Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review

E M O’Sullivan,1 I J Higginson2

ABSTRACT
Background Irradiation-induced xerostomia seriously reduces quality of life for patients with head and neck cancer (HNC). Anecdotal evidence suggests that acupuncture may be beneficial.

Objective To systematically review evidence on clinical effectiveness and safety of acupuncture in irradiation-induced xerostomia in patients with HNC.

Methods A detailed search was performed to identify randomised controlled trials (RCTs) and systematic reviews of RCTs on acupuncture in irradiation-induced xerostomia, using AMED, BNIAM, CINAHL, Cochrane, Embase, HPSI, PsycINFO and Medline. Grey literature was explored and 11 journals hand searched. Search terms included: acupuncture, xerostomia, salivary hypofunction, hyposalivation, dry mouth, radiotherapy, irradiation, brachytherapy, external beam. Two authors independently extracted data for analysis using predefined selection criteria and quality indicators.

Results 43 of the 61 articles identified were excluded on title/abstract. 18 articles underwent full-text review; three were deemed eligible for inclusion. Two trials had moderate risk of bias; one had high risk. Two trials compared acupuncture with sham acupuncture; one control arm received ‘usual care’. Outcome measurements included salivary flow rates (SFRs) in two trials and subjective questionnaires in three. All three trials reported 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). Insufficient evidence was presented to undertake risk/benefit assessment.

Conclusions Limited evidence suggests that acupuncture is beneficial for irradiation-induced xerostomia. Although current evidence is insufficient to recommend this intervention, it is sufficient to justify further studies. Highlighted methodological limitations must be dealt with.

INTRODUCTION
Xerostomia is defined as the subjective sensation of oral dryness which is usually, but not invariably, associated with a decrease in salivary production.1 The term ‘xerostomia’ is frequently ascribed to several related conditions—namely, ‘dry mouth’, ‘salivary gland dysfunction’, ‘hyposalivation’, ‘hyposial’ and ‘salivary gland hypofunction’. While the last terms should theoretically be reserved for cases with an objective change in the quality or quantity of saliva, these terms are frequently used interchangeably.2 Xerostomia is a common complaint affecting 10–29% of the general population.3 Many cases of dry mouth are drug related, as over 400 commonly used drugs are xerogenic1 4; however, the aetiology is frequently multifactorial.5 The prevalence is higher among older patients, those with multiple comorbidities, polypharmacy, advanced disease and those who have received head and neck irradiation.6 7 10 Thus it is a common concern to all areas of medicine, particularly primary care.

Irradiation-induced xerostomia
Radiation-induced xerostomia is common among patients with head and neck cancer (HNC), as radiotherapy fields frequently encompass many of the major salivary glands. Destruction of highly radiosensitive salivary acini causes a quantitative and qualitative reduction in salivary flow. The degree of dysfunction is directly related to the amount of salivary gland tissue lying within the irradiation fields and total dose delivered.10 Radiation damage to salivary gland tissue is rarely reversible once the accumulated dose exceeds 24–26 Gy, with severe dysfunction occurring above 52 Gy.11 12 As patients with HNC routinely receive 60–70 Gy, many (95–100%) may have chronic xerostomia,13 14 resulting in increased susceptibility to oral infections (candidiasis, caries, periodontitis, sialadenitis, cheilitis), taste disorders, sore throat, hoarseness, dry/crusted nasal passages, sleep disruption, fatigue and social isolation.1 3 15 16 The impact of radiation-induced xerostomia and its complications on quality of life (QoL) is well documented; …the chronic after-effects of radiation therapy may impair QoL more severely than cancer itself.17 Although the UK cancer reform strategy has emphasised the need for rehabilitative care of cancer survivors to improve QoL,18 therapeutic options for radiation-induced xerostomia remain limited.

Diagnosis
Diagnosis is generally based on the history and clinical assessment; additional investigations may include sialography, scintigraphy, microbiology, serology and histology. Clinically, the mucosa appears dry, red, shiny and sticky, while the tongue is atrophic, dry and fissured. Saliva appears viscous, ropy, foamy or non-existent.

