

ACUPUNCTURE FOR PALLIATIVE CARE

About palliative care

Palliative care is the active holistic care of patients with advanced progressive illness, such as those with advanced cancer, end-stage renal disease, AIDS, and chronic obstructive pulmonary disorder (COPD)(WHO 2002). Management includes treatments for pain and other symptoms (e.g. fatigue, nausea and vomiting, breathlessness, anxiety, depression, vasomotor symptoms, xerostomia), as well as the provision of psychological, social and spiritual support (NICE 2004). Up to 457,000 people in the UK need good palliative care services every year but around 92,000 people are not being reached (Hughes-Hallett 2011).

The goal of palliative care is to achieve the best quality of life for patients and their families, and to provide a support system to help patients live as actively as possible until death (WHO 2002). Ideally, palliative care is applied early in the course of illness in conjunction with other therapies intended to prolong life (such as chemotherapy or radiation therapy), and investigation and management of distressing clinical complications (NCHSPSCS 2002; DH 2000). Conventional treatments used in palliative care include drugs such as opioids, NSAIDs, antiemetics, corticosteroids, tranquillisers and laxatives; radio- and chemotherapy; and surgery (GP Notebook n.d.). People may be cared for in their own homes, hospices, care homes or hospitals (Hughes-Hallett 2011).

References

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Hughes-Hallett T et al. Palliative care funding review. The right care and support for everyone. July 2011 [online]. Available: <http://palliativecarefunding.org.uk/wp-content/uploads/2011/06/PCFRFinal%20Report.pdf>

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How acupuncture can help

Most research so far has focused on helping the side-effects of orthodox cancer treatments, and on relieving pain. First we consider those symptoms where there has been enough research to merit it being systematically reviewed.

Pain

Several randomised controlled trials (RCTs) have indicated that acupuncture may relieve pain in palliative settings and in addition it may reduce the need for cancer pain drugs (Lu 2008). One recent systematic review found (limited) evidence that acupuncture may provide long-term pain relief in patients with cancer (Paley 2011) and the most recent trials have strengthened the evidence (refer to the 'Acupuncture for Cancer Care' Fact Sheet, 2011).

Most research on acupuncture for chronic pain has been carried out in primary and secondary care with musculoskeletal conditions and headache, though also to some extent for visceral pain. Recent studies are demonstrating an effect over and above placebo (Hopton 2010). Palliative care patients, too, frequently suffer from non-cancer-specific pain and would be expected to benefit similarly from acupuncture.

Pain arising indirectly from cancer treatments may also be addressed with acupuncture, for example for chemotherapy-induced neuropathy (Donald 2011). Patients with HIV-associated neuropathic pain may also benefit (refer to the 'Acupuncture for Neuropathic Pain' Fact Sheet, 2012). Filshie (2003) reported that pain from cancer treatments is likely to respond better, and for longer, than that from the disease itself; nevertheless, there are still benefits possible for patients with late-stage cancer.

Dry mouth (xerostomia)

A systematic review found possible benefits with acupuncture for radiotherapy-induced xerostomia (O'Sullivan 2010). Not all the inter-group differences were significant but this is typical in trials comparing acupuncture with sham acupuncture, for the latter is commonly viewed as being an active treatment itself, not a placebo, and hence may underestimate the effects of the therapy (Lundeberg 2011; Sherman 2009; Paterson 2005). The RCTs to date are few in number and small in size. Although they have produced encouraging results, and are supported by observational studies (for example, Meidell 2009), larger trials are required to achieve more robust evidence. Acupuncture may also help with xerostomia dysphagia (swallowing difficulty) in late-stage palliative care (Filshie 2003).

Nausea and vomiting

Three systematic reviews found that moxibustion or acupuncture can help relieve chemotherapy-induced nausea and vomiting (Lee 2010; Chao 2009; Ezzo 2006), especially in acute situations, and even self-administered acupressure may be effective. There is little information on whether acupuncture is also effective for nausea and vomiting in advanced terminal care (unrelated to chemotherapy).

Breathlessness

Systematic reviews found low strength evidence that acupuncture/acupressure is helpful for breathlessness, with most of the studies on patients with COPD (Bausewein 2008). Semi-permanent indwelling needles have been used to prolong the effect and to give patients some control, by massaging them (Filshie 2003).

Hot flushes

The vasomotor symptoms brought on by chemotherapy treatment for breast and prostate cancer may be alleviated with acupuncture, though the evidence is not yet conclusive (Lee 2009a, 2009b; see Cancer Care Fact Sheet for details of more recent trials). Filshie (2005) provides details of the protocol used in a specialist UK cancer centre (which again includes self-treatment) together with positive audit results.

Other symptoms

Several pilot RCTs have found acupuncture to benefit patients with chemotherapy-related **fatigue** (Lu 2008). Acupuncture has also provided an alternative method for managing fatigue in patients with end-stage renal disease (Tsay 2004). Two recent observational studies have provided positive preliminary findings for **lymphoedema** (Cassileth 2011; de Valois 2011). Also in cancer patients, recent trials have suggested benefit for **insomnia and depression** (Feng 2011). Filshie (2011) has reported a wide range of other applications, especially for side effects of radiotherapy.

HIV patients may find adjunctive acupuncture useful for **gastrointestinal side-effects of anti-retroviral therapy** (Chang 2011), for **sleeplessness** (Philips 2001) and for **neuropathic pain** (discussed above).

