, use academic literature which is relevant and of good quality and follows reliable a research methodology. It is very important to use academic literature of good quality in a systematic review as the outcome of the systematic review will be to summarize all the data which have been found in that academic literature (Brink *et al.*, 2012:17) and thus the validity of the systematic review's conclusions would be influenced if unreliable sources were used. Best evidence as derived from the combination of numerous academic literature findings (Brink *et al.*, 2012:17-18) leads to better decisions regarding the best care for patients. This is confirmed by Fox (2017:88) who states that systematic reviews are used to inform numerous policies and evidence for best care and practice. To ensure that only good quality academic literature has been included all relevant studies were critically appraised by predetermined tools.

A systematic review consists of numerous steps, similar to those of traditional research methods (Botma *et al.*, 2010:241). These steps can fit broadly under the headings conceptual phase, empirical phase (search strategy and data extraction), interpretive phase (data synthesis) and communication phase as presented by Brink *et al.* (2013:55-58). According to Botma *et al.* (2010:241) the following eight steps have to be followed and these steps will form the outline of the discussion regarding the conducting of a systematic review (SR) under the headings conceptual phase, search strategy, data extraction and data synthesis:

1. Conceptual phase
 - 1.1. Step 1: The problem has to be identified;
 - 1.2. Step 2: A review protocol has to be established;
2. Search strategy
 - 2.1. Step 3: Literature relevant to the research question has to be located by the researcher;
 - 2.2. Step 4: Study selection;
 - 2.3. Step 5: The research quality has to be investigated;
3. Data-collection process
 - 3.1. Step 6: Individual literature sources are examined and data collected from them;
4. Data synthesis
 - 4.1. Step 7: Combining the findings of the literature used; and
 - 4.2. Step 8: The findings have to be documented and disseminated in the correct way.

2.2.1 Conceptual phase

This phase includes the first two steps of the SR method, namely the problem has to be identified and a review protocol has to be established.

Step 1: The problem has to be identified

First a problem has to be identified by the researcher and this will usually happen in a clinical setting (Botma *et al.*, 2010:241). If a systematic review study is done on a topic with limited research or a very new field then the research question could be very broad to make sure all information will be included (Joanna Briggs Institute, 2000:2). In such a broad study, the Joanna Briggs Institute (2000:2) further explains the aim to be to provide a summary of evidence available to inform future research of what research is needed in the specific field. In a study with a specific focus, there has to be sufficient academic literature available on the subject to do a systematic review (Milner, 2015:89). This systematic review aims to address a specific focus but the research question and inclusion criteria were broad so as to include all the information as the information in this field is limited.

The problem was identified as that no summary of the evidence about the use of essential oils for the relief of brain-malignancy-related symptoms could be found. This

led to the following research question: what is the best available evidence for the use of essential oils in the effective relief of specific brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety)?

The research question is very important as it will determine the course of the study and also which academic literature will be included and which will be excluded, as all academic literature must aim to answer the research question (Botma *et al.*, 2010:242). The research question has to be addressable through a proper search (Ten Ham-Baloyi & Jordan, 2016:123). The researcher also has to ensure that the review which is planned has not been done yet, thus a search has to be done to ensure that this study will not be a duplicate (Milner, 2015:90). To help with this search process it is valuable to search the specific registries for systematic reviews such as the Cochrane library (Milner, 2015:90). As discussed in Chapter 1, no systematic review could be retrieved on the same research question as this study this was confirmed by registration of the review on the PROSPERO website.

2.2.1.1 Eligibility criteria

The research question can at first be stated in free form and later be developed into the more specific PICO (Patient, Intervention, Comparison and Outcome) question (Khalid *et al.*, 2003:119) as requested by the PRISMA criteria checklist (Addendum H). The usage of the PICO helps the researcher to know exactly what the study will aim to search for (Milner, 2015:90). Time can also be added to the PICO but this will all depend on the purpose of the systematic review (Ten Ham-Baloyi & Jordan, 2016:123). The PICO question for this study has been established as follow:

Population –	People with brain malignancies.
Intervention –	Usage of essential oils for the relief of specific symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety) associated with brain malignancies.
Comparator –	Other modalities used to relieve specific brain malignancy-related symptoms.

Outcome – Relief brought by essential oils for brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety).

After the question has been formulated a review protocol can be developed (Botma *et al.*, 2010:243). The PICO question was used to help to determine the search words for conducting the literature review (Ten Ham-Baloyi & Jordan, 2016:123). The PICO was also used in formulating the inclusion criteria used to decide on which academic literature to include and which to exclude (The Joanna Briggs Institute 2000:3).

2.2.1.2 Literature review to determine key words

A literature review is important to help determine and define the symptoms related to brain malignancies. The academic literature was reviewed for symptoms related to brain malignancies and presented in Chapter 1. Here, a summary of those reviewed symptoms for adults follows. The summary only includes adults' symptoms as no research on the use of essential oils for paediatric symptoms is currently available to include in a systematic review.

Table 2.1 Summary of brain malignancy-related signs and symptoms in adults (ages 16+)

Gastro-intestinal signs and symptoms for adults			
Constipation	Diarrhoea	Nausea and vomiting	Difficulty swallowing
Eating problems			
General signs and symptoms for adults (ages 16+)			
Decreased immunity	Fatigue	Swelling in the neck	Pain
Retraction of eyelids	Cushing's triad	Headache	
Psychological signs and symptoms for adults			
Headache due to anxiety and depression	Struggling to cope with the diagnosis	Tiredness	Social isolation
Shock	Not enough sleep	Resentfulness	Blame
Anxiety	Irritability	Sluggishness	Depression
Stress	Emotional distress	Fear	Anger outbursts
Neurological signs and symptoms for adults			
Headaches	One-sided paralysis	Changes in behaviour	Hypopituitarism
Balance / walking difficulties	Changes in pupil reactions	Intracranial hypertension	Olfactory abnormalities
Distorted vision/double vision/decreased vision clarity	Runny nose	Attention deficits	Abnormal eye movements
Nausea and vomiting	Strabismus	Stroke	Hydrocephalus
Fits/seizures (without a fever)	Struggling to make decisions	Decreased cerebral blood flow	Constant buzzing in ears
Irritability	Loss of smell	Swelling of the optic nerve in the eye	Struggling to remember
Altering levels of consciousness	Brain herniation	Loss of control of body movements	Pain
Raised Intracranial pressure	Loss of motor function	Asymmetrical facial features	
Hormonal signs and symptoms for adults			
Decreased fertility	Decreased sexual drive	Hoarse voice	Impotence
Milky discharge from nipple not related to breastfeeding	Puberty problems such as loss of menstruation	Hormone changes	
Treatment related signs and symptoms for adults			
Nausea and vomiting	Changes in body image	Fluid retention	Stomach problems
Puberty problems	Fatigue	Skin itching	Deep vein thrombosis
Pain	Constipation	Scar at operation site	Hair loss
Increased blood pressure	Weakened immune system	Hyperglycaemia	Decreased sensory abilities
Weakness in legs	Sleeplessness		

Step 2: A review protocol / proposal is established

The review protocol or proposal consists of the systematic review steps which will be used to do the study and answer the research question as described in chapter one (Botma *et al.*, 2010:243). The research proposal is a critical part of the study as in it the researcher has to specify the process that will be followed to carry out the study and also give reasons as to why this specific method has been chosen (Botma *et al.*, 2010:243). In Chapter one every aspect of what information is needed from the literature was stated (Milner, 2015:90). Chapter one states the inclusion and exclusion criteria which will be used, keywords, where the academic literature will be sourced, and how the search will be documented (Ten Ham-Baloyi & Jordan, 2016:123). Botma *et al.* (2010:244) confirm the importance of clearly identifying the search terms in the proposal. The review protocol also helps to better the systematic review (Haddaway *et al.*, 2017:357). In this study, the proposal was scrutinised by the INSINQ scientific committee. This step is also very important as it will lay the ground work for the rest of the study (Milner, 2015:90). As this step aims to give an outline of the whole research it is important for the quality assurance of the systematic review as it is of value when even the process of a systematic review can be critically appraised (Joanna Briggs Institute, 2000:2).

2.2.2 Search strategy

This phase includes the literature review and steps 3, 4, and 5 in which the researcher identifies the relevant academic literature and collects it. After collection the relevant academic literature is assessed for quality.

2.2.2.1 Information sources and search

Step 3: The researcher has to locate the literature relevant to the research question

The search method has to be developed prior to beginning the search to ensure that anyone can redo the search and find the same results (Milner, 2015:90). The following databases were included: EbscoHost, Medline, eJournal, CAB abstracts, Health source, Academic search premier, CINAHL, Pubmed, Cochrane, Web of Science, Scopus, ScienceDirect, SAePublications, AHFS Consumer Medication information, SocINDEX and Masterfile. An example of the search strings is as follows: (brain malignancy or brain tumour or brain tumour or brain mass or brain cancer) AND (essential oils or

aromatherapy) AND (headache or migraine) OR (vomiting or emesis) OR (intracranial pressure or icp) OR (depression or anxiety) OR (seizures or epilepsy or seizure activity) OR (symptoms or signs) OR (treatment or intervention or therapy or management). These search terms were used in this manner according to the advice of the librarian and only the symptoms were adjusted to search individually for each symptom and not combined as listed in the above example. No time restraint was put on the academic literature gathered as essential oils have been used for an indefinite time period.

The researcher made use of the help of a team of which the subject librarian played an important role (Milner, 2015:90). Librarians can help the researcher in numerous ways to improve the study due to their expertise in the field (Ten Ham-Baloyi & Jordan, 2016:123). Furthermore the Joanna Briggs Institute (2000:3) states that the included articles' bibliographies should be searched to see if there is literature listed which could be of value for the current study being conducted. The academic literature giving information as secondary sources was used in that their bibliographies were searched so that the primary sources could be gathered. Also, the study supervisor acted as the second reviewer. It is important to record this process properly so that the study can be repeated if needed (Haddaway *et al.*, 2017:357). Eppi-reviewer 4 software was used to assist in recording the academic literature gathered from the searches and to remove duplicates.

Step 4: Study selection

First the academic literature was sifted to only include the relevant academic literature as determined by the inclusion and exclusion criteria, and then these academic literature sources were evaluated according to the quality thereof through the critical appraisal tools and lastly when the data were extracted even some more academic literature could be excluded due to errors found such as insufficient data (Hemingway & Brereton, 2009:4). Relevant academic literature was determined in accordance with the inclusion and exclusion criteria which have been formulated in the previous step (Botma *et al.*, 2010:244; Milner, 2015:90). The title (and if possibly relevant, the abstract) of all academic literature found was read to determine relevance. The full text of those found to be relevant was retrieved (Milner, 2015:90). It is important to keep proper record in this step so that reasons for inclusion and exclusion are clear (Botma *et al.*, 2010:244). Academic literature was included to ensure sensitivity and specificity (Ten Ham-Baloyi & Jordan, 2016:123). For sensitivity all academic literature that met the inclusion criteria

were recorded, even though some of them will later be removed again and for specificity the academic literature which is not applicable should be removed in the next step (Ten Ham-Baloyi & Jordan, 2016:124). All academic literature in question was checked and co-reviewed by a second reviewer to make a final decision regarding the usefulness and eligibility of the particular academic literature document (Milner, 2015:90).

In this step any duplicate academic literature should also be removed, and this is a very time-consuming action but it is necessary because of the usage of different databases when the literature is searched and thus duplication can happen (Kwon *et al.*, 2015:184). The removals of duplicates were done with the help of the Eppi-reviewer 4 software. Further the Eppi-reviewer 4 software was used to compile a list of academic literature after the title and abstract sifting.

Step 5: Investigate the quality of the research

Because the quality of academic literature may vary, all academic literature used for the systematic review had to be judged on their quality (Joanna Briggs Institute, 200:1). The quality control of a systematic review is also referred to as critical appraisal. In this step the academic literature was judged for any bias and errors, some of which could be minor and others could be major, which had been done in the research process of that particular study (Milner, 2015:891). In this step the researcher has to assess the academic literature for their methodological correctness, for their validity, any bias, and if their data-collection process was adequate and also assess if the search has been successful (Botma *et al.*, 2010:244). Haddaway *et al.* (2017:357) elaborate that both internal and external validity have to be explored as this step will aim to remove any academic literature that is not scientifically sufficient to be used. This is important because otherwise academic literature which has had poor information would lead to the systematic review also arriving at a poor conclusion (Milner, 2015:91).

The process and tools were used to determine the quality of the literature as stated in chapter one (Ten Ham-Baloyi & Jordan, 2016:124). The process of investigating the quality of the research is applicable to every step of the process and in this step a criterion checklist such as a critical appraisal tool could be used (Khalid *et al.*, 2003:118). Although critical appraisal tools are of much value, it must be kept in mind that there is not just one specific tool which would suit the need for all literature (Ten

Ham-Baloyi & Jordan, 2016:124). Different tools were used to critically appraise all the academic literature.

The Critical Appraisal Skills Programme (CASP) appraisal tools were used for Randomised Controlled Trials (Addendum C), Systematic Reviews (Addendum D), Cohort Studies (Addendum E), and Qualitative Studies (Addendum F). For mixed-method academic literature and for other designs that do not have a specific CASP tool, the Johns Hopkins Research Evidence Appraisal Tool (Addendum A) was used, while the Johns Hopkins Non-Research Evidence Appraisal Tool (Addendum B) was used for all non-research literature such as book chapters and journal-published academic literature.

The Johns Hopkins Tools first examine the general information regarding academic literature, such as author, journal, title, publication date, and whether the academic literature answers the research question. If the population of literature under review or research question is not correct the academic literature was excluded at this point in time. Furthermore the tools examined the sample size, asked whether the academic literature had valuable information, the interventions and control groups, the description of the data collection and analysis methods, and whether the results with recommendations and gaps identified are explained by the academic literature.

The CASP Tools do not collect the general data first as described above for the John Hopkins Tools. However, the CASP Tools also address some of the same aspects as the John Hopkins Tools. The CASP Tools start out with a few questions and after answering these starting questions a decision is made as to whether the reviewer will continue to critically appraise the academic literature or not. These questions are regarding the focus of the review, and if the methodology of the study is correct. If not the academic literature is excluded. The other questions also focus on the manner in which the academic literature was done and particular aspects such as randomization, or if the correct literature were included for a systematic review. In the end the answers to the questions can be calculated to determine if the academic literature should be included or excluded. If the academic literature scored more than 70% it was included (table 3.2 and addendum K).

2.2.3 Data-collection process

In this phase all the academic literature which had been collected and approved according to their quality was further examined for the data it contained.

Step 6: Individual literature sources are examined and data collected from them

A data-collection tool was created to make sure that the process of data collection ran smoothly (Botma *et al.*, 2010:245) and to collect all the applicable data. This data-collection tool which was used will help to improve the quality of the review (Milner, 2015:90). There are numerous data-collection tools which can be used (Ten Ham-Baloyi & Jordan, 2016:124), for example the Joanna Briggs Institute tools such as Mastari or Nortari. The researcher used tools as guidelines to develop a data extraction table specific for this study. All the data that will be used in this systematic review has now been removed from the whole body of data gathered (Ten Ham-Baloyi & Jordan, 2016:124).