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with reduced/absent salivary pooling. Subjective measurement tools include xerostomia inventory (XI),19 execution quotient (XQ) and XQ-10 (XI variants). Objective measurements include sialometry (salivary flow rates (SFRs)) and the presence/absence of salivary pooling. However, SFRs vary considerably among individuals and are further influenced by multiple factors such as stress, hydration, stimulation, season, time of day, etc. Furthermore, a patient’s subjective perception of dry mouth does not necessarily correlate with their objective signs of salivary gland dysfunction. This has led the Food and Drug Administration to acknowledge only subjective outcome measures for assessing benefit in patients with xerostomia.20

**Therapeutic options**

Conventional treatment focuses on (A) behaviour modification, fluoride supplements and xerogenic medication review; (B) salivary replacement treatment; (C) mechanical and pharmacological stimulants; (D) cytoprotectants and (E) improved radiation dosimetry. Unfortunately, salivary replacements are largely ineffective, providing short-term relief at best,6 while pharmacological stimulants may produce unpleasant adverse effects—for example, sweating, nausea, urinary frequency, cardiac arrhythmias, and are poorly tolerated or contraindicated in many patients.13 21 22  Concerns exist about the selectivity, safety and side effects of cytoprotectants such as amifostine, while access to advanced radiation techniques (intensity modulated radiation therapy, three-dimensional conformal radiotherapy) is currently restricted.23

**Role of acupuncture**

The failure of conventional medicine to alleviate this condition has led to a resurgence of interest in the age-old practice of acupuncture.13 24 Acupuncture has gained acceptance as a valid intervention for patients with cancer who have pain and nausea; emerging reports also suggest that acupuncture may be effective in the treatment of xerostomia and may offer long-lasting benefits of up to 3 years.25 Studies suggest that needling induces physiological effects, modulates neurological processes within the central nervous system, especially the spinal cord gating mechanisms, cerebral subcortical nuclei and hypothalamic-endocrine axis26; it promotes release of neuropeptides and endogenous opioids, stimulates the autonomic nervous system and increases peripheral blood flow.27 Salivary levels of vasoactive intestinal polypeptide and calcitonin gene-related peptide are also enhanced.28 29 However, the mechanism of action remains poorly understood. Furthermore, many fundamental questions remain unanswered about the relative value of the various consultation stages, optimal position/depth of needling and treatment duration/frequency. Even proponents of acupuncture admit it “has not been shown beyond doubt to be more efficacious than a placebo”.30 Up-to-date accurate information is clearly required to determine the efficacy, effectiveness and appropriateness of this intervention.

**Justification for systematic review**

A search of the database of abstracts of reviews of effects, Cochrane Database of Systematic Reviews (CDSR) and Scottish Intercollegiate Guidelines Network (SIGN) revealed the absence of any Cochrane review on this topic. CDSR listed just one ‘other review’ by Jedel.27 However, a review of this paper disclosed certain limitations, suggesting a comprehensive, up-to-date search examining the effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia was justified.

**METHODS: REVIEW PROTOCOL**

**Research question and objectives**

This review aimed to answer the following research question: Is acupuncture an effective and safe treatment for radiation-induced xerostomia in patients with HNC? The primary objectives were to assess whether patients with irradiation-induced xerostomia gain:

1. any objective relief from acupuncture
2. a subjective benefit from acupuncture.

The secondary objectives were to assess whether:

1. the acupuncture treatment protocols employed in the included trials were similar
2. the frequency and nature of adverse events is acceptable.

