

# Hypnosis for nausea and vomiting in cancer chemotherapy: a systematic review of the research evidence

J. RICHARDSON, BSC(HONS), PHD, RN, CPSYCHOL, PGCE, RNT, READER IN NURSING AND HEALTH STUDIES, *Faculty of Health and Social Work, Portland Square, University of Plymouth, Drake Circus, Plymouth, Devon*, J.E. SMITH, BA(HONS), MSC, FORMER RESEARCH ASSISTANT, *NHSP/CAMEO project, Research Council for Complementary Medicine*, G. MCCALL, DCR(T), MSC, APPLIED HYPNOSIS, SENIOR RESEARCH RADIOGRAPHER & PSYCHOLOGICAL SUPPORT, *South-East London Cancer Centre, St Thomas' Hospital, London*, A. RICHARDSON, BN(HONS), MSC, PHD, RN, PGDIPED, RNT, PROFESSOR OF CANCER AND PALLIATIVE NURSING CARE, *The Florence Nightingale School of Nursing and Midwifery, King's College London, Franklin Wilkins Building, London*, K. PILKINGTON, BPHARM(HONS), DIPINFSCI, MSC, PCME, MRPHARMS, *Project Manager/Senior Research Fellow, School of Integrated Health and Research Council for Complementary Medicine, University of Westminster, 115 New Cavendish Street, London*, & I. KIRSCH, BA, MA, PHD, PROFESSOR OF PSYCHOLOGY, *School of Applied Psychosocial Studies, Portland Square, University of Plymouth, Drake Circus, Plymouth, Devon, UK*

RICHARDSON J., SMITH J.E., MCCALL G., RICHARDSON A., PILKINGTON K. & KIRSCH I. (2007) *European Journal of Cancer Care* **16**, 402–412

## Hypnosis for nausea and vomiting in cancer chemotherapy: a systematic review of the research evidence

To systematically review the research evidence on the effectiveness of hypnosis for cancer chemotherapy-induced nausea and vomiting (CINV). A comprehensive search of major biomedical databases including MEDLINE, EMBASE, CINAHL, PsycINFO and the Cochrane Library was conducted. Specialist complementary and alternative medicine databases were searched and efforts were made to identify unpublished and ongoing research. Citations were included from the databases' inception to March 2005. Randomized controlled trials (RCTs) were appraised and meta-analysis undertaken. Clinical commentaries were obtained. Six RCTs evaluating the effectiveness of hypnosis in CINV were found. In five of these studies the participants were children. Studies report positive results including statistically significant reductions in anticipatory and CINV. **Meta-analysis revealed a large effect size of hypnotic treatment when compared with treatment as usual, and the effect was at least as large as that of cognitive-behavioural therapy. Meta-analysis has demonstrated that hypnosis could be a clinically valuable intervention for anticipatory and CINV in children with cancer.** Further research into the effectiveness, acceptance and feasibility of hypnosis in CINV, particularly in adults, is suggested. Future studies should assess suggestibility and provide full details of the hypnotic intervention.

*Keywords:* cancer, chemotherapy, hypnosis, nausea and vomiting, review, meta-analysis.

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Correspondence address: Dr Janet Richardson, Reader in Nursing and Health Studies, Faculty of Health and Social Work, Portland Square, University of Plymouth, Drake Circus, Plymouth, Devon PL4 8AA, UK (e-mail: janet.richardson@plymouth.ac.uk).

Accepted 18 September 2006

DOI: 10.1111/j.1365-2354.2006.00736.x

*European Journal of Cancer Care*, 2007, **16**, 402–412

## INTRODUCTION

Chemotherapy-induced nausea and vomiting (CINV) represents a significant problem for patients with cancer (Koeller *et al.* 2002). Despite advances in treating CINV, side effects continue to be clinically significant. Approximately 70–80% of all cancer patients receiving chemotherapy experience nausea and vomiting (Lindley *et al.*

1989; Morrow 1992). Emetic risk is higher (greater than 90% of patients) with some cytotoxic agents, for example, cisplatin and cyclophosphamide (<http://www.mascc.org>).

The presence of nausea and vomiting has been consistently demonstrated to impact on patients' quality of life and functional status and jeopardizes the delivery of optimal cancer treatment (Jenns 1994; Roscoe *et al.* 2000). Indeed, CINV has been shown to affect compliance as many patients may view the treatment and resulting discomfort as worse than the disease and are reluctant to subject themselves to repeated courses of treatment (Richardson *et al.* 1988).

