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The relative efficacy of topical non-steroidal anti-inflammatory drugs and capsaicin in osteoarthritis: A network meta-analysis of randomised controlled trials

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# 1 Title page

# 2 Title

- 3 The relative efficacy of topical non-steroidal anti-inflammatory drugs and
- 4 capsaicin in osteoarthritis: A network meta-analysis of randomised controlled
- 5 trials

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- 19 weiya.zhang@nottingham.ac.uk. Phone: +44 (0) 115 823 1756
- 20 Word count: 2622.
- 21 Abstract
- 22 **Objective**
- 23 To compare the efficacy of topical non-steroidal anti-inflammatory drugs
- 24 (NSAIDs) with topical capsaicin for pain relief in osteoarthritis (OA).

# 25 Design

- 26 A systematic literature search was conducted for randomised controlled trials
- 27 (RCTs) examining any topical NSAID or capsaicin in OA. Pain relief at or nearest
- 28 to four weeks was pooled using a random-effects network meta-analysis (NMA)
- 29 in a Frequentist and Bayesian setting. Analysis was conducted for all trials and

for trials using drugs listed as licenced for OA in the British National Formulary
 (BNF).

# 3 Results

4 The trial network comprised 28 RCTs (7372 participants), of which 17 RCTs

- 5 (3174 participants) were included in the as licensed analyses. No RCTs directly
- 6 compared topical NSAIDs with capsaicin. Placebo was the only common
- 7 comparator for topical NSAIDs and capsaicin. Frequentist and Bayesian effect
- 8 size (ES) estimates were in agreement. Topical NSAIDs were statistically
- 9 superior to placebo overall (ES 0.30, 95% confidence interval [CI] 0.19 to 0.41)
- and as licensed (ES 0.32, 95% CI 0.24 to 0.39). However, capsaicin was only
- 11 statistically superior to placebo when used at licensed doses (ES 0.41, 95% CI
- 12 0.17 to 0.64). No significant differences were observed in pain relief between
- 13 topical NSAIDs and capsaicin (overall: ES 0.04, 95% CI -0.26 to 0.33; as
- 14 licensed: ES-0.09, 95% CI -0.34 to 0.16).

# 15 **Conclusions**

- 16 Current evidence indicates that topical NSAIDs and capsaicin in licensed doses
- 17 may be equally effective for pain relief in OA. Whether the equivalence varies
- 18 between individuals remains unknown.

# 19 Systematic review registration number

20 2016:CRD42016035254

### 21 Keywords

- 22 Osteoarthritis, topical, capsaicin, non-steroidal anti-inflammatory drugs
- 23 (NSAIDs), network, meta-analysis

### 24 Running headline

- 25 Topical NSAIDs and capsaicin in OA
- 26

#### 1 Introduction

2 Osteoarthritis (OA) is a major cause of pain and disability for which two topical 3 treatments are used: non-steroidal anti-inflammatory drugs (NSAIDs) and capsaicin<sup>1-5</sup>. 4 Topical NSAIDs, such as ibuprofen and diclofenac, reversibly block the production of 5 prostanoids, thereby reducing pain and inflammation<sup>6</sup>. Topical NSAIDs, alongside 6 paracetamol, are recommended by the National Institute of Health and Care Excellence 7 (NICE) as first line pharmacological treatments<sup>1</sup>. Over £32 million's worth of 8 prescriptions of topical NSAIDs were dispensed in community pharmacies in England in 9 2016<sup>7</sup>. Topical NSAIDs are also freely available over-the-counter and are widely 10 advertised to consumers. Meanwhile, capsaicin, the substance responsible for the 11 warming spiciness of chili peppers, is primarily available on prescription in the UK. 12 Almost 200,000 tubes of 0.025% capsaicin were dispensed in 2016, amounting to over 13  $\pounds$ 4 million<sup>7</sup>. Capsaicin is thought to cause defunctionalisation of spontaneously active 14 peripheral nociceptors that otherwise maintain chronic pain conditions<sup>8</sup>.