**Eligibility criteria for the review (PICOS elements)**

Detailed information on the Participants, Interventions, Comparisons and Outcomes and types of Study (PICOS) to be included are provided in table 1, as advocated by the 2009 Centre for Reviews and Dissemination handbook.31 Since no clear definition of ‘placebo acupuncture’ currently exists, inactive control interventions such as sham acupuncture techniques (insertion of needles into non-acupuncture points or use of non-penetrating needles) are currently considered the most acceptable comparators for acupuncture studies.30 32 Timing of the

**Table 1** Prespecified eligibility criteria

<table>
<thead>
<tr>
<th>Participants</th>
<th>Interventions</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Study types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only studies involving patients with HNC, aged ≥18 years with irradiation-induced xerostomia will be included regardless of care setting, radiation modality or dosage</td>
<td>Only studies using traditional or manual acupuncture and electro-acupuncture included. Variations in dosage, intensity, mode of delivery, personnel, timing, frequency and duration will be tolerated. ‘Non-needling’ techniques will be excluded—for example, laser acupuncture, acupressure or acupuncture-like transcutaneous nerve stimulation</td>
<td>Placebo controls are required. Sham acupuncture using inactive points, superficial needling and non-penetrating needles are deemed acceptable</td>
<td>Only studies using one or more of these tools are eligible. Objective: Salivary flow rates (resting +/or stimulated)</td>
<td>Only RCTs and systematic reviews of RCTs will be included. If no such trials identified, high-quality non-RCTs will be included in the review</td>
</tr>
</tbody>
</table>

HNC, head and neck cancer; RCT, randomised controlled trial.

outcome assessment was grouped into three prespecified intervals—‘short-term’, ‘medium-term’ and ‘long-term’. Information on nature/timing/severity of adverse events was deemed desirable but not essential.

Study design
This review was limited to randomised controlled trials (RCTs) and systematic reviews of RCTs, accepting the likely paucity of such studies as these studies represent the highest level of evidence (level 1) currently available according to the SIGN revised grading system and Cochrane Handbook. Similarly, acupuncture research methodologists consider the highest level of evidence of effectiveness is a well-performed systematic review that considers appropriate, high-quality RCTs. As scope searching suggested a paucity of research in this area, the authors decided to apply a high level of sensitivity and low specificity to the search process and to include high-quality non-RCT studies (level 2++), if no RCTs could be identified.

Search strategy
A comprehensive search was undertaken, employing the following resources:
2. MESH headings and keywords included acupuncture, xerostomia, salivary hypofunction, hyposalivation, dry mouth, radiotherapy, irradiation, brachytherapy and external beam, combined using Boolean logic (AND, OR, NOT). To increase sensitivity, no restrictions were placed on language or study/trial/review type.

Applying selection/eligibility criteria to search results
Search results were merged using ReferenceManager 12 software, and duplicates/multiple reports were removed leaving 61 articles. Forty-three reports were excluded after review of the title and abstract (figure 1: PRISMA flow chart). Reasons for exclusion included inappropriate acupuncture techniques, xerostomia not a major focus, non-irradiation-induced xerostomia, study type (details available on request). Review process was undertaken by two reviewers independently, applying blinding to reduce bias.

Full texts of 18 reports were sought. The full-text reports were independently examined by both authors for compliance with eligibility criteria (table 2); 15 studies were excluded. Three RCTs were deemed suitable for inclusion. Basic study design characteristics were collected and tabulated (table 3), using a custom-designed data extraction form designed according to Cochrane review checklist 7.3a.

Critical appraisal and quality assessment
Research may vary considerably in methodological rigour and flaws in the design or conduct of a study can introduce bias, obscuring the benefit/harm of an intervention. Each study included in a review must therefore undergo a quality assessment (QA) process. The Cochrane Review Handbook (8.3.3) discourages the use of QA scales, advocating simple approaches for assessing validity that can be fully reported. The Jadad (1996) scale is explicitly discouraged as “it does not cover one of the most important potential biases in randomized trials—namely, allocation concealment.” The NHS Critical Appraisal Skills Programme (CASP) critical appraisal tool for RCTs was chosen for this review as it covers sequence generation, allocation sequence concealment, blinding, incomplete outcome data and selective outcome reporting.

