

The Acupuncture Evidence Project

A Comparative Literature Review

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Dr John McDonald was a co-author of three of the research papers referenced in this review. Professor Caroline Smith was a co-author of six of the research papers referenced in this review, and Associate Professor Zhen Zheng was co-author of one of the research papers in this review. There were no other conflicts of interest.

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ABSTRACT

Background

The acupuncture evidence project investigated the state of the evidence regarding acupuncture, with the focus on systematic reviews and meta-analysis. The Australian Department of Veterans' Affairs 2010 Alternative Therapies Review and United States Department of Veterans Affairs Acupuncture Evidence Map 2014 were used as baselines, then evidence levels were updated to reflect subsequent research.

Methods

A search of PubMed and Cochrane Library for systematic reviews and meta-analyses from March 2013 to September 2016 was conducted. Evidence levels were graded using NHMRC levels. Risk of bias was assessed using the Cochrane GRADE system where possible. All results were displayed in tables to demonstrate changes in evidence level over time, as well as the current state of evidence by clinical area.

Results

Of the 123 conditions reviewed, evidence of effect was found at various levels for 117 conditions. Six conditions were assessed as 'no evidence of effect'. The level of evidence had increased for 25 conditions since the previous reviews. The findings of this review are limited by the mounting evidence that sham/placebo controls used in acupuncture trials are not inert, which is likely to lead to a consistent underestimation of the true effect size of acupuncture interventions.

Conclusions

Systematic reviews published up to September 2016 indicate that acupuncture has a 'positive effect' on eight conditions (migraine prophylaxis, headache, chronic low back pain, allergic rhinitis, knee osteoarthritis, chemotherapy-induced nausea and vomiting, post-operative nausea and vomiting and post-operative pain), 'potential positive effect' on a further 38 conditions, 'unclear/insufficient evidence' for 71 conditions and 'no evidence of effect' for six conditions. Evidence of cost-effectiveness was identified for 10 conditions, and evidence for safety was identified for nine conditions.

PREFACE

Background

Evidence of effectiveness underpins the validity of all health care interventions. Acupuncture has been practised for thousands of years; however research into its effectiveness and cost effectiveness is in its relative infancy. The first significant attempt to identify the evidence validating the role of acupuncture was undertaken by the World Health Organization (WHO) in 1979 (1). WHO conducted a Delphi-like symposium in Beijing in 1979 where physicians from around the world identified 43 diseases which they believed acupuncture may benefit (1). The 1979 report was criticised because it was not based on clinical trials, rather the clinical experience of the participants (2).

The US Department of Health and Human Services National Institutes of Health (NIH) released a consensus statement on acupuncture in 1997 (3). The statement identified the efficacy of acupuncture for adult postoperative and chemotherapy nausea and vomiting, and for postoperative dental pain. In addition, the statement found support for the use of acupuncture for a range other conditions and identified the need for further research (3).

In 1996, WHO held a consultation on acupuncture in Cervia, Italy. At this meeting it was decided to review acupuncture again, this time focusing on the now-numerous controlled clinical trials. The result was a review of clinical trials up until early 1999 and culminated in 'Acupuncture: review and analysis of controlled clinical trials' published by WHO in 2002 (4). The report identified 28 conditions for which acupuncture was found to be effective, and nearly 100 others where there was a therapeutic effect (4). It was acknowledged at the time that there were problems with the methodology in some of the trials included in the review (4). Notwithstanding these limitations, the WHO report indicated a growing and convincing body of evidence indicating that there was more to acupuncture than the placebo effect (4).

The Acupuncture Evidence Project

Nearly 14 years after the WHO publication on acupuncture evidence there has been further refinement in the conduct of clinical trials, not just for acupuncture, but in health-care generally, with clearer guidelines on how to rate the quality of the evidence. The Australian Acupuncture and Chinese Medicine Association Ltd (AACMA) identified the need for an updated review of the literature with greater rigour than was possible in the past, and commissioned the acupuncture evidence project. AACMA engaged experienced clinician and researcher, Dr John McDonald PhD, to conduct the research and analysis for the project.

This review draws on two prior comprehensive literature reviews, one conducted for the Australian Department of Veterans' Affairs (DVA) in 2010 and another conducted for the United States Department of Veterans Affairs (USVA) in 2013 (5, 6). The research identified by these reviews was pooled, then a search of further literature from 2013 to 2016 was conducted. Trials were assessed using the National Health and Medical Research Council (NHMRC) levels of evidence, with risk of bias assessed using the Cochrane GRADE system (7, 8). Results have been tabulated to indicate not just the current state of the evidence, but to indicate how the quality and quantity of evidence has changed from 2005 to 2016. In this review, 123 conditions across 14 broad clinical areas were identified and, of these, only six conditions found 'no evidence of effect' for acupuncture. The level of evidence was found by this review to have increased for 25 conditions.

How to use this review

This project sets a new benchmark to inform acupuncturists, the public, researchers, health departments, governments, and other health providers that acupuncture has a valuable

contribution to make to global healthcare and to assist in reducing the global burden of disease. Acupuncturists should also take confidence from this report that their clinical expertise has been validated, and to confidently offer their services alongside other health professionals. Students and clinicians can use this report to identify areas of clinical interest which they may have overlooked. Researchers can find inspiration for areas of future investigation where the evidence is currently unclear. This review should also encourage educational institutions to maintain robust programs of study in acupuncture to continue to produce graduates capable of the broad scope of practice that this report indicates. It is no longer possible to say that the effectiveness of acupuncture can be attributed to the placebo effect or that it is useful only for musculoskeletal pain.

It is no longer possible to say that the effectiveness of acupuncture can be attributed to the placebo effect or that it is useful only for musculoskeletal pain.

The realisation that pharmacological and surgical interventions are not without their limitations has increased interest in drug-free treatments such as acupuncture (9-13). This review found eight conditions where acupuncture may be used to reduce reliance on pharmacological or surgical options. **Migraine** and **tension headaches** lead to loss of productivity and quality of life; a drug-free therapy has a major health impact and potential cost savings as well as maintaining participation in the workforce (14). Medication is not always an effective or acceptable therapy for **allergic rhinitis** and acupuncture improves the range of interventions available to improve quality of life (15). **Post-operative nausea and vomiting** and **post-operative pain** complicate post-operative management, with acupuncture offering another avenue to enhance care in the post-operative period and reduce reliance on medication alone (16, 17).

Knee osteoarthritis is on the increase globally and contributes not just to years lost to disability (YLD), but is an increasing burden on health budgets (18, 19). The option of a safe, drug-free treatment that may improve quality of life and potentially delay surgical intervention has significant potential to control these spiralling costs and YLD. **Low back pain** is a WHO priority disease, and is the single largest contributor to disability worldwide (20). The finding that acupuncture benefits chronic low back pain is arguably the most important finding from this report. Finally, **chemotherapy induced nausea and vomiting** is an unwanted complication of cancer treatment and is often not fully controlled even with state-of-the-art antiemetics. Acupuncture can assist in improving quality of life for these cancer patients (21).

It has been estimated that there is a 17-year time lag in translating clinical research into clinical practice (22). During this time patients are being deprived of the benefit of a proven therapy. Health policy makers now have eight clear conditions associated with a significant burden of disease where acupuncture should be integrated into current clinical guidelines without further delay. Placebo controlled clinical trials consistently underestimate the true effect size of acupuncture (as discussed in section 1.4), yet they have still demonstrated NHMRC Level 1 evidence for the effectiveness of acupuncture for a further 109 conditions. This review has found a significant improvement in both the quality of studies and the levels of evidence supporting acupuncture since the most recent reviews conducted by the Australian and US Departments of Veterans Affairs.

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GLOSSARY OF TERMS

AACMA	Australian Acupuncture and Chinese Medicine Association Ltd
CGRP	calcitonin gene-related peptide
DVA	Department of Veterans' Affairs
EA	electroacupuncture
ECP	eosinophilic cationic protein
FEV1	forced expiratory volume in one second
FEV1/FVC	ratio of FEV1 to forced ventilation capacity
GABA	gamma-amino-butyric-acid
GRADE	Grades of Recommendation, Assessment, Development and Evaluation
IgE	immunoglobulin E
IL	interleukin
MA	meta-analysis
MMSE	Mini Mental State Examination
NAD	neck pain and associated disorders
NHMRC	National Health and Medical Research Council
NIH	National Institutes of Health
NSAIDS	non-steroidal anti-inflammatory drugs
OHNSF	Otolaryngology Head Neck Surgery Foundation
PAR	persistent (perennial) allergic rhinitis
QoL	quality of life
RCT	randomised controlled trial
RQLQ	rhinoconjunctivitis quality of life questionnaire (Juniper)
SAR	seasonal (intermittent) allergic rhinitis
SP	substance P
SR	systematic review
TEAS	transcutaneous electrical acupoint stimulation
TRPV1	transient receptor potential vanilloid 1
USVA	United States Department of Veterans Affairs
VIP	vasoactive intestinal peptide
WAD	whiplash associated disorders
YLD	years lost to disability

1 INTRODUCTION

Increasing interest in acupuncture has led to the need for an updated review of its efficacy, effectiveness and cost effectiveness. Rather than starting from scratch, this review draws on two prior comprehensive literature reviews into acupuncture. The first was undertaken for the Australian Department of Veterans' Affairs (DVA) in 2010, the second for the United States Department of Veterans Affairs (USVA) in 2013 (5, 6). These reviews did not limit themselves to veteran-specific health issues but considered the evidence regarding acupuncture in the broadest health terms. A search was then conducted for studies after the USVA 2013 review and the evidence analysed, graded and tabulated. The advantage of this comparative approach is not only a pragmatic way of avoiding duplication of work; it also demonstrates the increasing quality and quantity of evidence supporting the effectiveness of acupuncture over the eleven-year period (2005 to 2016) from which studies were drawn.

Table 3 categorises the research literature by evidence levels. This table clearly demonstrates the increase in the volume and scope of research on acupuncture since the prior reviews. Table 4 summarises the changes in evidence levels among the reviews. Of note is the finding that eight conditions are now rated as 'evidence of positive effect'. Two of these had been listed as 'unclear' evidence and two as 'evidence of potential positive effect' prior to this review. Table 5 provides brief notes for each condition and the references justifying the change in evidence levels found by this review. Table 6 organises conditions by clinical areas, allowing the reader to get a snapshot of the state of the evidence for any particular clinical area, and identifies areas where further research needs to be undertaken.

Numerous clinical guidelines now recommend acupuncture for a range of conditions. Of the 123 conditions examined in this review, levels of evidence have increased for 25 conditions. There is now 'evidence of positive effect' for eight conditions and 'evidence of potential positive effect' for a further 38 conditions. Seventy-one conditions are rated as 'unclear/insufficient evidence' and only six conditions are currently rated at 'no evidence of effect'. Further statistics can be found at Table 2. The comparative approach used in this study serves as a reminder that a finding of 'no evidence of effect' or 'unclear' does not mean 'ineffective'. Many of the conditions currently rated as 'unclear' have consistently positive findings in systematic reviews, but because they represent new clinical areas for acupuncture research, the evidence is not yet sufficient to allow firm conclusions to be drawn on effectiveness or efficacy. Section 1.6 provides further assistance in interpreting the findings of this review. There are methodological challenges in investigating acupuncture such as the problems with placebo controlled trials (outlined in section 1.4) which are slowly being overcome.

1.1 Methods

A review of alternative therapies was published by the Australian Government Department of Veterans' Affairs in 2010 (5). In 2014, the US Department of Veterans Affairs published an Evidence Map of Acupuncture reviewing acupuncture research published in or before March 2013 (6). This review focuses on new evidence between March 2013 and September 2016. Like the two previous reviews, this review concentrates on systematic reviews (SR) and meta-analyses (MA), using Cochrane Systematic Reviews where available. The primary focus of this review is to examine evidence supporting the effectiveness and efficacy of acupuncture (see section 1.3 Efficacy versus effectiveness). Where available, evidence on cost-effectiveness and safety has been included (see Tables 7 and 8).

A search was undertaken on PubMed and the Cochrane Library using the search term ‘acupuncture’ with limits set for dates between March 2013 and September 2016, and restricted to reviews. All languages were included. Systematic reviews, meta-analyses, network meta-analyses, overviews of systematic reviews (NHMRC level I evidence) and some narrative reviews were included, but protocols for systematic reviews were excluded. Systematic reviews of non-invasive or nonpharmacological interventions or of complementary and/or alternative medicine (CAM) interventions were included if they included acupuncture studies. One systematic review from the Australian Journal of Acupuncture and Chinese Medicine was included although this journal is not included in PubMed listings. A total of 134 systematic reviews, including 27 Cochrane systematic reviews were included in this review, along with three network meta-analyses, nine reviews of reviews and 20 other reviews. Meta-analyses were conducted for 59 of the non-Cochrane systematic reviews. This review includes pooled data from more than 1,000 randomised controlled trials. Some of the included systematic reviews included studies which were not randomised controlled trials.

1.2 Assessment of the quality of evidence

The Australian DVA review (2010) used the National Health and Medical Research Council (NHMRC) levels of evidence (I-IV) which define the source of the evidence, with Level I being ‘evidence obtained from a systematic review of all relevant randomised controlled trials’, and Level II being ‘evidence obtained from at least one properly designed randomised controlled trial’ (7). By this definition, this review examined mainly Level I evidence as systematic reviews and meta-analyses were prioritised. Level II evidence from individual randomised controlled trials has been included occasionally where new high quality randomised trials may have changed the conclusions from the most recent systematic review.

Risk of bias in randomised controlled trials has mainly been assessed by the included systematic reviews using the Cochrane GRADE system of low, unclear or high risk of bias across a number of domains (8). The quality of evidence has also been assessed principally using the GRADE system with randomised controlled trials being assessed as high, moderate, low or very low quality evidence. See the Appendix, Table 10 for an outline of GRADE levels. Where systematic reviews have used other systems of quality assessment (such as PRISMA or Jadad) an attempt has been made to convert these scores to an equivalent within the GRADE system. Some systematic reviews have not reported an assessment of quality of evidence of included trials, and due to time constraints, this review has not attempted to make such an assessment.

Level	Description	GRADE level (8)
Evidence of positive effect	Reviews with consistent statistically significant positive effects and where authors have recommended the intervention.	Moderate or high quality
Evidence of potential positive effect	Reviews reporting all individual RCTs or pooled effects across RCTs as positive, but the reviewers deeming the evidence insufficient to draw firm conclusions.	Moderate or high quality
Unclear/insufficient evidence	Conflicting evidence between reviews or between authors within a review, with reviewers summarising the evidence as inconclusive.	Low or very low quality; or conflicting levels of evidence within or between reviews
No evidence of effect	Reviews have consistently found little support for acupuncture.	Consistently low or very low quality

In the US Veterans Affairs evidence map, evidence has been assessed at four levels: evidence of positive effect, evidence of potential positive effect, unclear evidence and evidence of no effect. In this review this terminology has largely been adopted with the exception that 'evidence of no effect' has been replaced with 'no evidence of effect' which seems to be more strictly accurate. 'Unclear evidence' was described as conflicting evidence between reviews or between authors within a review, with reviewers summarising the evidence as inconclusive. 'Evidence of potential positive effect' refers to reviews reporting all individual RCTs or pooled effects across RCTs as positive, however the reviewers deeming the evidence insufficient to draw firm conclusions. 'Evidence of positive effect' refers to reviews with consistent statistically significant positive effects and where authors have recommended the intervention (6).

There is not necessarily an exact equivalence between the 'insufficient evidence' category used in the Australian DVA review and 'unclear' in the USVA evidence map, as some conditions rated as 'insufficient evidence' in the former may appear in the 'evidence of potential positive effect' category in the latter. Generally speaking, conditions rated as positive or potential positive in this review are conditions for which evidence levels were either moderate or high quality evidence according to the GRADE definitions, and conditions with low or very low quality evidence were rated as unclear even when all included RCTs reported positive outcomes. Conditions previously rated as 'potential positive' have been down-graded to 'no evidence of effect' where subsequent Cochrane reviews have found little support for acupuncture.

1.3 Efficacy versus effectiveness

Efficacy refers to the ability of an intervention to achieve its intended effect in ideal conditions, i.e. a clinical trial, usually with a placebo control. Effectiveness refers to the result of an intervention in real world clinical practice.