15 Topical NSAIDs and capsaicin are applied directly to the skin over the painful joint and 16 little to no active drug is absorbed into the bloodstream, resulting in their favourable 17 safety profiles<sup>8-10</sup>. Topical administration therefore offers a safe and effective alternative 18 to oral analgesics for people with just one or a few painful peripheral joints, especially 19 for individuals with comorbidities, multiple medications, or those wishing to avoid tablets. The efficacy of topical NSAIDs and capsaicin in OA is documented<sup>6, 11-14</sup>, 20 21 however, no evidence for their relative efficacy is available so far to guide clinicians' 22 prescribing practice. We therefore undertook the present network meta-analysis (NMA) 23 to compare topical NSAIDs with capsaicin in people with symptomatic OA.

#### 24 Method

### 25 **Protocol and registration**

This work forms part of a project examining the relative efficacy of topical NSAIDs and
 capsaicin in OA and neuropathic pain. The protocol is published<sup>15</sup> and is also available on
 PROSPERO (2016:CRD42016035254).

### 4 Eligibility criteria

5 Randomised controlled trials (RCTs) comparing any topical NSAID or capsaicin to placebo 6 in participants with OA were included. No other comparators were included for this 7 analysis and only placebo-controlled trials were examined. Participants with painful 8 physician-diagnosed OA (clinical or radiographic) or chronic joint pain attributable to OA 9 at any site (excluding the spine) were included. Spinal pain was excluded as it is difficult 10 to differentiate between OA pain and back pain secondary to other aetiologies. Trials 11with pain due to multiple conditions were included if the data for OA could be extracted 12 separately.

13 Trials had to be a minimum of one week duration and report pain outcomes. Full texts14 published in any language and at any date were considered.

### 15 Identification and selection of trials

16 A search strategy, based on terms for (1) RCTs; (2) topical administration; (3) OA; and

17 (4) capsaicin or NSAIDs, was created (Supplementary Information).

18 Medline, Embase, Allied and Complementary Medicine Database (AMED), Cumulative

19 Index for Nursing and Allied Health Literature (CINAHL), Web of Science, and Cochrane

20 library were searched up to 16/11/2015. The searches were updated on 10/01/2018. In

21 addition, reference lists of included publications and meta-analyses in the area were

22 searched for eligible trials.

23 Citations were exported to Endnote where duplicates were removed before titles,

abstracts, and full texts were assessed for eligibility.

#### 25 Data collection and data items

1	The data were extracted independently by two authors (MSMP and JS) using a data				
2	extraction form created for this project. Publications in languages other than English				
3	were extracted by colleagues fluent in the language or using the Google Translate				
4	smartphone application. The following data were sought:				
5	Publication details: Author, journal, year				
6	• Trial details: Country of study, trial funder, study design, blinding, setting,				
7	duration				
8	• Participant details: Number of participants and withdrawals, age, gender				
9	distributions, body mass index, joint affected, method of diagnosing OA				

Intervention/placebo detail: Drug, formulation, dose/concentrations, frequency of
 application

• Endpoint: Pain scores

13 The primary end point was pain at or nearest to four weeks. Change from baseline pain 14 scores (extracted or calculated) were used. If unavailable, endpoint pain scores or 15 percent change from baseline were used. If pain was measured by more than one instrument in a study, the following hierarchy<sup>16-18</sup> was used to extract pain outcome 16 17 data: (1) visual analogue scale (VAS) global pain score; (2) categorical global pain 18 score; (3) pain during activity, such as walking; (4) Western Ontario and McMaster 19 Universities Osteoarthritis Index (WOMAC) pain subscale or pain subscale of other 20 disease-specific composite tools; (5) Short Form-36 (SF-36) bodily pain subscale; (6) 21 Health Assessment Questionnaire (HAQ) pain subscale, McGill pain questionnaire; (7) 22 tenderness; (8) physician's assessment of pain. Where multiple concentrations of a 23 study drug were examined within a study, they were combined as one prior to the effect size (ES) calculations for the overall analyses<sup>19</sup>. 24

### 25 Network structure

A network diagram was plotted to illustrate the treatment nodes, direct comparisons,and indirect comparisons within the NMA.

#### 1 Risk of bias within and across studies

2 Risk of bias assessment was carried out independently by two authors (MSMP and JS)

3 using a modified Cochrane Risk of Bias tool (Supplementary Material).