For most patients, the use of various emetogenic drugs forms the basis for the control of both acute and delayed CINV (Miller & Kearney 2004). Considerable progress has been made in the pharmacological management of CINV and numerous studies have provided evidence on the efficacy of anti-emetic therapies alone and in combination. While corticosteroids and dopamine antagonists have long been used in the treatment of acute emesis, the emergence of the selective serotonin (5-HT<sub>3</sub>) receptor antagonists in combination with dexamethasone has improved effectiveness and diminished treatment-related toxicity (Herrstedt *et al.* 1997). A number of professional organizations have published guidelines to direct the most appropriate use of anti-emetic therapy.<sup>1</sup> Nevertheless, a significant proportion of patients receiving chemotherapy still report symptoms of nausea and vomiting and a universally effective anti-emetic regime for CINV remains elusive. Furthermore, pharmacological anti-emetic treatment may be poorly tolerated in some patient groups and can produce a range of side effects (Miller & Kearney 2004). This creates ongoing challenges for those caring for patients who are receiving chemotherapy. Selecting and administering the appropriate anti-emetic therapy, be it pharmacological or behavioural, can significantly improve patients' quality of life and functional status facilitating the effectiveness of potentially curative therapy (Miller & Kearney 2004).

In addition to nausea and vomiting caused by pharmacological agents, there are several psychological triggers. Anticipatory nausea and vomiting (ANV) can begin even before the commencement of chemotherapy, influenced by patient beliefs, and expectations learned from other nauseating experiences (for example, pregnancy and travel sickness). Furthermore, healthcare staff may inadvertently trigger this response by talking about chemotherapy

side effects. After several pulses of chemotherapy, some patients develop classically conditioned nausea and vomiting (Walker 1992). For these reasons, it has been suggested that ANV should be managed primarily by psychological interventions (<http://www.mascc.org>). Moreover, the British National Institute for Clinical Excellence service guidance for improving outcomes in children and young people with cancer consultation guidelines recommend that 'there should be timely access to occupational and psychological or behavioural therapies for patients with anticipatory nausea and vomiting' (NICE 2005).

Hypnosis represents one possible therapy for limiting the emetic effects of chemotherapy. Hypnosis is a psychological approach during which a therapist suggests that a client will experience changes in sensation, perception, thought and behaviour (Kirsch *et al.* 1995). An 'induction' procedure is used prior to 'suggestion' in order to enhance relaxation. The 'suggestibility' of a person appears to be an important variable in the effectiveness of hypnosis and in long-term treatment effects (Patterson & Jensen 2003). Hypnosis has been used in a variety of conditions and settings. For example, Stalpers *et al.* (2005) found that hypnosis improved mental and overall well-being in cancer patients undergoing radiotherapy. Taylor and Ingleton (2003) used a qualitative approach in order to understand the experiences of cancer patients undergoing hypnotherapy and cognitive-behaviour therapy during cancer chemotherapy. Themes that emerged from the data included gaining help, individualized treatment, long-term benefits, patient satisfaction and patient information needs. Guided imagery in particular was highly valued by participants as it helped them to feel more in control.

A number of literature reviews and meta-analyses have examined the effectiveness of hypnosis. For example, Kirsch *et al.* (1995) conducted a meta-analysis of 18 studies of hypnosis as an adjunct to cognitive-behavioural psychotherapy in conditions such as anxiety and obesity and found that the addition of hypnosis substantially enhanced treatment outcome. In contrast, a meta-analysis carried out by Flammer and Bongartz (2003) produced contradictory results. Evidence from systematic reviews suggests that hypnosis has a positive impact on acute procedural and chronic pain conditions (Sellick & Zaza 1998; Hawkins 2001; Patterson & Jensen 2003), as well as for post-operative pain (Montgomery *et al.* 2002).

A number of reviews have examined the effects of psychological treatments on cancer patients (cf. Trijsburg *et al.* 1992; Smith *et al.* 1994; Devine & Westlake 1995; Milling & Constantino 2000; Redd *et al.* 2001; Newell *et al.* 2002; Mundy *et al.* 2003). These reviews have

<sup>1</sup>See, for example, The American Society of Clinical Oncology (<http://www.asco.org>), The National Comprehensive Cancer Network (<http://www.nccn.org>) and Multinational Association of Supportive Care in Cancer (<http://www.mascc.org>).

adopted different inclusion criteria resulting in different studies being included in the reviews. This highlights difficulties in the interpretation of findings when studies and interventions are heterogeneous. To date, a systematic review and meta-analysis specifically focusing on the effectiveness of hypnosis for CINV in cancer patients has not been published.

