Title:

The effects of menthol on exercise performance and thermal sensation: a meta-analysis

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Abbreviations:

NS, non-significant

PO, power output

Pt, point (on thermal sensation scale)

RPE, rating of perceived exertion

TRP, transient receptor potential

TS, thermal sensation

TT, time-trial

TTE, time-to-exhaustion

Wmax, maximal power output achieved in incremental ramp test

Abstract

Objectives: Menthol is an organic compound with non-thermal cooling properties that has been shown to relieve thermal strain associated with exercise in the heat; however, its effects on performance have not been systematically analysed. The aims were to determine the effects of menthol applied (1) internally and (2) externally on exercise performance and thermal sensation.

Design: Meta-analysis

Methods: A search was performed using various databases in August 2018. The studies were screened using search criteria for eligibility. Thirteen peer-reviewed articles were identified for inclusion in a primary analysis on the effect of menthol on exercise performance; subsequently eleven of these articles were included in a secondary analysis on the effect of menthol on thermal sensation during exercise. A sub-analysis examining the application method was also performed.

Results: Menthol improved overall exercise performance (Hedges' g = 0.33, 95 % CI -0.00, 0.65 P = 0.05), demonstrating greater effects when applied internally (Hedges' g = 0.40, 95 % CI 0.04, 0.76, P = 0.03). Thermal sensation was also lowered overall across all studies (Hedges' g = -0.54, 95 % CI -0.67, -0.42, $P < 0.001$).

Conclusions: Exercise performance can be improved by application of non-thermally cooling menthol, which also reduces perceptual measures of thermal sensation. Internal application appears to be the best strategy to improve performance.

Keywords: Heat, Cold, Thermoregulation, Sensory, Perception

Introduction

Menthol (2-Isopropyl-5-methylcyclohexanol) is a naturally occurring organic compound that invokes a range of biological responses [1]. Menthol acts on sensory nerves [2–4] and in smooth muscle of humans [5], as well as eliciting a cooling sensation when applied to the skin and mucosal surfaces [6]. Whilst found in many forms, the L isomer (L-menthol) is most commonly used because it elicits the strongest cooling sensations [7]. Menthol-induced cold hypersensitivity primarily relies on activation of the transient receptor potential melastatin 8 (TRPM8) channel expressed on small diameter Aδ and C- sensory nerve fibres - a subset of neuronal fibres dedicated to innocuous cold sensing [2–4]. These channels are activated below a temperature threshold of 25 °C, as well as by a range of chemical agonists, which include menthol [2]. However, menthol also displays bimodal actions on the TRPA1 channel, which is expressed on polymodal nociceptive neurons [8]. This might explain the ambiguous sensations of pain elicited by menthol when applied to the skin. Historically, menthol has been used for a range of conditions, including gastrointestinal disorders, common cold and respiratory illness, and for its analgesic properties on muscular skeletal pain [1].

Recent studies have explored menthol's non-thermal cooling properties in relieving the thermal strain associated with exercise in the heat. Whilst the detrimental effect of hot environments on exercise performance has been well described [9,10], much research has focussed on thermally-cooling interventions to offset rises in core body temperature, thus enhancing performance. For example, ice slurry ingestion [11–13], cold water immersion [14], face cooling [15] and cooling garments [16] have all been reported to provide pre- or per-cooling effects. However, non-thermal cooling can act as an alternative strategy to facilitate behavioural modifications in hot environments, and offers a more practical method to extend exercise performance. Menthol elicits sensations of coolness, without reductions in temperature, via activation of cold sensory pathways to the thalamus and the somatosensory cortex [4]. Here, reductions in perceived thermal sensation and thermal discomfort are thought to modulate perceived exertion to improve performance [17,18]. The application of menthol

may take multiple forms. For example, menthol can be applied externally to the skin via creams, gels, sprays or solutions, whereas internal applications are achieved through ingestion of a drink or mouth rinses. A recent review concluded that menthol has the greatest effect on exercise performance in the heat when applied internally [19]. However, it is important to integrate current available data on the use of menthol during exercise in the heat and describe its effects on lowering thermal sensation to provide clear and accurate guidance for prescription in sporting and occupational environmental conditions.