Table 2.2 An example of the data-extraction rubric that was used in this review

Authors and date	Title	Essential oil route, type and indication	Relevant findings

According to Milner (2015:90) it is best if two people do the data extraction and also if they have previous experience and training in this field and that the two researchers extract the data on their own and then thereafter come together to compare their findings. If the two reviewers doing the extraction have different views on a study then a third person can be brought in to help them to get to a conclusion (Milner, 2015:91). Also in this step consistency and objectivity are very important (Haddaway *et al.*, 2017:357). The data extractor has to measure the academic literature against the research question the whole time to make sure all the academic literature is on the right track (Milner, 2015:91). Furthermore, the reviewer has to search for the similarities and differences in the data while extracting it in the next step (Milner, 2015:91). At this stage, however, the researcher might find that some necessary data had been omitted in the academic literature being used and the researchers should be contacted to retrieve the data if possible (Botma *et al.*, 2010:245). This was done with regards to the studies where the specific essential oils used were not mentioned and the researchers were contacted, yet no response was received. The process of data collection should

be clearly documented and also any manipulation made to the data should also be clearly stated (Haddaway *et al.*, 2017:357). All the necessary information as described by the data extraction table titles was gathered from the included academic literature.

2.2.4 Data synthesis

This is the last phase and consists of steps 7 and 8. In this phase all the data retrieved from the academic literature is combined and disseminated accordingly.

Step 7: Combining the findings of the literature used

The aim of combining systematic review data is to summarize all the data which answer the research question, as could be achieved by compiling a data extraction table. (Botma *et al.*, 2010:245 and Ten Ham-Baloyi & Jordan, 2016:120). The data can be reported in different ways and the best way has to be determined so that the research question will be answered adequately (Botma *et al.*, 2010:245). Tables or statistical methods can be used to combine the data gathered (Khalid *et al.*, 2003:118). In this review statistical methods could not be used to combine findings from different academic sources. Data-synthesis was done through thematic analysis. Qualitative data could be analysed through thematic analysis (Braun & Clarke, 2006:87). Three steps for thematic analysis are listed by Thomas and Harden (2008:45): coding of the text, developing explanatory themes and lastly developing analytical themes. Data specific to the essential oils used, through what route it was administered and which symptoms were retrieved from the academic literature which were included. Data synthesis consisted of all the relevant data that had been generated from the included academic literature and combining it into a whole which then led to a summary which could answer the research question (Botma *et al.*, 2010:245).

Step 8: The findings have to be documented and disseminated in the correct way

The report writing includes the steps of an introduction, discussion of the methods, followed by the results, and ended with a conclusion and findings (Botma *et al.*, 2010:245). Tables are usually used to summarize all the information which had been retrieved, with headings such as population, intervention, effect of the intervention, outcomes and any issues which had confronted the study (Milner, 2015:91-92). Table 3.5 has been developed with the essential oils which had been used and the route of administration and for which symptom.

Recommendations were made and are supported by the gathered data (Khalid *et al.*, 2003:118). The recommendations which were made would be linked to the quality of the literature used; for if literature of high quality has been used then the recommendations made would also be of high quality (Milner, 2015:92). A systematic review can also be published in academic journals like research studies (Milner, 2015:92). There are other ways for dissemination as well, and not one is seen as the most effective method according to Milner (2015:92) and he states that using more than one method might be most effective. The dissemination process for this study will consist of a written article and a patient information leaflet. The leaflet consists of the information gathered from the study and is formulated in such a way that patients can use and understand it.

2.3 Conclusion

The process of conducting a systematic review of good quality and also disseminating the findings can be a long process (Milner, 2015:92). The process of conducting a systematic review as described above was used to guide this systematic review which was conducted. In the next chapter the results and discussion will be provided.

CHAPTER 3 REVIEW FINDINGS

3.1 Introduction

In this chapter the findings and discussion of the systematic review will be provided. A description of search outcomes and information related to the study topic will ensue, after which this information will be synthesised into a patient information leaflet. Thus this chapter will project the objectives of the study as presented in Chapter 1 after the methodology as discussed in Chapter 2 had been followed.

3.2 Academic literature selection

The initial search yielded 20 700 academic literature records. All the academic literature was uploaded into the Eppi-reviewer 4 software. With the help of Eppi-reviewer 4 software 6 068 academic literature records were excluded as duplicates. A further 13 564 academic literature records were excluded after title sifting and 745 academic literature records were excluded due to abstracts not being relevant to the study at hand. One article was excluded because no English abstract was available. The full texts of the remaining academic literature records were collected and 304 academic literature records were considered irrelevant with regards to the study focus. Two academic literature records from the initial search were unobtainable. A total of 15 academic literature records were found to be relevant to the research question. The reference lists of secondary sources such as systematic reviews, literature reviews, and book chapters` were searched to determine primary records mentioned in the case of these sources might be relevant for inclusion. Another 15 relevant academic literature sources were added from the reference lists of these secondary academic literature records. No additional academic literature from other primary literature's reference list was relevant for inclusion. Five of these were unobtainable.

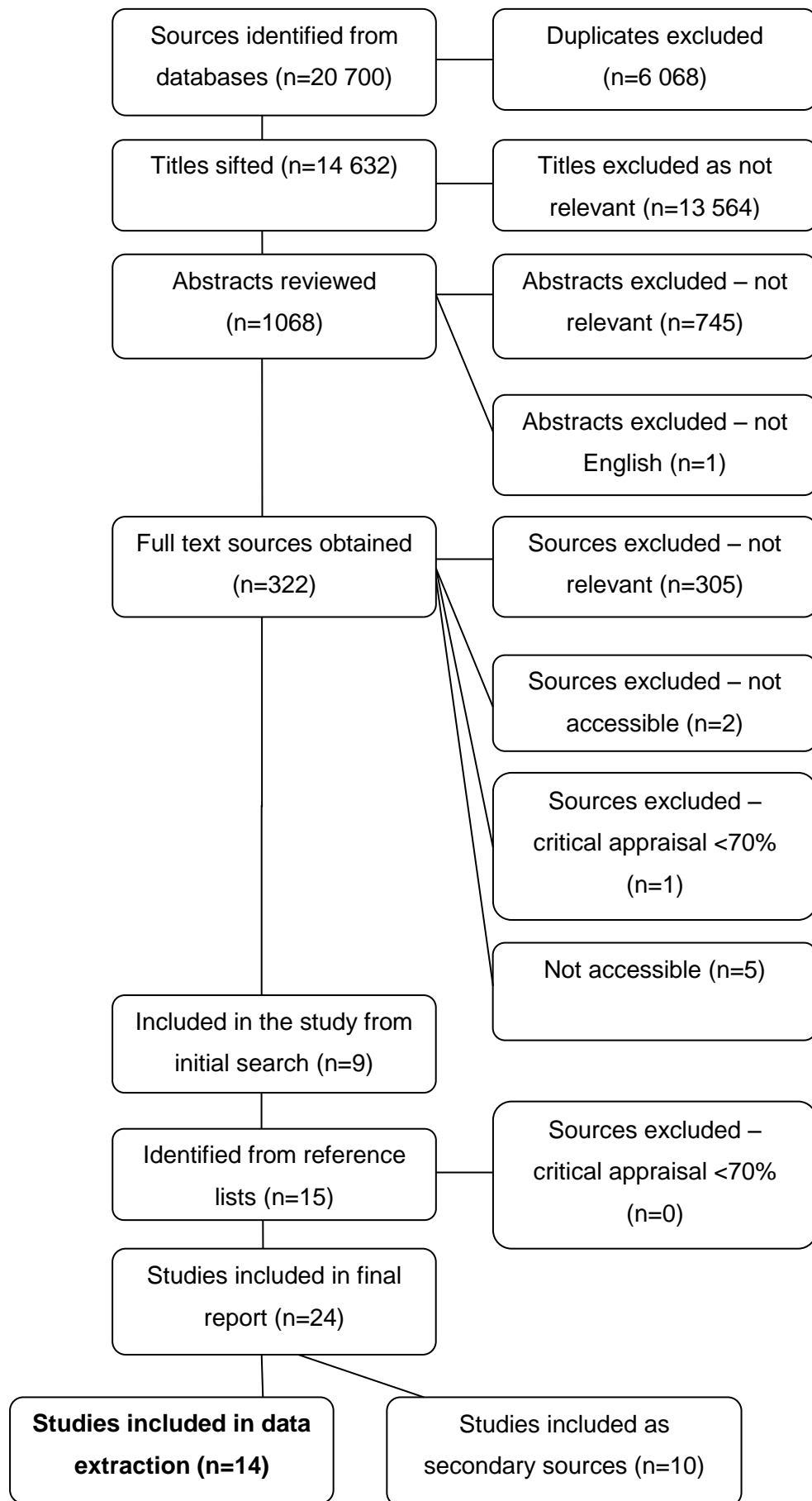


Figure 3.1: PRISMA flow diagram of search outcomes

3.3 Critical appraisal

Academic literature sources were included for data extraction if they scored 70% or more on the critical appraisal (see addendum K). All questions from critical appraisal tools were scored by indicating a yes as one, a no as zero or not applicable. Questions not applicable were excluded from the total from which percentages were calculated. A total of 25 academic literature records were critically appraised and one case study scored less than 70% and was excluded due to not being clearly formulated and not having clearly formulated conclusions linked to the results. Twenty four academic literature records were found to be both relevant and of good quality, and were included in the final report. The included academic literature focussed on the relief of specific symptoms by using essential oils. Table 3.2 was compiled with the headings of the tools used for the critical appraisal, as discussed in chapters one and two, and academic literature was individually examined accordingly and included in this table. Critical appraisal was done on all literature records (addendum K) however of these literature records ten were secondary sources and were only used to identify primary academic literature (table 3.3). Whereafter a total number of 14 primary academic literature records were used for data extraction (table 3.4). The calculation for the critical appraisal percentage was calculated by means of the following formulae (addendum K) where-in the number divided by indicates the total number of critical appraisal instrument items reviewed:

- Systematic review critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 8) x 100
- Literature review critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 5) x 100
- Expert opinion critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 4) x 100
- Case report critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 4) x 100
- Program/financieal evaluation/quality improvement critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 6) x 100
- Mixed method/quasi experimental academic literature critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 15 (or 12 when not applicable excluded)) x 100

- Randomised controlled trials critical appraisal score (%) = (number of elements of critical appraisal instrument complied with ÷ 11) x 100

The included primary academic literature used different instruments for measuring the symptoms that are used as outcomes in this review. Table 3.1 was created with all of the instrument acronyms accessed during data extraction for easier reference in the data extraction tool and also to provide an overview of symptoms measured by these tools.

Table 3.1: Scales or tools used to measure outcomes as mentioned in the academic literature

Acronym	Full Name	Used to measure
BPI-K	The Korean version of Brief Pain Inventory	Pain
CES-D	Center for Epidemiological Studies Depression	Depression
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer	Nausea Vomiting
HADS	Hospital Anxiety and Depression Scale	Anxiety Depression
MYMOP	Measure Yourself Medical Outcome Profile	Scale to measure intensity of symptoms on scale 0-7
POMS	Profile of Mood States	Depression Mood disturbance Fatigue
RSCL	Rotterdam Symptom Checklist	Physical Psychological symptom distress Activity level Global life quality
SAI	State Anxiety Inventor	Anxiety
SCID	Structured Clinical Interview	Anxiety Depression
SPHERE	Somatic and Psychological Health Report	Anxiety and depression
TAI	Trait Anxiety Inventory	Anxiety
VAS	Visual Analogue Scale	Anxiety Pain intensity
VSH	Verran and Snyder-Halpern	Sleep scale

The following data was extracted from the primary academic literature: authors, date, title of the literature, aim, methodology, route, type and indication of essential oils administered, findings related to the research question of the study at hand, strengths and limitations of the academic literature. Table 3.2 presents a summary of this data.

Table 3.2 Critical appraisal

Authors and date	Title	Aim	Methodology	Strenghts	Limitations	Critical appraisal score
Program evaluation / quality improvement						
De Valois (2001)	A retrospective assessment of 3 years of patient audit for an aromatherapy massage service for cancer patients.	To determine patients experience of aromatherapy received at a hospital.	<u>Sample</u> : 149 Patients. <u>Data collection</u> : Aromatherapy massage for inpatients and outpatients at a hospital was evaluated for a three year period (769 treatments) by staff-developed questionnaires. <u>Data analysis</u> : Descriptive statistics.	The study was done over a three year period. Adequate sample size.	Informal audit with no record of response rate. Patients had preconceived ideas about aromatherapy massage. Areas massaged not described.	83
Kite <i>et al.</i> (1998)	Development of an aromatherapy service at a cancer centre	To evaluate the effectiveness of aromatherapy to patients after chages has been made after the pilot study.	<u>Sample</u> : 89 patients referred for inclusion, 58 completed the study. <u>Data collection</u> : Patients completed a checklist of symptom severity and HADS pre- and post-treatment. Fieldnotes were made by aromatherapists. <u>Data analysis</u> : Descriptive statistics.	Interrator reliability ensured through co-observation by nurses and aromatherapists. Hawthorne effect accounted for as aromatherapy was a known treatment to sample.	10 Patients dropped out for unknown reasons. A number of patients dropped out due to illness or death. Do not specifically mention essential oils which were used.	83
Stringer & Donald (2011)	Aromasticks in cancer care: An innovation not to be Sniffed at.	To evaluate the effect of aromatherapy in an acute cancer care centre in the UK.	<u>Sample</u> : 160 cancer patients . <u>Data collection</u> : Therapists recorded frequency of use and perceived symptom relief on a checklist <u>Data analysis</u> : Descriptive and inferential statistics.	Good sample size, Standardised instrument used.	Baseline data was not recorded, randomization inadequate, and variables not controlled well. Vague about which essential oils were used.	83

Author and date	Title	Aim	Methodology	Strenghts	Limitations	Critical appraisal score
Case study						
Cooksley (2003)	An integrative aromatherapy intervention for palliative care.	To demonstrate how several holistic and integrative healing approaches were fused together with essential oil therapy to address numerous diagnoses and symptoms for a client in the end stages of her life.	<u>Sample</u> : One female patient (74year old) with metastatic adenocarcinoma of the lung (Stage IV). <u>Data collection</u> : Observation by RN over a three month period. <u>Data analysis</u> : Narrative report.	The author was one-on-one with the patient and a detailed diary was kept on wholistic observations.	Sample size limited to one patient.	75
Mixed method						
Hadfield (2001)	The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours	To find out if aromatherapy massage had an effect on anxiety as experienced by patients with a primary malignant brain tumour at the time of their first appointment after receiving radiotherapy.	<u>Sample</u> : 10 patients with brain malignancies (80% response rate) <u>Data collection</u> : Physical parameters measured and HADS completed pre- and post-treatment. Telephone interview one week after intervention. <u>Data analysis</u> : Descriptive and inferential statistics.	Three different measuring systems were used.	Small sample size. Co-variables not adequately accounted for. Different treatment options implemented and not ime given for massage duration.	75
Quasi-experimental						
Louis & Kowalski. (2002)	Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being	To measure the response of hospice cancer patients receiving lavender essential oil through humidification.	<u>Sample</u> : 17 terminal patients. <u>Data collection</u> : Vital signs monitored, 11-point scale used to measure anxiety and depression on three occasions: Twice after control treatments (no treatment or water humidification) and once after experimental treatment (3% Lavender inhalation) <u>Data analysis</u> : Descriptive and inferential statistics.	Treatment conducted at patients' homes, thus a known environment.	Small sample size was used and the tool used to measure well-being was confusing to the patients.	80