**Aim and objectives**

The aim of this review was to evaluate systematically the evidence for the effectiveness of hypnosis for the alleviation of nausea and vomiting in cancer chemotherapy.

**METHODS**

**Summary of the search strategy**

A comprehensive search for clinical research was carried out. Systematic searches were conducted on a range of databases and citations were sought from relevant reviews.

**Databases searched**

All searches covered databases from their inception and included all citations up to March 2005.

Systematic searches of major biomedical, nursing and specialist complementary and alternative medicine databases were carried out: Medline, Embase, AMED, CISCOM, CINAHL, PsycInfo, Cochrane Library. A search of specialist resources included Cochrane Complementary Field Registry. Search strategies were developed to accommodate the different indexing approaches used by the databases (Pilkington & Richardson 2003).

*Search terms*

The search strategy for this review included a combination of terms and text words for cancer and hypnosis. The cancer search strategy is broad and covers palliative and terminal care. Using this strategy, relevant citations for cancer-related nausea and vomiting have been identified.

Specific symptom terms or text words for nausea and vomiting were not included since they would have resulted in producing irrelevant citations for other conditions (for example, migraine, pregnancy, surgery-related symptoms). An additional search including the symptom terms and text words on PubMed and EMBASE identified irrelevant records and showed that any publications discussing these symptoms in cancer patients would have been retrieved by the cancer search strategy.

The basic search terms used included:

neoplasms (exp) or neoplas\* or tumour\* or tumour\* or melanoma\* or cancer\* or malignan\* or leukaemia\* or leukaemia\* or carcin\* or metastas\* or sarcoma\* or antineoplastic agents (exp) or chemotherapy or palliative care (exp) or palliative treatment (exp) or palliative therapy (exp) or terminal care (exp)

and

hypnosis or hypnosis (exp) or hypnotiz\* or hypnotis\* or hypnotherapy or hypnotizability or hypnotisability or hypnotic susceptibility or hypnotic-susceptibility (exp) or suggestibility (exp) or autosuggestion or autosuggestion (exp) or suggestion (exp) or autohypnosis (exp) or self-hypnosis or post-hypnotic or post-hypnotic suggestions or post-hypnotic suggestions (exp) or autogenic or autogenic-training (exp).

Efforts were made to identify unpublished and ongoing research using relevant databases such as the National Research Register (UK) and Clinicaltrials.gov (US). Reference lists of relevant articles were reviewed to identify further studies.

**Filtering**

Relevant research was categorized by study type (Table 1). Studies of adults or children were included. Animal research and basic lab-based research were not included in the categorization process.

No language restrictions were imposed at the search and filtering stage.

**Table 1.** Categories of study types used

RCT	Randomized controlled trials
CCT	Controlled clinical trials (without randomization)
UC studies	Uncontrolled studies including uncontrolled clinical trials and case series (further categorized according to the study population, i.e. random sample, consecutive series or 'best' series)
Case reports/studies	Reports of individual cases/patients
Qualitative research	Study designs with a qualitative approach (including in-depth interviews and focus groups)
Surveys	Large scale, primarily quantitative structured approaches
Other	Research studies not falling into above categories

## Selection criteria

### *Types of studies*

Controlled clinical trials of patients with a diagnosis of cancer undergoing chemotherapy.

### *Types of intervention*

An intervention defined by the study investigators as 'hypnosis' or 'hypnotherapy' that involved both 'induction' and 'suggestion'.

### *Types of control group*

Comparative therapy or no treatment controls.

### *Types of outcome measures*

Frequency and severity of nausea and vomiting.

### *Exclusion criteria*

Studies where the intervention investigated was not defined as hypnosis by the investigator, for example, relaxation studies. Studies that did not have CINV as the target symptom. Controlled clinical trials where only the abstract was available. Uncontrolled studies.

## Data collection and analysis

Data were extracted systematically using a specially designed data extraction form. Data extracted included details of selection criteria and procedure, the participants, the intervention and any comparison or control intervention, aspects of the methodology and outcome measures and results.

Clinical trials were appraised using a standardized appraisal framework specifically developed for this project and based on criteria recommended in the Centre for Reviews and Dissemination (2001, 2nd Edition) Report Number 4, Undertaking Systematic Reviews of Research on Effectiveness. Criteria included method of randomization, baseline comparison of characteristics, method of dealing with missing values, loss to follow-up/withdrawals, measures of compliance and outcomes measures reported. For each study, data extraction and appraisal were conducted independently by two researchers and any disagreements or discrepancies were resolved by discussion. Where consensus could not be obtained, a third reviewer was available for consultation.