Holistic care

Most patients in palliative care do not present with single symptoms and it may be advantageous to address them globally (Filshie 2011; Lim 2011). Further, although symptom control may be the main focus palliative care also emphasises patient dignity, autonomy and self-efficacy (Kauffman 2008; Lu 2008). Broad holistic benefits, covering multiple physical and mental symptoms and self-empowerment outcomes are characteristic of acupuncture (Rugg 2011).

Reviews of the evidence for acupuncture in palliative care have concluded that it is a promising adjunctive therapy (and potentially cost-effective), though more research is needed, especially with non-cancer patients (Filshie 2011; Couillot 2008; Lu 2008; Standish 2008).

A number of observational pilot studies in advanced cancer and haemodialysis populations have demonstrated change over a wide range of symptoms, alongside improved quality of life (Dean-Clower 2010), safety (Kim 2011), user endorsement of the service (Johnstone 2002), and the capability to stay living at home through the terminal stages (Takahashi 2009). A small RCT of acupuncture compared to nurse-led care in patients with incurable cancer reported global benefits without significant side-

effects or other tolerance issues (Lim 2011). Also, most symptom improvement was still evident 6 weeks after the end of treatment (though in practice, a regime of follow-on maintenance sessions would usually be advisable given the nature of the disease). For HIV patients with peripheral neuropathy RCT results indicated reduced attrition and mortality with acupuncture, though the effects on pain were inconclusive (Shiflett 2011).

For further details of cited research refer to the table below. For information about more of the individual trials, especially those published since the systematic reviews reported here, see the Cancer Care Fact Sheet. There is further information on the effects of acupuncture on symptoms associated with terminal illnesses in the Anxiety, Chronic Pain, COPD, Depression, Insomnia, Nausea and Vomiting, and Neuropathic Pain Fact Sheets.

Mechanisms

In general, acupuncture is believed to stimulate the nervous system and cause the release of neurochemical messenger molecules. The resulting biochemical changes influence the body's homeostatic mechanisms, thus promoting physical and emotional well-being.

Research has shown that acupuncture treatment may specifically benefit symptoms associated with palliative care by:

- Acting on areas of the brain known to reduce sensitivity to pain and stress, as well as promoting relaxation and deactivating the 'analytical' brain, which is responsible for anxiety and worry (Hui 2010; Hui 2009)
- Regulating neurotransmitters (or their modulators) and hormones such as serotonin, noradrenaline, dopamine, GABA, neuropeptide Y and ACTH; hence altering the brain's mood chemistry to help to combat negative affective states (Cheng 2009; Zhou 2008;
- Increasing the release of adenosine, which has antinociceptive properties (Goldman 2010)
- Improving muscle stiffness and joint mobility by increasing local microcirculation (Komori 2009), which aids dispersal of swelling
- Stimulating production of endogenous opioids that affect the autonomic nervous system, promoting relaxation and reduced stress Arranz 2007)
- Reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007, Zijlstra 2003)
- Reversing stress-induced changes in behaviour and biochemistry (Kim 2009)
- Increasing levels of T lymphocyte subsets such as CD(3), CD(4), and CD(8), as well as Natural Killer cells (Zhao 2010)
- Relieving nausea and vomiting via central opioid pathways (Tatewaki 2005), regulating gastric myo-electrical activity (Streitberger 2006) , modulating the actions

of the vagal nerve and autonomic nervous system (Huang 2005), and regulating vestibular activities in the cerebellum (Streitberger 2006)

- Enhancing levels of vasoactive intestinal polypeptide and calcitonin gene-related peptide (O'Sullivan 2010), which may relieve xerostomia and hot flushes

Safety and adverse effects

Acupuncture may be used to treat the person, some of the symptoms of cancer, and the side-effects of conventional cancer treatments, but it is not used to address the cancer itself.

Acupuncture needling is contraindicated in any area of actual or potential spinal instability due to cancer, as it potentially increases the risk of cord compression or transaction; directly over a tumour itself or nodules or related sites, such as ascites; when there is severely disordered clotting function; into a lymphoedematous limb (but see Cassileth 2011 below); directly above a prosthesis; or over any intracranial deficits following neurosurgery. Indwelling needles should not be used in patients at risk of bacteraemia, for instance in valvular heart disease and immune-compromised patients with neutropenia (Filshie 2003). It should be noted that acupuncture palliation of symptoms could mask both cancer and disease progression. Although the safety record of oncology acupuncture is extremely good, additional patient eligibility guidelines are in place in some countries, especially to protect against the possibility of infection in immune-compromised individuals (Lu 2010).

Filshie, J. National Guidelines for the Use of Complementary Therapies in Supportive and Palliative Care. Acupuncture. The Prince of Wales's Foundation for Integrated Health; National Council for Hospice and Specialist Palliative Care Services. May 2003

Lu Weidong et al. Recent advances in oncology acupuncture and safety considerations I practice. Current Treatment Options in Oncology 2010;11(3-4):141-146

About the British Acupuncture Council

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ACUPUNCTURE AND PALLIATIVE CARE

The evidence

Research

Conclusion

Overviews

Filshie J, Rubens C. Acupuncture in palliative care. *Acupunct Med.* 2011 Sep;29(3):166-7.

Lu WD et al. Recent advances in oncology acupuncture and safety considerations I practice. *Current Treatment Options in Oncology* 2010;11(3-4):141-146

Lu WD et al. The value of acupuncture in cancer care. *Haematol Oncol Clin N Amer.* 2008; 22(4):63-viii.

Filshie J. National Guidelines for the Use of Complementary Therapies in Supportive and Palliative Care. Acupuncture. The Prince of Wales's Foundation for Integrated Health; National Council for Hospice and Specialist Palliative Care Services. May 2003.