Therefore, this study systematically reviewed and meta-analysed all peer reviewed studies that have applied menthol to human subjects during exhaustive exercise (time to exhaustion at a fixed intensity), self-modulated exercise to exhaustion over a fixed distance (time-trial) or to a fixed point (core temperature or power output associated with a fixed-RPE). The aim of the meta-analysis was to determine the effects of menthol application on exercise performance and thermal sensation, thus identifying the method of application that will achieve the largest change in perceptions of thermal strain and elicit the greatest ergogenic effect.

Methods

Search strategy

All literature that investigated the effect of menthol on exercise performance and thermal sensation was searched and obtained using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines, with a pre-determined search strategy [20]. There was no limit on the status or language of the publication and the final searches were performed in PubMed, Science Direct, Web of Science, and SPORTDiscus (EBSCO) between the dates: 6th-22nd August, 2018. The search terms used were 'menthol AND exercise' OR 'menthol AND thermal sensation'.

Study selection

Once all of the articles were identified, two reviewers screened the titles and abstracts for inclusion or removal of duplicates. Another source was also identified from conference proceedings, which was later excluded. The reference lists of the initial articles were reviewed independently by two authors (OJ and MW), which did not reveal any additional articles. The remaining articles were then assessed by OJ and MW against the initial search criteria. To be included in this analysis, the studies must have: i) administered menthol to humans via any mechanism, ii) a control group without menthol and iii) been used during an exercise trial to either a fixed point or to exhaustion. Of the remaining papers, some were further removed for the reasons outlined in figure 1.

*******Insert Figure 1 near here*******

Data extraction and quality assessment

Data were extracted independently by two authors (OJ and MW) and entered into a custom excel spreadsheet. Collected data included: i) characteristics of the sample (sex, health status, age, training status); ii) study design; iii) menthol application method and dose; iv) performance type; v) performance outcomes; vi) thermal sensation outcomes; and vii) bias. Risk of bias was assessed by two authors (OJ and MW) according to Cochrane collaboration guidelines [21]. Where details of the study were unclear, the authors were contacted for further information to confirm details of the method. For the purposes of comparing data between time-to-exhaustion exercise tasks and time-trial exercise tasks, the latter data were converted to speed (m/s) for analysis. One study [22] did not include "final value" data for performance, therefore, the reported "change score" (the change in average power output in time trial 2 (T2) following the intervention, in relation to baseline time trial 1 (T1)) was added to the average T1 score for both conditions. These calculations matched the reported combined data value for T2. However, as measures of standard deviation (SD) were not available data was imputed [23] from the reported combined T1+T2 data for each condition. Here, the SD scores appeared to approximately match the differences in SD reported in the change scores and therefore considered appropriate. Data was analysed using standardised mean differences (Hedges' g) to reflect the different measurement outcomes.

Data extracted for thermal sensation (TS) were reported using three different analog scales. Three articles used a 7-point analog scale based on [24], six articles used a 9-point analog scale based on [25], and two articles used a 17-point analog scale that was comparable to the 9-point scale but with 0.5 point intervals [26]. Scores for thermal sensation were averaged across exercise trials following administration or application of menthol. Hence when menthol was applied at the beginning of exercise all data gathered during the test was averaged. However, in exercise trials were menthol was administered towards the end of exercise, TS values were averaged only from this point onwards. The reported differences in groups represent a decimal point change on the analog scale, i.e. 1.0-point may represent a decrease in thermal sensation from "very hot" = 9-point to "hot" = 8-

point. Analysis was conducted by reporting mean differences due to the close comparability between scales.

Statistical analysis

Data analyses were performed by one author (OJ) using Review Manager 5.3 according to the Cochrane guidelines. Raw data were extracted in the form of a mean, SD and sample size for the meta-analysis. Publicly available software (WebPlotDigitizer, Version 3.12) was used to extrapolate any unreported values from figures to raw mean and SD data. Heterogeneity was investigated using the I^2 statistic. A random effects model for the meta-analysis was used due to variability in experimental outcomes across studies (exercise performance), whereas a fixed effect model was used when it was assumed that the intervention produced an outcome with the same effect (in both magnitude and direction) in every study (thermal sensation) [27]. Hedges' g and 95 % confidence intervals were used to express the standardised means differences between menthol and control groups across studies. A sub-group analysis was also performed on both datasets based on the application of menthol internally or externally. The magnitudes of the effects were assessed using Cohen's definitions of: < 0.2, 0.3, 0.5 and 0.8 for trivial, small, moderate and large, respectively [28]. Statistical significance was set at $P < 0.05$ for all analyses.