The most common method used to assess efficacy is the randomised sham/placebo controlled blinded clinical trial. This methodology is derived from pharmaceutical research where an inert tablet ('a sugar pill') is compared to a medication. 'Efficacy' in this example is the measure of the effects of the medication on one group of test subjects minus the effects from the sugar pill on the other group of test subjects. The validity of this method of measuring efficacy rests heavily on the assumption that the sham protocol comparator intervention is inert. If the comparator intervention is not inert, this creates difficulties in measuring efficacy accurately, as discussed in the next section.

1.4 Problems with placebo controls in acupuncture trials

It has been observed from the over 8,000 randomised controlled trials which appear in the Cochrane Database of Controlled Clinical Trials, that in studies where acupuncture is compared with no treatment, waitlist or usual care, there is a significantly larger treatment effect than when acupuncture is compared with some form of sham, placebo or minimal acupuncture (23-27). The Society for Acupuncture Research has dubbed this phenomenon a paradox in acupuncture research (25). There is evidence that many, if not all, the forms of sham/placebo acupuncture treatment protocols used in acupuncture trials to date are not inert, and exert physiological, and possibly also placebo effects, making it extremely difficult (if not impossible) to accurately measure how much of the observed non-specific effects may be attributable to placebo and/or nocebo effects, and how much is due to the placebo not being inert (23, 26-29). Hence a

comparison of the effect size of acupuncture when compared to that of placebo acupuncture may result in a consistent underestimation of the true effect size (23, 28).

Some acupuncture researchers are now suggesting that clinical decisions regarding whether or not acupuncture should be recommended as a treatment option would be more accurately based on comparisons of acupuncture with usual care or acupuncture with other interventions (head-to-head studies and network meta-analyses) (25, 29). This trend of increased focus on pragmatic trials over explanatory trials is not limited to research into acupuncture, but has been identified as an issue in health research more generally (30). Further research on acupuncture mechanisms has also been recommended by both the Society for Acupuncture Research and the National Institutes for Health (NIH) in the USA which, at the Society for Acupuncture Research's biannual conference in Boston in October 2015, announced a new funding pool dedicated to acupuncture mechanism research (25). NIH have identified limited value in true versus sham acupuncture trials when investigating pain and have consigned such trials to a low programmatic priority (31). NIH has given high priority instead to pragmatic studies investigating acupuncture and pain management along with further research into the mechanisms of acupuncture (31).

The use of exit-debrief questionnaires in published sham/placebo-controlled acupuncture trials, which show no significant differences between the real and sham acupuncture groups in belief about which treatment they had received, suggests that in these trials placebo/nocebo effects are not an adequate explanation for any effects produced in the sham acupuncture group (32).

1.5 Acupuncture recommendations in clinical practice guidelines

In Australia, acupuncture has been included in clinical practice guidelines for various types of acute pain including post-operative pain, and for rotator cuff syndrome (33, 34). In 'Acute Pain Management: Scientific Evidence' published by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine in 2015, NHMRC Level I evidence was identified from Cochrane reviews for acupuncture for labour pain, oocyte retrieval pain, primary dysmenorrhoea, tension-type headaches and migraine, and from PRISMA reviews for postoperative pain, back pain and acute burns pain (33).

The development of guidelines requires quality levels of evidence adequate to support a given recommendation, even though they may fall below the highest level in some cases, and requires consideration of other factors including cost, clinical judgement, and patient preference.

In 'Clinical Practice Guidelines for the Management of Rotator Cuff Syndrome in the Workplace', published by The University of New South Wales in 2013, Recommendation 23 states that 'Clinicians may consider acupuncture in conjunction with exercise; both modalities should be provided by suitably qualified health care providers' (Grade C: 'Body of evidence provides some support for recommendation but care should be taken in its application to individual clinical and organisational circumstances') (34).

In 'Consensus Guidelines for the Management of Postoperative Nausea and Vomiting' published in USA by the Society for Ambulatory Anesthesia in 2014, acupuncture and point stimulation of PC6 were recommended as both prophylactic and treatment strategies [Category A recommendation: based on supportive literature which contains multiple randomised controlled trials which report statistically significant ($P < 0.01$) differences between clinical interventions for a clinical outcome, and aggregated findings are supported by meta-analysis] (35).

Between 2012 and 2015 four International Symposia of Evidence-Based Clinical Practice Guideline in Traditional Medicine have been held in Daejeon, South Korea hosted by the Korean Institute of Oriental Medicine (KIOM), bringing together participants from Korea, China, Japan, UK, Norway, Holland and Australia (36). By November 2015, over 870 recommendations for acupuncture were identified for over 100 conditions from multiple international groups and over 30 countries (36). Examples include: the Otolaryngology Head Neck Surgery Foundation’s clinical practice guidelines for allergic rhinitis in 2015 (37); the National Institute for Health and Care Excellence (NICE), UK inclusion of migraine and tension type headache in 2012 (38); the Scottish Intercollegiate Guidelines Network guideline for the Management of Chronic Pain, inclusion of acupuncture (Grade A recommendation) for chronic low back pain and osteoarthritis (39); and the National German Gynaecologic Oncology Association’s (Arbeitsgemeinschaft Gynakologische Onkologie) inclusion of acupuncture for 12 symptoms associated with breast cancer treatment in 2015 (36, 37).

Table 2. Statistical summary of findings of this review

Evidence Level	Number of Conditions	Changes in Level of Evidence	Number of Conditions
Evidence of Positive effect	8	Increase to positive effect	4
Evidence of Potential positive effect	38	Increase to potential positive effect	20
Unclear/insufficient evidence	71	Increase to unclear/insufficient evidence	1
No evidence of effect	6	Decreased evidence level	3
Total conditions with some evidence of effect (any level)	117	_____	_____
Total conditions reviewed	123	Total increases in evidence level since prior reviews	25

1.6 Interpreting the findings

This review set out to identify the current state of evidence regarding acupuncture, and has done so principally by examining systematic reviews and meta-analyses. Most of these systematic reviews were restricted to only randomised controlled clinical trials which examine efficacy, not effectiveness (NHMRC level I evidence); however some systematic reviews did include pragmatic trials and other uncontrolled studies. Consequently, studies which focused on effectiveness rather than efficacy such as cohort studies, case-control studies, or case series (NHMRC level III-IV evidence) were generally excluded from this review.

Placebo controlled clinical trials consistently underestimate the true effect size of acupuncture, yet over 1000 trials have still demonstrated NHMRC Level I evidence for the effectiveness of acupuncture for 117 conditions.

Earlier discussion has demonstrated the limitations of using placebo controlled clinical trials to assess acupuncture’s efficacy, with the NIH’s acknowledgement of this reflected in its current programmatic priorities which encourage pragmatic trials at the expense of RCT’s (31). Regardless of the limitations of acupuncture RCTs that under-report the true effect size of acupuncture (23, 28), for eight conditions across four clinical areas there is no longer any doubt of acupuncture’s efficacy.

For the reasons outlined above, it is not correct to infer that acupuncture is ineffective for conditions which fall outside of the 'evidence of positive effect' category. For a further 109 conditions examined positive results have been achieved from some trials in every case, with varying levels in the quality of the evidence. Even among the category of 'no evidence of effect' positive results have been found in some reviews. For example, in the assisted fertility category a 2013 Cochrane review indicated no evidence of effect, yet a more recent SR and MA found a positive effect for IVF support on the day of embryo transfer (40, 41). Due to the weighting of a Cochrane review over other SR and MA the evidence level has been reported at 'no evidence of effect', even though some positive results have been identified.

Acupuncture has already been incorporated into clinical guidelines for over 100 conditions even though its current evidence level is rated below 'evidence of positive effect' in most of these cases. This reflects the weighting of other factors in guideline development, and recognition that the quality of levels of evidence are adequate to support a given recommendation, even though they may fall below the highest level in some cases (8). As recommended by both the Society for Acupuncture Research and the NIH, future acupuncture research to inform clinical practice guidelines should be focused on pragmatic trials, head-to-head comparison studies with other interventions (especially currently-recommended usual care interventions) to compare effectiveness, safety and cost-effectiveness, underpinned by further mechanism studies (25, 31). It is accurate to state from this report that there is NHMRC Level 1 evidence for acupuncture's effectiveness for 117 conditions.

The number of conditions included in this review is significantly larger than in previous reviews for two reasons. Firstly, acupuncture researchers have just begun to research the effectiveness of acupuncture for conditions not previously studied. Secondly research has become more nuanced and targeted. For example, what was previously reviewed as 'cancer adverse effects' is now separated into 12 different cancer-related conditions such as pain, fatigue, insomnia and xerostomia.

1.7 Limitations

This review has several limitations. Literature before March 2013 was obtained by pooling results from the DVA 2010 and USVA 2013 reviews. Any MA or SR overlooked by those reviews were not identified in this review. MA's and SR's from March 2013 to September 2016 were identified via a PubMed search. MA's and SR's which were not indexed by PubMed were not identified in this review with one exception.

The findings of this review are limited by the mounting evidence that sham/placebo controls used in acupuncture trials are not inert, which is likely to lead to a consistent underestimation of the true effect size of acupuncture interventions (see sections 1.3 and 1.4 above).

By design this review aimed to update previous reviews, and focused on MA's and SR's. Studies which focus solely on effectiveness rather than efficacy such as cohort studies, case-control studies and case series were excluded by most of the SRs. This results in under-reporting studies on the effectiveness of acupuncture. For example, a PubMed search on 3 November 2016 for the following key words returned the following results:

- cohort AND acupuncture (208)
- case control AND acupuncture (377)
- case series AND acupuncture (150).

2 CONDITIONS NOW RATED AS ‘EVIDENCE OF POSITIVE EFFECT’ IN THIS REVIEW

2.1 Migraine prophylaxis [Positive effect]

For migraine prophylaxis, acupuncture was rated as ‘effective’ in the Australian DVA review (2010) and ‘evidence of positive effect’ in the USVA Evidence map of acupuncture (2014) (5, 6). Since March 2013 a narrative review of high quality randomised controlled trials and two systematic reviews including a Cochrane systematic review update, have confirmed that acupuncture is superior to sham acupuncture and seems to be at least as effective as conventional preventative medication in reducing migraine frequency (42-44). Moreover, acupuncture is described as ‘safe, long-lasting and cost effective’ (42). Subgroup analysis in the Cochrane systematic review found that 16 or more treatment sessions showed a larger effect size ($Z=4.06$) than 12 treatments or fewer ($Z=2.32$). Evidence levels in these three reviews was moderate to high quality.

2.2 Headache (chronic tension-type and chronic episodic) [Positive effect]

Chronic tension-type headaches and chronic episodic headaches were not reviewed in the Australian DVA review (2010) and rated as ‘evidence of positive effect’ in the USVA Evidence map of acupuncture (2014) (5, 6). The most recent Cochrane systematic review update confirmed that acupuncture is effective for frequent episodic and chronic tension-type headaches with moderate to low quality evidence (45). A brief review of systematic reviews and meta-analyses described acupuncture as having a ‘potentially important role as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders’ (46). Studies in Germany and the UK found acupuncture for chronic headaches to be cost-effective (46).

2.3 Low back pain [Chronic – positive effect; acute – potential positive effect]

For low back pain, acupuncture was rated as ‘effective (possibly)’ in the Australian DVA review (2010) and ‘unclear’ in the USVA Evidence map of acupuncture (2014) (5, 6). The main reason given for the ‘unclear’ rating in the USVA Evidence map was that ‘sham acupuncture controlled trials tended towards statistically nonsignificant results’ and a Cochrane systematic review in 2005 which drew no firm conclusions on the effectiveness of acupuncture for acute low back pain (6). The problems associated with the interpretation of the effects of sham acupuncture have already been discussed. When reviews separate the evidence on chronic low back pain from acute low back pain, as was done in the recent review by the US Agency for Healthcare Research and Quality, it was found that there is moderate quality evidence for the effectiveness of acupuncture in chronic low back pain for both pain intensity and function, but only low quality evidence for pain intensity and function in acute low back pain (47).

In a systematic review of 32 randomised controlled trials for acupuncture treatment of chronic non-specific low back pain, acupuncture was superior (both statistically and clinically significant) to sham acupuncture in pain reduction and improved function immediately after treatment (48). Acupuncture was equivalent but not superior to usual care in pain and function, but acupuncture plus usual care was superior to usual care alone (48). The reviewers rated the evidence level of their review as Level of Evidence I (48). A systematic review of 11 randomised controlled trials on acute low back pain, acupuncture was superior to NSAIDs for improving symptoms (small effect), and superior to sham for pain but not function (49). A narrative review of non-invasive and alternative treatments for chronic low back pain rated the evidence for the effectiveness of acupuncture as high and for acupressure as moderate (50).

A review of 16 systematic reviews found that acupuncture alone, or when added to usual care, provided short-term improvement in pain and function for chronic low back pain (medium to large clinical effects) and hence 'should be advocated in routine clinical practice' (51). For acute low back pain, the reviewers could not make firm conclusions about the effectiveness of acupuncture due to the inclusion of only two systematic reviews (51). Two studies found that acupuncture is likely to be cost-effective for low back pain or chronic non-specific low back pain, respectively (52, 53).

2.4 Knee osteoarthritis pain [Positive effect]

Knee osteoarthritis pain was not reviewed in the Australian DVA review (2010) and 'evidence of potential positive effect' in the USVA Evidence map of acupuncture (2014) (5, 6). In a network meta-analysis comparing 22 interventions in 152 studies, acupuncture was found to be equal to balneotherapy and superior to sham acupuncture, muscle-strengthening exercise, Tai Chi, weight loss, standard care and aerobic exercise (in ranked order) (54). Acupuncture was also superior to standard care and muscle-strengthening exercises in a sub-analysis of moderate to high quality studies (54). In a systematic review of 12 randomised controlled trials, acupuncture was found to significantly reduce pain intensity, to improve functional mobility and quality of life (55). Subgroup analysis showed greater reduction in pain intensity when treatment lasted for more than four weeks (55). The reviewers concluded that 'current evidence supports the use of acupuncture as an alternative for traditional analgesics in patients with osteoarthritis' (55).

2.5 Allergic rhinitis (seasonal and perennial/persistent) [Positive effect]

For allergic rhinitis, acupuncture was rated as 'effective' in the Australian DVA review (2010) and 'unclear' in the USVA Evidence map of acupuncture (2014) (5, 6). A systematic review of 13 randomised controlled trials concluded that 'acupuncture could be a safe and valid treatment option for allergic rhinitis' (moderate quality evidence) (56). Another systematic review (which included two large multi-centre randomised controlled trials, three comparisons of acupuncture versus medication and one cost-effectiveness study) concluded that there is high quality evidence of the efficacy and effectiveness of acupuncture and that it appears to be safe and cost-effective (15). Clinical practice guidelines for allergic rhinitis published by the Otolaryngology Head Neck Surgery Foundation in 2015 included acupuncture as Option five: 'Clinicians may offer acupuncture, or refer to a clinician who can offer acupuncture, for patients with AR who are interested in nonpharmacological therapy' (Aggregate evidence quality - Grade B) (37).

2.6 Chemotherapy-induced nausea and vomiting (CINV) [Positive effect]

For chemotherapy-induced nausea and vomiting, acupuncture was rated as 'effective' in the Australian DVA review (2010) and was not reviewed separately to 'cancer adverse effects' in the USVA Evidence map of acupuncture (2014) (5, 6). In 2013, a systematic review of seven acupuncture and six acupressure RCTs found that acupuncture reduced the frequency of acute vomiting and the dose of rescue medication but did not reduce acute nausea severity or frequency compared to control. Acupressure showed a decrease in frequency of nausea but not acute vomiting or delayed symptoms. All studies used state-of-the-art combination anti-emetics in addition to acupuncture/acupressure. The reviewers rated the quality of evidence in the acupuncture studies as low to moderate while the acupressure studies were moderate to high quality. There was insufficient evidence to draw firm conclusions due to underpowered studies

(21). However, an updated systematic review by Garcia et al in 2014 (using 18 new RCTs) found that acupuncture is an appropriate referral option for chemotherapy-induced nausea and vomiting (57). On this basis, CINV has been rated as positive rather than potential positive in this review.