Systematic reviews

Paley CA et al. Acupuncture for cancer pain in adults. *Cochrane Database Syst Rev.* 2011 Jan 19;(1):CD007753.

A systematic review that evaluated the efficacy of acupuncture for the relief of cancer-related pain in adults. It included three randomised controlled trials (involving a total of 204 patients) that evaluated any type of invasive acupuncture for pain directly related to cancer in adults of 18 years or over. One high quality study investigated the effect of auricular acupuncture compared with auricular acupuncture at 'placebo' points and with non-invasive ear seeds attached at 'placebo' points. Participants in the two acupuncture groups were blinded, but blinding was not possible in the ear seeds group because seeds were attached using tape. This may have biased results in favour of acupuncture groups. Participants in the real acupuncture group had lower pain scores at 2 month's follow-up than either the placebo or ear seeds group. There was high risk of bias in the other two studies because of low methodological quality. One study that compared acupuncture with medication concluded that both methods were effective in controlling pain, although acupuncture was the most effective. The second study compared acupuncture, point-injection and medication in participants with stomach cancer. Long-term pain relief was reported for both acupuncture and point-injection compared with medication during the last 10 days of treatment. The reviewers concluded that there was insufficient evidence to judge whether acupuncture is effective in treating cancer pain in adults.

Hopton A, MacPherson H. Acupuncture for chronic pain: is acupuncture more than an effective

A synthesis of evidence from systematic reviews on the pooled data of high-quality randomized controlled trials comparing acupuncture to sham acupuncture for chronic pain. For short-term

placebo? A systematic review of pooled data from meta-analyses. *Pain Pract* 2010; 10: 94-102.

outcomes, acupuncture showed significant superiority over sham for back pain, knee pain, and headache. For longer-term outcomes (6 to 12 months), acupuncture was significantly more effective for knee pain and tension-type headache but inconsistent for back pain (one positive and one inconclusive). The reviewers concluded that the accumulating evidence from recent reviews suggests acupuncture is more than a placebo for commonly occurring chronic pain conditions.

O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. *Acupunct Med* 2010; 28: 191-9.

A systematic review that looked at the evidence on clinical effectiveness and safety of acupuncture in irradiation-induced xerostomia in patients with head and neck cancer. In all, three randomised controlled trials were included. Two trials compared acupuncture with sham acupuncture, and the other had a control arm of 'usual care'. Outcome measurements included salivary flow rates (SFRs) in two trials and subjective questionnaires in three. All three trials reported a significant reduction in xerostomia versus baseline SFR ($p < 0.05$); one reported greater effect in the intervention group for stimulated SFR ($p < 0.01$). Subjective assessment reported significant differences between real acupuncture and control in two trials ($p < 0.02-0.05$). The reviewers concluded that there is limited evidence to suggest that acupuncture is beneficial for irradiation-induced xerostomia.

Lee MS et al. Moxibustion for cancer care: a systematic review and meta-analysis. *BMC Cancer* 2010; 10: 130.

A systematic review that assessed the effectiveness of moxibustion for supportive cancer care. It included five randomized controlled trials comparing the effects of moxibustion with conventional therapy. Four trials failed to show favourable effects of moxibustion for response rate compared with chemotherapy ($p = 0.43$). Two trials assessed the occurrence of side effects of chemotherapy and showed favourable effects of moxibustion. A meta-analysis showed significantly reduced nausea and vomiting from chemotherapy with moxibustion ($p = 0.0005$). The reviewers concluded that there is limited evidence to suggest moxibustion is an effective supportive cancer care in nausea and vomiting.

Chao LF et al. The efficacy of acupoint stimulation for the management of therapy-related adverse events in patients with breast cancer: a systematic review. *Breast Cancer Res Treat* 2009; 118: 255-67.

A systematic review that assessed the evidence on the use of acupoint stimulation for managing therapy-related adverse events in patients with breast cancer. A total of 26 clinical trials, 18 in English and eight in Chinese, were included. They assessed the application of acupoint stimulation on six disparate conditions related to anticancer therapies, including vasomotor syndrome, chemotherapy-induced nausea and vomiting, lymphoedema, post-operation pain, aromatase inhibitors-related joint pain and leukopenia. Methods of acupoint stimulation included traditional acupuncture, acupressure, electroacupuncture, and the use of a magnetic device on acupuncture points. Overall, 23 trials (88%) reported positive outcomes on at least one of the conditions examined. However, only nine trials (35%) were of high quality. Three of these found that acupoint stimulation on P6 was beneficial to chemotherapy-induced nausea and vomiting. For other adverse events, the quality of many of the trials identified was found to be poor and no conclusive remarks could be made. The reviewers concluded that acupoint stimulation, particularly acupressure on the P6 acupoint, appears to be beneficial in the

management of chemotherapy-induced nausea and vomiting, especially in the acute phase.

Lee MS et al. Acupuncture for treating hot flashes in breast cancer patients: a systematic review. *Breast Cancer Res Treat* 2009a; 115:497-503.

A systematic review that assessed the effectiveness of acupuncture as a treatment option for hot flashes in patients with breast cancer. Three randomised clinical trials comparing real with sham acupuncture were included. One trial showed favourable effects of acupuncture in reducing hot flashes frequency, while the other two failed to do so. The meta-analysis showed significant effects of acupuncture compared with sham acupuncture ($p=0.05$). One trial compared the effects of electroacupuncture (EA) with hormone replacement therapy. Hormone therapy was more effective than EA. Another trial compared acupuncture with venlafaxine and reported no significant intergroup difference. A further trial compared acupuncture with applied relaxation and failed to show a significant intergroup difference. The reviewers concluded that the evidence to suggest acupuncture is an effective treatment of hot flashes in patients with breast cancer was not convincing.