Results

Study Selection

The initial searches retrieved 907 articles, plus an additional 1 study through other sources. These were reduced to 722 after removal of duplicates. Further screening excluded 679 articles, with 43 articles left. These 43 articles were assessed for eligibility via full text and reference lists did not reveal any missing papers. The inclusion criteria stipulated a further removal of 30 articles due to not conforming to the correct exercise type, absence of a non-menthol control group and review articles. Thirteen articles remained, which were included in the primary meta-analysis examining the effect of menthol on exercise performance. Subsequently, eleven of these articles were included in a secondary analysis examining the effects of menthol on thermal sensation during exercise (see Figure 1).

Study Characteristics

Characteristics of the thirteen studies included in both meta-analysis are summarized in Table 1. The studies include a total of 135 participants, comprising healthy males of varying training status. All studies were crossover designs. Exercise protocols involved time-trials (*n* = 7), time-to-exhaustion trials (*n* = 3), fixed-RPE protocols (*n* = 2) and a time to a fixed core temperature (*n* = 1). Ambient temperature during the exercise tasks was 31 ± 5 ^{o}C, ranging from 20 ^{o}C to 35 ^{o}C. Menthol was applied via five different mechanisms: oral mouthrinse (*n* = 5), spray (*n* = 4), cream/gel (*n* = 2), ingestion of a drink (*n* = 1) and immersion (*n* = 1).

*******Insert Table 1 near here*******

Meta-analysis for exercise performance

The results of the meta-analysis examining performance are reported in Figure 2. Using a random-effects model and standardised mean differences, overall there was a small improvement in exercise performance, with menthol compared to control (Hedges' g = 0.33, 95 % CI -0.00, 0.65 P = 0.05). The I^2 statistic demonstrated 43% heterogeneity. However, when examining the methods of application, internal application of menthol (oral mouth-rinsing, ingestion) showed a greater but small effect (Hedges' g = 0.40, 95 % CI 0.04, 0.76, P = 0.03; I^2 = 0%) (n = 6). External application (spray, cream/gel and immersion) showed a trivial-to-small effect which was not significant (Hedges' g = 0.29, 95 % CI -0.34, 0.91, P = 0.37; I^2 = 70%) (n = 7).

*******Insert Figure 2 near here*******

Meta-analysis for thermal sensation during exercise

The results of the second meta-analysis examining thermal sensation are reported in Figure 3. Using a fixed-effects model and mean differences, overall there was a moderate-to-large reduction in thermal sensation during exercise with menthol compared to control (Hedges' g = -0.54, 95 % CI -0.67, -0.42, P < 0.001). The I^2 statistic demonstrated 67% heterogeneity. However, when examining the methods of application, internal application of menthol (oral mouth-rinsing, ingestion) showed a small effect (Hedges' g = -0.30, 95 % CI -0.50, -0.10, P = 0.004; I^2 = 0%) (n = 5). External application (spray, cream/gel and immersion) showed a moderate-to-large effect (Hedges' g = -0.71, 95 % CI -0.88, -0.54, P = < 0.001; I^2 = 74%) (n = 6).

*******Insert Figure 3 near here*******

Risk of Bias

The studies included generally had low or unclear risk of bias (Figure 4). Only three studies reported information on the randomisation procedure conducted to generate groups [29–31]. Attempts to conceal allocation to an intervention or control group were also not clearly reported in three studies [29,32,33]. However we acknowledge this may be difficult when administering menthol due to its distinctive sensory effect. Therefore, this is a limitation that must be acknowledged across the literature when there is not a sufficient placebo alternative. Only one study reported double-blinding [34] of participants and personnel to the interventions administered and all other studies were single-blinded. Therefore, the risk of bias on the outcome measure was deemed 'unclear'. Finally, in one study [22], performance data was only reported as the change from baseline which may have concealed differences at baseline for each condition or inflated outcome measures, therefore this was allocated as high risk for reporting bias.