#### 4 Statistical analysis

5 Hedges' ES and corresponding standard error (SE) were calculated for each study. The 6 estimates were combined using Frequentist and Bayesian random-effects NMAs. The 7 Frequentist ES and associated 95% confidence interval (CI) were calculated. A Bayesian 8 NMA was conducted using Markov chain Monte Carlo (MCMC) simulations. Noninformative prior distributions were set, normal likelihood distributions were assumed, 9 10 and three Markov chains with different initial values (chosen arbitrarily) were run 11simultaneously. The model fit was deemed appropriate, the chain converged within 12 10,000 simulations, and a total of 20,000 simulations comprised the burn-in period. The subsequent 50,000 iterations were examined. The median and the 2.5<sup>th</sup> and 97.5<sup>th</sup> 13 14 percentiles of the posterior distribution comprised the Bayesian ES and credible interval 15 (CrI). The probability of each treatment being the best were calculated.

16 An overall analysis was conducted using all drug concentrations and topical formulations. 17 Subgroup analysis was then conducted to examine topical NSAIDs and capsaicin used as recommended in the British National Formulary (BNF)<sup>20</sup> (Supplementary material). Trials 18 19 were excluded from the as licensed analysis if they examined (1) topical NSAIDs not 20 recommended in the BNF; (2) drugs used at concentrations lower than recommended; or 21 (3) licenced drugs in formulations not in the recommended list. The as licensed analysis 22 was conducted to guide clinical practice and inform decision-making based on the 23 medications currently available to physicians.

The frequentist NMA was conducted in Stata (StataCorp. 2015. Stata Statistical
 Software: Release 15. College Station, TX: StataCorp LP) using the "network" command
 <sup>21</sup>. The Bayesian analyses were conducted in WinBUGs software (version 1.4.3, MRS

Biostatistics Unit UK, 2007) using methods supplied by the NICE Decision Support Unit
 <sup>22</sup>.

#### 3 Results

#### 4 Study description

5 The results of the literature search and reasons for exclusion from this meta-analysis are 6 illustrated in Figure 1. Topical NSAIDs were compared to placebo in 32 RCTs. Data were 7 not available for extraction for nine of the studies <sup>23-31</sup> and the remaining 23 studies (6957 participants) <sup>32-54</sup> were included in the NMA. Of these, 13 trials <sup>34, 35, 37-42, 44, 46, 50,</sup> 8 <sup>52, 53</sup> used a topical NSAID at its recommended dose/formulation and were included in 9 10 the as licensed analysis. Six placebo-controlled RCTs examining capsaicin were 11 identified, of which five (415 participants) <sup>55-59</sup> were included in the NMA. Data from the sixth study<sup>60</sup> were not available for extraction. Four trials <sup>56-59</sup> used 0.025% capsaicin 12 13 four times per day, as recommended in the BNF.

All trials were described as double-blinded and all but one<sup>55</sup> were of parallel design. Data
from the first period were extracted for the crossover trial. One publication was in
Korean<sup>48</sup> and the remainder were in English. 24 trials were limited to participants with
knee OA, two to hand OA<sup>34, 57</sup>, and the two remaining trials<sup>56, 58</sup> included OA at multiple
sites (hand, wrist, elbow, shoulder, hip, knee, and ankle OA).

#### 19 **Risk of bias**

Trials were associated with considerable risks of bias (Figure 2). Although described as randomised, only 20 publications described the method of random number sequence generation in sufficient detail to ascertain its risk of bias. Furthermore, only 13 of the included trials adequately described the methods of allocation concealment. Although described as double-blinded, this was only considered adequate in 60-65% of all trials. No capsaicin trials were deemed to adequately blind their participants due to the

- 1 warming sensation experienced on its initial application. Across the body of evidence,
- 2 only six of the 28 studies analysed all participants that were randomised at baseline.

#### 3 Network meta-analysis

#### 4 **Overall analysis**

5 The trial network was comprised of 28 RCTs with 3473 participants on placebo (28

6 RCTs), 3693 on topical NSAIDs (23 RCTs), and 206 on capsaicin (5 RCTs) (Figure 3).

7 Direct evidence for topical NSAIDs vs placebo and capsaicin versus placebo were

8 available from placebo-controlled trials. No trials directly compared topical NSAIDs to

9 capsaicin, and the two treatments were therefore compared using placebo as a common

10 comparator (indirect evidence).