Lee MS et al. Acupuncture for treating hot flashes in men with prostate cancer: a systematic review. *Support Care Cancer* 2009b; 17: 763-70.

A systematic review that assessed the effects of acupuncture as a treatment for hot flashes in patients with prostate cancer. Six studies were included. One randomised clinical trial compared the effects of manual acupuncture with acupuncture plus electroacupuncture. The other five studies were uncontrolled observational studies and therefore had limitations. The reviewers concluded that the evidence to suggest an effect with acupuncture on hot flashes in patients with prostate cancer was not convincing.

Standish LJ et al. Acupuncture is underutilized in hospice and palliative medicine. *Am J Hosp Palliat Care*. 2008 Aug-Sep;25(4):298-308.

Of 27 RCTs on acupuncture for conditions seen frequently in palliative care 23 reported statistically significant, favourable results. The authors concluded that acupuncture is safe and clinically cost-effective for the management of common symptoms in palliative and end-of-life care.

Couilliot M, Delahaye G. Acupuncture in palliative care for cancer and non-cancer patients: a systematic review. *Palliative Medicine*. 22(4):552, June 2008. Abstracts of the 5th Research Forum of the European Association for Palliative Care (EAPC): Trondheim, Norway, 28-31 May 2008: EAPC Abstracts: Poster 490

The literature on acupuncture and palliative care has increased dramatically over the last 10 years, with most papers related to cancer. There are two main types: evaluations of the evidence for treating specific symptoms, and surveys on knowledge and use of acupuncture. It was concluded that although there is good evidence for cancer-related symptoms there is a shortage of high quality studies on non-cancer patients.

Bausewein C et al. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD005623. DOI: 10.1002/14651858.CD005623.pub2.

A systematic review that looked at the effectiveness of non-pharmacological and non-invasive interventions to relieve breathlessness in participants suffering from the five most common conditions causing breathlessness in advanced disease. It included 47 randomised controlled and controlled clinical trials involving a total of 2,532 participants described as suffering from breathlessness due to advanced stages of cancer, COPD, interstitial lung disease, chronic heart failure or motor neurone disease. Five of the trials were of acupuncture/acupressure, which provided low strength evidence that acupuncture/acupressure is

helpful. Most of the studies had been conducted in patients with COPD.

Ezzo JM et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database of Systematic Reviews.(2):CD002285, 2006.

A systematic review that assessed the effectiveness of acupuncture-point stimulation on acute and delayed chemotherapy-induced nausea and vomiting in cancer patients. Eleven randomised trials (involving a total of 1,247 patients) were pooled. Overall, acupuncture-point stimulation given by any method reduced the incidence of acute vomiting (RR $p=0.04$), but not acute or delayed nausea severity compared to control. By modality, stimulation with needles reduced the proportion of acute vomiting (RR $p=0.01$), but not acute nausea severity. Electroacupuncture reduced the proportion of acute vomiting ($p=0.02$), but manual acupuncture did not; delayed symptoms for acupuncture were not reported. Acupressure reduced mean acute nausea severity ($p=0.04$), but not acute vomiting or delayed symptoms. Non-invasive electrostimulation showed no benefit for any outcome. All trials used concomitant pharmacologic antiemetics, and all, except electroacupuncture trials, used state-of-the-art antiemetics. The reviewers concluded that this data complements that on post-operative nausea and vomiting, suggesting a biologic effect of acupuncture-point stimulation. They also concluded that electroacupuncture has demonstrated benefits for chemotherapy-induced acute vomiting, and that self-administered acupressure appears to have a protective effect for acute nausea and can readily be taught to patients.

Randomised controlled trials

Lim JT et al. Is there a role for acupuncture in the symptom management of patients receiving palliative care for cancer? A pilot study of 20 patients comparing acupuncture with nurse-led supportive care. *Acupunct Med* 2011; 29: 173-9.

A 4-week pilot randomised controlled study that documented changes in symptoms after acupuncture or nurse-led supportive care in 20 patients with incurable cancer and an estimated survival of at least 3 months. Edmonton Symptom Assessment System (ESAS) scores were obtained before and after each treatment, and weekly for 6 weeks after treatment by telephone. Total symptom scores were reduced by an average of 22% after each acupuncture visit and by 14% after each supportive care visit. Compared with baseline, ESAS scores at the end of the follow-up period were reduced by 19% for the acupuncture arm and 26% for nurse-led supportive care. The researchers concluded that patients appeared to benefit from incorporating acupuncture into the treatment of advanced incurable cancer, and that it was well tolerated with no significant or unexpected side effects. Acupuncture had an immediate effect on all symptoms, whereas nurse-led supportive care had a larger impact 6 weeks after the final session.

Chang BH, Sommers E. Acupuncture and the relaxation response for treating gastrointestinal symptoms in HIV patients on highly active antiretroviral therapy. *Acupunct Med*. 2011 Sep;29(3):180-7.