2.7 Post-operative nausea and vomiting (PONV) [Positive effect]

For post-operative nausea and vomiting (PONV), acupuncture was rated as ‘insufficient evidence’ in the Australian DVA review (2010) and ‘potential positive effect’ in the USVA Evidence map of acupuncture (2014) (5, 6). In a systematic review and meta-analysis of 30 RCTs on acupuncture and acupressure in 2013, both acupuncture and acupressure reduced the number of cases of early nausea and vomiting (up to 24 hours post-surgery) (58). In 2015, a Cochrane update of 59 RCTs on PC6 stimulation found that PC6 stimulation was superior to sham, and equivalent to modern anti-emetics (16).

2.8 Post-operative pain [Positive effect]

For post-operative pain, acupuncture was not reviewed in the Australian DVA review (2010) and rated as ‘unclear’ in the USVA Evidence map of acupuncture (2014) (5, 6). A systematic review and meta-analysis of 13 RCTs in 2016, found that acupuncture, electroacupuncture (EA) and transcutaneous electrical acupoint stimulation (TEAS) improved pain on day one after surgery and reduced opioid use (17). Subgroup analysis showed that acupuncture and TEAS were superior to EA (17). A systematic review specifically on acute pain after back surgery reviewed five RCTs (three of which were high quality) and found encouraging but limited evidence for the efficacy of acupuncture (59). A systematic review on complementary therapies for pain after knee surgery included three RCTs on acupuncture and one on acupressure (60). The review found that acupressure reduced pain, and while acupuncture did not reduce pain it did reduce ibuprofen use (60). An RCT on acupuncture for pain after total knee arthroplasty found that acupuncture was superior to sham in post-operative fentanyl use, time to first request for fentanyl and pain intensity (61).

3 RESEARCH INTO THE MECHANISMS OF ACUPUNCTURE

Mechanisms underlying acupuncture analgesia have been extensively researched for over 60 years. In animal models, acupuncture and/or electroacupuncture have been shown to be effective for the alleviation of inflammatory, neuropathic, cancer, and visceral pain (62). Ascending neural pathways involving A δ , A β and C sensory fibres have been mapped, the mesolimbic loop of analgesia in the brain and brain stem has been identified and descending pathways have also been mapped (63). Numerous mediators have been identified including opioid and non-opioid neuropeptides, serotonin, norepinephrine, dopamine, cytokines, glutamate, nitric oxide and gamma-amino-butyric-acid (GABA) (62, 63). Acupuncture analgesia has been shown to involve several classes of opioid neuropeptides including enkephalins, endorphins, dynorphins, endomorphins and nociceptin (also known as Orphanin FQ) (63-65). Among the non-opioid neuropeptides, substance P (SP), vasoactive intestinal peptide (VIP) and calcitonin gene-related peptide (CGRP) have been investigated for their roles in both the analgesic and anti-inflammatory effects of acupuncture (62, 66). Two recent reviews of acupuncture analgesia research further demonstrate the complexity of this area of study (63, 64).

The anti-inflammatory effects of acupuncture involve numerous mediators, receptors and signalling pathways, as outlined in two recent reviews (66, 67). The anti-inflammatory effects of acupuncture have particular relevance to allergic rhinitis, irritable bowel syndrome, post-surgical recovery, migraine, osteoarthritis and inflammatory aspects of a range of musculoskeletal conditions. In allergic rhinitis, acupuncture has been shown to down-regulate total and specific IgE, as well as SP and VIP (32, 68). Acupuncture has been shown to down-regulate transient receptor potential vanilloid 1 (TRPV1) in inflammatory pain and there is indirect evidence to suggest that acupuncture may down-regulate TRPV1 expression and sensitivity in allergic rhinitis (32, 66, 69). In irritable bowel syndrome, acupuncture has been shown to down-regulate SP, VIP and CGRP (70, 71). In migraine, acupuncture has been reported to down-regulate CGRP and SP which are also powerful vasodilators (72, 73).

In addition to the extensive research literature on acupuncture's efficacy, effectiveness and safety there is a body of research (largely using animal models) which has investigated physiological changes underpinning the effects of acupuncture in a broad range of clinical areas apart from pain and inflammation. To canvas this research in detail is beyond the scope of this review, however numerous reviews of this mechanism research have been published. A PubMed search on 18 September 2016, using the search terms 'acupuncture AND mechanism', yielded 1,943 hits.

For example:

- Acupuncture regulation of female reproductive function (74)
- Acupuncture regulation of gastrointestinal function (75)
- Acupuncture regulation of bladder function (75)
- Acupuncture regulation of circulation (76).

Table 3. Summary of effectiveness/efficacy in acupuncture research literature sorted by evidence levels

Australian DVA (Sept 2005 – Sept 2010)	USVA Evidence map (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)	
Effective	Evidence of positive effect	Moderate to high evidence/ positive	
<ul style="list-style-type: none"> - Allergic rhinitis (for up to 3 months) - Back or pelvic pain during pregnancy - Migraine prophylaxis (when used with routine care) - Vomiting after chemotherapy (with superseded anti-emetic drugs) 	<ul style="list-style-type: none"> - Chronic pain* - Headache - Migraine <p><i>* Chronic pain has been separated into different chronic pain conditions since USVA</i></p>	<ul style="list-style-type: none"> - Allergic rhinitis (perennial & seasonal) - Chemotherapy-induced nausea and vomiting (CINV) (with anti-emetics) - Chronic low back pain - Headache (tension-type and chronic) - Knee osteoarthritis - Migraine prophylaxis - Postoperative nausea & vomiting - Postoperative pain 	
Effective (possibly)	Evidence of potential positive effect		
<ul style="list-style-type: none"> - Lower back pain 	<ul style="list-style-type: none"> - Ankle sprain - Anxiety - Cancer pain - Constipation - Depression - Dysmenorrhoea - General pain - Insomnia - Labour pain - Obesity - Osteoarthritic pain - Plantar heel pain - Postoperative nausea and vomiting - Post-traumatic Stress Disorder - Pregnancy pain - Prostatitis pain - Restless leg syndrome - Schizophrenia - Smoking cessation - Temporomandibular pain 	<ul style="list-style-type: none"> - Acute low back pain - Acute stroke - Ambulatory anaesthesia - Anxiety - Aromatase-inhibitor-induced arthralgia - Asthma in adults - Back or pelvic pain during pregnancy - Cancer pain - Cancer-related fatigue - Constipation - Craniotomy anaesthesia - Depression (with antidepressants) - Dry eye - Hypertension (with medication) - Insomnia - Irritable bowel syndrome - Labour pain - Lateral elbow pain - Menopausal hot flushes - Modulating sensory perception thresholds - Neck pain (NAD, not WAD) 	<ul style="list-style-type: none"> - Obesity - Perimenopausal & postmenopausal insomnia - Plantar heel pain - Post-stroke insomnia - Post-stroke shoulder pain - Post-stroke spasticity - Post-traumatic stress disorder - Prostatitis pain/chronic pelvic pain syndrome - Recovery after colorectal cancer resection - Restless leg syndrome - Schizophrenia (with antipsychotics) - Sciatica - Shoulder impingement syndrome (early stage) (with exercise) - Shoulder pain - Smoking cessation (up to 3 months) - Stroke rehabilitation - Temporomandibular pain

Table 3. Summary of effectiveness/efficacy in acupuncture research literature sorted by evidence levels (contd)

Australian DVA (Sept 2005 – Sept 2010)	USVA Evidence map (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)	
Insufficient evidence	Unclear evidence	Unclear/insufficient evidence	
<ul style="list-style-type: none"> - Assisted conception (when used on the day of embryo transfer) - Asthma - Bell’s palsy - Breathlessness - Chronic neck pain - Cocaine addiction - Depression - Glaucoma - Induction of labour - Insomnia - Irritable bowel syndrome - Labour pain - Lateral elbow pain - Postnatal depression - Postoperative nausea and vomiting - Restless leg syndrome - Rheumatoid arthritis - Schizophrenia - Shoulder pain - Smoking cessation (up to 3 months) - Stroke - Uterine fibroids - Vascular dementia 	<ul style="list-style-type: none"> - Back pain - Cancer adverse effects - Chronic fatigue syndrome - Drug addiction - Dry eye - Erectile dysfunction - Exercise - Fibromyalgia pain - Gastrointestinal disease - High blood pressure - Irritable bowel syndrome - Menopausal symptoms - Neck pain - Opiate addiction - Postoperative pain - Premenstrual syndrome - Quality of life - Rheumatoid arthritis pain - Rhinitis - Shoulder pain - Surgical analgesia - Tinnitus - Xerostomia 	<ul style="list-style-type: none"> - Acupuncture in Emergency Department - Acute ankle sprain in adults - Alzheimer’s disease - Angina pectoris - Asthma in children - Atopic dermatitis - Attention Deficit Hyperactivity Disorder (ADHD) - Autism spectrum disorder (ASD) - Bell’s palsy - Bladder pain syndrome - Cancer-related insomnia - Cancer-related insomnia - Cancer-related psychological symptoms - Carpal tunnel syndrome - Chemotherapy-induced peripheral neuropathy - Chronic fatigue syndrome - Chronic kidney disease - Chronic obstructive pulmonary disease (COPD) - Chronic urinary retention due to spinal cord injury - Chronic urticaria - Dysmenorrhoea 	<ul style="list-style-type: none"> - Dyspepsia in diabetic gastroparesis (DGP) - Erectile dysfunction - Exercise performance & post-exercise recovery - Fatigue in systemic lupus erythematosus - Fibromyalgia - Functional dyspepsia - Gag reflex in dentistry - Glaucoma - Heart failure - Hot flushes in breast cancer - Hyperemesis gravidarum - Hypoxic ischemic encephalopathy in neonates - Induction of labour - Inflammatory bowel disease - Itch - Lumbar spinal stenosis - Melasma - Meniere’s disease/syndrome - Menopausal syndrome - Multiple sclerosis - Mumps in children - Myelosuppression after chemotherapy - Oocyte retrieval pain relief

Table 3. Summary of effectiveness/efficacy in acupuncture research literature sorted by evidence levels (contd)

Australian DVA (Sept 2005 – Sept 2010)	USVA Evidence map (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)	
Insufficient evidence	Unclear evidence	Unclear/insufficient evidence	
		<ul style="list-style-type: none"> - Opiate addiction - Opioid detoxification - Parkinson’s disease - Polycystic ovarian syndrome - Poor sperm quality - Postnatal depression - Postoperative gastroparesis syndrome (PGS) - Postoperative ileus - Post-stroke hiccoughs - Premenstrual syndrome - Primary ovarian insufficiency - Primary Sjogren’s syndrome - Psoriasis vulgaris - Rheumatoid arthritis 	<ul style="list-style-type: none"> - Slowing progression of myopia - Spinal cord injury - Stress urinary incontinence in adults - Sudden sensorineural hearing loss - Surgery analgesia - Tinnitus - Traumatic brain injury - Urinary incontinence - Uterine fibroids - Vascular cognitive impairment without dementia - Vascular dementia - Whiplash associated disorder (WAD) - Xerostomia in cancer
Not effective	Evidence of no effect	No evidence of effect	
<ul style="list-style-type: none"> - Assisted conception (if used around time of oocyte retrieval) - Epilepsy - Smoking cessation (more than 3 months) 	<ul style="list-style-type: none"> - Alcohol dependence - Carpal tunnel syndrome pain - Cocaine addiction - Nausea in pregnancy 	<ul style="list-style-type: none"> - Alcohol dependence - Cocaine addiction - Epilepsy - Improving pregnancy or live birth rates in ART - Nausea in pregnancy - Smoking cessation (more than 6 months) 	

Table 4. Summary of changes in evidence levels from 2005 to 2016

Conditions which have not changed in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Migraine prophylaxis	Effective	Positive effect	Positive effect
Headache (tension-type and chronic)	Not reviewed	Positive effect	Positive effect
Chemotherapy-induced nausea and vomiting	Effective	Not reviewed	Positive effect
Allergic rhinitis	Effective	Unclear	Positive effect
Anxiety	Not reviewed	Potential positive effect	Potential positive effect
Post-traumatic Stress Disorder	Not reviewed	Potential positive effect	Potential positive effect
Schizophrenia	Insufficient evidence	Potential positive effect	Potential positive effect
Smoking cessation			
Up to 3 months post-treatment	Insufficient evidence	Potential positive effect	Potential positive effect
More than 3 months post-treatment	Not effective		No evidence of effect (more than 6 months)
Temporomandibular pain		Potential positive effect	Potential positive effect
Plantar heel pain		Potential positive effect	Potential positive effect
Cancer pain	Not reviewed	Potential positive effect	Potential positive effect
Depression	Insufficient evidence	Potential positive effect	Potential positive effect
Insomnia	Insufficient evidence	Potential positive effect	Potential positive effect
Labour pain	Insufficient evidence	Potential positive effect	Potential positive effect
Back or pelvic pain during pregnancy	Effective	Potential positive effect	Potential positive effect
Prostatitis pain/chronic pelvic pain syndrome	Not reviewed	Potential positive effect	Potential positive effect
Constipation	Not reviewed	Potential positive effect	Potential positive effect
Obesity	Not reviewed	Potential positive effect	Potential positive effect
Restless leg syndrome	Insufficient evidence	Potential positive effect	Potential positive effect
Induction of labour	Insufficient evidence	Not reviewed	Unclear
Bell's palsy	Insufficient evidence	Not reviewed	Unclear
Glaucoma	Insufficient evidence	Not reviewed	Unclear
Uterine fibroids	Insufficient evidence	Not reviewed	Unclear
Vascular dementia	Insufficient evidence	Not reviewed	Unclear
Erectile dysfunction	Not reviewed	Unclear	Unclear
Tinnitus	Not reviewed	Unclear	Unclear
Improving exercise performance/recovery	Not reviewed	Unclear	Unclear
Opiate addiction	Not reviewed	Unclear	Unclear
Chronic fatigue syndrome	Not reviewed	Unclear	Unclear

Table 4. Summary of changes in evidence levels from 2005 to 2016 (contd)

Conditions which have not changed in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Fibromyalgia	Not reviewed	Unclear	Unclear
Premenstrual syndrome	Not reviewed	Unclear	Unclear
Rheumatoid arthritis	Insufficient evidence	Unclear	Unclear
Nausea in pregnancy	Not reviewed	Evidence of no effect	No evidence of effect
Alcohol dependence	Not reviewed	Evidence of no effect	No evidence of effect
Cocaine addiction	Insufficient evidence	Evidence of no effect	No evidence of effect
Epilepsy	Not effective	Not reviewed	No evidence of effect
Conditions which have increased in evidence level	Australian DVA (Sept 2005 –Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Low back pain	Possibly effective	Unclear	<i>Research has shown better outcomes for chronic low back pain than for acute low back pain</i>
Chronic low back pain			Positive effect
Acute low back pain			Potential positive effect
Knee osteoarthritis	Not reviewed	Potential positive effect	Positive effect
Postoperative nausea and vomiting	Insufficient evidence	Potential positive effect	Positive effect
Postoperative pain	Not reviewed	Unclear	Positive effect
Postoperative nausea and vomiting and pain after tonsillectomy			Positive effect
Postoperative pain – back surgery			Positive effect
Postoperative pain – knee surgery			Positive effect
Stroke	Insufficient evidence	Not reviewed	<i>Stroke research has now separated into several new topics</i>
Acute stroke			Potential positive effect
Stroke rehabilitation			Potential positive effect
Post-stroke spasticity			Potential positive effect
Post-stroke insomnia			Potential positive effect
Post-stroke shoulder pain			Potential positive effect
Post-stroke hiccoughs			Unclear

Table 4. Summary of changes in evidence levels from 2005 to 2016 (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 –Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Menopausal symptoms	Not reviewed	Unclear	<i>Menopausal symptom research has now separated into two new topics</i>
Menopausal hot flushes			Potential positive effect
Perimenopausal and postmenopausal sleep disturbance			Potential positive effect
Cancer adverse effects (not including cancer pain and chemotherapy-induced nausea and vomiting)	Not reviewed	Unclear	<i>Cancer adverse effects research has now separated into several new topics</i>
Cancer-related fatigue			Potential positive effect
Cancer-related insomnia			Unclear
Cancer-related peripheral neuropathy			Unclear
Hot flushes/flushes in breast cancer			Unclear
Xerostomia in cancer	Not reviewed	Unclear	Unclear
Recovery after colorectal cancer resection			Potential positive effect
Aromatase-inhibitor-induced arthralgia			Potential positive effect
Chemotherapy-induced peripheral neuropathy			Unclear
Myelosuppression after chemotherapy			Unclear
Cancer-related psychological symptoms			Unclear
Surgical analgesia	Not reviewed	Unclear	<i>Surgical analgesia research has now separated into several new topics</i>
Craniotomy anaesthesia			Potential positive effect
Ambulatory anaesthesia			Potential positive effect
Dry eye	Not reviewed	Unclear	Potential positive effect
Irritable bowel syndrome	Insufficient evidence	Unclear	Potential positive effect
Hypertension	Not reviewed	Unclear	Potential positive effect
Lateral elbow pain	Insufficient evidence	Not reviewed	Potential positive effect