RESULTS AND DATA SYNTHESIS
Data extraction sheets and CASP-QA forms were completed for each study. Interventions are assessed in table 5 using the revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) checklist. Meta-analysis was considered inappropriate for this review owing to the small number of included studies and differences in study methods. However, a brief qualitative analysis of the evidence is presented in narrative form, supplemented by tables 3 and 4.

Protocol issues
While the three trials (123 participants) included in this review were classified as ‘RCTs’, only Cho et al provided sufficient details of the randomisation process. In a preliminary report, Pfi ster et al said patients were randomised by patient or clinician preference; however, a recent report on the same study used a computer-generated randomisation list.

![Figure 1](http://aim.bmj.com/)

**Figure 1** PRISMA 2009 flow diagram. PRISMA, preferred reporting items for systematic reviews and meta-analyses; RCT, randomised controlled trial; RT, radiotherapy.
### Table 2  Characteristics of 18 for full-text review

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Title</th>
<th>Database UI</th>
<th>Eligible acupuncture technique used</th>
<th>Focus is RT-induced xerostomia</th>
<th>Study type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blom et al (1996)[^16^]</td>
<td>Acupuncture treatment of patients with radiation induced xerostomia</td>
<td>Ovid MEDLINE(R) UI – 8762786</td>
<td>Yes</td>
<td>Yes</td>
<td>RCT</td>
</tr>
<tr>
<td>Blom et al (1999)[^3^]</td>
<td>Prognostic value of the pilocarpine test to identify patients who may obtain long-term relief from xerostomia by acupuncture</td>
<td>EBSCO AN: 10326815</td>
<td>Yes</td>
<td>No</td>
<td>Before/after comparative study No control Not RCT</td>
</tr>
<tr>
<td>Blom and Lundberg (2000)[^5^]</td>
<td>Long-term follow-up of patients treated with acupuncture for xerostomia and the influence of additional treatment</td>
<td>Ovid MEDLINE(R) UI – 10673783</td>
<td>Yes</td>
<td>No</td>
<td>Before/after comparative study No control Not RCT</td>
</tr>
<tr>
<td>Deng et al (2008)[^2^]</td>
<td>Functional MRI changes and saliva production associated with acupuncture at LI2 acupuncture point: an RCT</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>RCT</td>
</tr>
<tr>
<td>Meidell and Holritz Rasmussen (2009)[^3^]</td>
<td>Acupuncture as an optional treatment for hospice patients with xerostomia: an intervention study</td>
<td>EBSCO AN –36221591</td>
<td>Yes</td>
<td>No</td>
<td>No control Not RCT</td>
</tr>
<tr>
<td>Pinkowish (2009)[^3^]</td>
<td>Acupuncture and acupuncture for side effects of RT</td>
<td>EMBASEUI – 2009496876</td>
<td>No</td>
<td>No</td>
<td>Commentary on Garcia et al</td>
</tr>
<tr>
<td>Taromina and Rooney (2006)[^2^]</td>
<td>Acupuncture for xerostomia</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