Meta-analysis was carried out for controlled trials on which post-treatment means and standard deviations for

nausea and/or vomiting had been reported. As these two outcomes were highly correlated, a single mean effect size was calculated for each comparison of hypnotic treatment against non-hypnotic treatment. However, when a clinical trial contained more than one comparator (e.g. treatment as usual, therapist contact and cognitive therapy), a separate effect size was calculated for each. Effect sizes were calculated as the standardized difference in post-treatment scores between the hypnosis and comparator treatment ( $d$ ). Mean effect sizes across trials ( $D$ ) were weighted for sample size (Hunter & Schmidt 1990).

## Clinical commentaries

Clinicians with relevant training and experience commented on each study focusing on clinical relevance and practical issues. Commentary frameworks were specifically developed for this project and these incorporate a number of closed and open questions with space for further comments. Summaries of these commentaries are provided in the table of studies.

## Main results

Six randomized controlled trials (RCTs) met the inclusion criteria (Zeltzer *et al.* 1984, 1991; Cotanch *et al.* 1985; Syrjala 1992; Jacknow *et al.* 1994; Hawkins *et al.* 1995).

No studies in languages other than English were located.

Ten of the retrieved studies did not meet the inclusion criteria (see Table 2).

## The evidence

Six RCTs were located for inclusion in the review. Five of the studies focused on CINV in children. In addition, a randomized clinical trial examining self-hypnosis for nausea and vomiting in cancer patients undergoing autologous bone marrow transplant was identified through the

**Table 2.** Excluded studies

Study	Reason for exclusion
Axelrod <i>et al.</i> (1988), Marchioro <i>et al.</i> (2000), Redd (1983), Walker <i>et al.</i> (1988), Walker <i>et al.</i> (1990)	Not a controlled study
Barr (1981) Rapkin <i>et al.</i> (1991), Shea (2003), Spiegel & Moore (1989)	Abstract only available Not nausea and vomiting
Syrjala <i>et al.</i> (1995)	Intervention not called hypnosis

National Research Register. Although this project status is given as 'complete', attempts to contact the author failed to produce a response and the study has not been published to date.

### Summary of each study

A summary of each study is presented in Table 3. Further details are provided below in narrative form together with consideration of the methodological issues raised from the critical appraisal of the studies.

Hawkins *et al.* (1995) randomized 30 patients (aged 5–17 years) known to have severe ANV undergoing chemotherapy for osteogenic sarcoma to one of three groups: usual treatment, therapist contact or hypnosis training. All patients were receiving an identical chemotherapy regime that included cisplatin and cyclophosphamide. All participants continued to receive anti-emetic drugs (ondansetron 30 min before chemotherapy) for the duration of the study. Participants in the hypnosis group were taught self-hypnosis by the therapist to be practised prior to and during chemotherapy. The therapist was not present at the time of self-hypnosis practice or during subsequent chemotherapy sessions. The 'usual treatment' group had no therapist intervention, whereas the 'therapist contact' control met with the therapist for the equivalent time and frequency as the hypnosis training group to control for therapist time and intervention. Nausea and vomiting/retching were assessed retrospectively using a visual analogue scale (VAS). Following the intervention, there was a significant difference in both nausea ( $P = 0.02$ ) and vomiting ( $P = 0.02$ ) scores between the hypnosis and the attention control group. The therapist attention control group showed a significant decrease in nausea but not vomiting compared with the usual treatment controls. The authors report that anecdotal evidence suggests the instruction to practise self-hypnosis at home was not adhered to.

In contrast to Hawkins *et al.* (1995), Jacknow *et al.* (1994) conducted an RCT of newly diagnosed children (aged 6–18 years) with no prior experience of chemotherapy. Twenty-four patients underwent a stratified randomization procedure that took account of the emetogenicity of their chemotherapy. The hypnotic technique (self-hypnosis) was age-specific and individually tailored to each child. The control group received the equivalent amount of time in informal conversation with the therapist. It is not clear if the therapist remained with the child throughout the chemotherapy. Patients in the control group received the standard anti-emetic regimen, whereas those in the hypnosis group only received as required

(prn.) anti-emetic treatment. Anticipatory nausea and vomiting was assessed at 1–2 and 4–6 months post diagnosis. Severity of nausea was assessed using five faces on a scale; a Likert scale (0–9) was used to assess vomiting. Lower use of prn. anti-emetic drugs in the hypnosis group for both pulses ( $P < 0.04$  and  $P < 0.02$ ), no differences were found between the two groups on nausea and vomiting scores. However, anticipatory nausea was significantly less ( $P < 0.02$ ) in the hypnosis group 1–2 months post diagnosis, but no between-group difference was found after 4–6 months. Practice declined after the end of the second course of chemotherapy; this may be linked to a decline in effectiveness.