*******Insert Figure 4 near here*******

Discussion

The main findings of this analysis were that menthol has an overall small positive effect on exercise performance (Hedges' *g* = 0.33). The effect is dependent on the method used to administer menthol, with internal strategies via mouth-rinsing or ingestion, indicating a stronger effect, albeit remaining small (Hedges' *g* = 0.40). External methods of menthol application via creams, gels, sprays and full-body immersion showed contrasting effects, both positive and negative, on exercise performance that resulted from the method of application used and physiological consequences (Hedges' *g* = 0.29). In a secondary analysis menthol was also shown to reduce thermal sensation across all exercise studies, irrespective of the application method (Hedges' *g* = -0.54).

Menthol is a non-thermal cooling stimulus that acts on thermoreceptors, eliciting sensations of coolness, without reductions in temperature when applied to the skin and mucosal surfaces [6]. Activation of sensory pathways transmit this information to the brain where perceptual lowering of the associated thermal strain occurs [4]. Overall, despite Hedges' g indicating a small effect of menthol on exercise performance, these changes could confer practically relevant effects. For example, pre-cooling strategies, such as cold water immersion or ingestion of ice slurries, lead to physiological reductions in core body temperature prior to exercise and facilitate an increased heat storage capacity to extend exercise performance in the heat [35]. Meta-analyses conducted on pre-cooling and exercise performance have reported small-moderate improvements in a range of temperate conditions (18-40 ^{o}C) (*d* = 0.41) [36], in a hot environment (27-35 ^{o}C) (*d* = 0.73) [37], or a hot (27-35 ^{o}C) and humid environment (RH 30-80 %) (*d* = 0.49) [38]. Indeed, small-to-moderate changes in performance have been reported following cold water-immersion (*d* = 0.53) [39] and cold water ingestion (*d* = 0.40) [40], ice ingestion (*d* = 0.20) [39] and wearing of an ice vest (*d* = 0.19) [40]. Therefore, the small effect sizes reported here using a non-thermal cooling strategy represents a substantial enhancement in performance.

279

280 Modulation of exercise intensity or performance when exposed to a non-thermal cooling stimulus,
281 such as menthol, provides interesting insights into human thermoregulatory behaviour. The current
282 analysis was performed to examine articles applying menthol during exercise that was either
283 exhaustive (time to exhaustion at a fixed intensity), self-modulated to exhaustion over a fixed
284 distance (time-trial) or to a fixed point (core temperature or power output associated with a fixed-
285 RPE). In addition, the method of menthol application was not restricted, thereby allowing multiple
286 comparisons between different methods. Although the use of non-thermal cooling would seem most
287 appropriate in a hot environment when physiological and perceptual thermal stresses are greater,
288 we also included articles that examined the use menthol in lower ambient temperatures. Including a
289 variety of studies was necessary to provide a broader insight into the benefits of menthol
290 application, yet based on the current findings, this added to the heterogeneity of the overall results
291 and contributed to smaller effect sizes. This is demonstrated most apparently in figure 2, where
292 internal applications improved performance with less variation and by a higher magnitude. The type
293 of menthol application is, therefore, worthy of further discussion.

294

295 Internal application via mouth-rising or ingestion of menthol resulted in greater effects on exercise
296 performance (Hedges' g = 0.40). Five articles included in this subsection administered menthol via an
297 oral mouth rinse, reporting an average ~6 % improvement (range 3-9 %) across a number of differing
298 experimental designs, such as, time trial [33,41], time to exhaustion [30,42] and RPE clamp [31]. Four of the
299 studies administered menthol frequently throughout the exercise trial (every kilometre or at 10
300 minute time intervals). In the fifth study, conducted in our own laboratory, oral menthol was
301 deliberately administered when thermal stress was high, towards the end of a constant-load
302 exercise trial (denoted by high body temp). Here, menthol was also capable of improving
303 performance by ~6% despite a single acute administration [30]. Interestingly, menthol yielded

304 comparable results to the ingestion of a thermally-cooling ice-slurry at the same time point. It was
305 postulated that menthol acted as a novel stimulus, despite increased thermal stress. This theory is
306 supported by a previous article [31], where it was noted that a reduction in performance over time was
307 not rescued by subsequent menthol application. Whether repeated applications of menthol or a
308 single dose when thermal load is high is most effective remains to be thoroughly explored.