Frequentist and Bayesian analyses were in agreement with identical ES and only minor 11 12 differences in the CI versus CrI (Table 1). Direct estimates indicated that topical NSAIDs 13 were superior to placebo for pain relief. In contrast, the ES estimate between capsaicin 14 and placebo was associated with considerable variability and did not reach statistical 15 significance. However, the indirect analyses found no statistically significant differences 16 between topical NSAIDs and capsaicin, although the ES favoured topical NSAIDs. Topical 17 NSAIDs had the highest probability of being the best treatment, followed by capsaicin 18 and then placebo (Table 2).

#### 19 As licensed analysis

Topical NSAIDs and capsaicin were used as licensed in 17 RCTs. 1705 participants on placebo (17 RCTs), 1328 on topical NSAID (13 RCTs), and 141 on capsaicin (4 RCTs) were included in the *as licensed* NMA. The results are presented in Table 1. Exclusion of non-licensed topical NSAIDs marginally raised the ES and it remained superior to placebo. In contrast, capsaicin at its licensed dose had a considerably increased ES that was statistically superior to placebo. Using placebo as a common comparator, no statistically significant differences remained between topical NSAIDs and capsaicin used

as licensed. However, the ES favoured capsaicin, which also had the highest probability
 of being the best treatment, followed by topical NSAIDs and placebo (Table 2).

#### 3 Discussion

4 Current evidence indicates that topical NSAIDs and capsaicin, when used as licensed, are 5 both superior to placebo for pain relief. No significant differences were identified in the 6 level of pain relief offered by topical NSAIDs compared to capsaicin. However, limited 7 and poor quality evidence for capsaicin in OA provides uncertainty. Displaying seemingly 8 negligible differences in efficacy, the decision of whether to prescribe topical NSAIDs or 9 capsaicin should be guided by patient preference, safety, costs, and subsequent 10 individual patient response.

Focusing on licensed doses of these two drugs renders the results of this meta-analysis more relevant for clinicians as they relate directly to the drugs recommended for prescription. The list of approved drugs was extracted from the BNF, a resource commonly used to guide prescribing practice in the UK<sup>61</sup>. The BNF was chosen as the leading authority on clinicians' selection of medicines in the UK, however it should be noted that they offer only recommendations of licenced medications and physicians can prescribe medications outside the recommended list<sup>61</sup>.

18 No direct or indirect (via NMA) quantitative evidence of the relative efficacy of topical 19 NSAIDs versus capsaicin has been published previously. Some guidelines, such as those 20 by Osteoarthritis Research Society International (OARSI) and European League Against Rheumatism (EULAR), provide equal recommendations for the two treatments<sup>2, 4, 5</sup>. This 21 22 may indicate a perceived equivalence in efficacy, in line with the findings of the current 23 meta-analysis. In contrast, a narrative review examining topical treatments in OA 24 concluded that capsaicin had less efficacy than topical NSAIDs<sup>62</sup>. Similarly, topical 25 NSAIDs are generally favoured in guidelines such as those by NICE and the American 26 College of Rheumatology (ACR), perhaps indicating a postulated greater efficacy for topical NSAIDs<sup>1, 3</sup>. In addition, OARSI guidelines granted topical NSAIDs a greater mean 27

1 benefit score (6.0/10) versus capsaicin  $(5.1/10)^2$ . However, the comparative efficacy of 2 the treatments in the narrative review was concluded primarily based on their 3 mechanism of action, rather than quantitative analysis. Capsaicin was thought to be less effective as it lacked significant tissue penetration and anti-inflammatory effects<sup>62</sup>. 4 5 Furthermore, guideline decisions are based not only on perceived efficacy, but on the 6 quality of evidence. Indeed, the preference of topical NSAIDs may reflect a greater 7 confidence in the evidence, rather than a perception of a larger effect. This is in keeping 8 with the wide confidence interval and associated uncertainty in the true effect of 9 capsaicin in the current meta-analysis.

10 Although pain in OA has traditionally been viewed as nociceptive in nature, it is now 11 widely accepted that some people experience pain with neuropathic-like pain 12 components. Pain descriptors indicative of neuropathic pain, such as "burning" and "shooting" pain are used by subsets of individuals with OA <sup>63</sup>. In fact, almost 15% of 13 people with knee pain report neuropathic-like pain<sup>64</sup>. This subgroup is of importance as 14 15 true neuropathic pain is often difficult to manage and commonly does not respond to traditional analgesics, such as NSAIDs<sup>65, 66</sup>. Capsaicin, however, is licensed and used in 16 17 neuropathic pain, where it is effective at higher doses<sup>67</sup>. It may therefore be that 18 individuals with predominantly nociceptive OA pain benefit from topical NSAIDs whilst 19 those with neuropathic pain components may benefit more from topical capsaicin. 20 Further evidence on pain phenotypes and response to these two commonly used topical 21 analgesics is warranted.