This was a 4-arm double-blind randomised controlled trial: real acupuncture+relaxation (AR), sham acupuncture + relaxation (SR), real acupuncture+health education (AE) or sham acupuncture + health education (SE). Participants listened to CDs with relaxation-eliciting instructions or health education while receiving acupuncture/sham. Interventions were provided twice weekly for 4 weeks and once weekly for another 4 weeks. Daily diaries recorded GI symptom severity ratings. 115 people with HIV/AIDS

who were on HAART (highly-active retroviral therapy) and had persistent GI symptoms started the intervention. The AR group had greater intervention effects for loose stools symptoms than the other three groups ($\beta=-0.149$, -0.151 and -0.144 , p value= 0.013 , 0.013 and 0.018 compared to AE, SR and SE, respectively). The AR group also had significant effects on reducing nausea symptoms when the intervention was given twice per week ($\beta=-0.218$, $p=0.001$). Conclusions: these preliminary data demonstrate the potential synergistic effects of acupuncture and relaxation for treating GI symptoms in HIV patients on HAART.

Feng Y et al. Clinical research of acupuncture on malignant tumor patients for improving depression and sleep quality. *J Tradit Chin Med*. 2011 Sep;31(3):199-202

Eighty cases of cancer related depression and sleep disorders received either acupuncture or Fluoxetine for 30 days. Before and after scores on the Hamilton Depression Rating Scale were 20.9 to 9.9 for acupuncture, and 20.7 to 13.7 for Fluoxetine. Sleep was assessed by the Pittsburgh Sleep Quality Index: acupuncture 14.5 to 7.9; Fluoxetine 13.0 to 11.4. In both cases the acupuncture group performed significantly better than the control. The authors concluded that acupuncture can effectively reduce malignant-related depression, improve sleep quality, and help to improve the quality of life of cancer patients.

Shiflett SC, Schwartz GE. Effects of acupuncture in reducing attrition and mortality in HIV-Infected men with peripheral neuropathy. *Explore (NY)*. 2011; 7: 148-54.

A reassessment of research assessing acupuncture versus amitriptyline for peripheral neuropathy in 114 HIV-infected patients study. The results were inconclusive for pain measures, but acupuncture had a strong and positive effect on attrition and mortality. Overall, acupuncture was associated with lower attrition rate (27.6% vs. 44.6%, $p=0.058$), and a zero mortality rate (0% vs. 12.5%, $p=0.047$) than amitriptyline. This protective effect of acupuncture was most pronounced among patients with poorest physical functioning at the beginning of the study (0% vs. 23.8%, $p=0.047$). The researchers concluded that acupuncture was clearly effective in reducing attrition and mortality in men with HIV and peripheral neuropathy, but that results for pain relief were mixed.

Tsay SL. Acupressure and fatigue in patients with end-stage renal disease- a randomized controlled trial. *Int J Nurs Stud* 2004; 41: 99-106.

A randomised controlled trial that investigated the effectiveness of acupressure on fatigue in patients with end-stage renal-disease (ESRD). A total of 106 patients were randomly assigned into acupressure, sham or control groups. Patients in the acupressure group had reduced fatigue ($p=0.003$). Comparisons indicated that there were significant differences between the acupressure group and the control group ($p=0.01$) and between the sham group and control group ($p=0.003$). The reviewers concluded that acupuncture provided an alternative method for healthcare providers in the management of ESRD patients with fatigue.

Observational studies

Cassileth BR et al. A safety and efficacy pilot study of acupuncture for the treatment of chronic lymphoedema. *Acupunct Med*. 2011 Sep;29(3):170-2.

This pilot study recruited women diagnosed with chronic lymphoedema (affected arm width >2 cm circumference than unaffected arm) after breast cancer surgery. They received acupuncture twice a week for 4 weeks, using a standardized prescription and needling into the affected as well as the unaffected limb. Nine subjects were treated before the study goal

	<p>was reached of obtaining four women with at least a 30% reduction in lymphoedema at 4 weeks when compared with baseline values. No serious adverse events occurred during or after 73 treatment sessions. It was concluded that acupuncture appears safe and may reduce lymphoedema associated with breast cancer surgery.</p>
<p>De Valois BA et al. Assessing the feasibility of using acupuncture and moxibustion to improve quality of life for cancer survivors with upper body lymphoedema. <i>Eur J Oncol Nurs.</i> 2011 Sep 12. [Epub ahead of print]</p>	<p>An exploratory single-arm observational study included breast (BC) and head and neck cancer (HNC) survivors with mild-to-moderate uncomplicated lymphoedema. They received seven individualised treatments (S1), and six optional additional treatments (S2). Of 35 participants recruited, 30 completed S1 and S2, three completed S1, two were lost to the study. Mean MYMOP profile change scores for BC participants were 1.28 points improvement on a 7-point scale for S1 (n=25), and 1.41 for S2 (n=24). For HNC the changes were 2.29 and 0.94 respectively (n=7; n=6). Some SF36 scores for BC patients also improved significantly to 4 weeks after treatment. There were no serious adverse effects, and the author concluded that acupuncture adjunctive to usual care is an acceptable treatment for cancer survivors with lymphoedema.</p>
<p>Donald GK et al. Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy. <i>Acupunct Med</i> 2011; 29 (3):230-3</p>	<p>Eighteen (18) patients referred by medical staff or self-referred received six weekly acupuncture treatments. The points were based on individual presentation. 82% (n=14) reported symptom improvement and some recorded additional benefits such as medication reduction and improved sleep. The conclusion was that acupuncture may be an option for patients with chemotherapy-induced peripheral neuropathy though further research is required.</p>
<p>Kim KH et al. Acupuncture for symptom management in hemodialysis patients: a prospective, observational pilot study. <i>J Altern Complement Med</i> 2011; 17: 741-8.</p>	<p>A prospective, observational pilot study that looked at the feasibility, safety, and possible benefits of acupuncture for symptom management in 24 patients undergoing haemodialysis. Acupuncture treatments were provided twice a week for 6 consecutive weeks on a non-dialysis day or on the day of haemodialysis prior to initiating treatment. Patients experienced a significant improvement of symptoms considered the most bothersome (p<0.0001). No serious adverse events related to acupuncture occurred. The researchers concluded that acupuncture seems feasible and safe for symptom management in patients undergoing haemodialysis.</p>
<p>Dean-Clower E et al. Acupuncture as palliative therapy for physical symptoms and quality of life for advanced cancer patients. <i>Integr Cancer Ther</i> 2010; 9: 158-67.</p>	<p>An 8-week single-armed prospective pilot study that looked at the feasibility of administering acupuncture as palliative therapy in 40 patients with advanced ovarian or breast cancer and to assess the effect on symptoms and quality of life (QOL). Among patients experiencing baseline symptoms, there was improvement in anxiety (p=0.001), fatigue (p=0.0002), pain (p=0.0002), and depression (p=0.003). QOL measures of pain severity and interference, physical and psychological distress, life satisfaction, and mood states showed improved scores during treatment, with sustained benefit at 12 weeks. The researchers concluded that their pilot study demonstrated that an 8-week outpatient acupuncture course is feasible for advanced cancer patients and produces a measurable benefit that should be evaluated in controlled trials.</p>