309

310 Ingestion of menthol with water (neutral temperature) also resulted in a 6% improvement in time-
311 trial performance [43]. Interestingly, in the same study, menthol ingestion with cold water / ice slurry
312 elicited greater effects on exercise performance than when ingested with water at a neutral
313 temperature or even cold water / ice slurry alone [43]. Future research should explore these
314 potentiating effects using mixed internal thermal cooling and menthol to benefit exercise
315 performance. However, the collective evidence presented here would suggest that when cool liquids
316 are not available, menthol does not need to be consumed to elicit a positive effect on performance
317 and can be orally rinsed and expectorated. Consumption of menthol in a beverage would
318 presumably still activate thermoreceptors located in the oral cavity, which is one of the most densely
319 innervated parts of the body in terms of peripheral receptors [44]. Therefore, either approach would
320 elicit cooling sensations via the same primary mechanism. The concentration of oral menthol applied
321 across all studies in this analysis was 0.01%. Interestingly, no performance studies have investigated
322 the physiological effects of increasing the menthol concentration and potential oral
323 stimulation/perception of cooling. However, one study has examined cooling perception when orally
324 rinsing with a range of menthol concentrations 0.005–0.105% [45] and reported no effect at rest. This
325 may be an interesting avenue for future studies during exercise.

326

327 External application of menthol via cream or gel produced contrasting results, with one study
328 reporting a 26% reduction in exercise [29] and another showing a 21% improvement [18]. The contrasting

effects reported most likely relate to the application method and associated physiological effects. Kounalakis et al. (2010) applied a menthol cream over the entire body, whereby the non-thermal cooling effects were secondary to a general vasoconstriction during the early stages of exercise. The ergolytic effects were explained by a delayed onset and total gain in sweat production, reducing the capacity to thermoregulate, as well as facilitating an earlier rise in core temperature. It should be noted that others have reported a vasodilatory response to local menthol application [46,47]. TRPM8 channel activation in smooth muscle has been shown to initiate vasoconstriction or vasodilation, dependent on previous vasomotor tone [5]. TRPM8 channels have also been suggested to act as 'thermostats of the skin' communicating skin temperature to the brain, whereby thermoregulatory changes occur to defend body temperature [48]. Therefore, the initial vasoconstriction described in the early stages of exercise that would precipitate a rise in skin temperature could be explained via these mechanisms. It is important to further establish the timing of menthol application to facilitate cutaneous blood flow during exercise, particularly in hot conditions. Interestingly, whole-body cold water immersion with menthol appeared to enhance subsequent time trial performance ~16% following a similar baseline test [22]. The mechanisms are unclear as the reduction in core temperature observed in the control bath immersion following the exercise task were not as great in the menthol bath suggesting that heat was retained by the body. The improvements in performance were suggested to relate to a shift in thermal sensation, however further studies are required to explore the effectiveness of this intervention strategy.

In contrast to whole-body application, Schlader et al. (2011) focussed application of a topical menthol gel to a much smaller area of the face. The face in particular, has been shown to contain a greater number of "hot spots" relative to the rest of the body, which is typically reported to reflect the density of peripheral thermoreceptors [49]. Indeed, the face has shown a greater sensitivity to cold (2-5 fold) than other parts of the body (forearm, thigh, leg and foot) [50]. Application of 8% menthol

gel to the entire face (dose of ~0.5 g/100 cm^2 of skin), did not induce a change in core temperature, nor changes in whole body and local sweat rates, and resulted in a 21% improvement in exercise performance [18]. This method initiated a shift to a cooler thermal sensation, independent of any change in facial temperature. Together, these studies crucially highlight the specificity of externally applied menthol in hot environments. There is little information on the dose-response effect of menthol applied to the skin, with studies here using ~4 – 8%. Perceptually, other studies have found that low concentrations of menthol (<2%) elicit cool sensations [51], moderate concentrations (2–5%) cause irritation and local anaesthesia [1], with higher concentrations (>10%) initiating burning sensations [52]. Whilst further work is needed to understand this method and concentration, it should be noted that the practical application of creams and gels during exercise largely restrict its use to pre-exercise.