The present meta-analysis is subject to several limitations. Firstly, the conclusions drawn are limited by the scarcity of data available on capsaicin in OA. Only four trials compare 0.025% capsaicin to placebo and no direct estimates were available to compare topical NSAIDs to capsaicin. The low number of studies and participants on capsaicin resulted in an estimate with much uncertainty. The equivalence of the drugs may therefore be an artefact of the wide confidence intervals. Secondly, the probability of being the best treatment is based predominantly on the ES, not on the uncertainty of the estimate. The

1 probability of being the best was chosen to facilitate the translation of results to clinical 2 practice, however the results should be interpreted with caution and in conjunction with 3 the ES estimates. Thirdly, risk of bias assessment identified concerns over the high risk 4 of bias in included trials. Poor compliance with complete outcome data reporting, 5 analysis of all randomised participants, and pre-specification of published outcomes all 6 have the potential to overestimate the results of this meta-analysis. Fourthly, because 7 capsaicin is associated with a warming sensation on application, making it difficult to 8 blind, it was deemed a high risk of bias domain for all capsaicin trials. This may results in 9 inherent differences in the placebo group across the trial network, threatening the 10 assumption of transitivity. Furthermore, the efficacy data for topical NSAIDs is 11predominantly based on knee OA (22 of 23 studies), whilst the trial population for 12 capsaicin included hand, wrist, elbow, shoulder, hip, knee, and ankle OA. The differences 13 in study populations may limit comparisons between the two treatments, however, it 14 was not possible to conduct subgroup analyses by joint type due to limited data. Finally, 15 by the very nature of analyses conducted at trial-level, the results of this NMA relate to 16 populations of individuals with OA and may not be reflected at the individual patient 17 level. In addition, data were unavailable to examine the efficacy of topical NSAIDs and 18 capsaicin in subgroups with differing OA phenotypes (e.g. nociceptive versus 19 neuropathic-like pain). Studies at the individual patient level are still required.

In conclusion, current evidence indicates that topical NSAIDs and capsaicin offer similar
levels of pain relief in OA. Larger and better conducted RCTs, particularly for capsaicin,
are required to confirm this. However, it is unknown whether individuals with different
pain phenotypes respond differently to these two commonly used topical analgesics.
Further work on phenotypic features of OA pain and their response to these two drugs is
warranted.

#### 26 **Declarations**

#### 27 Acknowledgments

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2 screening and data extraction of publications in Japanese, German, and Chinese.

#### 3 Author contributions

MSMP conceived the work, developed and ran the search strategy, screened trials for eligibility, designed data collection tools, performed data collection, analysed the data, and drafted and revised the paper. JS extracted data for validation and revised the paper. DAW, MD, and WZ were involved in the conceptualisation of the work, interpretation of the data, and revision of the paper. WZ is the guarantor. All authors discussed the results, commented on the manuscript, and have approved the final version of the paper.

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13 had no role in study design, data collection, data synthesis, data interpretation, or

14 writing the report.

#### 15 **Conflicts of interest**

16 MSMP, JS, and JK declare no support from any organisation for the submitted work; no 17 financial relationships with any organisations that might have an interest in the 18 submitted work in the previous three years; no other relationships or activities that could 19 appear to have influenced the submitted work. DAW reports grants from Arthritis 20 Research UK, during the conduct of the study; grants and personal fees from Pfizer Ltd, 21 personal fees from GSK Consumer Healthcare, outside the submitted work. MD reports 22 grants from AstraZeneca funding a non-drug PI-led study in Nottingham (Sons of Gout 23 Study), grants from Arthritis Research UK during the conduct of the study, and personal 24 fees from Ad hoc Advisory Boards on osteoarthritis and gout for AstraZeneca, 25 Grunenthal, Mallinckrodt and Roche, outside the submitted work. WZ grants from 26 Arthritis Research UK Pain Centre, during the conduct of the study; personal fees from