<p>Takahashi H. Effects of acupuncture on terminal cancer patients in the home care setting. <i>Med Acupunct</i> 2009; 21: 123-9.</p>	<p>A study that evaluated the efficacy of acupuncture on various symptoms in 12 terminal cancer patients receiving home care who had been evaluated as having less than 1 month to live at the time of discharge from hospital. The patients presented with a variety of symptoms, including pain, nausea, vomiting, constipation, dyspnoea, and general fatigue. All patients survived at least 1 month after the initiation of the acupuncture treatment at home (mean length of stay at home, 133 days). There was a moderate to significant reduction in the severity of constipation, dyspnoea, and general fatigue; the effects on pain and nausea were variable. No patient required hospitalisation for palliation of symptoms, nor did any patients experience anxiety or other psychological problems that needed further medical attention. All patients were able to remain home until death. The researchers concluded that acupuncture appeared to significantly contribute to the palliation of symptoms experienced by terminal cancer patients.</p>
<p>Meidell L et al. Acupuncture as an optional treatment for hospice patients with xerostomia: an intervention study. <i>Int J Palliat Nurs</i> 2009; 15: 12-20.</p>	<p>A 5-week study that investigated whether treatment with acupuncture is a viable option for 14 hospice patients with xerostomia. Only eight patients completed the study. The effect of acupuncture was assessed using a visual analogue scale, and by measuring the saliva production before and after treatment. All the patients experienced alleviation of dryness of the mouth and the associated symptoms. However, conducting a 5-week acupuncture intervention study was not feasible due to the patients being too close to death.</p>
<p>Kaufman K, Salkeld EJ. Home hospice acupuncture: a preliminary report of treatment delivery and outcomes. <i>Perm J</i>. 2008 Winter; 12(1):23-6</p>	<p>A hospice report comprising a one-year summary of patient chart data (n=71) and interviews with the two acupuncturists in the programme. 63% of patients had a cancer diagnosis. The commonest complaints were pain (70%), anxiety (45%), shortness of breath (27%) and nausea/vomiting (14%). With a median of 3 treatments excellent/good results were noted for 22-31% of patients, depending on the complaint. The practitioners described a greater focus on symptoms than is typical in traditional acupuncture practice, though benefits in psycho-socio-spiritual domains were also observed. Conclusions: acupuncture is a promising adjunctive therapy for those nearing the end of life in the home hospice setting; more detailed and precise assessment is warranted.</p>

Filshie J et al. Acupuncture and self acupuncture for long-term treatment of vasomotor symptoms in cancer patients--audit and treatment algorithm. *Acupunct Med.* 2005 dec;23(4):171-80

An acupuncture protocol was developed for treating cancer patients with vasomotor symptoms. Initially six weekly treatments were given using distal and upper sternal points, but avoiding lymphoedematous limbs. If there were no contraindications, patients were told how to perform self acupuncture, weekly for up to six years, for long term maintenance. A retrospective audit of 159 patients (predominantly female, and with breast or prostate cancer) showed that 114 (79%) gained a 50% or greater reduction in hot flushes and 30 (21%) a less than 50% reduction. The duration of treatment varied from one month to over six years (mean, nine months). Seventeen patients (9%) experienced minor side effects over the six year period, mostly minor rashes. Hence acupuncture is associated with long-term relief of vasomotor symptoms in cancer patients. Treatment is safe and costs appear to be low.

Johnstone PA et al. Integration of acupuncture into the oncology clinic. *Palliat Med* 2002; 16: 235-9.

A paper describing the physical integration of acupuncture into an oncology clinic, and patient perspectives on its availability and efficacy. A practice outcome analysis was performed on 89 patients receiving therapy between 1 January 2000 and 30 April 2000. Major reasons for referral to the clinic included pain (53%), xerostomia (32%), hot flashes (6%) and nausea/loss of appetite (6%). Patients had a mean of five acupuncture visits (range 1-9). Most patients (60%) showed at least 30% improvement in their symptoms. About one-third of patients had no change in severity of symptoms. There were no untoward effects reported related to the acupuncture. When analysed by diagnosis, these values persist. Irrespective of response to therapy, 86% of respondents considered provision of the acupuncture service to be 'very important'. The researchers concluded that acupuncture may contribute to control of symptoms for cancer patients.

Phillips KD, Skelton WD. Effects of individualized acupuncture on sleep quality in HIV disease. *J Assoc Nurses Aids Care.* 2001;12(1):27-39.