Table 4. Summary of changes in evidence levels from 2005 to 2016 (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 –Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Neck pain			
Neck pain and associated disorders (NAD)	Insufficient evidence	Unclear	Potential positive effect
Whiplash associated disorders (WAD)			Unclear
Shoulder pain	Insufficient evidence	Unclear	Potential positive effect
Asthma	Insufficient evidence	Not reviewed	Potential positive effect (in adults)
Carpal tunnel syndrome	Not reviewed	Evidence of no effect	Unclear
Conditions which have decreased in evidence level	Australian DVA (Sept 2005 - Sept 2010)	USVA (Jan 2005 - Mar 2013) (to Mar 2013)	The Acupuncture Evidence Project (to September 2016)
	<i>Baseline evidence in bold</i>		
Dysmenorrhoea	Not reviewed	Potential positive effect	Unclear
Ankle sprain	Not reviewed	Potential positive effect	Unclear
Assisted conception in ART	Not effective when used for oocyte retrieval Insufficient evidence when used for embryo transfer	Not reviewed	No evidence of effect

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references

Conditions which remain unchanged	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 – Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Migraine prophylaxis	Effective	Positive effect	<p>Acupuncture seems to be at least as effective as conventional preventative medication for migraine and is safe, long lasting, and cost-effective (citing Witt et al 2008) (Da Silva 2015 - Narrative review of large high quality RCTs)(42)</p> <p>Acupuncture reduces migraine frequency. Acupuncture superior to sham and may be as effective as prophylactic drugs; subgroup analysis showed larger effect size when 16 or more treatments given ($Z = 4.06$) compared to 12 treatments or less ($Z = 2.32$); Moderate quality evidence (Linde 2016 - Cochrane SR of 22 RCTs of at least 8 weeks duration)(43)</p> <p>Acupuncture superior to sham in effectiveness and reduced risk of recurrence; Moderate to high quality evidence (Yang 2016 - SR of 10 RCTs)(44)</p>
Chemotherapy-induced nausea and vomiting	Effective	Not reviewed	<p>Acupuncture reduced the frequency of acute vomiting and the dose of rescue medication but did not reduce acute nausea severity or frequency compared to control. Acupressure showed a decrease in frequency of nausea but not acute vomiting or delayed symptoms. All studies used state-of-the-art combination anti-emetics. Insufficient evidence due to underpowered studies; acupuncture low to moderate quality evidence; acupressure moderate to high quality evidence (McKeon 2013 - SR of 7 acupuncture and 6 acupressure RCTs)(21)</p> <p>Acupuncture is an appropriate referral option for chemotherapy-induced nausea and vomiting (Garcia 2014 - SR update: 18 new RCTs)(57)</p>
Allergic rhinitis	Effective	Unclear	<p>Acupuncture could be a safe and valid treatment for allergic rhinitis; Moderate quality evidence (Feng 2015 - SR of 13 RCTs)(56)</p> <p>High quality evidence of efficacy and effectiveness (Taw 2015 - SR of 2 large multi-centre RCTs, 3 acupuncture vs medication RCTs and 1 cost-effectiveness study)(15)</p> <p>OHNSF clinical practice guideline: Option 5: Clinicians may offer acupuncture, or refer to a clinician who can offer acupuncture, for patients with AR who are interested in nonpharmacologic therapy; Aggregate evidence quality - Grade B (Seidman 2015)(37)</p> <p>Acupuncture is cost-effective for allergic rhinitis (Kim 2012, Witt 2010)(77, 78)</p> <p>SAR - Acupuncture significantly superior to rescue medication in QALY gained, but may cost more short term (Reinhold 2013)(79, 80)</p>

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which remain unchanged	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 – Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Anxiety	Not reviewed	Potential positive effect	Acupuncture has ‘potential use’ (Bazzan 2014 - Narrative review)(81) Positive and statistically significant effects; Moderate to high quality evidence (Goyata 2016 - Integrative review of 19 studies including 6 RCTs; 11 high quality studies; 5 moderate)(82)
Post-traumatic Stress Disorder	Not reviewed	Potential positive effect	One new RCT - Acupuncture plus usual care superior to usual care in PTSD severity, depression, pain and physical and mental functioning (Engel 2015 - RCT acupuncture plus usual care vs usual care, n = 55)(83)
Schizophrenia	Insufficient evidence	Potential positive effect	Acupuncture effective for schizophrenia, especially in improving sleep, mood and QoL by modulating and normalizing the limbic–paralimbic–neocortical network (LPNN), including the default mode network (DMN); limited evidence (Bosch 2015 - Review of SRs & MAs)(84) Acupuncture plus antipsychotic medication superior to antipsychotic medication alone, in terms of mental state and length of hospitalisation (moderate quality evidence) with fewer adverse effects (low quality evidence) (Shen 2014 – Cochrane update of 30 RCTs)(85)
Smoking cessation	Insufficient evidence (up to 3 months); Not effective (more than 3 months)	Potential positive effect (short term)	Potential short-term effects (low quality evidence), Insufficient evidence (more than 6 months) (White 2014 – Cochrane update)(86)
Temperomandibular pain		Potential positive effect	One new RCT: Acupuncture was equivalent to occlusal splint in pain intensity and range of mouth opening (Grillo 2015 - RCT acupuncture vs occlusal splint, n = 40)(87)
Plantar heel pain		Potential positive effect	No updates
Cancer pain	Not reviewed	Potential positive effect	Conflicting SRs Insufficient evidence; low to very low quality evidence (Paley 2015 - Cochrane SR of 5 RCTs) (88) Acupuncture relieved malignancy-related and surgery-induced pain but not pain induced by chemotherapy, radiotherapy or hormone therapy; Reviewers recommend acupuncture be included in multimodal treatment regimens (Chiu 2016 - SR of 29 RCTs)(89)

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which remain unchanged	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Depression	Insufficient evidence	Potential positive effect	<p>Acupuncture plus SSRIs superior to SSRIs alone, with an early onset of action and was safe and well-tolerated; EA had greater effect than manual acupuncture (Chan 2015 – SR of 13 RCTs: 1 high quality trial, 5 moderate, 7 low) (90)</p> <p>Effective and safe for major depressive disorder, especially in improving sleep, mood and QoL by modulating and normalizing the limbic–paralimbic–neocortical network (LPNN), including the default mode network (DMN); ‘promising evidence’ (Bosch 2015 - Review of SRs & MAs)(84)</p> <p>Acupuncture is cost-effective compared with counselling or usual care alone, although the ranking of counselling and acupuncture depends on the relative cost of delivering these interventions (Spackman 2015 –cost-effectiveness in one RCT)(91)</p>
Insomnia	Insufficient evidence	Potential positive effect	<p>Acupuncture may be superior to medication. Acupuncture for insomnia is potentially mediated by norepinephrine, melatonin, gamma-aminobutyric acid, and beta-endorphin; insufficient evidence (Zhao 2013 - book chapter)(92)</p> <p>Acupuncture statistically superior to sham (3 studies) and medication (27 studies); low quality evidence (Shergis 2016 - SR)(93)</p>
Labour pain	Insufficient evidence	Potential positive effect	<p>Acupuncture & acupressure ‘promising’ – Conflicting results due to heterogeneity in study designs, research questions, treatment protocols and outcomes measures (Levett 2014 - Review of SRs)(94)</p>
Back or pelvic pain during pregnancy	Effective	Potential positive effect	<p>Promising results; low quality evidence (Selva Olid 2013)(95)</p> <p>Clinically important and statistically significant changes (Close 2014 - SR of CAM; 2 high quality studies)(96)</p> <p>Moderate quality evidence that acupuncture or exercise, tailored to the stage of pregnancy, significantly reduced evening pelvic or lumbo-pelvic pain. Acupuncture superior to exercise for reducing evening pelvic pain; Both acupuncture and exercise superior to usual care; Insufficient evidence (Liddle 2015 - Cochrane SR: Comparison of interventions)(97)</p>

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which remain unchanged	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Prostatitis pain/chronic pelvic pain syndrome	Not reviewed	Potential positive effect	Acupuncture superior to both sham and to usual care and safe, thus it should be offered when available (Chang 2016 - SR of 7 RCTs: 3 high quality studies, 1 moderate and 3 low)(98) Acupuncture superior to sham in pain, voiding and QoL; acupuncture superior to medication in pain relief but no different in voiding and QoL; acupuncture as an adjunctive treatment for symptom control should be considered (Qin 2016 - SR of 7 RCTs: 3 high quality studies, 1 moderate and 3 low)(99)
Constipation	Not reviewed	Potential positive effect	No updates
Obesity	Not reviewed	Potential positive effect	Acupuncture superior to medication, sham and lifestyle modification; low to very low quality evidence (Esteghamati 2015 - Critical review of 3 SRs)(100)
Restless leg syndrome	Insufficient evidence	Potential positive effect	Insufficient evidence (Bega 2016 – Overview of alternative treatment of restless leg syndrome)(101)
Induction of labour	Insufficient evidence	Not reviewed	Insufficient evidence; included studies ranged from high to low quality evidence (Smith 2013 - Cochrane update with 14 RCTs)(102) Acupressure may reduce the duration of labour especially the first stage; insufficient evidence (Mollart 2015 – SR of 7 RCTs)(103)
Bell's palsy	Insufficient evidence	Not reviewed	Seems to be effective; insufficient evidence of efficacy and safety; low quality evidence (Li 2015 – SR & MA of 14 RCTs)(56) Acupuncture superior to waitlist in physical and social function (Kwon 2015 - RCT acupuncture (n=36) vs waitlist (n=13))(104)
Glaucoma	Insufficient evidence	Not reviewed	Insufficient evidence; low quality evidence (Law 2013 - Cochrane SR; 1 RCT on auricular acupressure)(105)
Uterine fibroids	Insufficient evidence	Not reviewed	Acupuncture may be a treatment option as part of a CAM treatment approach (Dalton-Brewer 2016 - Narrative review of CAM)(106)
Vascular dementia	Insufficient evidence	Not reviewed	Acupuncture plus other therapies significantly improved Mini Mental State scores; low quality evidence (Cao 2013 – SR of 12 RCTs)(107)
Erectile dysfunction	Not reviewed	Unclear	Insufficient evidence; low quality evidence (Cui 2016 - SR of 3 RCTs)(108)
Tinnitus	Not reviewed	Unclear	EA - Insufficient evidence; low quality evidence (He 2016 - SR of 5 RCTs)(109)

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which remain unchanged	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Improving exercise performance and post-exercise recovery	Not reviewed	Unclear	No updates
Opiate addiction	Not reviewed	Unclear	Acupuncture is effective in opiate detoxification (and associated depression and anxiety) which is mediated by endogenous dynorphin; no effect on opioid cravings; low quality evidence (Wu 2016 – Narrative review)(110) Acupuncture superior to controls for withdrawal/craving and anxiety post-treatment but not long term; low quality evidence (Grant 2016 - SR & MA of 41 RCTs on substance use disorders)(111)
Chronic fatigue syndrome	Not reviewed	Unclear	Acupuncture plus usual care may improve fatigue in chronic fatigue syndrome and idiopathic chronic fatigue (Kim 2015 - Multi-centre nonblinded RCT, n = 150)(112)
Fibromyalgia	Not reviewed	Unclear	Acupuncture superior to no treatment or standard care in reducing pain and stiffness; low to moderate quality evidence Acupuncture not different from sham in reducing pain, fatigue or improving sleep and global wellbeing; moderate quality evidence EA is probably better than manual acupuncture in reducing pain and stiffness and improving global well-being, sleep and fatigue. (Deare 2013 – Cochrane SR of 9 RCTs)(113) Insufficient evidence; low quality evidence (Yang 2014 – SR of RCTs)(114) Inconsistent evidence (Lauche 2015 – SR of reviews; 2 high and 2 low quality reviews)(115)
Premenstrual syndrome	Not reviewed	Unclear	A SR in 2014 included no new evidence (116) Insufficient evidence (Hofmeister 2016 - Narrative review) (117)
Rheumatoid arthritis	Insufficient evidence	Unclear	A SR in 2016 included no new evidence (Fernandez-Llanio Camella 2016 -SR of CAM)(118)
Nausea in pregnancy	Not reviewed	Evidence of no effect	No significant difference between real and sham acupuncture; low quality evidence (Matthews 2015 - Cochrane SR of interventions for nausea in pregnancy; 2 RCTs on acupuncture)(119)
Alcohol dependence	Not reviewed	Evidence of no effect	Low to very low quality evidence (Grant 2016 - SR & MA of 41 RCTs: 12 opioids, 9 cocaine, 11 alcohol, 9 mixed/not reported/other)(111)
Cocaine addiction	Insufficient evidence	Evidence of no effect	Low to very low quality evidence (Grant 2016 - SR & MA of 41 RCTs: 12 opioids, 9 cocaine, 11 alcohol, 9 mixed/not reported/other)(111)
Epilepsy	Not effective	Not reviewed	No evidence of effect (Cheuk 2014 – Cochrane update)(120)

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 – Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Low back pain	Possibly effective	Unclear	<i>Research has shown better outcomes for chronic low back pain than for acute low back pain</i>
Chronic low back pain			High quality evidence for acupuncture; moderate quality evidence for acupressure (Wellington 2014 – SR of noninvasive interventions)(50) Acupuncture alone or as an adjunct to usual care provided short-term improvement in pain and function; low to high quality evidence; ‘should be advocated in routine clinical practice’ (Liu 2015 - Overview of 16 SRs)(51) Moderate quality evidence for pain and function (Chou 2016 [AHRQ Comparative Effectiveness review])(47) Upgrade to positive
Acute low back pain			Acupuncture superior to NSAIDS for improving symptoms; acupuncture superior to sham for pain but not function (Lee 2013 - SR of 11 RCTs)(49) Low quality evidence for pain and function (Chou 2016 - AHRQ Comparative Effectiveness review)(47) Upgrade to potential positive
Headache (frequent episodic or chronic tension-type)	Not reviewed	Potential positive effect	Acupuncture is cost effective for headache (Kim 2012)(78) A potentially important role for acupuncture as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders. Cost-effective in Germany and UK (Coeytaux 2016 - Brief review of selected SRs and MAs)(46) Acupuncture can reduce workplace headache pain intensity, frequency and related disability; low quality evidence (Lardon 2016 - SR of 15 RCTs)(121) Effective for frequent episodic or chronic tension-type headaches; Moderate or low quality evidence (Linde 2016 - Cochrane SR of 12 RCTs)(45) Acupuncture has been included in the NICE guidelines for headache since 2012(38) Upgrade to positive
Knee osteoarthritis	Not reviewed	Potential positive effect	Acupuncture was equal to balneotherapy and superior to sham acupuncture, muscle-strengthening exercise, Tai Chi, weight loss, standard care and aerobic exercise (in ranked order). Acupuncture superior to standard care and muscle-strengthening exercises in sub-analysis of moderate to high quality studies (Corbett 2013: Network meta-analysis (152 studies on 22 interventions: 12 RCTs included in network MA) (54) Upgrade to positive