Authors and date	Title	Aim	Methodology	Strenghts	Limitations	Critical appraisal score
Randomised controlled trials						
Chang (2008)	Effects of aroma hand massage on pain, state anxiety, and depression in hospice patients with terminal cancer.	To determine what effect hand massage had on pain, state anxiety and depression in patients with terminal cancer receiving care at a hospice.	<u>Sample</u> : 58 hospitalized patients with terminal cancer (56 patients completed the study). <u>Data collection</u> : The one group received aromatherapy hand massage and the control group only received carrier oil hand massage. Tools used were BPI-K, SAI and completed before and after each session. <u>Data analysis</u> : Descriptive and inferential statistics	Study is well described. Researcher well read in the field of aromatherapy.	Possible Hawthorne effect because the same researcher offered the massages and had the questionnaires completed.	91
Graham <i>et al.</i> (2003)	Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial	To find out if the inhalation of essential oils reduced anxiety in patients during radiotherapy.	<u>Sample</u> : 313 patients undergoing radiotherapy. <u>Data collection</u> : HADS and SPHERE completed at the beginning and end of the treatment. Patients divided into three groups. <u>Data analysis</u> : Descriptive and inferential statistics	Large sample group (statistically adequate). Some of the participants had previously used aromatherapy.	None of the authors were qualified aromatherapists. Variables in oils were not controlled adequately across groups.	91
Kyle (2006)	Evaluating the effectiveness of aromatherapy inreducing levels of anxiety in palliative care patients.	To determine the effectiveness of aromatherapy massage to reduce anxiety in patients receiving palliative care in four countries.	<u>Sample</u> : Pilot study of 80 palliative care patients, 58% drop-out rate. <u>Data collection</u> : Three groups were created. VAS was used before and after each 20 minute aromatherapy massages session administered daily for four weeks. STAI was completed before and after the four weeks. <u>Data analysis</u> : Descriptive statistics	All groups had the same level of anxiety prior to the research.	Randomisation was not consistent. Only 34 patients completed intervention schedule.	82

Authors and date	Title	Aim	Methodology	Strenghts	Limitations	Critical appraisal score
Soden <i>et al.</i> (2004)	A randomized controlled trial of aromatherapy massage in a hospice setting	To determine the effect of aromatherapy massage over a four week period for patients with advanced cancer versus receiving massage without aromatherapy.	<u>Sample</u> : 36 hospice patients. <u>Data collection</u> : VAS, VSH, HADS, RSCL scales were used to determine the effect of weekly aromatherapy massages, massages with carrier oil, or no treatment for four weeks in a randomised and blinded trial. <u>Data analysis</u> : Descriptive and inferential statistics	Different tools were used to assess the symptoms. Data were tested for each session as well as overall sessions.	Six patients did not complete the study as three were too ill and three passed away. Thus, the sample size was small. Control and intervention group had the same results.	82
Tayarani-Najaran <i>et al.</i> (2013)	Antiemetic activity of volatile oil from <i>Mentha spicata</i> and <i>Mentha x piperita</i> in chemotherapy-induced nausea and vomiting	To determine the effectivity of two essential oils (<i>Mentha spicata</i> and <i>Mentha x piperita</i>) to help prevent nausea caused by chemotherapy.	<u>Sample</u> : 200 cancer patients. <u>Data collection</u> : Patients were divided into four groups (control group, placebo group, two experimental groups). A questionnaire measuring the intensity of nausea and vomiting in 24 hours post chemotherapy was completed. <u>Data analysis</u> : Descriptive and inferential statistics	Randomisation and control exercised adequately.	The intervention was only done once-off. Patients still received their normal medication regimens which might have influenced the results.	91
Wilcock <i>et al.</i> (2004)	Does aromatherapy massage benefit patients with cancer attending a specialist palliative care dae centre?	To examine what effect aromatherapy massage had on the mood, quality of life and physical symptoms experienced by patients with cancer attending a palliative centre.	<u>Sample</u> : 46 palliative day care patients (29 completed). <u>Data collection</u> : MYMOP was used to report two symptoms and its intensity at the beginning and weekly. POMS was completed at the same intervals. Patients assigned to control or experimental group. <u>Data analysis</u> : Descriptive and inferential statistics	Good control and randomisation applied.	Small sample size: 17 patients did not complete the study, mostly due to being unwell. Control and intervention group had the same results.	73

Authors and date	Title	Aim	Methodology	Strenghts	Limitations	Critical appraisal score
Wilkinson <i>et al.</i> (1999)	An evaluation of aromatherapy massage in palliative care	To determine the effect of massage and aromatherapy massage given to patients with cancer at a palliative centre.	<u>Sample</u> : 103 cancer patients in palliative care, 87 completed the study. <u>Data collection</u> : Four nurses trained in massage did the aromatherapy massages. RSCL was completed in the week before the intervention and the week after the interventions. SAI were completed at the beginning and end of each session. TAI was completed in the week after the interventions. A semi-structured questionnaire was sent to the patients two weeks after the completion of the interventions. <u>Data analysis</u> : Descriptive and inferential statistics	Different tools were used to measure outcomes. Triangulation increased rigour.	16 Patients did not complete the study as 13 passed away, and another three were too sick to complete the intervention. Massage time duration is not mentioned.	82
Wilkinson <i>et al.</i> (2007)	Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer.	To determine the effectiveness of the addition of aromatherapy massage to the normal supportive care to manage anxiety and depression experienced by cancer patients.	<u>Sample</u> : 288 cancer patients, 231 completed the study. <u>Data collection</u> : the patients were randomly allocated to receive normal supportive care or normal supportive care and an aromatherapy massage of 1 hour every week for four weeks. The SAI, EORTC QLQ-C30 and Ces-D tools were completed initially and then at six and ten weeks after the treatment. <u>Data analysis</u> : Descriptive and inferential statistics	A large, statistically supported sample size was used.	The essential oil names and the massage sites were not documented. 8% of participants passed away and 15% were too ill to complete the assesements at ten weeks.	77

3.4 Study characteristics

No information was found to address symptoms of Intracranial pressure or epilepsy; though evidence of treatment of all other specified brain malignancy-related symptoms with application of essential oils were found. In total, 24 academic literature records were included in the data extraction table. These 24 consisted of three systematic reviews, one case study, three programme evaluations/quality improvements, three literature reviews, four chapters from books, one mixed-method study, one quasi-experimental design, and eight randomized controlled trials.

All the systematic reviews contained information regarding aromatherapy massage. The literature reviews also mostly reported aromatherapy massage, though some of the routes of administration and specific essential oils used were not fully described. The book chapters had information regarding inhalation of the essential oils, aromatherapy massage, oral intake of essential oils, and also some unknown routes. Systematic reviews, literature reviews and book chapters gave secondary information and thus were only used to access more primary sources as presented in table 3.3 in order to maintain comprehensiveness in the current report. This will limit reporting bias by preventing duplication of the information.

3.5 Data extraction

Data extraction for the secondary academic literature listed as systematic reviews, literature reviews and book chapters only included the references of primary academic literature records extracted from reference lists which were applicable to answering the research question. All the primary academic literature found from these secondary sources is listed in table 3.3, indicating which secondary sources quoted which primary source. After the ten secondary academic literature records had been tabulated, data extraction from the 14 remaining primary academic literature records will be presented.

Table 3.3 Secondary academic literature used to identify primary academic literature

Authors and date	Title	Study references
Systematic reviews		
Perry <i>et al.</i> (2012)	Is lavender an anxiolytic drug? A systematic review of randomised clinical trials	Soden, K., Vincent, K., Craske, S., Lucas, C. & Ashley, S. 2004. A randomized controlled trial of aromatherapy massage in a hospice setting. <i>Palliative medicine</i> , 18:87-92.
Shin <i>et al.</i> (2016)	Massage with or without aromatherapy for symptom relief in people with cancer.	Soden, K., Vincent, K., Craske, S., Lucas, C. & Ashley, S. 2004. A randomized controlled trial of aromatherapy massage in a hospice setting. <i>Palliative medicine</i> , 18:87-92.
		Wilkinson, S.M., Love, S.B., Westcombe, A.M., Gambles, M.A., Burgess, C.C., Cargill, A., Young, T., Maher, E.J. & Ramirez, A.J. 2007. Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer: a multicenter randomized controlled trial. <i>Journal of clinical oncology</i> , 25(5):532-539.
		Wilkinson, S., Aldridge, J., Salmon, I., Cain, E. & Wilson, B. 1999. An evaluation of aromatherapy massage in palliative care. <i>Palliative medicine</i> , 13:409-417.
		Wilcock, A., Manderson, C., Weller, R., Walker, G., Carr, D., Carey, A., Broadhurst, D., Mew, J. & Ernst, E. 2004. Does aromatherapy massage benefit patients with cancer attending a specialist palliative care dae centre? <i>Palliative medicine</i> , 18:287-290.
Yim <i>et al.</i> (2009)	A review of the effects of aromatherapy for patients with depressive symptoms	Soden, K., Vincent, K., Craske, S., Lucas, C. & Ashley, S. 2004. A randomized controlled trial of aromatherapy massage in a hospice setting. <i>Palliative medicine</i> , 18:87-92.
		Wilkinson, S. 1995. Aromatherapy and massage in palliative care. <i>International journal of palliative nursing</i> , 1(1):21-30.
		Hadfield, N. 2001. The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours. <i>International journal of palliative nursing</i> , 7(6):279-285.
Literature reviews		
Filshie (2005)	Complementary Medicine (CM) for cancer pain control	Kite, S.M., Maher, E.J., Anderson, K., Young, T., Young, J., Wood, J., Howells, N. & Bradburn, J. 1998. Development of an aromatherapy service at a cancer centre. <i>Palliative medicine</i> , 12:171-180.
Filshie and Rubens (2006)	Complementary and alternative medicine	Kite, S.M., Maher, E.J., Anderson, K., Young, T., Young, J., Wood, J., Howells, N. & Bradburn, J. 1998. Development of an aromatherapy service at a cancer centre. <i>Palliative medicine</i> , 12:171-180.
		Wilkinson, S. 1995. Aromatherapy and massage in palliative care. <i>International Journal of Palliative Care</i> , 1:21-30.
		De Valois, B. 2001. A retrospective assessment of 3 years of patient audit for an aromatherapy massage service for cancer patients. <i>The international journal of aromatherapy</i> , 11(3):134-142.

Authors and date	Title	Study references
Stefflitch and Steflitch (2008)	Clinical aromatherapy	Wilkinson, S. 1995. Aromatherapy and massage in palliative care. <i>International Journal of Palliative Care</i> , 1:21-30.
		Hadfield, N. 2001. The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours. <i>International journal of palliative nursing</i> , 7(6):279-285.
		Louis, M. & Kowalski, S.D. 2002. Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being. <i>American journal of hospice and palliative care</i> , 19(6):381-386.
Book chapters		
Buckle (2016[a])	Chapter 16: Oncology	Stringer, J. & Donald, G. 2011. Aroma sticks in cancer care: An innovation not to be Sniffed at. <i>Complementary therapies in clinical practice</i> , 17:116-121.
		Graham P, Browne L, Cox H, Graham J. 2003. Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial. <i>Journal of Clinical Oncology</i> . 21(12):2372–2376.
		Chang, S.Y. 2008. Effects of aroma hand massage on pain, state anxiety, and depression in hospice patients with terminal cancer. <i>Journal of Korean academy of nursing</i> , 38(4):493-502.
Buckle (2016[b])	Chapter 9: Nausea and vomiting	Stringer, J. & Donald, G. 2011. Aroma sticks in cancer care: An innovation not to be Sniffed at. <i>Complementary therapies in clinical practice</i> , 17:116-121.
		Tayarani-Najaran, Z., Talasaz-Firoozi, E., Nasiri, R., Jalali, N. & Hassanzadeh, M.K. 2013. Antiemetic activity of volatile oil from Mentha spicata and Mentha x piperita in chemotherapy-induced nausea and vomiting. <i>Ecancermedicalscience</i> , 7:290-295.
Buckle (2016[c])	Chapter 2: How essential oils work	Stringer, J. & Donald, G. 2011. Aroma sticks in cancer care: An innovation not to be Sniffed at. <i>Complementary therapies in clinical practice</i> , 17:116-121.
		Tayarani-Najaran, Z., Talasaz-Firoozi, E., Nasiri, R., Jalali, N. & Hassanzadeh, M.K. 2013. Antiemetic activity of volatile oil from Mentha spicata and Mentha x piperita in chemotherapy-induced nausea and vomiting. <i>Ecancermedicalscience</i> , 7:290-295.
Srivastava and Gupta (2009)	Chapter 8: Health-promoting benefits of Chamomile in the elderly population	Wilcock, A., Manderson, C., Weller, R., Walker, G., Carr, D., Carey, A., Broadhurst, D., Mew, J. & Ernst, E. 2004. Does aromatherapy massage benefit patients with cancer attending a specialist palliative care dae centre? <i>Palliative medicine</i> , 18:287-290.
		Graham P, Browne L, Cox H, Graham J. 2003. Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial. <i>Journal of Clinical Oncology</i> , 21(12):2372–2376.
		Hadfield, N. 2001. The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours. <i>International journal of palliative nursing</i> , 7(6):279-285.
		Soden, K., Vincent, K., Craske, S., Lucas, C. & Ashley, S. 2004. A randomized controlled trial of aromatherapy massage in a hospice setting. <i>Palliative medicine</i> , 18:87-92.

Table 3.4 indicates the findings relevant to this review as extracted from the included academic literature. The type of oil, route and indication as well as a summary of the findings is presented.

Table 3.4: Data extraction of primary academic literature

Authors and date	Title	Essential oil route, type and indication	Relevant findings
Case study			
Cooksley (2003)	An integrative aromatherapy intervention for palliative care.	<u>Topical</u> : Lavender, Roman chamomile, Basil and Indian Frankincense for headaches; Spikenard and Frankincense for mild depression; and Lavender for anxiety. <u>Inhalation</u> : Lavender for stress and mild headaches.	Essential oils helped alleviate symptoms.
Program evaluation / quality improvement			
De Valois (2001)	A retrospective assessment of 3 years of patient audit for an aromatherapy massage service for cancer patients.	<u>Topical</u> (Aromatherapy massage): Lavender, Rosewood, Orange, Sandalwood, Geranium Cyprus and Eucalyptus used for pain, nausea, poor appetite, constipation, insomnia, tension and emotional distress.	All patients reported improvement. The symptoms listed as most improved was tension, emotional distress, insomnia and pain. Transient side-effects were noted, viz. insomnia, dizziness and chronic arthritis aggravation.
Kite <i>et al</i> (1998)	Development of an aromatherapy service at a cancer centre	<u>Topical</u> : (Aromatherapy massage): Rose, Bergamot, Lavender, Chamomile, Juniper, Geranium, and Jasmine for anxiety, nausea depression, and vomiting.	Improvement in symptoms were reported by 50% or more of patients. Stress, anxiety/fear and tension improved the most.
Stringer & Donald (2011)	Aroma sticks in cancer care: An innovation not to be Sniffed at.	<u>Inhalation</u> : Aroma sticks containing a variety of essential oils of which names were not publicised.	77% of all patients reported at least one benefit after aroma stick use. Reduction in anxiety, stress, insomnia and nausea noted specifically.
Mixed method			
Hadfield (2001)	The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours	<u>Topical</u> (Aromatherapy massage): Lavender (six patients) and Roman Chamomile (two patients) for anxiety and depression.	Statistically significant reduction in anxiety (measured by physical parameters). Reduction in anxiety and depression post-treatment, although not statistically significant (measured by HADS). Interviews reflected positive experience of massages.