HNC, head and neck cancer; RCT, randomised controlled trial; RT, radiotherapy.
### Table 3: Characteristics of included studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Participants (n)</th>
<th>Intervention and comparator interventions</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blom et al (1996)</td>
<td>Number: 41 enrolled; 38 included in analysis</td>
<td>1. Acupuncture rationale: traditional Chinese acupuncture; limited reasoning provided for treatment. Treatment partially individualised</td>
<td>Measured and reported</td>
<td>Significant improvement in 50% of both groups. No significant difference between real and sham acupuncture (SA) groups</td>
</tr>
<tr>
<td></td>
<td>PMH: all HNC</td>
<td>2. Needling details: Needle insertions per case per session: not stated</td>
<td>Defined: SFR defined but subjective tool not defined</td>
<td>Adverse events: brief mention of tiredness + small haematomas in a few patients but group unspecified</td>
</tr>
<tr>
<td></td>
<td>Age: 35–82 years</td>
<td>Points used: various points from list of 28</td>
<td>Tools: (A) SFR: stimulated + unstimulated</td>
<td>(B) Subjective assessment Scales not explained</td>
</tr>
<tr>
<td></td>
<td>Median: control 64 years intervention 61.5 years</td>
<td>Depth of insertion: not stated</td>
<td>Measured, reported and defined</td>
<td>Significantly improved in 50% of both groups. No significant difference between real and sham acupuncture (SA) groups</td>
</tr>
<tr>
<td></td>
<td>Gender: M:F was 26:12</td>
<td>Responses sought: needling response O/</td>
<td>Tools: (A) SFR: stimulated + unstimulated</td>
<td>(B) Execution Quotient (XQ) Questionnaire subjective assessment but only 4 of the 8 questions used</td>
</tr>
<tr>
<td></td>
<td>Xerostomia: subjective</td>
<td>Needle retention time: 20 min implied</td>
<td>Scales explained</td>
<td>Adverse events: no information provided</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria: none</td>
<td>Needle type: Chinese Cloud &amp; Dragon 0.30 mm diameter, 15 and 30 mm long</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td>Cho et al (2008)</td>
<td>Number: 12 enrolled</td>
<td>1. Acupuncture rationale: manual acupuncture; little reasoning provided for treatment. Treatment variation none</td>
<td>Measured, reported and defined</td>
<td>Significant difference in SFR + XQ scores between baseline and 6 weeks in the active group, but no significant difference in scores between active and control. XQ improved by 2.33 points in RA vs 0.33 in SA group (p &lt; 0.05)</td>
</tr>
<tr>
<td></td>
<td>PMH: all HNC</td>
<td>2. Needling details: Needle insertions per case per session: not stated</td>
<td>Tools: (A) SFR: stimulated + unstimulated</td>
<td>(B) Execution Quotient (XQ) Questionnaire subjective assessment but only 4 of the 8 questions used</td>
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<tr>
<td></td>
<td>All post-RT &gt;35 Gy</td>
<td>Points used: ST6, LI4, ST36, SP6</td>
<td>Scales explained</td>
<td>Follow-up: medium-term 1 year</td>
</tr>
<tr>
<td></td>
<td>Age: 37–72 years</td>
<td>Depth of insertion: 1.5 cm</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median age: 44 years</td>
<td>Responses sought: not stated</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gender: M:F was 10:2</td>
<td>Needle retention time: 20 min</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All women in control group</td>
<td>Needle type: Zeus Korea Acupuncture Dev Co diameter 0.20 mm, length 30 mm</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria: ECOG &gt;2, treatment for inflammatory disease, distant metastases</td>
<td>Number of sessions: 12</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Treatment regimen:</td>
<td>Frequency: twice weekly</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number of sessions: 12</td>
<td>Duration of sessions: 20 min per session</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
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<tr>
<td></td>
<td>Frequency: twice weekly</td>
<td>Duration of sessions: 20 min per session</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
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<tr>
<td></td>
<td>4. Other components of treatment: none stated</td>
<td>Setting: unspecified</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Setting: unspecified</td>
<td>5. Practitioner background: unspecified</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6. Control or comparator: sham acupuncture using inactive points 2 cm from active points and superficial intradermal needling with no stimulation</td>
<td>Follow-up: medium-term 1 year</td>
<td>Follow-up: medium-term 1 year</td>
<td></td>
</tr>
</tbody>
</table>

Continued
### Table 3

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Participants (n)</th>
<th>Intervention and comparator interventions</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acupuncture rationale: traditional Chinese acupuncture; limited reasoning provided for treatment.</td>
<td>Partly</td>
<td>Measured, reported and defined</td>
<td>Significantly greater reduction in acupuncture group (mean XI score 52.6±21.6 compared with 61.8±18.9 in ‘usual care’ group; p&lt;0.02)</td>
<td>Adverse events: no serious adverse events; 27 minor events: pain, minor bruising or bleeding and GIT upset</td>
</tr>
</tbody>
</table>