Zeltzer *et al.* (1991) randomized 54 patients to receive hypnosis, non-hypnotic distraction or attention control. All participants were children (aged 5–17 years) reporting significant chemotherapy-related nausea and vomiting. Children in the hypnosis group underwent hypnotic induction including imaginative fantasy with suggestions, for example, holding or cuddling a pet. The non-hypnotic distraction group had active cognitive distraction/relaxation therapy (such as counting objects). The therapist attention control group received the same amount of time with the therapist, but this was spent in 'casual conversation'. The therapist was present with each child during the chemotherapy administration for all groups. Chemotherapy regimens included at least one cytotoxic agent classified as high emetic risk. Anticipatory nausea and vomiting was measured by observation and semi-structured interview. A post-chemotherapy telephone interview was conducted 24 h following the cessation of chemotherapy-related symptoms and included a nausea and vomiting rating scale. Nausea was significantly shorter in duration for the hypnosis group ( $P < 0.001$ ) and the non-hypnotic distraction group ( $P < 0.01$ ) when compared with controls. Vomiting was of significantly shorter duration in the hypnosis group ( $P < 0.005$ ) compared with the attention control group. The greatest improvement in ANV was shown in the hypnosis group, whereas children in the control group had worsening symptoms ( $P < 0.05$ ).

Cotanch *et al.* (1985) assessed self-hypnosis in children (aged 10–18 years) who reported CINV. Twelve children were randomized to receive the hypnotic intervention or standard treatment (not specified) and were monitored for four courses of chemotherapy. Post-hypnotic suggestions included feeling good about their ability to help themselves (ego strengthening). The control condition involved distraction, such as focusing on an object in the room. The actual amount of vomiting was measured by nursing staff. The children assessed their nausea and vomiting using a VAS drawn in the form of a thermometer. Psychophysical

Table 3. Hypnosis for nausea and vomiting for cancer patients

Study	Study design	Sample	Inclusion criteria	Hypnosis intervention	Control Tx	Outcome measure(s)	Results	Methodology comments	Clinical comments
Hawkins <i>et al.</i> (1995) (Greece)	RCT three-armed trial Unknown recruitment criteria	n = 30 Hypnosis = 10 Attention control = 10 Usual treatment = 10 Age range 5–17 years.	Paediatric outpatients undergoing chemotherapy with severe anticipatory nausea and vomiting.	One hour pre-admission training session and 20-min post-admission booster sessions in hypnotherapy with instructions for self-hypnosis.	(1) Therapist attention control group had equal time as hypnosis group but spent in discussion. (2) Treatment as usual group, no therapist contact.	Retrospective assessment of anticipatory nausea for one chemotherapy pulse by parents /children and independently by staff with a 10-cm Visual Analogue Scale. Retching/vomiting measured by frequency counts.	Significant difference (prior to, during or within 15 min of infusion) between hypnosis and attention control for vomiting and nausea.	Small sample, no power analysis. Unknown method of randomization or blinding of assessors. Anti-emetic and cytotoxic drug dose not specified.	Appropriate use of intervention, controls and outcome measures. 15 min follow-up time relevant for anticipatory symptoms. Good use of direct and indirect suggestions in self-hypnosis leading to increased self-efficacy.
Jacknow <i>et al.</i> (1994) (USA)	RCT two-armed trial	n = 24 (20 completed) Hypnosis = 10 Attention control = 10 Age range 6–18 years.	Newly diagnosed paediatric cancer patients undergoing chemotherapy.	Hypnosis group received two to three 45-min individualized training sessions in self-hypnosis (to practise twice daily with the aid of an audio tape) plus additional suggestive prompts.	Equivalent time and attention as hypnosis group spent in conversation with the therapist.	Anticipatory nausea and chemo-induced nausea and vomiting measured by face and Likert rating scales. Use of prn. antiemetics recorded. Daily score computed for each hospitalization.	Hypnosis group used significantly less prn. antiemetic medication than control group for both pulses. Anticipatory nausea significantly less in the hypnosis group 1–2 months post diagnosis.	Small sample size, no power analysis. Unknown method of randomization. Assessor was blind to subject group for patient assessment. Four lost to follow up, no intention to treat analysis.	Appropriate use of intervention and controls. Appropriate outcome measures and reporting of outcomes. Follow-up time relevant.