Authors and date	Title	Essential oil route, type and indication	Relevant findings
Quasi-experimental			
Louis & Kowalski (2002)	Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being	<u>Inhalation</u> : 3% Lavender for anxiety and depression	Small physical and psychological improvements noted after lavender and water inhalation (not statistically significant). Improvement noted after control with no treatment, although not in anxiety and pain.
Randomised controlled trials			
Chang (2008)	Effects of aroma hand massage on pain, state anxiety, and depression in hospice patients with terminal cancer.	<u>Topical</u> (Aromatherapy massage): Bergamot, Lavender and Frankincense in ratio 1:1:1 used for pain, anxiety and depression.	Pain, state anxiety and depression scores decreased for the aromatherapy massage group.
Graham et al (2003)	Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial	<u>Inhalation</u> : Experimental group - Lavender, Bergamot and Cedarwood in the ratio 2:1:1 used for depression and anxiety. Control group 1 – same oil blend in weaker concentrations. Control group 2 – only carrier oil.	All the patients experienced a decrease in their anxiety levels over the course of time. The control group receiving only the carrier oil had the highest drop in anxiety level as measured by HADS. The conclusion was that aromatherapy does not decrease levels of anxiety or depression in patients undergoing radiotherapy.
Kyle (2006)	Evaluating the effectiveness of aromatherapy in reducing levels of anxiety in palliative care patients.	<u>Topical</u> : Aromatherapy massage with Sandalwood or sweet almond oil carrier oil, or aromastone massage for anxiety.	Sandalwood aromatherapy and aromastone massages proved to be most effective in relieving anxiety.
Soden et al (2004)	A randomized controlled trial of aromatherapy massage in a hospice setting	<u>Topical</u> (Aromatherapy massage): 1% Lavender for anxiety, pain, sleep quality, depression, physical and psychological distress, and global life quality.	Both the experimental group and control group receiving massages slept better. Massages led to perceived decreases in anxiety and depression. Aromatherapy massage revealed no advantage over normal massage.

Authors and date	Title	Essential oil route, type and indication	Relevant findings
Tayarani-Najaran <i>et al</i> (2013)	Antiemetic activity of volatile oil from <i>Mentha spicata</i> and <i>Mentha x piperita</i> in chemotherapy-induced nausea and vomiting	<u>Oral</u> : Experimental groups - Spearmint or Peppermint used for nausea and vomiting.	The patients treated with the essential oils had statistically less vomiting episodes the 24 hours after chemotherapy than the placebo group. No difference was found between the two essential oils. No adverse events were noted. The cost of using the essential oils are lower than using the prescribed drugs.
Wilcock <i>et al</i> (2004)	Does aromatherapy massage benefit patients with cancer attending a specialist palliative care centre?	<u>Topical</u> (Aromatherapy massage): Lavender and Chamomile used for general symptoms, vigour, fatigue, tension, anger, confusion and depression.	There was no significant difference between the two groups in quality of life, physical symptoms or mood disturbances. Yet all patients wanted to continue with the aromatherapy after completion of the study due to them experiencing it as overall positive. A rash was reported by one patient as side-effect to the intervention.
Wilkinson <i>et al</i> (1999)	An evaluation of aromatherapy massage in palliative care	<u>Topical</u> (Aromatherapy massage): Group 1 - Roman Chamomile for anxiety, tension, pain and depression. Group 2 - only sweet almond carrier oil.	RSCL showed that aromatherapy group experienced relief in physical and psychological symptoms and increase in quality of life, but deterioration in activity scale. SAI showed improvement for both groups. Massage, whether with or without essential oils improve certain malignancy-related symptoms.
Wilkinson <i>et al</i> (2007)	Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer.	<u>Topical</u> (aromatherapy massage): 20 unidentified oils used for anxiety, nausea and vomiting, and depression.	63% of patients (experimental and control group) had improved anxiety and depression scores 10 weeks post- intervention. The experimental group showed better anxiety and depression relief 6 weeks post-treatment. Aromatherapy showed no advantage over normal supportive care in improvement of global quality of life, sleep, pain, or nausea and vomiting.

3.6 Risk of bias across studies

Possible reporting bias across academic literature was noted in the form of cross-referencing between the same small reference pool of literature available on the topic. This was mitigated by only extracting data from primary sources of data. Furthermore reporting bias was minimized by reporting data both supporting and contradicting the efficacy of essential oils in the treatment of brain malignancy-related symptoms.

3.7 Synthesis of results

Data extracted from different academic literature was grouped according to administration route and will be discussed below:

3.7.1 Topical application

In the case study a registered nurse recorded her holistic treatment of a patient over a three-month period (Cooksley, 2003:128-135). The patient had primary adenocarcinoma of the lung with metastases to the brain and adrenal glands. Different essential oils were used to relieve symptoms as they appeared. The following symptoms, correlating with the symptoms addressed in the current study were mentioned: stress, headaches, mild depression and anxiety. The patient still continued with conventional treatments and the essential oils were used as adjuvant measures. *Lavandula angustifolia* (Lavender), *Anthemis nobilis* (Roman Chamomile), *Ocimum bacilicum* (Basil) and *Boswellia serrata* (Indian Frankincense) were added to calendula-infused olive oil in a 4% dilution ratio and this oil mixture was applied to the temples and the back of the neck for relief of mild headaches. *Lavandula angustifolia* (Lavender) was used in a natural white lotion in 2% dilution and applied to the patient's body as needed to reduce feelings of anxiety.

Mild depression was treated with a sacred anointing oil made from *Nardostachys jatamansi* (Spikenard) and *Boswellia carteri* (Frankincense). This anointing oil was applied to her forehead and the centre of her chest and her feet. This academic literature confirmed the usefulness of essential oils in alleviating these symptoms through anecdotal evidence of perceived effectiveness.

A total number of nine academic literature records were found using aromatherapy massage as administration route of the essential oils. Six of these were randomised-controlled trials (Chang, 2008:493; Kyle, 2006:148; Soden *et al.*, 2004:87; Wilcock *et al.*, 2004:287; Wilkinson *et al.*, 1999:411; and Wilkinson *et al.*, 2007:532), two were under the programme evaluation/quality improvement category (De Valois, 2001:134 and Kite *et al.*, 1998:171), and one used a mixed-method design (Hadfield, 2001:281). Five of the randomized-controlled trials used a control group receiving a massage with only the carrier oil (mostly almond oil) and the intervention group receiving an aromatherapy massage with other essential oils (Chang, 2008:495; Soden *et al.*,

2004:88; Wilcock *et al.*, 2004:287; Wilkinson *et al.*, 1999:411; and Wilkinson *et al.*, 2007:533). Kyle (2006:151) divided the participants into three groups where group A received an aromatherapy massage, group B received a massage with carrier oil (almond oil) and group C received a massage with essential oils with an aromastone. De Valois (2001:145) used carrier oil consisting of half walnut oil and the other half organic sunflower oil and all participants received the carrier oil mixed with essential oils in a 1% dilution ratio.

The most commonly massaged areas were the hands, feet, shoulders, neck and back (Hadfield, 2001:282; Kite *et al.*, 1998:173-174; Kyle, 2006:151; and Wilcock *et al.*, 2004:288). The study done by Soden *et al.* (2004:88) only massaged the back, Chang (2008:493) did hand massages of both hands per session and Wilkinson *et al.*, (1999:411) did a full body massage. De Valois (2001:134-142) and Wilkinson *et al.* (2007:533) did not describe the massage site. The site of the tumour of the patient had an influence on where the massage was done, as the tumour site was generally avoided.

The massage duration differed for the studies and ranged between 15-60 minutes per session. Two studies (Hadfield, 2001:279-285, and Wilkinson *et al.*, 1999:409-417) did not mention the duration of the massage session. Kite *et al.*'s., (1998:176) massage sessions ranged from 15-60 minutes, Chang's (2008:493) and Kyle's (2006:151) massage sessions were 20 minutes, Soden *et al.*'s (2004:88) and Wilcock *et al.*'s (2004:288) massage sessions were 30 minutes, De Valois (2001:135) had massage sessions lasting for 20 minutes to 30 minutes and Wilkinson *et al.*'s. (2007:533) massage sessions lasted 60 minutes.

The studies ranged from a once-off session (Hadfield, 2001:282) to six weeks of sessions (Kite *et al.*, 1998:173). De Valois (2001:134) conducted the study over a three-year period with different participants over the years and participants could receive four or more sessions per week. Most studies were done during a four-week period where the participants received one massage per week (Kyle, 2006:151; Soden *et al.*, 2004:88; Wilcock *et al.*, 2004:288 and Wilkinson *et al.*, 2007:533). Wilkinson *et al.* (1999:411) offered three sessions, roughly divided as one session per week. Chang (2008:493) presented the only study in which participants received one massage session per day for a week.

The symptoms assessed by these academic literature that were applicable to this systematic review is anxiety, depression and nausea/vomiting (Kite *et al.*, 1998:173-174 and Wilkinson *et al.*, 2007:533), only anxiety (Kyle, 2006:153-155), only depression (Wilcock *et al.*, 2004:287-288), emotional distress such as anxiety, nausea and headaches (De Valois, 2001:134-135). Most academic literature examined both anxiety and depression (Chang, 2008:493; Hadfield, 2001:282; Soden *et al.*, 2004:88; Wilkinson *et al.*, 1999:411). To measure these symptoms the HADS scale was mostly used (Hadfield, 2001:282; Kite *et al.*, 1998:173-174 and Soden *et al.*, 2004:88) or SAI tool (Chang, 2008:495-496; Wilkinson *et al.*, 1999:411; and Wilkinson *et al.*, 2007:533). Other tools used was VAS (Kyle, 2006:152), RSCL (Soden *et al.*, 2004:88), CES-D, EORTC (Wilkinson *et al.*, 2007:533), MYMOP and POMS (Wilcock *et al.*, 2004:287-288).

A number of different essential oils were used. Kite *et al.* (1998:176) and Wilkinson *et al.* (2007:533) only mention 20 different essential oils that were used and do not state the specific oils used. Kite *et al.* (1998:176) list a few of the oils used as Rose, Bergamot, Lavender, Chamomile, Juniper, Geranium and Jasmine and also mention that some participants used different oils for each session consisting of a mixture of 2-4 essential oils. De Valois (2001:135-136) also used numerous oils and the participants could choose from the following oils: *Lavandula angustifolia* (Lavender), *Aniba rosaeodora* (Rosewood), *Citrus sinensis* (Orange), *Santalum album* (Indian Sandalwood), *Pelargonium graveolens* (Geranium), *Cupresses sempervirens* (Mediterranean cypress) and *Eucalyptus globulus* (Eucalyptus) with the assistance of an aromatherapist. Most people chose Lavender or Rosewood and people with breathing difficulties preferred Eucalyptus. Cypress and Geranium were the least chosen oils. The oils used by the other records were Sandalwood (Kyle, 2006:151), Lavender (Soden *et al.*, 2004:88), Roman Chamomile (Wilkinson *et al.*, 1999:411), Lavender and Roman Chamomile (Hadfield, 2001:282, Wilcock *et al.*, 2004:288), and Lavender, Frankincense and Bergamot (Chang, 2008:493). Lavender was the most used oil for topical application, with Roman chamomile second most used.

Two randomised controlled trials (Soden *et al.*, 2004:89-91 and Wilcock *et al.*, 2004:288-290) had the same results for the control and intervention group, yet all patients in Wilcock *et al.* (2004:289) wanted to continue with the aromatherapy massage as the patients reported they experienced it as positive. All other academic

literature (Chang, 2008:493; de Valois, 2001:136-142; Hadfield, 2001:282-285; Kite *et al.*, 1998:176; Kyle, 2006:153-155; Wilkinson *et al.*, 1999:412-416; and Wilkinson *et al.*, 2007:534-538;) showed an improvement in the symptoms examined for the intervention groups receiving aromatherapy massage. Wilkinson *et al.* (2007:534-538) found that both groups had the same score for improvement at ten weeks after the intervention although at six weeks after the intervention the aromatherapy group showed more improvement in their symptoms. Wilkinson *et al.* (1999:412-416) showed an improvement on the RSCL scale where the aromatherapy massage group showed more improvement and on the SAI scale though both groups had the same improvement. According to Kite *et al.* (1998:176) half of the participants (no control group, all received aromatherapy massage) listed improvements in their symptoms of which anxiety was one of the symptoms most listed as improved.

3.7.2 Oral intake

One randomised controlled trial (Tayarani-Najaran *et al.*, 2013:291-295) was done on chemotherapy-induced nausea. This study used two drops *Mentha spicata* (Spearmint) or *Mentha x piperitaone* (Peppermint) essential oil taken orally in capsules. The capsules were prepared by adding two drops of the essential oil to sugar and putting it in the capsule. The capsules with the two drops of essential oils of either *Mentha spicata* (Spearmint) or *Mentha x piperitaone* (Peppermint) were given 30 minutes before chemotherapy and at four-hour intervals twice after the chemotherapy. The patients were divided into four groups with 50 patients each – one group as control, one group receiving a placebo, one group receiving a capsule with two drops *Mentha spicata* (Spearmint) essential oil and one group receiving a capsule with two drops *Mentha x piperitaone* (Peppermint) essential oil. The patients treated with the capsules with the two drops of essential oils of either *Mentha spicata* (Spearmint) or *Mentha x piperitaone* (Peppermint) experienced statistically significantly fewer vomiting episodes in the 24 hours following their chemotherapy session than the placebo or control group. There was no statistical difference noted between the two different essential oils and no adverse events were reported. An added positive note by the author was that the cost of using the essential oils are lower than using prescribed antiemetic drugs.

3.7.3 Inhalation administration

Four academic literature records used the inhalation of essential oils as administration route. Stringer and Donald (2001:116) conducted a programme evaluation/quality improvement and Louis and Kowalski (2002:383) conducted a quasi-experimental design study. Another was the case study of Cooksley (2003:128-135) and lastly Graham *et al.* (2003:2372) who did a randomized-controlled trial. In Stringer and Donald (2001:117) aroma sticks were used and in Louis and Kowalski (2002:383) humidified inhalation of the essential oil was used. Cooksley (2003:130,133) used numerous inhalation methods such as applying the essential oil to tissue paper or the patient's gown or creating a spritzer to spray into the air for inhalation and Graham *et al.* (2003:2373) had patients wear a necklace with a plastic and paper bib (similar to a dentist office bib) onto which the essential oils and carrier oils were added. The aroma sticks were used for numerous symptoms and symptoms relevant to this study for depression, nausea and anxiety. The humidified inhalation of the essential oil and the bibs applications were applied for the symptoms of depression and anxiety. Cooksley (2003:130,133) confirms the use of inhaled essential oils for stress, while adding headaches to symptoms treated via this administration route.