Participants were 21 HIV-infected men and women aged 29 - 50 years, who reported sleep disturbance three or more times per week and who scored greater than 5 on the Pittsburgh Sleep Quality Index. The Wrist Actigraph was used to measure sleep activity, and the Current Sleep Quality Index was used to measure sleep quality for 2 nights before and after a 5-week acupuncture intervention (10 treatments). Acupuncture was individualized to address insomnia and other symptoms reported by the participants. Sleep activity and sleep quality significantly improved after treatment.

Possible mechanisms of acupuncture

Goldman N et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nat Neurosci* 2010; May 30.

A study showing that the neuromodulator adenosine, which has anti-nociceptive properties, was released during acupuncture in mice, and that its anti-nociceptive actions required adenosine A1 receptor expression. Direct injection of an adenosine A1 receptor agonist replicated the analgesic effect of acupuncture. Inhibition of enzymes involved in adenosine degradation potentiated the acupuncture-elicited increase in adenosine, as well as its anti-nociceptive effect. The researchers concluded that their observations indicate that adenosine mediates the effects of acupuncture and that interfering with adenosine metabolism may

prolong the clinical benefit of acupuncture.

Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. *Auton Neurosci* 2010; 157: 81-90.

Studies have shown that acupuncture stimulation, when associated with sensations comprising deqi, evokes deactivation of a limbic-paralimbic-neocortical network, as well as activation of somatosensory brain regions. These networks closely match the default mode network and the anti-correlated task-positive network. The effect of acupuncture on the brain is integrated at multiple levels, down to the brainstem and cerebellum and appears to go beyond either simple placebo or somatosensory needling effects. Needling needs to be done carefully, as very strong or painful sensations can attenuate or even reverse the desired effects. Their results suggest that acupuncture mobilizes the functionally anti-correlated networks of the brain to mediate its actions, and that the effect is dependent on the psychophysical response. They discuss potential clinical application to disease states including chronic pain, major depression, schizophrenia, autism, and Alzheimer's disease.

Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. *Human Brain Mapping* 2009; 30: 1196-206.

This study assessed the results of fMRI on 10 healthy adults during manual acupuncture at 3 acupuncture points and a sham point on the dorsum of the foot. Although certain differences were seen between real and sham points, the hemodynamic and psychophysical responses were generally similar for all 4 points. Acupuncture produced extensive deactivation of the limbic-paralimbic-neocortical system. Clusters of deactivated regions were seen in the medial prefrontal cortex, the temporal lobe and the posterior medial cortex. The sensorimotor cortices, thalamus and occasional paralimbic structures such as the insula and anterior middle cingulate cortex showed activation. The researchers concluded that their results provided additional evidence that acupuncture modulates the limbic-paralimbic-neocortical network. They hypothesised that acupuncture may mediate its analgesic, anti-anxiety, and other therapeutic effects via this intrinsic neural circuit that plays a central role in the affective and cognitive dimensions of pain.

Zhao CL et al. Effect of acupuncture on the activity of the peripheral blood T lymphocyte subsets and NK cells in patients with colorectal cancer liver metastasis. *Zhongguo Zhen Jiu* 2010; 30: 10-2.

A study that looked at the effect of acupuncture on the immune function of 60 patients with colorectal cancer liver metastasis. The value of T lymphocyte subsets such as CD(3) , CD(4), and CD(8) , as well as Natural Killer cells were obviously increased after treatment, and there were significant differences between them before and after treatment.

Cheng CH et al. Endogenous Opiates in the Nucleus Tractus Solitarius Mediate Electroacupuncture-induced Sleep Activities in Rats. *Evid Based Complement Alternat Med* 2009; Sep 3.

An animal study that investigated the involvement of the nucleus tractus solitarius opioidergic system in electroacupuncture-induced alterations in sleep, the findings of which suggested that mechanisms of sleep enhancement may be mediated, in part, by cholinergic activation, stimulation of the opioidergic neurons to increase the concentrations of beta-endorphin and the involvement of the μ -opioid receptors.

Kim H et al. The effects of acupuncture stimulation at PC6 (Neiguan) on chronic mild stress-

The effects of acupuncture on the behavioural responses induced by chronic mild stress (CMS) were evaluated in rats by using a maze and a sucrose intake test. C-fos expression in the brain was

<p>induced biochemical and behavioral responses. <i>Neuroscience Letters</i>. 2009; 460: 56-60.</p>	<p>examined by immunohistochemistry. Acupuncture stimulation at point P6 (3 min) (but not at point SJ5) reversed stress-induced behavioural changes and significantly attenuated c-fos expression in the hypothalamus, suggesting that acupuncture has a therapeutic effect on chronic stress-related diseases such as depression and anxiety.</p>
<p>Komori M et al. Microcirculatory responses to acupuncture stimulation and phototherapy. <i>Anesth Analg</i> 2009; 108: 635-40.</p>	<p>Experimental study on rabbits in which acupuncture stimulation was directly observed to increase diameter and blood flow velocity of peripheral arterioles, enhancing local microcirculation.</p>
<p>Zhou Q et al. The effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the CNS of rats with chronic emotional stress-induced anxiety. <i>Int J Clin Acupunct</i> 2008; 17: 79-84.</p>	<p>A study of the regulatory effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the central nervous system of rats with chronic emotional stress-induced anxiety. The levels of serotonin, noradrenaline and dopamine fell significantly, while GABA levels were significantly higher in the rats given acupuncture ($P < 0.05$, or $P < 0.0$). The researchers concluded that the anti-anxiety effect of electro-acupuncture may relate to its regulation of the imbalance of neurotransmitters.</p>
<p>Arranz L et al. Effect of acupuncture treatment on the immune function impairment found in anxious women. <i>American Journal of Chinese Medicine</i>. 2007;35(1):35-51</p>	<p>A study in which 34 women with anxiety received 10 acupuncture treatments over a year, until complete remission. Twenty healthy, non-anxious women formed the controls. Impaired immune functions in anxious women (chemotaxis, phagocytosis, lymphoproliferation and NK activity) were significantly improved by acupuncture, coming to the values of the healthy controls. The effects peaked 72 hours after a session and lasted up to a month after the course finished.</p>
<p>Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. <i>Integr Cancer Ther</i> 2007; 6: 251-7.</p>	<p>Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.</p>
<p>Streitberger K et al. Acupuncture for nausea and vomiting: an update of clinical and experimental studies. <i>Auton Neurosci</i> 2006; 129: 107-17.</p>	<p>An overview of clinical and experimental studies. The latter showed effects of P6-stimulation on gastric myo-electrical activity, vagal modulation and cerebella vestibular activities in functional magnetic resonance imaging. A growing number of experimental studies suggest mechanisms of action for acupuncture's effect on nausea/vomiting.</p>