**Table 3.** *Continued*

Study	Study design	Sample	Inclusion criteria	Hypnosis intervention	Control Tx	Outcome measure(s)	Results	Methodology comments	Clinical comments
Syriala (1992) (USA)	RCT four-armed trial	n = 67 (45 completed) Hypnosis = 12 Cognitive coping = 11 Therapist attention = 12 Usual treatment = 10 Age range 19–49 years.	Adult cancer patients with haematologic lymphoma about to receive a bone marrow transplant. Anticipated survival for 19 days post transplant.	Relaxation, imagery and tailored hypnosis with suggestions. Instruction for home practice. 2 × 90-min outpatient training sessions and 10 × 30-min 'booster sessions' twice weekly after admission.	(1) Cognitive-behavioural training: relaxation and cognitive restructuring (2) Therapist contact control group as specified in (3) Usual treatment control.	Brief symptom inventory. Sickness impact profile. Nausea and pain was rated 24 h preceding transplant on a 100-mm VAS. Emesis was rated on patients charts on a scale of 0–3. Opioid use was recorded.	Nausea, emesis and opioid use did not differ significantly between treatment groups.	Unknown method of randomization or blinding of assessors, unknown compliance. 33% lost to follow up. No ITT analysis. Potentially underpowered study.	Adequate intervention and control group, however, more therapist-directed sessions earlier would be advisable to give the patient confidence to use self-hypnosis at times of distress. Adequate outcome measures and follow-up time.
Zeltzer <i>et al.</i> (1991) (USA)	RCT three-armed trial	n = 54 Hypnosis = 21 Non-hypnotic distraction = 16 Attention control = 17 Age range 5–17 years.	Paediatric cancer patients with chemotherapy-related nausea and vomiting of >3 on a 0–10 scale.	15–30 min of pre-hypnotic interview followed by imaginative fantasy with suggestions.	(1) Non-hypnotic distraction: active cognitive distraction /relaxation therapy. (2) Therapist attention time as in other two conditions spent in casual conversation.	Anticipatory and post-chemotherapy nausea, vomiting, distress and functional disruption. Pre-chemotherapy interview, observations, monitoring of anti-emetic use and a post-chemotherapy telephone interview for parent and child.	Nausea of shorter duration for the hypnosis group and non-hypnotic distraction group compared with controls. Vomiting shorter duration in the hypnosis group.	Unknown measure of randomization, blinding or compliance. Co-interventions of anti-emetics. Ten refused to participate.	Appropriate intervention, control, outcome measures and reporting of outcomes. Phone surveys may not be appropriate in young children. Detailed breakdown of symptom evaluation is clinically relevant. Excellent use of involvement in distraction and dissociation of pre-hypnotic suggestions.

Cotanch <i>et al.</i> (1985) (USA)	RCT two-armed trial	<p><i>n</i> = 12 Hypnosis = 6 Usual treatment = 6 Age range 10–18 years.</p>	<p>Paediatric patients undergoing chemotherapy requiring at least 48 h hospitalization with troublesome chemotherapy-related nausea and vomiting.</p>	<p>30–40-min therapist directed training in self-hypnosis with suggestions individually tailored to the child and a post-hypnotic session.</p>	<p>The control group received standard care (deep breaths and distraction).</p>	<p>Vomiting and oral intake assessed by staff following two courses of chemotherapy infusion. Nausea and vomiting were reported by the child on a VAS. Psychophysical scaling to determine severity and intensity of nausea.</p>	<p>Hypnosis group reported a significant decrease in the frequency, amount, severity and duration of vomiting. Also significant decrease in intensity and duration of nausea. Control group more likely to vomit.</p>	<p>Small sample and no power analysis. Unknown method of randomization, checks on blinding of assessors, or compliance. Chemotherapy type and dose not reported. Different numbers of subjects reported in the</p>	<p>Intervention appropriate for this patient group but unclear how methods used. Appropriate control, however, distraction by something in the room can itself be hypnotic. Outcomes appropriately reported. Over ambitious and unsuccessful outcome measures used for the younger ages.</p>
Zeltzer <i>et al.</i> (1984) (USA)	RCT two-armed	<p><i>n</i> = 19 Hypnosis Tx = 9 Supportive therapy Tx = 10 Age range 6–17 years.</p>	<p>Cancer diagnosis, chemotherapy-induced nausea and vomiting symptoms.</p>	<p>After the baseline assessment, each patient met with the therapist once (for 30 min) to practise techniques (individualized imagery and fantasy with suggestions) to be used thereafter in chemotherapy sessions.</p>	<p>Supportive therapy consisted of distracting the child during chemotherapy.</p>	<p>Likert scale completed by parents and children for the severity of the child's nausea and vomiting. Stanford Hypnotic Clinical Scale for Children. Anti-emetic usage.</p>	<p>Significant reductions were found in nausea, vomiting and both for hypnosis and supportive counselling interventions. No significant between-group differences. No significant relationship between hypnotisability and symptom reduction.</p>	<p>Small sample with high (53%) attrition rate. No intention to treat analysis. Oncologists were blind to subject group.</p>	<p>Appropriate intervention and controls. Outcome measures appropriately used and results reported adequately. Results not particularly useful due to small sample. Delay in post-treatment measures to allow for cumulative toxicity is clinically useful.</p>