Stringer and Donald (2001:117) are vague about which 20 essential oils were used in the study. One hundred and sixty cancer patients who wanted to try the use of aroma sticks for their symptoms received various essential oil-infused aroma sticks. The participants could use the aroma sticks as often as needed and used them by smelling the aromastick. Louis and Kowalski (2002:383) used Lavender essential oil in a dilution of 3% (50cc of water with 30 drops of Lavender essential oil was used to humidify the room for 60 minutes). As control, no intervention was implemented on the first post-chemotherapy day, while humidified water was used for 60 minutes on the second day and the third day was seen as the test day where the above-mentioned essential oil humidification was applied. In Cooksley (2003:130,133) *Lavandula angustifolia* (Lavender) was placed on the patient's gown and facial tissues for inhalation in treatment of stress during scans. A lavender hydrosol mist was also sprayed to inhale and used as needed for headaches. Graham *et al.* (2003:2372-2373) used essential oils of Lavender, Bergamot and Cedarwood in a ratio of 2:1:1. Three drops of the essential oil mixture were applied to a plastic-paper bib which the patient wore as a necklace. The second group received the same oils but diluted with one part of essential oil blend to

two parts carrier oil. The carrier oil was sweet almond oil. The third group only received sweet almond oil.

Stringer and Donald (2001:117-120) measured the symptoms with a checklist to firstly identify the symptoms present in the patient, and then to evaluate the results one week later, indicating which symptoms had improved and how often the aroma stick had been used. Louis and Kowalski (2002:383-384) measured the patients' vital signs, and had a 11-point scale on which to measure depression and anxiety. The Lavender humidified water showed improvement in the symptoms of the patients and most patients continued using this humidification method. Contrary to previous recorded results, Graham *et al.* (2003:2373-2374) disagreed with the findings from the above mentioned studies using inhalation of essential oils as route of administration, as the experimental group did not exhibit greater symptom relief, thus the conclusion was that aromatherapy does not decrease levels of anxiety or depression in patients undergoing radiotherapy.

3.7.4 Side-effects

Only two of the included academic literature records noted side-effects. De Valois (2001:141) noted side-effects in three participants which were transient in nature. One participant experienced increased difficulty in sleeping, and one participant with chronic arthritis had increased bodily pains after the aromatherapy massage. The other participant felt uneasy on her feet, couldn't concentrate properly and felt unwell after the aromatherapy massage sessions. Lastly, Wilcock *et al.* (2004:289) noted a rash in one of the participants.

In table 3.5 a summary of above-mentioned information is provided. The essential oils used, the route of administration and the specific symptoms targeted are presented.

Table 3.5 Summary of essential oils used for specific brain malignancy-related symptoms

Symptom	Essential oils used to alleviate the symptom	Route of administration of oil
Stress	Lavender	Inhalation through application on clothes or tissue
Headaches	Mixture of calendula infused olive oil in 4% dilution of Lavender, Roman Chamomile, Basil, and Indian Frankincense	Topical application on temples and back of neck
	Lavender hydrosol	Used as a mist to spray in the room and inhale
Depression	Spikenard and Frankincense in an oil basis	Topical application on the forehead, middle of the chest and feet
	Lavender essential oil in a dilution of 3% (50cc of water with 30 drops of Lavender essential oil)	Inhalation through humidifying the water with oil for 60 minutes into the room
	1% Lavender and Roman Chamomile essential oil in a sweet almond carrier oil.	Back, neck, shoulders or hand massage (once a week for 30 minutes)
Anxiety	2% Lavender essential oil in a lotion	Topical application on the body
	Sandalwood 1% in sweet almond carrier oil	Leg and foot massage (once a week for 20 minutes)
	Lavender, Rosewood, Orange, Indian Sandalwood, Geranium, Mediterranean cypress, and Eucalyptus essential oils in a 1% dilution with a carrier oil consisting of half walnut oil and half organic sunflower oil.	Massage to parts of body for 20 to 30 minutes for four or more sessions per week.
Anxiety and depression	Lavender or Roman Chamomile	Shoulder, neck or foot massage
	1% lavender essential oil mixed in carrier oil of sweet almond oil	Back massage (once a week for 30 minutes)
	Roman Chamomile	Full body massage
	1,5% dilution Bergamot, Lavender and Frankincense in a ratio 1:1:1 used in 50ml carrier oil.	Hand massage (every day for 10 minutes per hand)
	Rose, bergamot, lavender, chamomile. juniper, geranium, and jasmine essential oils	Massage of hands, feet, face, legs, scalp, arms, neck, or shoulders (once per week for 15-60 minutes)
Nausea and vomiting	Spearmint or Peppermint essential oil	Capsules with two drops essential oil of either spearmint or peppermint in a capsule given 30 minutes before chemotherapy and then in four hour intervals after chemotherapy until three doses in total had been given

3.8 Development of leaflet

A patient information leaflet was developed to assist nursing personnel in giving patient education regarding the use of essential oils (type and route) for brain malignancy related symptoms, including headache, nausea and vomiting, depression and anxiety. This leaflet will be printed front and back on an A5 flyer (figures 3.2 and 3.3).


	<p>Essential oils (EO) are extracts taken out of plants with the essence of the plant still in it. This essence is seen as the life of the plants (Stewart, 2012:xv-xvi).⁸</p> <p>Different types of carrier oils are used as preferred by the researchers who conducted the studies (see heading: further reading). Carrier oils are used to dilute the essential oils in to create a specified dilution as mentioned for each application procedure.</p>	<p>*Mix Lavender, Roman Chamomile, Basil and Frankincense (<i>Boswellia Serrata</i>) EO in a 4% dilution (4 drops EO in each 5ml of carrier oil) of calendula infused olive oil. Apply topically to temples and back of neck for relief.²</p> <p>*Put Lavender EO hydrosol in a spray bottle and spray a mist in the room to inhale for relief from mild headaches.²</p>	<p>Two drops Spearmint or Peppermint EO put in a capsule with guidance of a qualified aromatherapist and given 30 minutes before chemotherapy and then in four hour intervals after chemotherapy until three doses in total have been given.⁹</p>
	What are essential oils?	Headache	Nausea / Vomiting
	<h2>USING ESSENTIAL OILS (EO) TO IMPROVE YOUR BRAIN MALIGNANCY-RELATED SYMPTOMS</h2>		
	<p>*Mix Sandalwood EO in a 1% dilution (1 drop EO in each 5ml of carrier oil) of sweet almond oil. Massage oil onto legs and feet once a week for 20 minutes.⁶</p> <p>*Apply a few drops of Lavender EO on clothes or on a tissue paper to keep nearby during stressful times. Mix Lavender EO and a body cream in a 2% dilution (20 drops EO in 50ml cream). Apply to body when anxious.²</p>	<p>*Massage any body part for 20-30 minutes per day for four or more days per week with an essential oil mix of Lavender, Rosewood, Orange, Sandalwood, Geranium, Mediterranean cypress, or Eucalyptus in a 1% dilution (1drop of desired EO in each 5ml of carrier oil) of Walnut and Sunflower carrier oil.³</p>	<p>*Mix Lavender, Roman Chamomile, Rose, Bergamot, Juniper, Geranium, and Jasmine EO in a 1% dilution (1 drop EO in each 5ml of carrier oil) of sweet Almond carrier oil. Massage hands, feet, face, legs, scalp, arms, neck, back, full body or shoulders for 15-60 minutes per week.^{5,10}</p>
	Anxiety	Depression and Anxiety	

Figure 3.2 Front of leaflet


	<p>*1,5% dilution (15 drops EO in 50ml of carrier oil) of Bergamot, Lavender and Frankincense EO in a ratio 1:1:1 used in 50ml carrier oil. Hand massage (every day for 10 minutes per hand).¹</p>	<p>*Lavender (EO) in a dilution of 3% (30 drops EO in 50ml water). Inhalation through humidifying the water with the oil for 60 minutes into the room.⁷</p> <p>*Mix Spikenard and Frankincense EO in a carrier oil basis. Apply topically to forehead, middle of the chest and feet when feeling depressed.²</p>	<p>*Mix Lavender and Roman Chamomile in a 1% dilution (1 drop EO in each 5ml of carrier oil) of sweet Almond carrier oil. Massage back, neck, shoulders or hands once a week for 30 minutes.⁴</p>
	Depression and Anxiety	Depression	
	<p>This patient information leaflet was compiled from the following dissertation: “The use of essential oils in relieving symptoms specific to brain malignancies: A systematic review” done by M Durr. You can contact the researcher directly if more information is required at e-mail: maridv92@gmail.com</p>		
	<p>After an aromatherapy massage you might experience insomnia, a feeling of light headedness, and an increase in general chronic arthritis pains, though these side-effects should dissipate quickly.³</p> <p>A rash following aromatherapy massage is a rare side-effect.¹¹</p>	<ol style="list-style-type: none">1. Chang, S.Y. 2008. Effects of aroma hand massage on pain, state anxiety, and depression in hospice patients with terminal cancer. <i>J Korean Acad Nurs</i>, 38(4):493-502.2. Cooksley, V. 2003. An integrative aromatherapy intervention for palliative care. <i>Int J Aromather</i>, 13(2/3):128-137.3. De Valois, B. 2001. A retrospective assessment of 3 years of patient audit for an aromatherapy massage service for cancer patients. <i>Int J Aromather</i>, 11(3):134-142.4. Hadfield, N. 2001. The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours. <i>Int J Palliat Nurs</i>, 7(6):279-285.5. Kite, S.M., Maher, E.J., Anderson, K., Young, T., Young, J., Wood, J., Howells, N. & Bradburn, J. 1998. Development of an aromatherapy service at a cancer centre. <i>Palliat Med</i>, 12:171-180.6. Kyle, G. 2006. Evaluating the effectiveness of aromatherapy in reducing levels of anxiety in palliative care patients: results of a pilot study. <i>Complement Ther Med</i>, 12:148-155.	<ol style="list-style-type: none">7. Louis, M. & Kowalski, S.D. 2002. Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being. <i>Am J Hosp Palliat Med</i>, 19(6):381-386.8. Stewart, D. 2012. Healing oils of the bible. 1st ed. Marble Hill, Missouri: Care publications.9. Tavarani-Najaran, Z., Talasaz-Firoozi, E., Nasiri, R., Jalali, N. & Hassanzadeh, M.K. 2013. Antiemetic activity of volatile oil from <i>Mentha spicata</i> and <i>Mentha x piperita</i> in chemotherapy-induced nausea and vomiting. <i>Ecancermedicallscience</i>, 7:290-295.10. Wilkinson, S., Aldridge, J., Salmon, I., Cain, E. & Wilson, B. 1999. An evaluation of aromatherapy massage in palliative care. <i>Palliat med</i>, 13:409-417.11. Wilcock, A., Manderson, C., Weller, R., Walker, G., Carr, D., Carey, A., Broadhurst, D., Mew, J. & Ernst, E. 2004. Does aromatherapy massage benefit patients with cancer attending a specialist palliative care centre? <i>Palliat med</i>, 18:287-290.
Side-effects	Further reading		

Figure 3.3 Back of leaflet

3.9 Limitations of included literature

A number of limitations as briefly mentioned table 3.2 merit further elaboration in unbiased reporting of results:

- A number of the academic literature sources revealed high attrition rates due to the patients being either too sick to continue or dying. This led to academic literature with small sample sizes and even studies not obtaining their determined number of participants. Thus long term research on the population group of people with brain malignancies is difficult to attain and most research is only done on short duration. Yet the academic literature with small sample sizes also showed the value of the usage of essential oils for symptom relief correlating with the results of studies with adequate sample sizes. For this reason, inclusion in this review was considered applicable.
- Some of the academic literature sources were vague on which oils were used. Although attempts were made to contact researchers to address this vagueness, no response were received. However, the overall theme of support in the use of essential oils for brain malignancy-related symptoms was confirmed by these studies and therefore important for inclusion in this review.
- The dilution ratio and how often essential oils were used were not mentioned in all the included academic literature. These administration factors are also deemed important to report as it could influence effectively of administrated oils on specific symptoms. However, even in the low dosages reported in these literature sources, confirmation for the use of essential oils in treatment of some of the mentioned symptoms could be derived, thus supporting this study's findings.

Although several literature limitations were noted, none of these limitations appeared to have seriously impeded the results of this review.

3.10 Conclusion

Essential oils were found to be useful in alleviating brain-malignancy related symptoms (such as stress, headaches, anxiety, depression, nausea and vomiting). Different routes of administration were used, including inhalation, topical application, and oral intake. Lavender essential oil was applied to relieve symptoms of stress, anxiety, depression, and headaches. Spearmint or peppermint essential oil assisted to alleviate nausea

arising from chemotherapy. Roman Chamomile, Basil, and Indian Frankincense (*Boswellia Serrata*) were shown to be useful for relief for headaches. Lastly anxiety and depression were improved by use of Spikenard, Frankincense, Lavender, Sandalwood, Roman Chamomile, Rose, Bergamot, Lavender, Chamomile, Juniper, Geranium, and Jasmine essential oils.

CHAPTER 4 CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

4.1 Introduction

In this chapter the main focus will be on recommendations and limitations as derived from the systematic review. It will be presented with regards to the included academic literature and also observations made by the researcher, based on an evaluation of the study.

4.2 Evaluation of the study

The main aim of this study was to provide a summary of the best available evidence regarding the use of essential oils to relief specific brain malignancy-related symptoms (such as headaches, seizures, increased intra-cranial pressure, vomiting/nausea, depression and anxiety) and to design a patient information leaflet containing the findings of the study. The following objectives were identified to reach the abovementioned aim:

- To review the evidence regarding which essential oils can be used and the route of administration of these oils to relieve specific brain malignancy-related symptoms such as headaches, seizures, increased intra cranial pressure, vomiting/nausea, depression and anxiety.
- To design a patient information leaflet with the findings of the study.

Although evidence retrieved could not be seen as strong (most included literature had small samples and limited control over variables), a summary was provided of some of the symptoms of brain malignancies. Literature pertaining to all the symptoms could not be found. Seizures and Intracranial pressure could not be addressed due to an absence of literature on the usage of essential oils in the alleviation of these symptoms in brain malignancy patients. The academic literature on headaches and vomiting/nausea was limited and most literature pertained to depression and anxiety.

There was enough information found to compile a patient information leaflet. The information focussed on headaches, vomiting/nausea and depression/anxiety and the essential oils which could be used to alleviate these symptoms effectively. There was

also enough information gathered to inform the patient on how to use the essential oils to alleviate their symptoms.

From the information gathered from the literature, nursing personnel can educate patients on how to use the essential oils and which essential oils to use to alleviate specific symptoms. From this education patients will be able to make more informed decisions regarding the alleviation of their symptoms.

4.3 Summary of evidence

In this systematic review it was found that essential oils could be used to help alleviate specific brain-malignancy related symptoms. The essential oils were administered by different routes (inhalation, topical application and oral intake) to reach the desired outcomes (alleviation of stress, headaches, anxiety, depression, nausea and vomiting). The most common route of administration was through aromatherapy massage (topical application) for symptoms of depression and anxiety. The oils used differed in the studies (Lavender, Spearmint, Peppermint, Roman Chamomile, Basil, Indian Frankincense, Spikenard, Frankincense, Lavender, Sandalwood, Roman Chamomile, Rose, Bergamot, Lavender, Chamomile, Juniper, Geranium, and Jasmine essential oils) and the essential oil of Lavender was most commonly used.

Thus the main aim was achieved by implementing two set objectives. Though certain limitations of the study need to be considered, recommendations for nursing practice, nursing research, nursing education and policy could be derived.