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Postoperative nausea and vomiting	Insufficient evidence	Potential positive effect	Acupuncture and acupressure reduced number of cases of early nausea and vomiting (up to 24 hours); low quality evidence (Cheong 2013 - SR of 30 RCTs)(58) PC 6 stimulation was superior to sham; low quality evidence; no difference between PC 6 stimulation and anti-emetics (moderate quality evidence); insufficient evidence that PC 6 plus anti-emetics is superior to anti-emetics alone (Lee 2015 - Cochrane update with 59 RCTs of PC 6 stimulation)(16) Upgrade to positive
Postoperative nausea and vomiting and pain after tonsillectomy			Pain scores, analgesic need and nausea and vomiting were reduced (acupuncture vs control); no significant adverse events; insufficient evidence (Cho 2016 - MA of 12 RCTs; 7 high quality)(122) Acupuncture superior to controls and cost-effective; insufficient evidence (Shin 2016 - SR & MA - 4 RCTs [3 high quality]; 3 randomised prospective studies and 1 pilot)(123) Upgrade to positive
Postoperative pain	Not reviewed	Unclear	Some forms of acupuncture (acupuncture, EA and TEAS) improved pain on day 1 after surgery and reduced opioid use; subgroup analysis showed acupuncture and TEAS superior to EA; moderate quality evidence (Wu 2016 - SR & MA of 13 RCTs)(17) Upgrade to positive
Postoperative pain – back surgery			Encouraging but limited evidence (Cho 2015 - SR of 5 RCTs; 3 high quality)(59) Upgrade to positive
Postoperative pain – knee surgery			Acupressure reduced pain; acupuncture did not reduce pain but resulted in reduced use of ibuprofen; low quality evidence (Barlow 2013 - SR of CAM – 3 acupuncture & 1 acupressure RCTs)(60) Acupuncture superior to sham in post-operative fentanyl use, time to first request for fentanyl and pain intensity (Chen 2015 - RCT acupuncture vs sham, n=60)(61) Upgrade to positive

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Stroke	Insufficient evidence	Not reviewed	<i>Stroke research has now become nuanced into several new topics</i> Acupuncture may be effective for treating post-stroke neurological impairment and dysfunction such as dysphagia, but does not prevent post-stroke death; (Zhang 2014 - Review of SRs: 8 reviews high quality, 6 moderate, 10 low)(124) <i>Upgrade to potential positive</i>
Acute stroke			Acupuncture plus rehabilitation superior to rehabilitation alone for acute and subacute stroke sequelae (Vados 2015 – SR of 17 RCTs; 5 high quality)(125) Acute ischaemic stroke: EA superior to usual care in Barthel Index, Fugl-Meyer Assessment, National Institutes of Health Stroke Scale, and Revised Scandinavian Stroke Scale; Moderate to high quality evidence (Liu 2015 - MA of 18 RCTs)(126) <i>Upgrade to potential positive</i>
Stroke rehabilitation			May have beneficial effects on improving dependency, global neurological deficiency, and some specific neurological impairments; insufficient evidence; low to very low quality evidence (Yang 2016 – Cochrane update)(127) <i>Upgrade to potential positive</i>
Post-stroke spasticity			Acupuncture or EA significantly decreased spasticity after stroke; low quality evidence (Lim 2015 – SR & MA of 5 RCTs)(128) Acupuncture improved passive resistance to stretching, degree of personal dependence and motor function; insufficient evidence; 6 high quality studies; 3 moderate quality (Rodriguez-Mansilla 2016 – SR of 9 RCTs or controlled studies)(129) <i>Upgrade to potential positive</i>
Post-stroke insomnia			Acupuncture superior to sham acupuncture and to medication; insufficient evidence; low to moderate evidence (Lee 2016 – SR & MA of 13 RCTs)(130) <i>Upgrade to potential positive</i>
Post-stroke shoulder pain			Acupuncture plus rehabilitation superior to rehabilitation alone; insufficient evidence; low to moderate evidence (Lee 2016 – SR of 12 RCTs)(131) <i>Upgrade to potential positive</i>
Post-stroke hiccoughs			Acupuncture may be effective as an adjunctive but not as a stand-alone treatment; low quality evidence (Yue 2016 – SR & MA of 5 RCTs)(132) <i>Unclear</i>

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Menopausal symptoms	Not reviewed	Unclear	<i>Menopausal symptom research has now separated into two new topics</i>
Menopausal hot flushes			Acupuncture improves hot flash frequency and severity, menopause-related symptoms, and QoL (vasomotor domain) in natural menopause (Chiu 2015 - MA of 12 studies; 2 high quality studies, 8 moderate and 2 low)(133) Promising results; low quality evidence (Selva Ovid 2013 (Review of 8 SRs and 9 RCTs))(95) Acupuncture superior to wait-list or no treatment; low quality evidence Acupuncture superior to sham in reducing severity but not frequency; very low quality evidence Acupuncture inferior to hormone therapy in QoL and frequency; no difference in severity; low quality evidence (Dodin 2013 - Cochrane SR of 16 RCTs)(134) <i>Upgrade to potential positive</i>
Perimenopausal and postmenopausal sleep disturbance			Significant reduction in sleep disturbance which appears to be associated with changes in serum estradiol, FSH and LH; acupuncture recommended as adjunctive therapy in improving sleep disturbances in perimenopausal and postmenopausal women (Chiu 2016 - SR of 34 studies; 4 high quality)(135) Improved sleep quality; limited evidence; moderate to high quality evidence (Bezerra 2015 - SR of 7 RCTs; 4 high quality; no studies with high risk of bias)(136) <i>Upgrade to potential positive</i>
Cancer adverse effects (not including cancer pain and chemotherapy-induced nausea and vomiting)	Not reviewed	Unclear	<i>Cancer adverse effects research has now become nuanced into several new topics</i> Acupuncture plus usual care superior to usual care alone in reducing pain, fatigue, and in improving QoL. Acupuncture’s effectiveness for managing anorexia, reducing constipation, paraesthesia and dysaesthesia, insomnia, and limb oedema is unclear; low to very low quality evidence (Lau 2016 - SR & MA of 13 RCTs)(137) Acupuncture may be effective for cancer pain, post-operative pain, aromatase inhibitor related joint pain and neck dissection pain and dysfunction, as well as opioid related constipation and pruritus and chemotherapy-induced nausea and vomiting and neuropathy; no assessment of quality of evidence (Lu 2013 - Narrative review)(138) Acupuncture effective for treatment-related nausea and vomiting, cancer pain, fatigue, hot flushes, xerostomia, dyspnoea and anxiety; low quality evidence (Towler 2013 - Review of 17 reviews)(139) Acupuncture may be appropriate adjunctive therapy for a range of cancer-related symptoms including adverse effects of chemotherapy and radiotherapy and cancer pain (Lian 2014 - SR of 33 RCTs)(140)

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 – Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Cancer-related fatigue			<p>Acupuncture and moxibustion appear to be efficacious adjunctive therapy; Insufficient evidence; low quality evidence (He 2013 - SR of 7 RCTs)(134)</p> <p>Acupuncture and acupressure tend to be effective, acupuncture more than acupressure; low quality evidence (Ling 2013 - SR)(141)</p> <p>Conflicting evidence: 4 studies showed acupuncture or acupuncture plus usual care superior to sham, usual care, enhanced usual care or no treatment; 3 studies showed no difference between acupuncture and sham; very low quality evidence (Posadzki 2013 - SR of 7 RCTs)(142)</p> <p>Acupuncture may reduce fatigue after cancer treatment; low quality evidence (Finnegan-John 2013 - SR of CAM 20 studies; 3 acupuncture/acupressure RCTs)(143)</p> <p>Acupuncture plus education superior to usual care; low quality evidence (Zeng 2014 (SR of 7 RCTs)(144)</p> <p>Upgrade to potential positive</p>
Cancer-related insomnia			<p>Acupuncture may be superior to sham acupuncture, drugs or hormones therapy. Number of studies and effect size are small for clinical significance; low quality evidence (Choi 2016 - SR of 6 RCTs)(145)</p> <p>Unclear</p>
Hot flushes/flushes in breast cancer			<p>Acupuncture superior to sham in some studies and superior to baseline in all studies; low quality evidence (Garcia 2015 - SR of 8 RCTs)(146)</p> <p>Acupuncture had similar efficacy to venlafaxine and gabapentin but may have longer durability after completing treatment and fewer side effects (Johns 2016 - SR of interventions; 2 acupuncture vs medication studies)(147)</p> <p>Acupuncture superior to sham in 3 studies; no different from sham in 6 studies; inferior to hormone therapy in 2 studies; low quality evidence (Chen 2016 - SR of 12 RCTs)(148)</p> <p>Conflicting evidence; low quality evidence (Salehi 2016 - SR of 12 studies)(149)</p> <p>Acupuncture yielded small-size effects on reducing hot-flash frequency and the severity of menopause-related symptoms; Insufficient or conflicting evidence; Low to high quality studies (Chiu 2016 - SR of 7 studies; 4 high quality studies)(89)</p> <p>Unclear</p>

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Xerostomia in cancer	Not reviewed	Unclear	Insufficient evidence (Zhuang 2013 - SR of 4 studies)(150) Small increase in saliva production; low quality evidence (Furness 2013 - Cochrane SR of non-pharmacological interventions - 9 RCTs; 5 acupuncture)(151) Acupuncture was superior to sham; low quality evidence (Hanchanale 2015 - SR of 6 RCTs)(152) Unclear
Recovery after colorectal cancer resection			Acupuncture efficacious and effective; Low to moderate quality evidence (Kim 2016 - SR of 7 RCTs)(153) Upgrade to potential positive
Aromatase-inhibitor-induced arthralgia			Acupuncture superior to sham in 2 high quality studies; no different from sham in 2 low-quality studies (Bae 2015 - SR of 4 RCTs)(154) Acupuncture reduces joint pain and stiffness but not superior to sham; moderate to high quality evidence (Chien 2015 - SR of 5 RCTs)(155) Upgrade to potential positive
Chemotherapy-induced peripheral neuropathy			Acupuncture superior to sham in one RCT; very low quality evidence (Franconi 2013 - SR of 3 RCTs, 3 case series, 1 rat study)(156) Unclear
Myelosuppression after chemotherapy			Insufficient evidence; low to very low quality evidence (Fu 2015 - Narrative review includes 7 RCTs)(157) Unclear
Cancer-related psychological symptoms			All included studies suggest benefits in depression, anxiety, sleep disturbance, and for improving QoL; strong evidence for safety; no assessment of quality of evidence (Haddad 2014 - SR of 12 studies; 8 RCTs)(158) Unclear
Surgical analgesia	Not reviewed	Unclear	<i>Surgical analgesia has now become nuanced into several new topics</i> Conflicting evidence; insufficient evidence; no assessment of quality of evidence (Lee 2014 - Overview of 12 SRs on postsurgical nausea and vomiting and postsurgical pain)(159)

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Craniotomy anaesthesia			Acupuncture significantly reduced the amount of volatile anaesthetics and led to faster extubation time and postoperative patient recovery and reduced postoperative nausea and vomiting. In addition, significantly reduced blood levels of the brain tissue injury marker S100beta 48 hours after operation; low quality studies excluded from MA, hence moderate to high quality evidence (Asmussen 2016 - MA of 10 RCTs)(160) Upgrade to potential positive
Ambulatory anaesthesia			Acupuncture may reduce preoperative anxiety, and postoperative pain, nausea, vomiting, shivering and emergence delirium. Acupuncture is safe and cost-effective. Acupuncture may be a beneficial adjunctive therapy for ambulatory anaesthesia; insufficient evidence; high quality studies favour acupuncture (Liiodden 2013 - Narrative review)(161) Upgrade to potential positive
Postoperative nausea and vomiting and pain after tonsillectomy			Pain scores, analgesic need and nausea and vomiting were reduced (acupuncture vs control); no significant adverse events; insufficient evidence (Cho 2016 - MA of 12 RCTs; 7 high quality)(122) Acupuncture superior to controls and cost-effective; insufficient evidence (Shin 2016 - SR & MA - 4 RCTs [3 high quality]; 3 randomised prospective studies and 1 pilot)(123) Upgrade to potential positive
Dry eye	Not reviewed	Unclear	Acupuncture was significantly superior to artificial tears in tear break-up time, Schirmer I test, and cornea fluorescein staining; Low to moderate quality evidence (Yang 2015 - SR & MA of 7 RCTs)(162) Upgrade to potential positive

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Carpal tunnel syndrome	Not reviewed	Evidence of no effect	Acupuncture superior to ibuprofen in function and symptoms (Hadianfard et al 2015 - RCT comparing acupuncture plus night wrist splints with ibuprofen plus night wrist splints, n=50)(177) Upgrade to unclear
Irritable bowel syndrome	Insufficient evidence	Unclear	Insufficient evidence; low to moderate quality evidence (Manheimer 2012 - Cochrane SR of 17 RCTs)(163) Acupuncture superior to usual care on IBS symptom severity score at 6, 9 and 12 months but not at 24 months (MacPherson 2016 - high quality RCT)(164) Upgrade to potential positive
Hypertension	Not reviewed	Unclear	Acupuncture plus medication superior to sham plus medication; low quality evidence (Wang 2013 - SR of 35 RCTs)(165) Acupuncture plus medication superior to medication, but acupuncture not superior to medication; high quality evidence (Li 2014 - SR of 4 RCTs) (166) Acupuncture plus medication superior to medication, but acupuncture not superior to medication; risk of bias unclear for most domains (Zhao 2015 – 23 RCTs)(167) Upgrade to potential positive
Lateral elbow pain	Insufficient evidence	Not reviewed	Acupuncture superior to sham; moderate quality evidence (Gadua 2014 - SR of 19 RCTs)(168) Insufficient evidence: low to very low quality evidence (Tang 2015 - SR of 4 RCTs)(169) Upgrade to potential positive
Neck pain	Insufficient evidence	Unclear	Acupuncture plus usual medical care is cost-effective for neck pain and its associated disorders (NAD) (Van der Velde 2015 – SR of 6 studies)(170) Acupuncture superior to sham acupuncture or inactive treatment (at completion of treatment and short-term follow-up) for pain relief; Moderate quality evidence (Trinh 2016 - Cochrane update with 27 RCTs)(171) Limited evidence of effectiveness; low quality evidence (Moon 2014 – 6 RCTs on whiplash associated disorder [WAD])(172) Moderate quality evidence for NAD, but low quality evidence for WAD Upgrade to potential positive for NAD, but leave WAD as unclear

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)			
Conditions which have increased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Shoulder pain	Insufficient evidence	Unclear	For non-operative treatment options at an early stage of Shoulder Impingement Syndrome (SIS), exercise combined with therapies such as kinesio taping, specific exercises, and acupuncture should be considered as the first line choices (2 included high quality acupuncture studies) (Dong 2015 - SR and network MA)(173) <i>Upgrade to potential positive</i>
Asthma	Insufficient evidence	Not reviewed	Acupuncture may improve peak expiratory flow or peak expiratory flow variability in children; low quality evidence (Liu 2015 – SR of 7 RCTs)(174) Acupoint herbal patches superior to sham in improving FEV1 and asthma symptoms; low quality evidence (Lee 2016 – SR & MA of 16 RCTs)(175) Acupuncture improved FEV1, FEV1/FVC, IL and IgE (moderate quality evidence), but not ECP (Su 2016 - SR & MA of 8 RCTs)(176) <i>Upgrade to potential positive</i>

Table 5. Evidence levels from 2005 to 2016: explanatory notes with references (contd)

Conditions which have decreased in evidence level	Australian DVA (Sept 2005 – Sept 2010)	USVA (Jan 2005 - Mar 2013)	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)
	<i>Baseline evidence in bold</i>		
Dysmenorrhoea	Not reviewed	Potential positive effect	<p>Conflicting SRs (3 positive SRs; Cochrane SR insufficient evidence)</p> <p>Acupuncture is effective and acupressure may be effective for pain relief; acupuncture trials had low to moderate risk of bias; acupressure trials high risk of bias (Chen et al, 2013 – MA of 3 acupuncture and 4 acupressure RCTs)(178)</p> <p>Acupoint stimulation superior to controls for pain relief; low to moderate quality evidence (Xu et al, 2014 MA of 20 RCTs of acupoint stimulation)(179)</p> <p>Acupuncture and acupressure (vs placebo, waitlist or medication) reduced pain intensity, while acupuncture also improved quality of life; moderate quality evidence (Abaraogu 2015 – SR of 8 RCTs and MA of 4 RCTs)(180)</p> <p>Insufficient evidence; low to very low quality evidence (Smith 2016 - Cochrane update)(181)</p> <p><i>Downgrade to unclear</i></p>
Ankle sprain	Not reviewed	Potential positive effect	<p>Insufficient evidence; low to very low quality evidence (Kim 2014 – Cochrane SR of 15 RCTs, 5 quasi-randomised trials)(182)</p> <p><i>Downgrade to unclear</i></p>
Assisted conception in ART	<p>Insufficient evidence when used around embryo transfer;</p> <p>Not effective when used around oocyte retrieval</p>	Not reviewed	<p>No evidence that acupuncture improves live birth or pregnancy rates in ART regardless of whether performed around the time of oocyte retrieval or embryo transfer (Cheong 2013 - Cochrane update with 20 RCTs)(40). Contradictory finding from Shen 2015 who found acupuncture ineffective when used only on the day of oocyte retrieval but effective when used on the day of embryo transfer. Shen 2015 (SR & MA) (41).</p> <p>Due to the weighting of the Cochrane review over other SR and MA the evidence level has been reported at ‘no evidence of effect’, even though a more recent SR and MA reports some positive results.</p> <p><i>Downgrade to no evidence of effect</i></p>