<p>Huang ST et al. Increase in the vagal modulation by acupuncture at Neiguan point in the healthy subjects. <i>American Journal of Chinese Medicine</i> 2005; 33: 157-64.</p>	<p>A study that investigated whether acupuncture at the P6 point could improve vagal modulation by using heart rate variability analysis. In all, 39 subjects received acupuncture at the P6 point, 38 subjects received sham acupuncture, and 34 subjects received no treatment., and the low-/high-frequency power ratio was used as the index of sympathovagal balance. The normalised high-frequency power (a measure of vagal modulation) after acupuncture (but not sham) increased significantly. In both the P6 and sham acupuncture groups, the mean RR interval (the intervals between consecutive R waves in the electrocardiogram) increased significantly. In the no-treatment group, there was no significant change in any heart rate variability measures. The researchers concluded that acupuncture at the P6 point can increase vagal modulation of the subjects.</p>
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<p>Tatewaki M et al. Effects of acupuncture on vasopressin-induced emesis in conscious dogs. <i>American Journal of Physiology - Regulatory Integrative and Comparative Physiology</i> 2005. 288: 57-2.</p>	<p>Vasopressin, a posterior pituitary hormone, is involved in nausea and vomiting in humans and dogs. To investigate the antiemetic effects of acupuncture on vasopressin-induced emesis, gastroduodenal motor activity and the frequency of retching and vomiting were simultaneously recorded in conscious dogs. Electroacupuncture (EA) at P6 significantly reduced the number of episodes of retching and vomiting induced by vasopressin. It also suppressed retrograde peristaltic contractions. In contrast, EA at two other acupoints had no antiemetic effects. The antiemetic effect of EA was abolished by pre-treatment with naloxone (but not naloxone methiodide), suggesting that it is mediated via the central opioid pathway.</p>
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<p>Zijlstra FJ et al. Anti-inflammatory actions of acupuncture. <i>Mediators Inflamm</i> 2003; 12: 59-69.</p>	<p>An article that suggests a hypothesis for anti-inflammatory action of acupuncture: Insertion of acupuncture needles initially stimulates production of beta-endorphins, CGRP and substance P, leading to further stimulation of cytokines and NO. While high levels of CGRP have been shown to be pro-inflammatory, CGRP in low concentrations exerts potent anti-inflammatory actions. Therefore, a frequently applied 'low-dose' treatment of acupuncture could provoke a sustained release of CGRP with anti-inflammatory activity, without stimulation of pro-inflammatory cells.</p>
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Methodological considerations concerning acupuncture trials

<p>Lundeberg T et al. Is Placebo Acupuncture What It is Intended to Be? <i>Evid Based Complement Alternat Med.</i> 2011;2011:932407</p>	<p>Discusses the concerns with sham acupuncture and recommends instead that the therapy be evaluated by comparisons with standard treatments</p>
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<p>Sherman KJ, Coeytaux RR. Acupuncture for Improving Chronic Back Pain, Osteoarthritis and Headache. <i>J Clin Outcomes Manag.</i> 2009 May 1;16(5):224-230</p>	<p>An overview of the clinical research on acupuncture for three chronic pain conditions, back pain, osteoarthritis and headache (tension headache and migraine). Also discusses the nature of acupuncture and points out the problems with sham interventions</p>
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<p>Paterson C, Dieppe P. Characteristic and incidental (placebo) effects in complex interventions such as acupuncture. <i>BMJ.</i> 2005 May 21;330(7501):1202-5</p>	<p>Discusses how complex interventions such as acupuncture differ profoundly from drugs such that placebo/sham trial designs are no longer appropriate and may even generate false negative results.</p>
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General effects of acupuncture

Rugg S et al. Traditional acupuncture for people with medically unexplained symptoms: a longitudinal qualitative study of patients' experiences. *Br J Gen Pract.* 2011 Jun;61(587):e306-15

20 participants in a trial of acupuncture for medically unexplained symptoms were interviewed at the start and end of the 6-month treatment period. Acupuncture was valued for the amount of time allotted with a caring practitioner and for the interactive and holistic nature of the sessions. Patients were encouraged to take an active role in their treatment, including cognitive or behavioural lifestyle changes. They noticed health changes across physical, psychological, and social dimensions, including an increase in physical and/or mental energy and feelings of greater personal control, calmness and relaxation.