4.4 Limitations

- This review mostly includes academic literature with small sample sizes, which influenced the results of this study, as small sample sizes influenced the critical appraisal scores negatively and also could have led to unclear or unreliable results. Yet, as comparative literature to support the use of specific essential oils were often found across included literature, this triangulation between sources again mitigated this limitation.
- Although this review was focused on the use of essential oils via any administration route, most included literature evaluated aromatherapy massage versus massage without aromatherapy. Massage on its own could also be seen as an intervention

and thus does not necessarily give a definite result of the usage of the aromatherapy for symptoms other than anxiety and depression. More academic literature is needed in the field of the usage of essential oils for symptom relief for patients with brain malignancies which is more focussed on establishing the value of the oils on their own and not in combination with another intervention. However, some academic literature had a control group receiving massage without aromatherapy where aromatherapy massage revealed an advantage over normal massage in improving symptoms, thus showing that aromatherapy is effective even when combined with another intervention such as massage.

- Vague included literature (treatment process not properly described such as essential oils used not mentioned) could have influenced the specificity of outcomes, as these vagueness led to assumptions regarding which oils were used, on the bases of oils often used in other sources. However, the general theme that essential oils might be beneficial in the treatment of brain malignancy-related symptoms was confirmed.
- A small range of academic literature records was collected and included ten secondary sources which referenced the same primary sources. This leads to little data being available, and reusing of the same data repeatedly through different studies. Even though the data were limited most academic literature agreed that essential oils did help to alleviate symptoms. This was supported by the unique primary studies.

4.5 Recommendations

4.5.1 Recommendations for nursing practice

The usage of essential oils is more specific to the practice of aromatherapy than nursing, yet it is important for nursing practitioners working with cancer patients to have knowledge in this field. In nursing practice, nursing practitioners have to educate patients with regard to their treatment options. Symptoms are a burden to many patients and nursing practitioners have to educate patients on how to help alleviate these symptoms. Essential oils as found by this study have a great role to play in this alleviation of symptoms.

As seen in one of the academic literature records (Stringer and Donald, 2001:116-117), the essential oils were accessible in the hospital to the patients with help from the nursing personnel. This could be a great addition to any hospital for the nursing personnel to be trained in the usage of predetermined essential oils for the alleviation of symptoms in their patients, specifically in the speciality of oncology as traditional pharmaceutical treatments might be ineffective or contradicted.

4.5.2 Recommendations for nursing research

Most academic literature included aromatherapy massage. Massage on its own could also be seen as an intervention and thus it is argued that it does not give a clear result of the workings of the essential oils. The academic literature used only a number of essential oils out of the many available essential oils. The academic literature included patients suffering from a variety of malignancies, and not much academic literature was focused on people with brain-malignancies as their primary concern. There was no information found on the usage of essential oils for the relief of seizures or increased Intra-cranial pressure which is normally one of the main concerns of people with brain malignancies. The academic literature also focussed mainly on depression and anxiety and not on all the other symptoms experienced by people with brain-malignancies such as headaches. The dosages presented in the academic literature were low as most interventions were only carried out once a week. The following recommendations for nursing research emanate from this:

- As limited research on the topic could be found, and mostly being of lower research evidence levels, more high-evidence level research such as randomized controlled trials should be applied to the use of essential oils in the treatment of brain malignancy-related symptoms which is a vulnerable group of people;
- More research is needed specifically focused on how to use essential oils to alleviate brain malignancy-related symptoms and not cancer symptoms in general;
- The research has to focus on the specific symptoms experienced by this population group and how to use essential oils to help alleviate these symptoms and not only depression and anxiety;
- More research is also needed with regards to which essential oils work, as Lavender essential oil was mostly used and there are numerous more essential oils which

could help to alleviate these symptoms and could even be more effective than Lavender essential oil to treat certain symptoms;

- More research is needed with regards to which dosages of the essential oils are most effective so that the essential oils could work to their full potential.
- More research is needed with regards to the usage of essential oils for increased Intracranial pressure and also seizures as these are symptoms which people with brain-malignancies experience regularly.
- More research regarding the use of essential oils is necessary on human participants as the mechanisms of working will be different in humans as compared to laboratories or animals; and
- More research is also needed using a different route of administration other than aromatherapy massage to examine the working of the essential oils alone.

4.5.3 Recommendations for nursing education

As nurses are involved in the holistic care of patients, they need to be prepared for caring for oncology patients who might need alternative treatment options for malignancy related symptoms. Therefore the following recommendations for nursing education are proposed:

- Nursing practitioners have to increase their knowledge with regards to the usage of essential oils to alleviate brain malignancy-related symptoms. As many cancers spread to the brain and cancer statistics are on the rise, more and more nursing practitioners will have to care for cancer patients with primary brain-malignancies or metastases of the brain;
- Nursing practitioners have to know how to use the essential oils safely with regards to dosage, route and which oils are safe for the individual patient. This is necessary for nursing practitioners to be able to care for their patients in a holistic manner. It is also important to know about the essential oils so that better patient education could be given; and
- Nursing personnel working with patients who are burdened with symptoms such as in oncology wards could receive training in essential oil usage for symptom relief. This would improve the nurse-patient relationship as nursing personnel would have to spend more time with the patients to educate them on how to use the essential

oils. Further the nurses could also be educated themselves with regards to the usage of essential oils to relieve symptoms in patients.

4.5.4 Recommendations for policy

Policies are important for the effective implementation of treatment given by nursing personnel to patients. The usage of essential oils for relief of brain-malignancy related symptoms has to be incorporated into policies so that proper guidance will be available to nursing practitioners. The following recommendations for policies have been formulated:

- Policies have to be created to inform the health science of nursing with regards to the usage of essential oils in practice as to what is applicable and what not in nursing practice. This could be incorporated in standing orders for symptoms such as anxiety or nausea;
- Hospitals also have to draw up policies and guidelines as how and which oils may be used and for which symptoms in the wards. This will improve the patient education given by the nursing personnel as well as the care;
- Policies with regards to the scope of practice for nursing practitioners having knowledge and qualifications in the aromatherapy field as to how the nursing personnel can incorporate their aromatherapy knowledge into the day-to-day care of patients should be developed;
- Hospitals could implement policies to allow aroma therapists to administer aromatherapy to patients for symptom relief and also to introduce nursing personnel to aromatherapy; and
- Lastly hospitals could develop policies to allow aroma therapists to work hours specific to oncology wards to administer aromatherapy to patients. This will also increase the number of nursing personnel who could study aromatherapy as they would be able to work as nursing personnel and aromatherapists.

4.6 Conclusion

Through this systematic review literature was gathered on the usage of essential oils to relieve specific brain malignancy-related symptoms (such as headaches, seizures, increased Intracranial pressure, vomiting/nausea, depression and anxiety). The oils were administered through topical application, oral intake, aromatherapy massage or

inhalation. Aromatherapy was mostly used and secondly different inhalation methods were used. The essential oils were found to be useful to relieve specific brain malignancy-related symptoms such as headaches, vomiting/nausea, depression and anxiety. The essential oils which were used to improve these symptoms were Lavender, Spearmint or Peppermint, Roman Chamomile, Basil, Indian Frankincense, Spikenard, Sandalwood, Rose, Bergamot, Juniper, Geranium and Jasmine. From this systematic review it was concluded that essential oils could be used to relieve certain brain-malignancy related symptoms.

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ADDENDUM A: JOHNS HOPKINS RESEARCH EVIDENCE APPRAISAL TOOL

Johns Hopkins Nursing Evidence-Based Practice Appendix E: Research Evidence Appraisal Tool

Evidence Level and Quality: _____

Article Title:		Number:	
Author(s):		Publication Date:	
Journal:			
Setting:		Sample (Composition & size):	
Does this evidence address my EBP question?	<input type="checkbox"/> Yes	<input type="checkbox"/> No Do not proceed with appraisal of this evidence	
Level of Evidence (Study Design)			
<p>A. Is this a report of a single research study? <i>If No, go to B.</i></p> <p>1. Was there an intervention?</p> <p>2. Was there a control group?</p> <p>3. Were study participants randomly assigned to the intervention and control groups?</p>		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No
<p>If Yes to all three, this is a Randomized Controlled Trial (RCT) or Experimental Study →</p>		<input type="checkbox"/> LEVEL I	
<p>If Yes to #1 and #2 and No to #3, OR Yes to #1 and No to #2 and #3, this is Quasi Experimental (some degree of investigator control, some manipulation of an independent variable, lacks random assignment to groups, may have a control group) →</p>		<input type="checkbox"/> LEVEL II	
<p>If Yes to #1 only, OR No to #1, #2, and #3, this is Non-Experimental (no manipulation of independent variable, can be descriptive, comparative, or correlational, often uses secondary data) or Qualitative (exploratory in nature such as interviews or focus groups, a starting point for studies for which little research currently exists, has small sample sizes, may use results to design empirical studies) →</p>		<input type="checkbox"/> LEVEL III	
<p>NEXT, COMPLETE THE BOTTOM SECTION ON THE FOLLOWING PAGE, "STUDY FINDINGS THAT HELP YOU ANSWER THE EBP QUESTION"</p>			

**Johns Hopkins Nursing Evidence-Based Practice
Appendix E: Research Evidence Appraisal Tool**

<p>B. Is this a summary of multiple research studies? <i>If No, go to Non-Research Evidence Appraisal Form.</i></p> <p>1. Does it employ a comprehensive search strategy and rigorous appraisal method (Systematic Review)? <i>If No, use Non-Research Evidence Appraisal Tool; if Yes:</i></p> <p>a. Does it combine and analyze results from the studies to generate a new statistic (effect size)? (Systematic review with meta-analysis)</p> <p>b. Does it analyze and synthesize concepts from qualitative studies? (Systematic review with meta-synthesis)</p> <p><i>If Yes to either a or b, go to #2B below.</i></p> <p>2. For Systematic Reviews and Systematic Reviews with meta-analysis or meta-synthesis:</p> <p>a. Are all studies included RCTs? →</p> <p>b. Are the studies a combination of RCTs and quasi-experimental or quasi-experimental only? →</p> <p>c. Are the studies a combination of RCTs, quasi-experimental and non-experimental or non-experimental only? →</p> <p>d. Are any or all of the included studies qualitative? →</p> <p>COMPLETE THE NEXT SECTION, "STUDY FINDINGS THAT HELP YOU ANSWER THE EBP QUESTION"</p>	<p>→ <input type="checkbox"/> LEVEL I</p> <p>→ <input type="checkbox"/> LEVEL II</p> <p>→ <input type="checkbox"/> LEVEL III</p> <p>→ <input type="checkbox"/> LEVEL III</p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>	<p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p> <p><input type="checkbox"/>Yes <input type="checkbox"/>No</p>
<p>STUDY FINDINGS THAT HELP YOU ANSWER THE EBP QUESTION:</p>			

NOW COMPLETE THE FOLLOWING PAGE, "QUALITY APPRAISAL OF RESEARCH STUDIES", AND ASSIGN A QUALITY SCORE TO YOUR ARTICLE

**Johns Hopkins Nursing Evidence-Based Practice
Appendix E: Research Evidence Appraisal Tool**

Quality Appraisal of Research Studies					
<ul style="list-style-type: none"> • Does the researcher identify what is known and not known about the problem and how the study will address any gaps in knowledge? • Was the purpose of the study clearly presented? • Was the literature review current (most sources within last 5 years or classic)? • Was sample size sufficient based on study design and rationale? • If there is a control group: <ul style="list-style-type: none"> ◦ Were the characteristics and/or demographics similar in both the control and intervention groups? ◦ If multiple settings were used, were the settings similar? ◦ Were all groups equally treated except for the intervention group(s)? • Are data collection methods described clearly? • Were the instruments reliable (Cronbach's α [alpha] ≥ 0.70)? • Was instrument validity discussed? • If surveys/questionnaires were used, was the response rate $\geq 25\%$? • Were the results presented clearly? • If tables were presented, was the narrative consistent with the table content? • Were study limitations identified and addressed? • Were conclusions based on results? 	<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No			
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ADDENDUM B: JOHNS HOPKINS NON-RESEARCH EVIDENCE APPRAISAL TOOL

Johns Hopkins Nursing Evidence-Based Practice Appendix F: Non-Research Evidence Appraisal Tool

Evidence Level & Quality: _____

Article Title:		Number:	
Author(s):		Publication Date:	
Journal:			
Does this evidence address the EBP question?	<input type="checkbox"/> Yes	<input type="checkbox"/> No Do not proceed with appraisal of this evidence	
<input type="checkbox"/> Clinical Practice Guidelines: Systematically developed recommendations from nationally recognized experts based on research evidence or expert consensus panel. LEVEL IV			
<input type="checkbox"/> Consensus or Position Statement: Systematically developed recommendations based on research and nationally recognized expert opinion that guides members of a professional organization in decision-making for an issue of concern. LEVEL IV			
<ul style="list-style-type: none"> • Are the types of evidence included identified? • Were appropriate stakeholders involved in the development of recommendations? • Are groups to which recommendations apply and do not apply clearly stated? • Have potential biases been eliminated? • Were recommendations valid (reproducible search, expert consensus, independent review, current, and level of supporting evidence identified for each recommendation)? • Were the recommendations supported by evidence? • Are recommendations clear? 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No
<input type="checkbox"/> Literature Review: Summary of published literature without systematic appraisal of evidence quality or strength. LEVEL V			
<ul style="list-style-type: none"> • Is subject matter to be reviewed clearly stated? • Is relevant, up-to-date literature included in the review (most sources within last 5 years or classic)? • Is there a meaningful analysis of the conclusions in the literature? • Are gaps in the literature identified? • Are recommendations made for future practice or study? 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No
<input type="checkbox"/> Expert Opinion: Opinion of one or more individuals based on clinical expertise. LEVEL V			
<ul style="list-style-type: none"> • Has the individual published or presented on the topic? • Is author's opinion based on scientific evidence? • Is the author's opinion clearly stated? • Are potential biases acknowledged? 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No

Johns Hopkins Nursing Evidence-Based Practice Appendix F: Non-Research Evidence Appraisal Tool

Organizational Experience:			
<input type="checkbox"/> Quality Improvement: Cyclical method to examine organization-specific processes at the local level. LEVEL V			
<input type="checkbox"/> Financial Evaluation: Economic evaluation that applies analytic techniques to identify, measure, and compare the cost and outcomes of two or more alternative programs or interventions. LEVEL V			
<input type="checkbox"/> Program Evaluation: Systematic assessment of the processes and/or outcomes of a program and can involve both quantitative and qualitative methods. LEVEL V			
Setting:		Sample (composition/size):	
<ul style="list-style-type: none"> Was the aim of the project clearly stated? Was the method adequately described? Were process or outcome measures identified? Were results adequately described? Was interpretation clear and appropriate? Are components of cost/benefit analysis described? 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> N/A
<input type="checkbox"/> Case Report: In-depth look at a person, group, or other social unit. LEVEL V			
<ul style="list-style-type: none"> Is the purpose of the case report clearly stated? Is the case report clearly presented? Are the findings of the case report supported by relevant theory or research? Are the recommendations clearly stated and linked to the findings? 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> No
Community Standard, Clinician Experience, or Consumer Preference			
<input type="checkbox"/> Community Standard: Current practice for comparable settings in the community LEVEL V			
<input type="checkbox"/> Clinician Experience: Knowledge gained through practice experience LEVEL V			
<input type="checkbox"/> Consumer Preference: Knowledge gained through life experience LEVEL V			
Information Source(s):		Number of Sources:	
<ul style="list-style-type: none"> Source of information has credible experience. Opinions are clearly stated. Identified practices are consistent. 		<input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes	<input type="checkbox"/> No <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/> No <input type="checkbox"/> N/A
Findings that help you answer the EBP question:			