Table 6. All conditions reviewed sorted by clinical areas

Condition	<p align="center">THE ACUPUNCTURE EVIDENCE PROJECT (updates from March 2013 to August 2016) systematic reviews, meta-analyses, network meta-analyses, narrative reviews, cost effectiveness reviews <i>Cochrane reviews highlighted in bold</i></p>	Comments
Cardiovascular/respiratory conditions		
Angina pectoris	<p>Xu 2013 (Narrative review)(184): Acupuncture shows effectiveness rates of 80% to 92.6% without adverse effects of medication; no assessment of quality of evidence</p> <p>Yu 2015 (SR of 25 RCTs)(185): Improvement in symptoms and ECG; very low quality evidence</p> <p>Zhang 2015 (SR & MA of 15 RCTs)(186): Acupuncture plus medication superior to medication alone in improving symptoms and ECG; insufficient evidence; no assessment of quality of evidence</p>	<i>Unclear</i>
Asthma	<p>Liu 2015 [Childhood asthma] (SR of 7 RCTs)(174): Acupuncture may improve peak expiratory flow or peak expiratory flow variability; insufficient evidence; low quality evidence</p> <p>Lee 2016 [Acupoint herbal patches] (SR & MA of 16 RCTs)(175): Superior to sham in improving FEV1 and asthma symptoms; low quality evidence</p> <p>Su 2016 [Acupoint application in adults] (SR & MA of 8 RCTs)(176): Acupuncture improved FEV1, FEV1/FVC, IL and IgE (moderate quality evidence) but not ECP</p>	<p>Moderate quality evidence of lung function improvements in adults -<i>Potential positive</i> (adults)</p> <p><i>Unclear</i> (children)</p>
Chronic obstructive pulmonary disease (COPD)	Coyle 2014 (SR of 16 RCTs)(183): Clinically significant improvements in QoL and dyspnoea, but not lung function; moderate quality evidence	<i>Unclear</i>
Heart failure	Lee 2016 (SR of 7 RCTs)(187): Acupuncture improved exercise capacity, quality of life, hemodynamic parameters, and time domain heart rate variability parameters; low quality evidence	<i>Unclear</i>
Hypertension	<p>Wang 2013 (SR of 35 RCTs)(165): Acupuncture plus medication superior to sham plus medication; low quality evidence</p> <p>Li 2014 (SR of 4 RCTs)(166): Acupuncture plus medication superior to medication, but acupuncture not superior to medication; high quality evidence</p> <p>Zhao 2015 (SR & MA of 23 RCTs)(167): Acupuncture plus medication superior to medication, but acupuncture not superior to medication; risk of bias unclear for most domains</p>	<p>Low to high quality evidence for acupuncture plus medication</p> <p><i>Potential positive</i> (with medication)</p>
Vascular cognitive impairment without dementia	Min 2016 (MA of 15 studies)(188): Acupuncture superior to usual care or medication; low quality evidence	<i>Unclear</i>

Table 6. All conditions reviewed sorted by clinical areas		
Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Cardiovascular/respiratory conditions (contd)		
Vascular dementia	Cao 2013 (SR of 12 RCTs)(107): Acupuncture plus other therapies significantly improved Mini Mental State scores; low quality evidence	Unclear
Musculoskeletal disorders		
Acute ankle sprain in adults	Park 2013 (SR of 17 RCTs; 2 high quality, 15 low quality)(194): Acupuncture superior to various controls in relieving pain, facilitating return to normal activity, and promoting QoL based on subgroup analysis of 2 high quality studies Kim 2014 (Cochrane SR of 15 RCTs, 5 quasi-randomised trials)(182): Insufficient evidence; Low to very low quality evidence	Potential positive in USVA review 2014; Insufficient evidence/ low to very low quality evidence (Cochrane) Downgrade to unclear
Carpal tunnel syndrome	Hadianfard 2015 (RCT comparing acupuncture plus night wrist splints with ibuprofen plus night wrist splints, n=50)(177): Acupuncture superior to ibuprofen in function and symptoms	USVA review 2014 ‘Evidence of no effect’; 1 positive RCT in 2015 Upgrade to unclear
Fibromyalgia	Deare 2013 (Cochrane SR of 9 RCTs)(113): Acupuncture superior to no treatment or standard care in reducing pain and stiffness; low to moderate quality evidence Acupuncture not different from sham in reducing pain, fatigue or improving sleep and global wellbeing; moderate quality evidence EA is probably better than manual acupuncture in reducing pain and stiffness and improving global well-being, sleep and fatigue. Yang 2014 (MA of 9 RCTs)(114): Insufficient evidence; low quality evidence Lauche 2015 (SR of reviews; 2 high and 2 low quality reviews)(115): Inconsistent evidence	Unclear
Lateral elbow pain	Gadau 2014 (SR of 19 RCTs)(168): Acupuncture superior to sham; moderate quality evidence Tang 2015 (SR of 4 RCTs)(169): Insufficient evidence: low to very low quality evidence	Moderate quality evidence when 19 RCTs included – Upgrade to potential positive
Lumbar spinal stenosis	Kim 2013 (SR of 6 RCTs, 6 controlled trials) (190): Acupuncture superior to controls in pain intensity, functional improvements and QoL; Low quality evidence	Unclear

Table 6. All conditions reviewed sorted by clinical areas

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Musculoskeletal disorders (contd)		
Low back pain	Taylor 2014 (53): Cost effective for chronic low back pain Andronis 2016 (52): Likely to be cost effective	Chronic and acute low back pain need to be differentiated in SRs
Acute low back pain	Lee 2013 (SR of 11 RCTs; 5 low risk of bias, 6 high)(49): Acupuncture superior to NSAIDs for improving symptoms; acupuncture superior to sham for pain but not function; Chou 2016 [AHRQ Comparative Effectiveness review](47): Low quality evidence for pain and function	Upgrade to potential positive
Chronic low back pain	Lam 2013 (32 RCTs; 25 in MA)(48): Acupuncture may be effective for pain and functional limitation in chronic non-specific low back pain: Evidence Level 1 Wellington 2014 (SR of non-invasive interventions)(50): High quality evidence for acupuncture; moderate quality evidence for acupressure Liu 2015 (Overview of 16 SRs)(51): Acupuncture alone or as an adjunct to usual care provided short-term improvement in pain and function; low to high quality evidence; ‘should be advocated in routine clinical practice’ Chou 2016 [AHRQ Comparative Effectiveness review](47): Moderate quality evidence for pain and function Nahin 2016 (4 RCTs; Excluded studies not performed in USA or by US researchers)(189): Acupuncture superior to usual care; Acupuncture superior to sham in 1 RCT, but not superior in 2 RCTs	Moderate to high quality evidence Cost effective, safe Upgrade to positive
Neck pain	Van der Velde 2015 (SR of 6 studies)(170): Acupuncture plus usual medical care is cost-effective for neck pain and its associated disorders (NAD) Trinh 2016 (Cochrane update with 27 RCTS)(171): Acupuncture superior to sham acupuncture or inactive treatment (at completion of treatment and short-term follow-up) for pain relief; Moderate quality evidence	Moderate quality evidence (Cochrane update); Acupuncture plus medication is cost-effective Potential positive for NAD
Knee osteoarthritis pain	Corbett 2013 (Network meta-analysis - 152 studies on 22 interventions: 12 RCTs included in network MA)(54): Acupuncture was equal to balneotherapy and superior to sham acupuncture, muscle-strengthening exercise, Tai Chi, weight loss, standard care and aerobic exercise (in ranked order). Acupuncture superior to standard care and muscle-strengthening exercises in sub-analysis of moderate to high quality studies Nahin 2016 (4 RCTs; Excluded studies not performed in USA or by US researchers)(189): Acupuncture superior to attention control or usual care in 3/4 studies; Acupuncture superior to sham in 2/4 studies	Moderate to high quality evidence Upgrade to positive

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Musculoskeletal disorders (contd)		
Osteoarthritis	Kim 2012 (Cost effectiveness analysis)(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache Manyanga 2014 (SR & MA of 12 trials)(55): Significant reductions in pain intensity, improvement in functional mobility and quality of life; low quality evidence	Cost-effective
Plantar heel pain		Potential positive in USVA review 2014; no updates
Restless leg syndrome	Bega 2016 (Overview of alternative treatment of restless leg syndrome)(101): insufficient evidence	Potential positive
Sciatica	Lewis 2015 (Network MA of 21 interventions)(191): Acupuncture 2 nd out of 21 interventions for global effect and pain intensity Qin 2015 (SR & MA of 11 RCTs; 10 acupuncture vs medications; 1 acupuncture vs sham)(192): Acupuncture may be superior to drugs and may enhance the effect of drugs for patients with sciatica; low quality evidence Ji 2015 (SR of 12 RCTs)(193): Acupuncture superior to conventional Western medicine in outcomes effectiveness, pain intensity and pain threshold; low quality evidence	Acupuncture 2 nd out of 21 interventions for global effect and pain intensity Potential positive
Shoulder pain: Shoulder impingement syndrome (SIS)	Dong 2015 (SR and network MA; 2 high quality acupuncture studies)(173): For non-operative treatment options at an early stage of SIS, exercise combined with therapies such as kinesio taping, specific exercises, and acupuncture should be considered as the first-line choices, whereas pulsed electromagnetic field therapy, localized corticosteroid injection, diacutaneous fibrolysis, and ultrasound therapy may be considered as the second-line treatment choices; however, low-level laser therapy and the localized injection of NSAIDs are not recommended	Moderate to high quality evidence Potential positive
Whiplash associated disorder (WAD)	Moon 2014 (SR of 6 RCTs)(172): Limited evidence of effectiveness; low quality evidence	Unclear for WAD

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Neurological disorders		
Acute stroke	Vados 2015 (SR of 17 RCTs; 5 high quality)(125) Acupuncture plus rehabilitation superior to rehabilitation alone for acute and subacute stroke sequelae Liu 2015 (MA of 18 RCTs)(126): Acute ischaemic stroke: EA superior to usual care in Barthel Index, Fugl-Meyer Assessment, National Institutes of Health Stroke Scale, and Revised Scandinavian Stroke Scale; Moderate to high quality evidence Liu 2015: (Acute ischaemic stroke) EA superior to usual care in Barthel Index, Fugl-Meyer Assessment, National Institutes of Health Stroke Scale, and Revised Scandinavian Stroke Scale; Moderate to high quality evidence	Moderate to high quality evidence Potential positive
Bell's palsy	Li 2015 (SR & MA of 14 RCTs)(56): Seems to be effective; insufficient evidence of efficacy and safety; low quality evidence Kwon 2015 (RCT acupuncture (n=36) vs waitlist (n=13))(104): RCT acupuncture vs waitlist (n=26 vs 13) Acupuncture superior to waitlist in physical and social function	Unclear
Epilepsy	Cheuk 2014 (Cochrane update)(120): No evidence of effect; low quality evidence	No evidence of effect (Cochrane update)
Parkinson's disease	Kim 2014 (Review of 11 studies: 6 RCTs, 4 uncontrolled open label studies & 1 crossover trial)(195): Insufficient evidence; low to very low quality evidence	Unclear
Post-stroke spasticity	Lim 2015 (SR & MA of 5 RCTs)(128): Acupuncture or EA significantly decreased spasticity after stroke; low quality evidence Rodriguez-Mansilla 2016 (SR of 9 RCTs or controlled studies: 6 high quality; 3 moderate) (129) Acupuncture improved passive resistance to stretching, degree of personal dependence and motor function; insufficient evidence	Potential positive
Stroke	Zhang 2014 (Review of SRs: 8 reviews high quality, 6 moderate, 10 low)(124): Acupuncture may be effective for treating post-stroke neurological impairment and dysfunction such as dysphagia, but does not prevent post-stroke death	Moderate to high quality evidence
Stroke rehabilitation	Yang 2016 (Cochrane update)(127): May have beneficial effects on improving dependency, global neurological deficiency, and some specific neurological impairments; low to very low quality evidence	Potential positive (Cochrane update)

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Mental health		
Anxiety	Bazzan 2014 (Narrative review)(81): Acupuncture has ‘potential use’ Goyata 2016 (Integrative review of 19 studies including 6 RCTs; 11 high quality studies; 5 moderate)(82): Positive and statistically significant effects; Moderate to high quality evidence	Moderate to high quality evidence Potential positive
Alzheimers disease	Zhou 2015 (SR & MA of 10 RCTs)(197): Acupuncture superior to medication in improving cognitive function on MMSE. Acupuncture plus medication superior to medication alone. Acupuncture is safe; no assessment of quality of evidence	Unclear
Chronic fatigue syndrome	Kim 2015 (Multi-centre non-blinded RCT, n=150)(112): Acupuncture plus usual care may improve fatigue in chronic fatigue syndrome and idiopathic chronic fatigue	Unclear
Depression	Chan 2015 (SR & MA of 13 RCTs;1 high quality, 5 moderate, 7 low)(90): Acupuncture plus SSRIs superior to SSRIs alone, with an early onset of action and was safe and well-tolerated; EA had greater effect than manual acupuncture Bosch 2015 (Review of SRs & MAs)(84): Effective and safe for major depressive disorder, especially in improving sleep, mood and QoL by modulating and normalizing the limbic–paralimbic–neocortical network (LPNN), including the default mode network (DMN); ‘promising’ evidence Spackman 2015 (Cost-effectiveness analysis)(91): Acupuncture is cost-effective compared with counselling or usual care alone, although the ranking of counselling and acupuncture depends on the relative cost of delivering these interventions	Potential positive in USVA 2014; 2 positive SRs since Cost-effective
Insomnia	Zhao 2013 (SR)(92): Acupuncture may be superior to medication. Acupuncture for insomnia is potentially mediated by norepinephrine, melatonin, gamma-aminobutyric acid, and beta-endorphin; Insufficient evidence Shergis 2016 (SR of 30 studies)(93): Acupuncture statistically superior to sham (3 studies) and medication (27 studies); low quality evidence	Potential positive in USVA 2014; 2 positive SRs since
Opioid detoxification	Wu 2016 (110): Acupuncture is effective in opiate detoxification (and associated depression and anxiety) which is mediated by endogenous dynorphin; no effect on opioid cravings; low quality evidence	Unclear
Post-traumatic stress disorder	Engel 2015 (RCT acupuncture plus usual care vs usual care, n=55)(83): Acupuncture plus usual care superior to usual care in PTSD severity, depression, pain and physical and mental functioning	Potential positive in USVA 2014; positive RCT in 2015
Pre-treatment anxiety	Au 2015 (SR of 7 RCTs, MA of 5)(196): Acupressure effective in reducing anxiety; Moderate to high quality evidence	Moderate to high quality evidence Potential positive