**Tools:**
- Xerostomia inventory (XI) questionnaire with questions ‘modified slightly for American use’ and modified scoring
- Scales explained
- Follow-up: Short-term – 4 weeks

**Bias:**
- There was no statistically significant difference in symptomatic relief (improved quality of saliva, taste, appetite, sleep and a reduction in hoarseness, nausea, pain and weight loss). However, patients in the experimental group experienced symptomatic relief between the experimental and control groups. Cho et al found acupuncture significantly improved the XQ score by 2.33 points (11.17±4.31 vs 13.5±3.56) compared with only 0.33 points (7.67±0.82 vs 7.33±1.37, p<0.05). Pfister et al reported a significantly greater reduction in XI scores for the acupuncture group (mean score 52.6±21.6) compared with ‘usual care’ group (61.8±18.9, p<0.02). This review concludes that there is no evidence that patients with radiation-induced xerostomia derive any objective benefit from acupuncture.

**Assessment of the uniformity of acupuncture treatment protocols employed**

This review highlighted the complete lack of uniformity or consistency seen in just three studies as the number of acupuncture points ranged from four to 29, while the number of sessions ranged from four to 24. Duration of follow-up varied from 2 to 4 weeks.

**Review of objectives**

**Do patients with irradiation-induced xerostomia gain any objective relief from acupuncture?**

Only two trials used objective outcome measurements: Blom et al reported an improvement of >20% in both stimulated and unstimulated SFR in the experimental group. However, the control group also showed positive changes in SFR, albeit at a lower level. Significant differences were reported between baseline levels of unstimulated saliva (p<0.05–0.01) and stimulated saliva (p<0.01) within groups but not between the experimental and control group. Similarly, Cho et al found acupuncture significantly increased unstimulated SFR compared with the baseline scores (0.04±0.064 to 0.071±0.071, p<0.05). However, flow rates also improved in the control group and no significant differences were seen between the active and control groups. As a change from baseline over time in the experimental group is not generally accepted as evidence of an effect unless the change is greater than the change in the control group, this review concludes that there is no evidence that patients with radiation-induced xerostomia derive any objective benefit from acupuncture.

**Do patients with irradiation-induced xerostomia gain any subjective benefit from acupuncture?**

All three studies undertook subjective assessment, using a variety of measurement tools. Blom et al reported that many patients in the experimental group experienced symptomatic relief (improved quality of saliva, taste, appetite, sleep and a reduction in hoarseness, nausea, pain and weight loss). However, there was no statistically significant difference in symptomatic relief between the experimental and control groups. Cho et al found that acupuncture significantly improved saliva flow rate. Blom et al reported a significantly greater reduction in XI scores for the acupuncture group (mean score 52.6±21.6) compared with ‘usual care’ group (61.8±18.9, p<0.02). This review concludes that there is no evidence that patients with radiation-induced xerostomia derive a subjective benefit from acupuncture. However, this evidence is based on two RCTs of moderate quality and moderate risk of bias and one RCT of poor quality with a high risk of bias—that is, level 1 evidence which is deemed inadequate for making any recommendation to introduce this intervention based on National Institute for Health and Clinical Excellence guidelines for evidence grading.
Trial of poor quality with high risk of bias in relation to the use of acupuncture in treatment of xerostomia. However, xerostomia was a secondary end point in this study. Adequate evidence is currently insufficient evidence to determine the safety of this intervention. Adverse events were reported; the frequency of ‘minor’ events is insufficient evidence to determine the safety of this intervention. Acupuncture is associated with minimal risk as no serious adverse events were reported; the frequency of ‘minor’ events has merit. However, this systematic review indicates that there is currently insufficient ‘high-quality’ evidence to advocate the use of acupuncture as a treatment for irradiation-induced xerostomia. The lack of evidence may be due to true lack of effect or to our failure to:

1. Appreciate the multifactorial nature of xerostomia and to understand the true bio-physiological basis of acupuncture; this may result in a lack of appropriate stratification for confounding factors.
2. Establish the relative value of each component of the acupuncture consultation: discussion, listening, nurturing, needling and stimulation.
3. Provide full details on adverse events, thus hindering meaningful risk/benefit analysis.
4. Resolve protocol issues—for example, relative value of specific acupuncture points, number of points to include, optimal intervention frequency and comparability of various techniques (manual, traditional Chinese, acupuncture, TENS/ALTENS-acupuncture, electro-acupuncture), dosage (level and method of stimulation, depth of needling and stimulation).

Is the frequency and nature of adverse events acceptable?
Attempts to ascertain the risk/benefit ratio for this intervention were hampered by a paucity of information, as one study (Cho et al46) provided no information. The other authors claimed that acupuncture is associated with minimal risk as no serious adverse events were reported; the frequency of ‘minor’ events ranged from ‘a few’ to 27. This review therefore finds that there is insufficient evidence to determine the safety of this intervention.

DISCUSSION
Anecdotal and clinical evidence suggest a potentially beneficial role for acupuncture in the treatment of radiation-induced xerostomia. Indeed, several high-quality phase II non-randomised and non-controlled studies have suggested that this intervention has merit. However, this systematic review indicates that there is currently insufficient ‘high-quality’ evidence to advocate the use of acupuncture as a treatment for irradiation-induced xerostomia. The lack of evidence may be due to true lack of effect or to our failure to:

1. Appreciate the multifactorial nature of xerostomia and to understand the true bio-physiological basis of acupuncture; this may result in a lack of appropriate stratification for confounding factors.
2. Establish the relative value of each component of the acupuncture consultation: discussion, listening, nurturing, needling and stimulation.
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RCT, randomised controlled trial.

### Table 4 Quality assessment (QA) overview

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needing). Indeed, the lack of standardisation and transparency poses a major ‘stumbling block’ in complementary and alternative medicine (CAM) research generally. This problem is difficult to resolve as no ‘gold standard’ acupuncture protocol exists for treating xerostomia.20 Furthermore, the personalised nature of the treatment given to each individual is considered a crucial component of care in traditional Chinese acupuncture and CAM. Skilled practitioners may therefore consider the introduction of any single ‘gold standard’ acupuncture protocol restrictive and counterproductive.

5. Resolve the placebo controversy, which thus remains a major obstacle to future work. No agreement exists about what constitutes an acceptable comparator for acupuncture as non-needling techniques do not accurately replicate the experience while needling ‘inactive’ points appears to produce a positive physiological response. Identification of a validated, inert comparator must be considered a priority, to prevent future RCTs being doomed to failure.

CONCLUSION

The profound impact of chronic radiation-induced xerostomia on the QoL of patients with HNC is beyond dispute. This condition is inadequately dealt with by conventional medicine, but a growing body of clinical evidence suggests that acupuncture may provide significant symptomatic relief. However, this review indicates that there is still insufficient evidence from high-quality RCTs to support acupuncture as an effective treatment for radiation-induced xerostomia.

This review also highlights many important methodological issues that must be dealt with before an effective RCT can be undertaken, particularly the need to standardise treatment and to develop a valid comparator. The introduction of additional outcome measures—for example, a diary of daily fluid intake and record of sleep disturbance, might be beneficial. The use of the revised STRICTA guidelines39 for future publications is encouraged as this will facilitate review and replication. The search for an appropriate comparator can best be resolved by international collaboration and co-ordinated East–West medical research so that all can benefit from the vast body of wisdom accumulated in Eastern countries about this ancient skill.

REFERENCES


Summary points

► Irradiation-induced xerostomia is debilitating and difficult to treat.
► Previous reports have suggested a therapeutic role for acupuncture.
► A systematic review of three studies found no evidence of objective benefit but suggests that acupuncture may provide significant symptomatic relief.
► Further research is warranted.

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Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review
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