Johns Hopkins Nursing Evidence-Based Practice Appendix F: Non-Research Evidence Appraisal Tool

<p>QUALITY RATING FOR CLINICAL PRACTICE GUIDELINES, CONSENSUS OR POSITION STATEMENTS (LEVEL IV)</p> <p>A <u>High quality</u>: Material officially sponsored by a professional, public, private organization, or government agency; documentation of a systematic literature search strategy; consistent results with sufficient numbers of well-designed studies; criteria-based evaluation of overall scientific strength and quality of included studies and definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years.</p> <p>B <u>Good quality</u>: Material officially sponsored by a professional, public, private organization, or government agency; reasonably thorough and appropriate systematic literature search strategy; reasonably consistent results, sufficient numbers of well-designed studies; evaluation of strengths and limitations of included studies with fairly definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years.</p> <p>C <u>Low quality or major flaws</u>: Material not sponsored by an official organization or agency; undefined, poorly defined, or limited literature search strategy; no evaluation of strengths and limitations of included studies, insufficient evidence with inconsistent results, conclusions cannot be drawn; not revised within the last 5 years.</p>
<p>QUALITY RATING FOR ORGANIZATIONAL EXPERIENCE (LEVEL V)</p> <p>A <u>High quality</u>: Clear aims and objectives; consistent results across multiple settings; formal quality improvement or financial evaluation methods used; definitive conclusions; consistent recommendations with thorough reference to scientific evidence</p> <p>B <u>Good quality</u>: Clear aims and objectives; formal quality improvement or financial evaluation methods used; consistent results in a single setting; reasonably consistent recommendations with some reference to scientific evidence</p> <p>C <u>Low quality or major flaws</u>: Unclear or missing aims and objectives; inconsistent results; poorly defined quality improvement/financial analysis method; recommendations cannot be made</p>
<p>QUALITY RATING FOR LITERATURE REVIEW, EXPERT OPINION, COMMUNITY STANDARD, CLINICIAN EXPERIENCE, CONSUMER PREFERENCE (LEVEL V)</p> <p>A <u>High quality</u>: Expertise is clearly evident; draws definitive conclusions; provides scientific rationale; thought leader in the field</p> <p>B <u>Good quality</u>: Expertise appears to be credible; draws fairly definitive conclusions; provides logical argument for opinions</p> <p>C <u>Low quality or major flaws</u>: Expertise is not discernable or is dubious; conclusions cannot be drawn</p>

ADDENDUM C: CRITICAL APPRAISAL SKILLS PROGRAMME (CASP)

TOOL: RANDOMISED CONTROLLED TRIAL



11 questions to help you make sense of a trial

How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a randomised controlled trial:

- Are the results of the trial valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 11 questions on the following pages are designed to help you think about these issues systematically.

The first two questions are screening questions and can be answered quickly. If the answer to both is yes, it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a yes, no or can't tell to most of the questions. A number of prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

There will not be time in the small groups to answer them all in detail!

These checklists were designed to be used as educational tools as part of a workshop

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(A) Are the results of the trial valid?

Screening Questions

1. Did the trial address a clearly focused issue?

☐

Yes

☐

Can't tell

☐

No

Consider: An issue can be 'focused' in terms of

- The population studied
- The intervention given
- The comparator given
- The outcomes considered

2. Was the assignment of patients to treatments randomised?

☐

Yes

☐

Can't tell

☐

No

Consider:

- How was this carried out, some methods may produce broken allocation concealment
- Was the allocation concealed from researchers?

Is it worth continuing?



Detailed questions

3. Were patients, health workers and study personnel blinded?

☐ Yes

☐ Can't tell

☐ No

Consider:

- Health workers could be: clinicians, nurses etc
- Study personnel – especially outcome assessors

4. Were the groups similar at the start of the trial?

☐ Yes

☐ Can't tell

☐ No

Consider: Look at

- Other factors that might affect the outcome such as age, sex, social class, these may be called baseline characteristics

5. Aside from the experimental intervention, were the groups treated equally?

☐ Yes

☐ Can't tell

☐ No

6. Were all of the patients who entered the trial properly accounted for at its conclusion?

☐ Yes

☐ Can't tell

☐ No

Consider:

- Was the trial stopped early?
- Were patients analysed in the groups to which they were randomised?

(B) What are the results?

7. How large was the treatment effect?

Consider:

- What outcomes were measured?
- Is the primary outcome clearly specified?
- What results were found for each outcome?
- Is there evidence of selective reporting of outcomes?

8. How precise was the estimate of the treatment effect?

Consider:

- What are the confidence limits?
- Were they statistically significant?

(C) Will the results help locally?

9. Can the results be applied in your context?
(or to the local population?)

☐

Yes

☐

Can't tell

☐

No

Consider:

- Do you have reason to believe that your population of interest is different to that in the trial
 - If so, in what way?
-

10. Were all clinically important outcomes considered?

☐

Yes

☐

Can't tell

☐

No

Consider:

- Is there other information you would like to have seen?
 - Was the need for this trial clearly described?
-

11. Are the benefits worth the harms and costs?

☐

Yes

☐

Can't tell

☐

No

Consider:

- Even if this is not addressed by the trial, what do you think?
-

ADDENDUM D: CRITICAL APPRAISAL SKILLS PROGRAMME (CASP)

TOOL: SYSTEMATIC REVIEWS

(A) Are the results of the review valid?

Screening Questions

1. Did the review address a clearly focused question?

☐ Yes

☐ Can't tell

☐ No

HINT: An issue can be 'focused' in terms of

- The population studied
- The intervention given
- The outcome considered

2. Did the authors look for the right type of papers?

☐ Yes

☐ Can't tell

☐ No

HINT: 'The best sort of studies' would

- Address the reviews question
- Have an appropriate study design (usually RCTs for papers evaluating interventions)

Is it worth continuing?



Detailed questions

3. Do you think all the important, relevant studies were included?

☐ Yes

☐ Can't tell

☐ No

HINT: Look for

- Which bibliographic databases were used
 - Follow up from reference lists
 - Personal contact with experts
 - Search for unpublished as well as published studies
 - Search for non-English language studies
-

4. Did the review's authors do enough to assess the quality of the included studies?

☐ Yes

☐ Can't tell

☐ No

HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results. ("All that glisters is not gold" Merchant of Venice – Act II Scene 7)

5. If the results of the review have been combined, was it reasonable to do so?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider whether

- The results were similar from study to study
- The results of all the included studies are clearly displayed
- The results of the different studies are similar
- The reasons for any variations in results are discussed

(B) What are the results?

6. What are the overall results of the review?

HINT: Consider

- If you are clear about the review's 'bottom line' results
 - What these are (numerically if appropriate)
 - How were the results expressed (NNT, odds ratio etc)
-

7. How precise are the results?

HINT: Look at the confidence intervals, if given

(C) Will the results help locally?

8. Can the results be applied to the local population?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider whether

- The patients covered by the review could be sufficiently different to your population to cause concern
- Your local setting is likely to differ much from that of the review

9. Were all important outcomes considered?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider whether

- Is there other information you would like to have seen

10. Are the benefits worth the harms and costs?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- Even if this is not addressed by the review, what do you think?

ADDENDUM E: CRITICAL APPRAISAL SKILLS PROGRAMME (CASP)

TOOL: COHORT STUDY



12 questions to help you make sense of cohort study

How to use this appraisal tool

Three broad issues need to be considered when appraising a cohort study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 12 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is “yes”, it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a “yes”, “no” or “can’t tell” to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

These checklists were designed to be used as educational tools as part of a workshop setting

There will not be time in the small groups to answer them all in detail!

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(A) Are the results of the study valid?

Screening Questions

1. Did the study address a clearly focused issue?

☐

Yes

☐

Can't tell

☐

No

HINT: A question can be 'focused' in terms of

- The population studied
- The risk factors studied
- The outcomes considered
- Is it clear whether the study tried to detect a beneficial or harmful effect?

2. Was the cohort recruited in an acceptable way?

☐

Yes

☐

Can't tell

☐

No

HINT: Look for selection bias which might compromise the generalisability of the findings:

- Was the cohort representative of a defined population?
- Was there something special about the cohort?
- Was everybody included who should have been included?

Is it worth continuing?



Detailed questions

3. Was the exposure accurately measured to minimise bias?

☐ Yes

☐ Can't tell

☐ No

HINT: Look for measurement or classification bias:

- Did they use subjective or objective measurements?
- Do the measurements truly reflect what you want them to (have they been validated)?
- Were all the subjects classified into exposure groups using the same procedure

4. Was the outcome accurately measured to minimise bias?

☐ Yes

☐ Can't tell

☐ No

HINT: Look for measurement or classification bias:

- Did they use subjective or objective measurements?
- Do the measures truly reflect what you want them to (have they been validated)?
- Has a reliable system been established for detecting all the cases (for measuring disease occurrence)?
- Were the measurement methods similar in the different groups?
- Were the subjects and/or the outcome assessor blinded to exposure (does this matter)?

5. (a) Have the authors identified all important confounding factors?

☐ Yes ☐ Can't tell ☐ No

List the ones you think might be important, that the author missed.

(b) Have they taken account of the confounding factors in the design and/or analysis?

☐ Yes ☐ Can't tell ☐ No

List:

HINT: Look for restriction in design, and techniques e.g. modelling, stratified-, regression-, or sensitivity analysis to correct, control or adjust for confounding factors

6. (a) Was the follow up of subjects complete enough?

☐ Yes ☐ Can't tell ☐ No

(b) Was the follow up of subjects long enough?

☐ Yes ☐ Can't tell ☐ No

HINT: Consider

- The good or bad effects should have had long enough to reveal themselves
- The persons that are lost to follow-up may have different outcomes than those available for assessment
- In an open or dynamic cohort, was there anything special about the outcome of the people leaving, or the exposure of the people entering the cohort?

(B) What are the results?

7. What are the results of this study?

HINT: Consider

- What are the bottom line results?
 - Have they reported the rate or the proportion between the exposed/unexposed, the ratio/the rate difference?
 - How strong is the association between exposure and outcome (RR_r)?
 - What is the absolute risk reduction (ARR)?
-

8. How precise are the results?

HINT: Look for the range of the confidence intervals, if given.

9. Do you believe the results?

☐ Yes ☐ Can't tell ☐ No

HINT: Consider

- Big effect is hard to ignore!
- Can it be due to bias, chance or confounding?
- Are the design and methods of this study sufficiently flawed to make the results unreliable?
- Bradford Hills criteria (e.g. time sequence, dose-response gradient, biological plausibility, consistency)

(C) Will the results help locally?

10. Can the results be applied to the local population?

☐

Yes

☐

Can't tell

☐

No

HINT: Consider whether

- A cohort study was the appropriate method to answer this question
- The subjects covered in this study could be sufficiently different from your population to cause concern
- Your local setting is likely to differ much from that of the study
- You can quantify the local benefits and harms

11. Do the results of this study fit with other
available evidence?

☐

Yes

☐

Can't tell

☐

No

12. What are the implications of this study for practice?

HINT: Consider

- One observational study rarely provides sufficiently robust evidence to recommend changes to clinical practice or within health policy decision making
- For certain questions observational studies provide the only evidence
- Recommendations from observational studies are always stronger when supported by other evidence

ADDENDUM F: CRITICAL APPRAISAL SKILLS PROGRAMME (CASP)

TOOL: QUALITATIVE STUDY



10 questions to help you make sense of qualitative research

How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a qualitative research:

- Are the results of the review valid?
- What are the results?
- Will the results help locally?

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is “yes”, it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a “yes”, “no” or “can’t tell” to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

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There will not be time in the small groups to answer them all in detail!

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Screening Questions

1. Was there a clear statement of the aims of the research?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- What was the goal of the research?
- Why it was thought important?
- Its relevance

2. Is a qualitative methodology appropriate?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants
- Is qualitative research the right methodology for addressing the research goal?

Is it worth continuing?



Detailed questions

3. Was the research design appropriate to address the aims of the research?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- If the researcher has justified the research design (e.g. have they discussed how they decided which method to use)?

4. Was the recruitment strategy appropriate to the aims of the research?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)

5. Was the data collected in a way that addressed the research issue?

☐

Yes

☐

Can't tell

☐

No

HINT: Consider

- If the setting for data collection was justified
 - If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
 - If the researcher has justified the methods chosen
 - If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
 - If methods were modified during the study. If so, has the researcher explained how and why?
 - If the form of data is clear (e.g. tape recordings, video material, notes etc)
 - If the researcher has discussed saturation of data
-

6. Has the relationship between researcher and participants been adequately considered?

☐

Yes

☐

Can't tell

☐

No

HINT: Consider

- If the researcher critically examined their own role, potential bias and influence during
 - (a) Formulation of the research questions
 - (b) Data collection, including sample recruitment and choice of location
- How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

7. Have ethical issues been taken into consideration?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained
- If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)
- If approval has been sought from the ethics committee

8. Was the data analysis sufficiently rigorous?

☐ Yes

☐ Can't tell

☐ No

HINT: Consider

- If there is an in-depth description of the analysis process
- If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data?
- Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process
- If sufficient data are presented to support the findings
- To what extent contradictory data are taken into account
- Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation

9. Is there a clear statement of findings?

☐ Yes ☐ Can't tell ☐ No

HINT: Consider

- If the findings are explicit
 - If there is adequate discussion of the evidence both for and against the researchers arguments
 - If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst)
 - If the findings are discussed in relation to the original research question
-

10. How valuable is the research?

HINT: Consider

- If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g. do they consider the findings in relation to current practice or policy?, or relevant research-based literature?
- If they identify new areas where research is necessary
- If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

ADDENDUM G: PROOF OF ETHICAL TRAINING



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YUNIBESITHI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT
POTCHEFSTROOM CAMPUS

Private Bag X6001, Potchefstroom
South Africa 2520

Tel: 018 299-1111/2222
Web: <http://www.nwu.ac.za>

Health Sciences Ethics Office for Research,
Training and Support
Tel: 018 299 2092
Fax:
Email: minnie.greeff@nwu.ac.za

10 February 2017

Dear Mej Mari-Louise Durr (HPCSA registration number: _____)

PROOF OF ATTENDANCE

This letter certifies that you have attended the 2 day ethics training, entitled:

The Basics of Health Research Ethics

(Accreditation number: UP1163 from University of Pretoria CPD accreditation department)

presented by Prof Minnie Greeff (Head of the Health Sciences Ethics Office for Research, Training and Support) on 23 and 24 January 2017.

This proof of attendance, as recognised by HREC and the Ethics Office, NWU, is valid for 3 years and expires on the 24th of January 2020. Where applicable, Ethics CEUs awarded: 27 Ethics CEUs

Yours sincerely

A handwritten signature in black ink, appearing to be 'M. Greeff'.

Prof Minnie Greeff
Head of Health Sciences Ethics
Office for Research, Training and Support

A handwritten signature in black ink, appearing to be 'A. Kotzé'.