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Mental health (contd)		
Schizophrenia	<p>Bosch 2015 (Review of SRs & MAs)(84): Acupuncture effective for schizophrenia, especially in improving sleep, mood and QoL by modulating and normalizing the limbic–paralimbic–neocortical network (LPNN), including the default mode network (DMN); limited evidence</p> <p>Shen 2014 (Cochrane update of 30 RCTs)(85): Acupuncture plus antipsychotic medication superior to antipsychotic medication alone, in terms of mental state and length of hospitalisation (moderate quality evidence) with fewer adverse effects (low quality evidence)</p>	<p>Moderate quality evidence for acupuncture with antipsychotics</p> <p>Potential positive</p>
Smoking cessation	<p>White 2014 (Cochrane SR Of 38 RCTs)(86): Acupuncture and acupressure superior to sham short-term; low quality evidence</p> <p>Insufficient evidence of effects for 6 months or more</p>	<p>Potential positive short term effects</p> <p>No evidence of effect after 6 months (Cochrane update)</p>
Gynaecology and obstetrics		
Back or pelvic pain during pregnancy	<p>Selva Olid 2013 (Review of 8 SRs and 9 RCTs)(95): Promising results; low quality evidence</p> <p>Close 2014 (SR of 8 RCTs on CAM; 2 acupuncture RCTs with low risk of bias)(96): Clinically important and statistically significant changes</p> <p>Liddle 2015 (Cochrane SR: Comparison of interventions 26 RCTs – 7 acupuncture RCTs)(97): Moderate quality evidence showed that acupuncture or exercise, tailored to the stage of pregnancy, significantly reduced evening pelvic or lumbo-pelvic pain. Acupuncture superior to exercise for reducing evening pelvic pain; Both acupuncture and exercise were superior to usual care; Insufficient evidence</p>	<p>Potential positive</p>
Dysmenorrhoea	<p>Chen et al, 2013 (MA of 3 acupuncture and 4 acupressure RCTs)(204): Acupuncture is effective and acupressure may be effective for pain relief; acupuncture trials had low to moderate risk of bias; acupressure trials high risk of bias</p> <p>Xu 2014 (MA of 20 RCTs of acupoint stimulation)(179): Acupoint stimulation superior to controls for pain relief; low to moderate quality evidence</p> <p>Abaraogu 2015 (SR of 8 RCTs and MA of 4 RCTs)(180): Acupuncture and acupressure vs placebo, waitlist or medication reduced pain intensity, while acupuncture also improved physical and mental aspects of QoL; moderate quality evidence</p> <p>Smith 2016 (Cochrane update)(181): Insufficient evidence; low to very low quality evidence</p> <p>Kim 2012(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache</p>	<p>Conflicting SRs (3 positive SRs vs Cochrane SR insufficient evidence)</p> <p>Moderate quality evidence vs low to very low quality evidence;</p> <p>Cost effective</p> <p>Downgrade to unclear</p>

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Gynaecology and obstetrics (contd)		
Hyperemesis gravidarum	Boelig 2016 (SR of interventions - 1 acupuncture study)(200): Insufficient evidence to identify clear differences between acupuncture and metoclopramide; very low quality evidence	<i>Unclear</i>
Induction of labour	Smith 2013 (Cochrane SR of 14 RCTs)(102) : Insufficient evidence; included studies ranged from high to low quality evidence Mollart 2015 (SR of 7 RCTs)(103): Acupuncture may reduce the duration of labour especially the first stage; insufficient evidence	<i>Unclear</i> (Cochrane update)
Labour pain	Levett 2014 (Critical narrative review of SRs)(94): Acupuncture & acupressure ‘promising’ – Conflicting results due to heterogeneity in study designs, research questions, treatment protocols and outcomes measures	<i>Potential positive</i>
Melasma	Chai 2015 (SR of 8 RCTs; 2 high quality studies; 6 low to moderate)(201): Acupuncture appeared to be effective and safe; insufficient evidence	<i>Unclear</i>
Menopausal hot flushes	Chiu 2015 (MA of 12 studies; 2 high quality, 8 moderate and 2 low)(133): Acupuncture improves hot flash frequency and severity, menopause-related symptoms, and QoL (vasomotor domain) in natural menopause Selva Ovid 2013 (Review of 8 SRs and 9 RCTs) (95): Promising results; low quality evidence Dodin 2013 (Cochrane SR of 16 RCTs)(134) : Acupuncture superior to wait-list or no treatment; low quality evidence Acupuncture superior to sham in reducing severity but not frequency; very low quality evidence Acupuncture inferior to hormone therapy in QoL and frequency; no difference in severity; low quality evidence Chen 2016 (SR of 12 RCTs) (148): Seems to be effective; insufficient evidence; low quality evidence	‘Promising’; very low to moderate quality evidence <i>Upgrade to potential positive</i>
Nausea in pregnancy	Matthews 2015 (Cochrane SR of interventions for nausea in pregnancy; 2 RCTs on acupuncture) (119) : No significant difference between real and sham acupuncture; low quality evidence	<i>No evidence of effect</i>
Oocyte retrieval pain relief	Kwan 2013 (Cochrane SR of 21 RCTs)(199) : Insufficient evidence; low quality evidence	<i>Unclear</i> (Cochrane update)

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Gynaecology and obstetrics (contd)		
Perimenopausal and postmenopausal sleep disturbance	Chiu 2016 (SR of 34 RCTs; 4 high quality)(135): Significant reduction in sleep disturbance which appears to be associated with changes in serum estradiol, FSH and LH; acupuncture recommended as adjunctive therapy in improving sleep disturbances in perimenopausal and postmenopausal women Bezerra 2015 (SR of 7 RCTs; 4 high quality; no studies with high risk of bias)(136): Improved sleep quality; limited evidence; moderate to high quality evidence	High quality studies favour acupuncture as adjunctive therapy; moderate to high quality evidence Potential positive
Pregnancy rates in IVF support	Manheimer 2013 (SR & MA of 16 RCTs) (198): Insufficient evidence Cheong 2013 (Cochrane SR of 20 RCTs)(40): No evidence that acupuncture improves live birth or pregnancy rates in ART regardless of whether performed around the time of oocyte retrieval or embryo transfer	No evidence of effect (Cochrane update)
IVF support: around oocyte retrieval	Shen 2015 (SR & MA)(41): Only at time of ET – ineffective	No evidence of effect
IVF support: day of embryo transfer	Shen 2015 (SR & MA) (41): at follicle phase and 25 min before and after ET, as well as 30 min after ET and implantation phase - effective	Effective – contradictory to Cheong 2013 Cochrane SR finding of ineffective
Polycystic ovarian syndrome	Ren 2014 (SR & MA of 31 studies)(202): Acupuncture may be effective; low quality evidence Lim 2016 (Cochrane SR of 5 RCTs)(203): Insufficient evidence; low to very low quality evidence	Unclear
Premenstrual syndrome	A SR review in 2014 included only studies before 2012, hence no new evidence (Jang 2014)(116) Insufficient evidence (Hofmeister 2016 - Narrative review)(117)	Unclear in USVA review 2014; no change in level
Primary ovarian insufficiency	Jo 2015 (SR of 8 RCTs & MA)(205): Acupuncture significantly lowered serum FSH levels and more women receiving acupuncture reported resumption of menses; low quality evidence	Unclear
Uterine fibroids	Dalton-Brewer 2016 (Narrative review of CAM)(106): Acupuncture may be a treatment option as part of a CAM treatment approach	Unclear

Table 6. All conditions reviewed sorted by clinical areas (contd)		
Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Gastrointestinal disorders		
Constipation		Potential positive - USVA review 2014; no updates
Dyspepsia in diabetic gastroparesis (DGP)	Yang 2013 (SR of 14 RCTs)(209): May be effective for dyspepsia in DGP; insufficient evidence; low quality evidence	Unclear
Functional dyspepsia	Lan 2014 (Cochrane SR of X RCTs)(207): Insufficient evidence; low quality evidence Kim 2015 (SR of 20 RCTs; high risk of bias)(208): Acupuncture significantly superior to sham and medication; low quality evidence	Unclear
Inflammatory bowel disease	Langhorst 2015 (SR of 2 RCTs: one on Crohn's disease, one on ulcerative colitis)(206): Acupuncture superior to sham in disease activity and wellbeing but no different in QoL; low quality evidence (2 studies with low risk of bias but small samples)	Unclear
Irritable bowel syndrome	MacPherson 2016 (High quality RCT)(164): Acupuncture superior to usual care on IBS symptom severity score at 6, 9 and 12 months but not at 24 months	Unclear in USVA review 2014; Upgrade to potential positive - positive high quality RCT in 2016
Obesity	Esteghamati 2015 (Critical review of 3 SRs)(100): Acupuncture superior to medication, sham and lifestyle modification; low to very low quality evidence	Potential positive - USVA review 2014; no updates
Headache and migraine		
Headache	Kim 2012(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache Coeytaux 2016 (Brief review of selected SRs and MAs)(46): A potentially important role for acupuncture as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders. Cost-effective in Germany and UK Lardon 2016 (SR of 15 RCTs)(121): Acupuncture can reduce workplace headache pain intensity, frequency and related disability; low quality evidence	'A potentially important role for acupuncture' as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders. Positive

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Headache and migraine (contd)		
Migraines	<p>(Da Silva 2015 - Narrative review of large high quality RCTs)(42): Acupuncture seems to be at least as effective as conventional preventative medication for migraine and is safe, long lasting, and cost-effective</p> <p>Linde 2016 (Cochrane SR of 22 RCTs of at least 8 weeks duration)(43): Acupuncture reduces migraine frequency. Acupuncture superior to sham and may be as effective as prophylactic drugs; subgroup analysis showed larger effect size when 16 or more treatments given (Z = 4.06) compared to 12 treatments or less (Z = 2.32); Moderate quality evidence</p> <p>Yang 2016 (SR of 10 RCTs)(44): Acupuncture superior to sham in effectiveness and reduced risk of recurrence; Moderate to high quality evidence</p>	Moderate to high quality evidence, safe and cost-effective (including Cochrane update); 16 or more treatments more effective than 12 treatments or less - Positive
Tension-type headache	Linde 2016 (Cochrane SR of 12 RCTs)(45): Effective for frequent episodic or chronic tension-type headaches; Moderate or low quality evidence	Positive
Genitourinary/sexual disorders		
Chronic kidney disease	Kim 2016 (Cochrane SR of 24 RCTs or quasi-randomised CTs)(211): Insufficient evidence; low to very low quality evidence	Unclear
Erectile dysfunction	Cui 2016 (SR of 3 RCTs): Insufficient evidence; low quality evidence	Unclear
Poor sperm quality	Jerng 2014 (SR of 4 RCTs)(210): Insufficient evidence; low quality evidence	Unclear
Prostatitis pain/chronic pelvic pain syndrome	<p>Chang 2016 (SR of 7 RCTs: 3 high quality, 1 moderate and 3 low)(98): Acupuncture superior to both sham and to usual care and safe, thus it should be offered when available</p> <p>Qin 2016 (SR of 7 RCTs)(99): Acupuncture superior to sham in pain, voiding and QoL; acupuncture superior to medication in pain relief but no different in voiding and QoL; acupuncture as an adjunctive treatment for symptom control should be considered; (3 high quality studies, 1 moderate and 3 low)</p>	Potential positive
Stress urinary incontinence in adults	Wang 2013 (Cochrane SR of 1 study: acupuncture vs midodrine)(213): Insufficient evidence; low quality evidence	Unclear
Urinary incontinence	Paik 2013 (SR of 4 RCTs)(212): Limited support for acupuncture or acupressure; Insufficient evidence; low to very low quality evidence	Unclear

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Surgery		
Surgical conditions	Lee 2014 (Overview of 12 SRs on postsurgical nausea and vomiting and postsurgical pain)(159): Conflicting evidence; insufficient evidence	Generic systematic reviews on surgical conditions need to be more targeted to specific conditions
Ambulatory anaesthesia	Liodden 2013 (Narrative review)(161): Acupuncture may reduce preoperative anxiety, and postoperative pain, nausea, vomiting, shivering and emergence delirium. Acupuncture is safe and cost-effective. Acupuncture may be a beneficial adjunctive therapy for ambulatory anaesthesia.	Acupuncture safe, cost-effective and effective as an adjunctive therapy; no assessment of quality of evidence Potential positive
Postoperative nausea & vomiting	Cheong 2013 (SR of 30 RCTs)(58): Acupuncture and acupressure reduced number of cases of early nausea and vomiting (up to 24 hours); low quality evidence Lee 2015 (Cochrane SR of 59 RCTs of PC 6 stimulation)(16): PC 6 stimulation was superior to sham (low quality evidence); no difference between PC 6 stimulation and anti-emetics (moderate quality evidence); insufficient evidence that PC 6 plus anti-emetics is superior to anti-emetics alone.	Upgrade to positive (Cochrane update)
Postoperative nausea and vomiting and pain after tonsillectomy	Cho 2016 (MA of 12 RCTs; 7 high quality)(122): Pain scores, analgesic need and nausea and vomiting were reduced (acupuncture vs control); no significant adverse events; insufficient evidence Shin 2016 (SR & MA - 4 RCTs – 3 with low risk of bias; 3 randomised prospective studies and 1 pilot)(123): Acupuncture superior to controls and cost-effective; insufficient evidence	Upgrade to positive Cost effective
Postoperative pain	Wu 2016 (SR & MA of 13 RCTs)(17): Some forms of acupuncture (acupuncture, EA and TEAS) improved pain on day 1 after surgery and reduced opioid use; subgroup analysis showed acupuncture and TEAS superior to EA; moderate quality evidence	Upgrade to positive
Postoperative pain – back surgery	Cho 2015 (SR of 5 RCTs – 3 high quality)(59): Encouraging but limited evidence	Upgrade to positive
Postoperative pain – knee surgery	Barlow 2013 (SR of 5 RCTs: 3 acupuncture; 1 acupressure)(60): Acupressure reduced pain; acupuncture did not reduce pain but resulted in reduced use of ibuprofen; low quality evidence Chen 2015 (RCT acupuncture vs sham, n=60)(61): Acupuncture superior to sham in post-operative fentanyl use, time to first request for fentanyl and pain intensity	Upgrade to positive

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Surgery (contd)		
Craniotomy anaesthesia	Asmussen 2016 (MA of 10 RCTs)(160): Acupuncture significantly reduced the amount of volatile anaesthetics and led to faster extubation time and postoperative patient recovery and reduced postoperative nausea and vomiting. In addition, significantly reduced blood levels of the brain tissue injury marker S100beta 48 hours after operation; (low quality studies excluded from MA)	MA which excluded low quality studies found positive effects; moderate to high quality evidence, but not definitive - Potential positive
Dentistry	Naik 2014 (Narrative review of 40 RCTs)(216): Acupuncture effective for inducing dental analgesia, relieving dental pain, myofascial pain and TMJ pain, controlling gag reflex, reducing dental anxiety and reducing post-operative pain and inflammation; no assessment of quality of evidence	'Promising' narrative review; no assessment of quality of evidence Unclear
Postoperative gastroparesis syndrome (PGS)	Cheong 2014 (SR of 16 RCTs; MA of 7)(215): Might be effective; insufficient evidence; low quality evidence	Insufficient evidence; low quality evidence Unclear
Postoperative ileus	Cheong 2016 (SR of 8 RCTs; MA of 4)(214): Acupuncture might be effective in reducing postoperative ileus; low quality evidence	Unclear
Oncology		
Aromatase-inhibitor-induced arthralgia	Bae 2015 (SR of 4 RCTs)(154): Acupuncture superior to sham in 2 high quality studies; no different from sham in 2 low-quality studies Chien 2015 (SR of 5 RCTs)(155): Acupuncture reduces joint pain and stiffness but not superior to sham; moderate to high quality evidence	Potential positive
Cancer-related insomnia	Choi 2016 (SR of 6 RCTs)(145): Acupuncture may be superior to sham acupuncture, drugs or hormones therapy. Number of studies and effect size are small for clinical significance; low quality evidence	Unclear
Cancer pain	Pailey 2015 (Cochrane SR of 5 RCTs)(88): Insufficient evidence; low to very low quality evidence Hu 2016 (SR of 20 RCTs)(217): Acupuncture plus medication superior to medication alone; very low quality evidence Chiu 2016 (SR of 29 RCTs)(89): Acupuncture relieved malignancy-related and surgery-induced pain but not pain induced by chemotherapy, radiotherapy or hormone therapy	Conflicting evidence Unclear