ITT, intention to treat; RCT, randomized controlled trial; Tx, treatment; VAS, visual analogue scale.



scaling was used to determine the severity and intensity of nausea using an adapted version of the Pain Perception Profile (Tursky *et al.* 1982). The hypnosis group reported a significant decrease in the frequency ( $P = 0.002$ ), amount ( $P = 0.002$ ), severity ( $P = 0.005$ ) and duration ( $P = 0.05$ ) of vomiting, and a significant decrease in intensity ( $P = 0.001$ ) and duration ( $P = 0.01$ ) of nausea. Children in the control group were more likely to vomit ( $P < 0.05$ ). Furthermore, children in the hypnosis group reported being 'less bothered' by chemotherapy ( $P < 0.04$ ). Although children in the hypnosis group had greater oral intake 24 h following chemotherapy infusion, this was not statistically significant ( $P = 0.07$ ). The psychophysical measures for nausea and oral intake did not show statistically significant between-group differences. However, children aged 12 years and younger were unable to complete the ratings in the psychophysical measures; therefore, 50% of data were lost for this scale. This highlights the importance of the use of scales appropriate to age/developmental level.

Zeltzer *et al.* (1984) assessed 19 patients (aged 6–17 years) with leukaemia, lymphoma or bone tumours who experienced CINV. Patients were randomly assigned to receive either hypnosis ( $n = 9$ ) or supportive counselling ( $n = 10$ ). Randomization took into account age and emetic potential of chemotherapy agents. The intervention was used on two chemotherapy cycles. Children in the hypnotic group were helped to become intensely involved in imagery and fantasy, and were given post-hypnotic suggestions to use at home (such as to have a good appetite and to have a restful night's sleep) to be used thereafter in chemotherapy sessions. Supportive counselling consisted of distracting the child's attention during chemotherapy administration. The therapist was present for each course of chemotherapy during the intervention period. Oncologists were blinded to the patients' assigned group. Patients were assessed 3–5 days after the last administered dose in a chemotherapy course. Significant reductions were found in nausea ( $P < 0.001$ ), vomiting ( $P < 0.001$ ) and both ( $P < 0.001$ ) for both hypnosis and supportive counselling interventions with no significant between-group differences. However, as sequential data were only available for nine patients, resulting in an attrition rate of 53%, this may be an artefact of the small sample. No significant relationship ( $P > 0.10$ ) was found between hypnotisability and symptom reduction.

Syrjala (1992) randomized 67 adult patients undergoing bone marrow transplant for haematological malignancies prior to beginning transplantation conditioning to one of four groups: hypnosis training; cognitive-behavioural cop-

ing skills training; therapist contact control; usual treatment control. Hypnosis involved relaxation and imagery tailored to patient preferences. Sessions were tape-recorded for patient use between sessions. Outcomes were assessed using the Brief Symptom Inventory and Sickness Impact Profile. Only 45 completed the study. Oral pain and nausea were assessed daily in the hospital, from a week prior to transplant until 20 days post transplant using VASs. Nausea, emesis and opioid use did not differ significantly between treatment groups.