1 AstraZeneca and Hisun Pharm, royalties to his institution from EULAR, non-financial 2 support from Peking University, Xiangya Hospital, outside the submitted work. 3 References 4 1. NICE. Osteoarthritis: Care and management in adults [CG177]2014 16/10/2015; 5 (CG177). Available from: http://www.nice.org.uk/guidance/cg177/evidence/cg177-6 osteoarthritis-full-guideline3. 7 2. McAlindon T, Bannuru R, Sullivan M, Arden N, Berenbaum F, Bierma-Zeinstra S, 8 et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. 9 Osteoarthritis and Cartilage. 2014;22(3):363-88. 10 3. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. 11 American College of Rheumatology 2012 recommendations for the use of 12 nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis care & research. 2012;64(4):465-74. 13 14 4. Zhang W, Doherty M, Leeb B, Alekseeva L, Arden N, Bijlsma J, et al. EULAR 15 evidence based recommendations for the management of hand osteoarthritis: report of a 16 Task Force of the EULAR Standing Committee for International Clinical Studies Including 17 Therapeutics (ESCISIT). Annals of the rheumatic diseases. 2007;66(3):377-88. 18 5. Jordan K, Arden N, Doherty M, Bannwarth B, Bijlsma J, Dieppe P, et al. EULAR 19 Recommendations 2003: an evidence based approach to the management of knee 20 osteoarthritis: Report of a Task Force of the Standing Committee for International 21 Clinical Studies Including Therapeutic Trials (ESCISIT). Annals of the rheumatic diseases. 22 2003;62(12):1145-55. 23 6. Derry S, Conaghan P, Da Silva JAP, Wiffen PJ, Moore RA. Topical NSAIDs for 24 chronic musculoskeletal pain in adults. The Cochrane Library. 2016. 25 7. Prescribing & Medicines Team P. Prescription Cost Analysis, England - 2016. 26 Health and Social Care Information Centre; 2017 [updated 30/03/2017; cited 2017 27 17/08/2017]; Available from: http://content.digital.nhs.uk/article/2021/Website-

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## 1 Figure legends

- 2 Figure 1 PRISMA flow diagram. Results of the systematic literature search for placebo-
- 3 controlled trials of topical NSAIDs and capsaicin in OA
- Figure 2 Risk of bias assessment. Risk of bias scores for all studies included in the
   overall analysis.
- 6 **Figure 3** Trial network diagram. Nodes (circles) are weighted to represent the number
- 7 of participants using each intervention. The solid lines represent the direct comparisons
- 8 of the treatments in RCTs. The dotted line represents indirect comparisons generated
- 9 through the NMA. The lines are weighted to represent the number of comparisons

**Table 1 – Effect size (ES) and Frequentist confidence interval (CI)/Bayesian credible interval (CrI)**. Results of the overall and *as licensed* subgroup analysis of topical NSAIDs and capsaicin in OA.

			Frequentist		Bayes	sian
Comparison	Туре	Ν	ES	CI	ES	CrI
All trials						
Topical NSAID vs placebo	Direct	23	0.30	0.19 to 0.41	0.30	0.19 to 0.43
Capsaicin vs placebo	Direct	5	0.27	-0.01 to 0.54	0.27	-0.02 to 0.56
Topical NSAIDs vs capsaicin	Indirect	28	0.04	-0.26 to 0.33	0.04	-0.28 to 0.35
As licensed						$\mathbf{N}$
Topical NSAID vs placebo	Direct	13	0.32	0.24 to 0.39	0.32	0.24 to 0.42
Capsaicin vs placebo	Direct	4	0.41	0.17 to 0.64	0.41	0.16 to 0.66
Topical NSAIDs vs capsaicin	Indirect	17	-0.09	-0.34 to 0.16	-0.09	-0.35 to 0.18

ES: effect size, CI: confidence interval, CrI: credible interval, N: number of studies

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**Table 2 – Treatment rankings.** The probability of each treatment being the "best" using Frequentist and Bayesian approaches

	Probability of be Frequentist	eing the best (%) Bayesian
All trials		
Topical NSAID	61.9	58.9
Capsaicin	38.1	41.1
Placebo	0.0	0.0
As licensed		
Topical NSAID	23.5	25.9
Capsaicin	76.5	74.1
Placebo	0.0	0.0





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