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Oncology (contd)		
Cancer-related fatigue	<p>He 2013 (SR of 7 RCTs)(134): Acupuncture and moxibustion appear to be efficacious adjunctive therapy; Insufficient evidence; low quality evidence</p> <p>Ling 2013 (SR of RCTs)(141): Acupuncture and acupressure tend to be effective, acupuncture more than acupressure; low quality evidence</p> <p>Posadzki 2013 (SR of 7 RCTs)(142): Conflicting evidence: 4 studies showed acupuncture or acupuncture plus usual care superior to sham, usual care, enhanced usual care or no treatment; 3 studies showed no difference between acupuncture and sham; very low quality evidence</p> <p>Finnegan-John 2013 (SR of CAM 20 studies; 3 acupuncture/acupressure RCTs)(143): Acupuncture may reduce fatigue after cancer treatment; low quality evidence</p> <p>Zeng 2014 (MA of 7 studies)(144): Acupuncture plus education superior to usual care; low quality evidence</p>	<i>Potential positive</i>
Cancer-related psychological symptoms	Haddad 2014 (SR of 12 studies; 8 RCTs)(158): All included studies suggest benefits in depression, anxiety, sleep disturbance, and for improving QoL; strong evidence for safety; no assessment of quality of evidence	<i>Unclear</i>
Chemotherapy-induced nausea & vomiting (CINV)	<p>McKeon 2013 (SR of 7 acupuncture, 6 acupressure RCTs)(21): Acupuncture reduced the frequency of acute vomiting and the dose of rescue medication but did not reduce acute nausea severity or frequency compared to control. Acupressure showed a decrease in frequency of nausea but not acute vomiting or delayed symptoms. All studies used state-of-the-art combination antiemetics. Insufficient evidence due to underpowered studies; acupuncture low to moderate quality evidence; acupressure moderate to high quality evidence</p> <p>Garcia 2014 (SR update: 18 new RCTs)(57): Acupuncture is an appropriate referral option for chemotherapy-induced nausea and vomiting</p>	<i>Positive</i>
Chemotherapy-induced peripheral neuropathy	Franconi 2013 (SR of 3 RCTs, 3 case series, 1 rat study)(156): Acupuncture superior to sham in one RCT; very low quality evidence	<i>Unclear</i>
Myelosuppression after chemotherapy	Fu 2015 (Narrative review of 7 RCTs)(157): Insufficient evidence; low to very low quality evidence	<i>Unclear</i>
Recovery after colorectal cancer resection	Kim 2016 (SR of 7 RCTs)(153): Acupuncture efficacious and effective; Low to moderate quality evidence	<i>Potential positive</i>

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Oncology (contd)		
Hot flushes in breast cancer	<p>Garcia 2015 (SR of 8 RCTs)(146): Acupuncture superior to sham in some studies and superior to baseline in all studies; low quality evidence</p> <p>Johns 2016: (SR of interventions; 2 acupuncture vs medication studies)(147): Acupuncture had similar efficacy to venlafaxine and gabapentin but may have longer durability after completing treatment and fewer side effects</p> <p>Chen 2016 (SR of 12 RCTs)(148): Acupuncture superior to sham in 3 studies; no different from sham in 6 studies; inferior to hormone therapy in 2 studies; low quality evidence</p> <p>Salehi 2016 (SR of 12 studies)(149): Conflicting evidence; low quality evidence</p> <p>Chiu 2016 (SR of 7 studies; 4 high quality)(89): Acupuncture yielded small-size effects on reducing hot-flash frequency and the severity of menopause-related symptoms</p>	<p>Insufficient or conflicting evidence; Low to high quality studies</p> <p>Unclear</p>
Xerostomia in cancer	<p>Zhuang 2013 (SR of 4 studies)(150): Insufficient evidence</p> <p>Furness 2013 (Cochrane SR of non-pharmacological interventions 9 RCTs; 5 acupuncture)(151): Small increase in saliva production; Low quality evidence</p> <p>Hanchanale 2015 (SR of 6 RCTs)(152): Acupuncture was superior to sham; low quality evidence</p>	<p>Unclear</p>
Eye, ear, nose, throat		
Allergic rhinitis	<p>Feng 2015 (SR of 13 RCTs)(56): Significant improvements in nasal symptoms scores and RQLQ; Moderate quality evidence</p> <p>Taw 2015 (SR of 2 large multi-centre RCTs, 3 acupuncture vs medication RCTs and 1 cost-effectiveness study)(15): High quality evidence of efficacy and effectiveness</p> <p>Seidman 2015 (OHNSF clinical practice guideline)(37): Option 5: Clinicians may offer acupuncture, or refer to a clinician who can offer acupuncture, for patients with AR who are interested in non-pharmacologic therapy; Aggregate evidence quality - Grade B</p> <p>McDonald 2016 (High quality RCT)(32): PAR - Significant improvements in symptoms, QoL, and reductions in total IgE and dust mite specific IgE and Substance P; high quality evidence</p> <p>Xue 2015 (High quality RCT)(218): SAR - Significant improvement in symptoms; high quality evidence</p> <p>Kim 2012(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache</p> <p>Reinhold 2103(79): SAR - Acupuncture significantly superior to rescue medication in QALY gained, but may cost more short term</p>	<p>Moderate to high quality evidence; safe and cost-effective for both SAR and PAR</p> <p>Evidence of positive effect</p>
Dry eye	<p>Yang 2015 (SR of 7 RCTs)(162): Acupuncture was superior to artificial tears in tear break-up time, Schirmer I test, and cornea fluorescein staining; Low to moderate quality evidence</p>	<p>Upgrade from unclear to potential positive effect</p>

Table 6. All conditions reviewed sorted by clinical areas (contd)		
Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Eye, ear, nose, throat (contd)		
Glaucoma	Law 2013 (Cochrane SR; 1 RCT on auricular acupressure)(105): Insufficient evidence; low quality evidence	<i>Unclear</i>
Meniere's disease/syndrome	He 2016 (SR of 12 RCTs)(220): Acupoint stimulation significantly effective in controlling vertigo but did not improve hearing loss; very low evidence	<i>Unclear</i>
Sudden sensorineural hearing loss	Zhang 2015 (SR of 12 RCTs)(219): Acupuncture plus usual care superior to usual care alone; low to very low quality evidence	<i>Unclear</i>
Tinnitus	He 2016 (SR of 5 RCTs)(109): EA - Insufficient evidence; low quality evidence	<i>Unclear</i>
Paediatrics		
Attention Deficit Hyperactivity Disorder (ADHD)	Li 2011: (Cochrane SR; No eligible studies)(222): Insufficient evidence	<i>Unclear</i> [not included in previous reviews]
Autism spectrum disorder (ASD)	Cheuk 2011 (Cochrane SR of 10 RCTs)(221): (4 high quality studies; 6 low quality) Insufficient evidence; low quality evidence	<i>Unclear</i> [not included in previous reviews]
Hypoxic ischemic encephalopathy in neonates	Wong 2013 (Cochrane SR; No eligible studies)(223): Insufficient evidence	<i>Unclear</i> [not included in previous reviews]
Mumps in children	He 2015 (Cochrane SR; No eligible studies)(224): Insufficient evidence	<i>Unclear</i> [not included in previous reviews]
Slowing progression of myopia	Wei 2011 (Cochrane SR of 2 RCTs): (2 high quality studies) Insufficient evidence; low quality evidence	<i>Unclear</i> [not included in previous reviews]
Dermatology		
Dermatology	Ma 2015 (SR of 15 RCTs: 3 Level I RCTs; 12 Level II)(225): Acupuncture improves outcome measures in the treatment of dermatitis, chloasma, pruritus, urticaria, hyperhidrosis, and facial elasticity	<i>Unclear</i>
Atopic dermatitis	Tan 2015 (SR: no eligible RCTs)(227): Insufficient evidence Vieira 2016 (Evidence-based review of CAM)(228): Acupuncture and acupressure 'promising therapies'; insufficient evidence	<i>Unclear</i>
Chronic urticaria	Yao 2015 (SR of 6 RCTs)(229): Acupuncture might be effective and safe for relieving symptoms of chronic urticaria; low level evidence	<i>Unclear</i>

Table 6. All conditions reviewed sorted by clinical areas (contd)

Condition	THE ACUPUNCTURE EVIDENCE PROJECT	Comments
Dermatology (contd)		
Itch	Yu 2015 (SR & MA of 3 RCTs)(230): Acupuncture superior to sham and no treatment in alleviating itch; acupuncture might be effective for treating itch; insufficient evidence	<i>Unclear</i>
Psoriasis vulgaris	Coyle 2015 (SR of 6 RCTs)(226): Some evidence of benefit but also conflicting evidence; low quality evidence	<i>Unclear</i>
Miscellaneous conditions		
Acupuncture in Emergency Department	Kim 2013 (SR of 2 RCTs & 2 observational studies)(232): Insufficient evidence; low quality evidence	<i>Unclear</i>
Exercise performance & post-exercise recovery	USVA review 2014 ‘unclear’; no updates	<i>Unclear</i>
Fatigue in systemic lupus erythematosus	del Pino-Sedeno 2016 (SR of non-pharmacological interventions; 1 acupuncture study)(233): Acupuncture and minimal acupuncture superior to usual care; moderate quality study	<i>Unclear</i>
Primary Sjogren’s syndrome	Hackett 2015 (SR of non-pharmacological interventions; 1 acupuncture study)(234): Acupuncture not superior to usual care in increasing salivary flow rate; moderate quality study	<i>Unclear</i>
Sensory perception	Baeumler 2014 (MA of 85 high quality studies)(231): Acupuncture effects sensory thresholds especially pressure pain threshold; high quality evidence	<i>Potential positive effect</i>

Table 7. Conditions reported in this review with evidence of cost-effectiveness

Condition	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)	Comments
Allergic Rhinitis	Taw 2015 (SR of 2 large multi-centre RCTs, 3 acupuncture vs medication RCTs and 1 cost-effectiveness study) Kim 2012(Cost effectiveness analysis)(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache.	Safe and cost-effective for both SAR and PAR.
Ambulatory Anaesthesia	Liodden 2013 (Narrative review)(161): Acupuncture may reduce preoperative anxiety, and postoperative pain, nausea, vomiting, shivering and emergence delirium. Acupuncture is safe and cost-effective. Acupuncture may be a beneficial adjunctive therapy for ambulatory anaesthesia.	Acupuncture safe, cost-effective and effective as an adjunctive therapy.
Depression	Spackman 2015 (Cost-effectiveness analysis)(91): Acupuncture is cost-effective compared with counselling or usual care alone, although the ranking of counselling and acupuncture depends on the relative cost of delivering these interventions.	Cost-effective
Dysmenorrhoea	Kim 2012(Cost effectiveness analysis)(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache.	Cost effective
Headache	Kim 2012(Cost effectiveness analysis)(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache. Coeytaux 2016 (Brief review of selected SRs and MAs)(46): A potentially important role for acupuncture as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders. Cost-effective in Germany and UK.	A potentially important role for acupuncture' as part of a treatment plan for migraine, tension-type headache, and several different types of chronic headache disorders. Cost effective
Low back pain	Taylor 2014 (Cost effectiveness analysis/MA)(53): Cost effective for chronic low back pain. Andronis 2016 (SR of 33 studdies)(52): Likely to be cost effective.	Moderate to high quality evidence Cost effective , safe.
Migraine	Da Silva 2015 (Narrative review of large high quality RCTs)(42): Acupuncture seems to be at least as effective as conventional preventative medication for migraine and is safe, long lasting, and cost-effective.	Moderate to high quality evidence, safe and cost-effective (including Cochrane update); 16 or more treatments more effective than 12 treatments or less.
Neck Pain	Van der Velde 2015 (SR of 6 studies)(170): Acupuncture plus usual medical care is cost-effective for neck pain and its associated disorders (NAD).	Moderate quality evidence (Cochrane update); Acupuncture plus medication is cost-effective .
Osteoarthritis	Kim 2012 (Cost effectiveness analysis)(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache.	Cost-effective
Post-operative nausea and vomiting	Shin 2016 (SR & MA - 4 RCTs – 3 with low risk of bias; 3 randomised prospective studies and 1 pilot)(123): Acupuncture superior to controls and cost-effective.	Cost effective

Table 8. Conditions reported in this review with evidence of safety

Condition	The Acupuncture Evidence Project (Mar 2013 - Sept 2016)	Comments
Acupuncture generally prior to this review	Zhang et al 2010 (Review of 98 case reports and 17 case series)(235) ‘Various types of acupuncture-related adverse events have been reported in China. Similar events have been reported by other countries, usually as a result of inappropriate technique. Acupuncture can be considered inherently safe in the hands of well-trained practitioners.’	Acupuncture can be considered inherently safe in the hands of well-trained practitioners.
Allergic Rhinitis	Taw 2015 (SR of 2 large multi-centre RCTs, 3 acupuncture vs medication RCTs and 1 cost-effectiveness study). Kim 2012(78): Acupuncture is cost effective for dysmenorrhoea, allergic rhinitis, osteoarthritis & headache.	Safe and cost-effective for both SAR and PAR.
Ambulatory Anaesthesia	Liodden 2013 (Narrative review)(161): Acupuncture may reduce preoperative anxiety, and postoperative pain, nausea, vomiting, shivering and emergence delirium. Acupuncture is safe and cost-effective. Acupuncture may be a beneficial adjunctive therapy for ambulatory anaesthesia.	Acupuncture safe , cost-effective and effective as an adjunctive therapy.
Alzheimer's disease	Zhou 2015 (SR & MA of 10 RCTs)(197): Acupuncture superior to medication in improving cognitive function on MMSE. Acupuncture plus medication superior to medication alone. Acupuncture is safe.	Acupuncture is Safe .
Cancer-related psychological symptoms	Haddad 2014 (SR of 12 studies; 8 RCTs)(158): All included studies suggest benefits in depression, anxiety, sleep disturbance, and for improving QoL; strong evidence for safety; no assessment of quality of evidence.	Strong evidence for safety .
Depression	Chan 2015 (SR & MA of 13 RCTs; 1 high quality, 5 moderate, 7 low)(90): Acupuncture plus SSRIs superior to SSRIs alone, with an early onset of action and was safe and well-tolerated; EA had greater effect than manual acupuncture. Bosch 2015 (Review of SRs & MAs)(84): Effective and safe for major depressive disorder, especially in improving sleep, mood and QoL by modulating and normalizing the limbic-paralimbic-neocortical network (LPNN), including the default mode network (DMN); ‘promising’ evidence.	Safe and well tolerated. Effective and safe for major depressive disorder.
Low back pain	Nahin 2016 (4 RCTs; Excluded studies not performed in USA or by US researchers)(189): Acupuncture superior to usual care; Acupuncture superior to sham in 1 RCT, but not superior in 2 RCTs. NIH (2016) Promise in the following for safety and effectiveness in treating pain: Acupuncture and yoga for back pain, acupuncture and tai chi for osteoarthritis of the knee (236). Chou et al 2016 (Comparative effectiveness review) (47): Serious adverse events were not reported in any trial.	Moderate to high quality evidence Cost effective. Promise in safety and effectiveness. Serious adverse events were not reported in any trial.
Migraine	Da Silva 2015 (Narrative review of large high quality RCTs)(42): Acupuncture seems to be at least as effective as conventional preventative medication for migraine and is safe, long lasting, and cost-effective.	Moderate to high quality evidence, safe and cost-effective (including Cochrane update); 16 or more treatments more effective than 12 treatments or less.
Osteoarthritis of the Knee	Nahin 2016 (4 RCTs; Excluded studies not performed in USA or by US researchers)(189). NIH 2016 (236): Promise in the following for safety and effectiveness in treating pain: Acupuncture and yoga for back pain, acupuncture and tai chi for osteoarthritis of the knee.	Promise in safety and effectiveness.
Prostatitis pain/chronic pelvic pain syndrome	Chang 2016 (SR of 7 RCTs: 3 high quality studies, 1 moderate and 3 low)(98) Acupuncture superior to both sham and to usual care and safe, thus it should be offered when available.	Acupuncture superior to both sham and to usual care and safe .

APPENDIX

Level	Intervention	Diagnostic accuracy	Prognosis	Aetiology	Screening Intervention
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive persons with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> ▪ Non-randomised, experimental trial ▪ Cohort study ▪ Case-control study ▪ Interrupted time series with a control group 	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: <ul style="list-style-type: none"> ▪ Non-randomised, experimental trial ▪ Cohort study ▪ Case-control study
III-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> ▪ Historical control study ▪ Two or more single arm study ▪ Interrupted time series without a parallel control group 	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: <ul style="list-style-type: none"> ▪ Historical control study ▪ Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series	Case series

GRADE and guideline development

GRADE quality levels reflect how much confidence the reviewers have that the estimate of effect is close to the true effect in a systematic review. GRADE considers five factors in making this judgement: imprecision, inconsistency, indirectness of study results, publication bias and bias generally. GRADE levels do not necessarily infer a recommendation, and the GRADE process is separate to the process of making recommendations. Although a high level of evidence is likely to lead to a recommendation, low or very low evidence can lead to a strong recommendation in some cases. The development of recommendations involves more than just the quality of evidence and requires consideration of other factors including cost, clinical judgement and patient preference (8).

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

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