### Meta-analysis

Post-treatment means and standard deviations for hypnosis and comparator conditions were supplied in four studies (Zeltzer *et al.* 1991; Syrjala 1992; Jacknow *et al.* 1994; Hawkins *et al.* 1995). Effect sizes (displayed in Table 4) varied considerably between studies and as a function of type of treatment to which hypnosis was compared. Nevertheless, all but one of the effect sizes were positive, indicating that hypnosis was generally more effective than comparison procedures in controlling nausea and vomiting. Weighted mean effect sizes indicated that hypnosis was most effective when compared with treatment as usual ( $D = 0.99$ ), followed by therapist contact ( $D = 0.43$ ), and cognitive-behaviour therapy ( $D = 0.18$ ).

## DISCUSSION

The emetogenicity of chemotherapy agents and limitations of conventional anti-emetic treatments continue to pose a challenge in cancer care. This systematic review aimed to evaluate the effectiveness of a psychological intervention (hypnosis) in the treatment of both CINV and ANV. Six RCTs were found. Positive results were reported for nausea and/or vomiting in all five studies assessing children. Positive results were found for ANV in both chemotherapy-experienced and chemotherapy-naive

**Table 4.** Effect sizes

Comparator	Study	<i>n</i>	<i>d</i>
Treatment as usual	Syrjala (1992)	22	-0.02
	Jacknow <i>et al.</i> (1994)	20	0.90
	Hawkins <i>et al.</i> (1995)	20	2.40
Therapist contact	Zeltzer <i>et al.</i> (1991)	38	0.08
	Syrjala (1992)	24	0.23
	Hawkins <i>et al.</i> (1995)	20	1.35
CBT	Zeltzer <i>et al.</i> (1991)	37	0.20
	Syrjala (1992)	23	0.16

CBT, cognitive-behaviour therapy.

patients. These results were supported by the meta-analysis. Only one of the studies we found involved adults and in this study there were no significant differences between groups.

Studies tended to have small sample sizes. To compensate for this, we undertook a meta-analysis to summarize treatment effects across studies and weighted effect sizes as a function of sample size. This analysis indicated a large effect for hypnosis compared with treatment as usual, a moderate effect for hypnosis compared with therapist contact and a small effect for hypnosis compared with cognitive-behaviour therapy.

The meta-analysis also revealed substantial differences in outcome across studies. This may have been due to variations in the hypnotic intervention administered. For example, the initial pre-chemotherapy hypnosis training session varied in length, and the hypnotherapist was present during chemotherapy in some but not all studies. This may have important implications for effectiveness. All the studies involved some form of 'induction' and 'suggestion' in the hypnosis group. Hypnotizability/suggestibility was only assessed in the study by Zeltzer *et al.* (1984). However, various validated scales that measure hypnotic ability are available and these correlate strongly with one another. For example, the Stanford Scale of Hypnotic Susceptibility, Form C (Weitzenhoffer & Hilgard 1962), has become the 'gold standard' research tool. However, as this is time-consuming, the shorter Stanford Clinical Scale for Adults and the Stanford Clinical Scale for Children have been designed for clinical application (Morgan & Hilgard 1978–1979a,b).

The content of the 'script' varied across studies and was mostly targetted towards the development stage of the patient (in the case of children). Explicit reporting of the hypnosis procedure and 'standardization' of techniques assists in the planning of future studies and support implementation into clinical practice. As the studies included a broad range of ages, it was not possible to establish whether the intervention was more or less effective with some age groups.

This systematic review is limited in that the inclusion criteria explicitly focused on studies where the authors had defined their intervention as 'hypnosis'. This resulted in only a small number of studies being selected for review in contrast with other larger reviews that have included a wide range of psychological-behavioural interventions. This highlights a number of challenges in searching and appraising hypnosis studies, as there appears to be some overlap in the components of some relaxation/hypnotic interventions, and similar interventions may be given dif-

ferent names. This has implications for those receiving the intervention as their expectancy of the power of the intervention could be related to what they perceive the intervention to involve.

## CONCLUSIONS

Meta-analysis reported in this review has demonstrated that hypnosis could be a clinically valuable intervention for anticipatory and CINV, in children in particular. The studies generally had small samples; nonetheless, meta-analysis revealed a large effect size of hypnotic treatment when compared with treatment as usual, and the effect was at least as large as that of cognitive-behaviour therapy. Further methodologically rigorous, appropriately powered studies into the feasibility, acceptability and effectiveness of hypnosis in children, adolescents and adults are required. These should provide full details of the hypnotic intervention, and take account of 'suggestibility', presence or absence of the therapist, measuring both actual and anticipatory nausea and vomiting.

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