Prof Awie Kotzé
Dean of Faculty of Health Sciences

ADDENDUM H: PRISMA CRITERIA

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

ADDENDUM I: EPPI-REVIEWER 4

Features

EPPI-Reviewer 4 is the EPPI-Centre's comprehensive online software tool for research synthesis. It is a web-based software program for managing and analysing data in literature review and has been developed for all types of systematic review such as meta-analysis, framework synthesis and thematic synthesis.

Systematic review

EPPI-Reviewer 4 has the functionality to help manage your systematic review through all stages of the process from bibliographic management, screening, coding and right through to synthesis.

It manages references, stores PDF files, facilitates qualitative and quantitative analyses and allows easy export of review data to enable use with other software programmes.

The software allows multiple concurrent users to access the system and being web-based allows members of a review group to be located in different geographic locations.

EPPI-Reviewer 4 supports many different analytic functions for synthesis including meta-analysis, empirical synthesis and qualitative thematic synthesis. It allows you to present your data in summary diagrams and customisable reports.

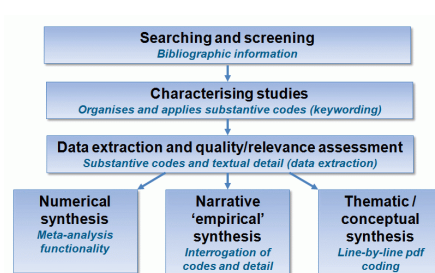
Recent additions to the software include text mining, data clustering, classification and term extraction which are leading to new possibilities in the field of systematic reviewing.

The only system requirements to run EPPI-Reviewer 4 are that you must be connected to the internet and your computer will need to have the free Microsoft Silverlight browser plug-in installed. This plug-in is available for both PCs and Macs and is available [here](#).

You can start using EPPI-Reviewer 4 today by signing up for a free one month trial [here](#)!

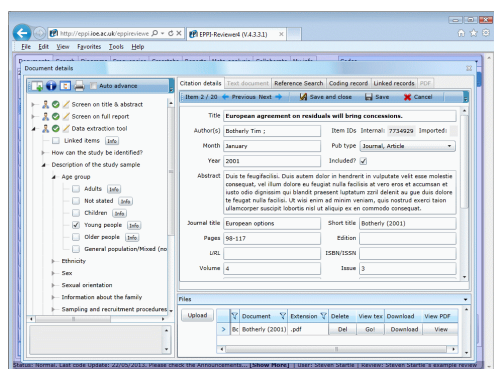
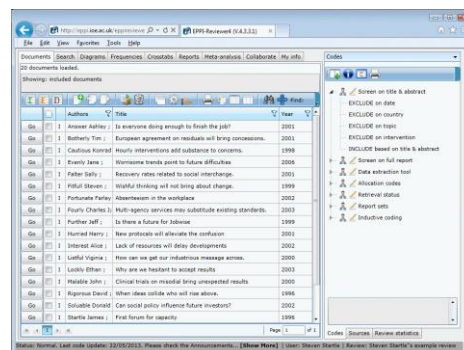
Detailed features and functions

A more detailed description of its many functions include:



Reference management

- Managing the thousands of references that often result from comprehensive searches of electronic databases
- Importing references in a wide variety of 'tagged' formats
- Duplicate checking using 'fuzzy logic'. (Potential duplicates can be checked manually and / or automatically classified as duplicates, depending on how similar they are.)
- Document storage: store the original document file (such as pdf, doc etc) along with the study record.
- 'Linked documents': the 'unit of analysis' in a systematic review is usually the study, but there are often multiple publications originating from the same study; EPPI-Reviewer 4 helps reviewers to use the correct 'unit'.
- Direct access to PubMed through web services. EPPI-Reviewer 4 makes use of this capability to allow direct searching and search result data transfer from PubMed.

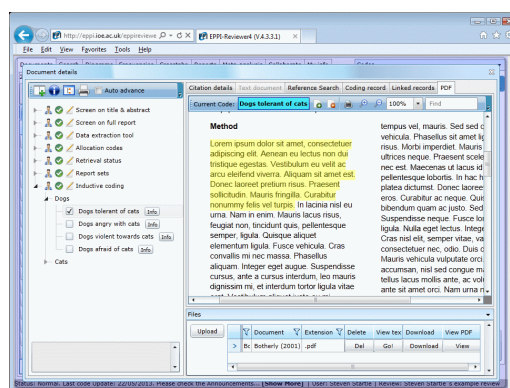


Study classification and data extraction

- Flexible coding schemas for classifying studies:
 - Inclusion / exclusion / eligibility criteria;
 - Codes for descriptive 'mapping' of research activity.
 - Codes to capture detailed information about a study.
- Concurrent multi-user classification: multiple users can classify studies independently and then compare their results; EPPI-Reviewer 4 works throughout this process, producing summary discrepancy reports and an interface to facilitate the process of agreeing final decisions.
- Bulk application / removal of codes to selected studies
- Calculation of common measures of effect (odds ratios, risk ratios, risk differences, standardized mean differences, mean differences) from a variety of statistics (2 x 2 tables, means, standard deviations, confidence intervals, p, t and r values).
- Text mining: automatic term recognition and document clustering.

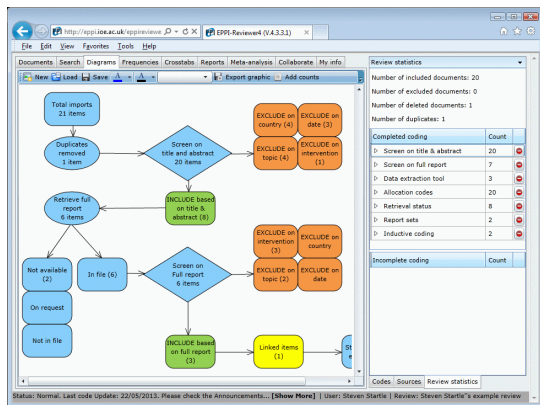
Synthesis

- Running meta-analyses (fixed and random effects models); calculating I-squared and supporting sub-group analyses using analog to the anova
- A powerful search engine enabling users to search by categories and text and combine searches using Boolean terms
- Producing reports of categorical, numeric and textual data in a wide variety of formats from frequency reports, crosstabs and full-text reports, to tabular summary reports and summary statistics of numeric data
- Text mining functionality. Automatic document clustering, using text mining, is one way of describing the range of studies you have identified at the click of a button. Text mining can assist with searching by identifying significant terms in the documents you have



already included.

- Inductive coding functionality. This allows line by line coding of textual data and organising and structuring these codes graphically into 'conceptual relationship diagrams to display analytic and descriptive themes found through inductive coding.
- Fulltext reference searching using the uploaded pdfs.
- Diagrams to summarise e.g. qualitative syntheses and theories of change for interventions.



Review Management

- The ability to create an unlimited number of non-shareable reviews.
- Allocation of classification tasks (e.g. screening / data extraction) to individual users.
- Work progress reporting.
- Individual reviewer permissions (forthcoming)
- Review flow charts which update automatically (e.g. with counts of how many studies have been included / excluded according to which criterion in order to generate PRISMA flow-diagrams).
- Easy export of review data to enable use with other software programmes and to enable long term independent storage of data.

Under development

We have been developing ways of using emerging text mining technologies in systematic reviews. Currently used during the searching and screening stages of a review, you can read a paper which outlines their potential published in Research Synthesis Methods*. We have also written up our early findings in the [NCRM Newsletter](#) and in a poster presented at the [2011 Cochrane Colloquium](#). Methods to use these technologies are still in their infancy and require significant further evaluation. While automatic term recognition and document clustering are available for all users, document classification often requires significant server processing time and support; therefore this technology is not yet generally available in EPPI-Reviewer. However, if you would like to use a classifier in your review, please contact us to discuss your particular requirements.

Citing EPPI-Reviewer 4

Thomas J, Brunton J, Graziosi S (2010) EPPI-Reviewer 4: software for research synthesis. EPPI-Centre Software. London: Social Science Research Unit, UCL Institute of Education.

ADDENDUM J: ETHICAL CLEARANCE CERTIFICATE



NORTH-WEST UNIVERSITY
YUNIBESITHI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

Private Bag X8501, Potchefstroom,
South Africa, 2520

Tel: (018) 299-4900

Fax: (018) 299-4910

Web: <http://www.nwu.ac.za>

Research Ethics Regulatory Committee

Tel: +27 18 299 4849

Email: Ethics@nwu.ac.za

ETHICS APPROVAL CERTIFICATE OF STUDY

Based on approval by Health Research Ethics Committee (HREC) on 08/11/2017, the North-West University Research Ethics Regulatory Committee (NWU-RERC) hereby approves your study as indicated below. This implies that the NWU-RERC grants its permission that provided the special conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: The use of essential oils in relieving symptoms specific to brain malignancies: A systematic review														
Study Leader/Supervisor: AJ Bilgaut														
Student: M Durr-22744764														
Ethics number:														
N	W	U	-	0	0	1	1	3	-	1	7	-	A	1
Institution			Study Number						Year		Status			
<small>Legend: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation</small>														
Application Type: Systematic review														
Commencement date: 03/11/2017														
													Risk:	Minimal
Approval of the study is initially provided for a year, after which continuation of the study is dependent on receipt of the annual (or as otherwise stipulated) monitoring report and the concomitant issuing of a letter of continuation.														

Special conditions of the approval (if applicable):

- It is requested that the applicants please submit the data collection tool for review and approval, once it has been created.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:

- The study leader (principle investigator) must report in the prescribed format to the NWU-RERC via HREC:
 - annually (or as otherwise requested) on the monitoring of the study, and upon completion of the study
 - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.
- Annually a number of studies may be randomly selected for an external audit.
- The approval applies strictly to the proposal as stipulated in the application form. Should any changes to the proposal be deemed necessary during the course of the study, the study leader must apply for approval of these amendments at the HREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the study may be started.
- In the interest of ethical responsibility the NWU-RERC and HREC retains the right to:
 - request access to any information or data at any time during the course or after completion of the study;
 - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process.
 - withdraw or postpone approval if:
 - any unethical principles or practices of the study are revealed or suspected,
 - it becomes apparent that any relevant information was withheld from the HREC or that information has been false or misrepresented,
 - the required amendments, annual (or otherwise stipulated) report and reporting of adverse events or incidents was not done in a timely manner and accurately,
 - new institutional rules, national legislation or international conventions deem it necessary.
- HREC can be contacted for further information or any report templates via Ethics-HRECAdmin@nwu.ac.za or 018 299 1208.

The RERC would like to remain at your service as scientist and researcher, and wishes you well with your study. Please do not hesitate to contact the RERC or HREC for any further enquiries or requests for assistance.

Yours sincerely,

Prof. Refilwe Phaswana-Mafuya

Chair NWU Research Ethics Regulatory Committee (RERC)

ADDENDUM K: CRITICAL APPRAISAL SCORE

Systematic reviews (CASP)									
	All relevant studies included?	Quality of studies assessed adequately?	Reasonable to combine results?	What are the overall results?	Precision of results?	Results applicable to local population?	Were all important outcomes considered?	Are the benefits worth the harms and cost?	
Perry <i>et al.</i> (2012)	✓	✓	✓	½	✓	✓	✓	✓	94
Shin <i>et al.</i> (2016)	✓	✓	✓	½	✓	✓	✓	✓	94
Yim <i>et al.</i> (2009)	✓	X	✓	½	✓	✓	✓	✓	81

Literature review (Johns Hopkins)						
	Is subject matter to be reviewed clearly stated?	Is relevant, up-to-date literature used?	Is there a meaningful analysis of the conclusions?	Are gaps in literature identified?	Are recommendations made?	
Filshie (2005)	✓	X	✓	✓	½	70
Filshie and Rubens (2006)	✓	½	✓	✓	✓	80
Steflitch and Steflitch (2008)	✓	X	✓	✓	✓	80

Expert opinion (Johns Hopkins)					
	Has the individual published or presented on the topic?	Is author's opinion based on scientific evidence?	Is the author's opinion clearly stated?	Are potential biases acknowledged?	
Buckle (2016[a])	✓	✓	✓	X	75
Buckle (2016[b])	✓	✓	✓	X	75
Buckle (2016[c])	✓	✓	✓	X	75
Srivastava & Gupta (2009)	✓	✓	✓	X	75

Case report (Johns Hopkins)					
	Purpose of the case report stated?	Is the case report clearly presented?	Are the findings supported by research or theory?	Are the recommendations clearly stated and linked to findings?	
Cooksley (2003)	✓	✓	✓	X	75
Gilligan (2005)	✓	X	✓	X	50

Program / financial evaluation / quality improvement (Johns Hopkins)							
	Aim of project clearly stated?	Method adequately described?	Process of outcomes measures described?	Results adequately described?	Interpretation clear and appropriate?	Is cost / benefit analysis described?	
De Valois (2001)	✓	X	✓	✓	✓	✓	83
Kite <i>et al.</i> (1998)	✓	X	✓	✓	✓	✓	83
Stringer and Donald (2011)	✓	✓	✓	✓	✓	X	83

Mixed method / Quasi experimental academic literature (Johns Hopkins)																
	What is known/not known identified?	Purpose clearly presented?	Literature recently (<5years)?	Sample size sufficient?	Control group similar?	Control group settings similar?	Control group equally treated except for intervention?	Data collection described clearly?	Instrument reliable (Cronbach Alpha >0.70)	Instrument validity discussed?	Response rate >25%	Results presented clearly?	Tables consistent with narrative?	Limitations identified and addressed?	Conclusions based on results?	
Hadfield (2001)	✓	✓	X	X	n.a	n.a	n.a	✓	X	✓	✓	✓	✓	✓	✓	75
Louis & Kowalski (2002)	✓	✓	✓	X	✓	✓	✓	✓	X	X	✓	✓	✓	✓	✓	80

Randomised controlled trials (CASP)												
	Did the trial address a clearly focused issue?	Assignment of patients to treatment randomised?	Patients, health workers and study personnel blinded?	Groups similar at start of trial?	Were groups treated equally except for intervention?	Were all participants accounted for at conclusion?	How large was the treatment effect?	How precise was the estimate of treatment effect?	Can results be applied locally?	Were all clinically important outcomes considered?	Are the benefits worth the harms and costs?	
Chang (2008)	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	91
Graham <i>et al.</i> (2003)	✓	✓	✓	✓	✓	✓	½	½	✓	✓	✓	91
Kyle (2006)	✓	✓	✓	X	✓	✓	X	✓	✓	✓	✓	82
Soden <i>et al.</i> (2004)	✓	✓	✓	✓	✓	✓	½	½	X	✓	✓	82
Tayarani-Najaran <i>et al.</i> (2013)	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	91
Wilcock <i>et al.</i> (2004)	✓	✓	X	✓	✓	✓	X	✓	✓	X	✓	73
Wilkinson <i>et al.</i> (1999)	✓	✓	✓	✓	✓	✓	½	½	X	✓	✓	82
Wilkinson <i>et al.</i> (2007)	✓	✓	✓	✓	✓	✓	✓	½	X	X	✓	77

ADDENDUM L: PROOF OF LANGUAGE EDITING

Declaration

This is to declare that I, Annette L Combrink, accredited language editor and translator of the South African Translators' Institute, have language-edited the mini-dissertation by

ML Durr

with the title

**The use of essential oils in relieving
symptoms specific to brain malignancies: A
systematic review**



Prof Annette L Combrink

Accredited translator and language editor

South African Translators' Institute

Membership No. 1000356

Date: 16 November 2017