An alternative strategy for the application of menthol was in a spray vaporised form [32,34,53,54]. In three studies, menthol was sprayed onto the participant's garment at various stages of exercise; however, these interventions did not modify exercise performance. The application of menthol in a spray is further supported by a body of research that examined the optimal concentration, reported as 0.05 %, to minimize thermoeffector responses of menthol, while preserving the cool sensations [55–57]. Interestingly, it was also reported that perceptual differences were sustained for up to 25 min after spraying; however, this was not during exhaustive exercise, meaning further research is required to confirm this. It is also interesting that no effect on performance was noted when menthol was sprayed at the beginning [32] or towards the end [34] of exercise, contrasting the positive effects of orally applied menthol in similar experimental designs [30,31]. Together this may suggest that menthol delivered in a spray may rapidly lose effectiveness during exercise. Interestingly, a menthol spray targeted at the neck did show a ~11% improvement in performance [54]. Therefore, the differential

sensitivity of body regions could also explain the lack of effect when applied on the torso compared to the neck and face.

A moderate-to-large reduction (Hedges' *g* = -0.54) in thermal sensation was consistently reported, with external application showing greater effects (Hedges' *g* = -0.71) than internal (Hedges' *g* -0.30). All articles examined in this secondary meta-analysis required inclusion in the primary analysis examining exhaustive performance in order to understand the relationship between reductions in thermal sensation and exercise performance. All articles included demonstrated a lowering of thermal sensation, with effects ranging from -0.2 to -3.04. Scores for thermal sensation were averaged across the trials from the first point of menthol administration. Therefore, larger reductions were observed when menthol was delivered acutely at the end of exercise via mouth rinse (Hedges' *g* -0.60) [30] or spray (Hedges' *g* -1.56) [34]. The small changes across exercise tasks following internal administration may reflect the reducing potency of menthol upon repeated applications as discussed previously. Application of menthol externally elicited greater reductions in thermal sensation that may be explained by a persistent aroma facilitated by evaporative mechanisms or convective air movements during exercise, which elicit continual nasal receptor stimulation. The cool sensation of nasal airflow is mediated by the same cold receptors in oral mucosa and this largely determines the sensation of breathing, rather than a sense of respiration [58]. The largest reported changes in thermal sensation were evidenced in three studies where menthol was applied via a vaporised spray to the torso; however, as previously discussed, there were no performance changes. Therefore, reductions in thermal sensation following the application of menthol cannot fully explain improvements in exercise performance in the heat. Flouris and Schlader [17] have argued that it is perception of effort that dictates behaviour and that thermal perception may play a modulatory role. Indeed, at rest it is thermal discomfort and not thermal sensation that acts as the primary motivation for thermoregulatory behaviour [17]. However, while the

role of thermal discomfort during exercise in the heat is less well understood, menthol applied as a cream to the face initiated reductions in both thermal discomfort and thermal sensation, which subsequently leads to a reduction in the perception of effort associated with a fixed exercise intensity [18]. Future studies should explore menthol's effectiveness in modulating thermal discomfort and thermal sensation during exercise in the heat.

It should be noted that a number of studies could not be included in this meta-analysis due to the absence of a comparable non-menthol control group [59,60]. This is unfortunate, as the addition of these papers might have strengthened the overall effects reported. This highlights the need for greater experimental control in this area. The risk of bias of the articles included were generally low; however, 12/13 studies were single-blinded, demonstrating "unclear" risk to the outcomes of the study. Whilst it is practically challenging to conduct double-blind experiments in research of this type, improvements in research design could be achieved in this way, which would substantiate the effects of menthol on exercise performance.

Conclusion

Human performance can be improved by application of non-thermally cooling menthol and can consistently reduce thermal sensation during exercise. Oral administration appears to be the most effective method to enhance exercise capacity, predominantly in hot environments. Targeted external application of sensitive anatomical regions may also be a useful strategy in improving exercise performance, whereas whole-body coverage appears to be detrimental to performance. Irrespective of the application mode, the use of menthol is a relatively simple way to increase exercise performance. This is in contrast to various cooling strategies that often require access to refrigerators, ice, baths or cold fluids, notwithstanding the thermal benefits they confer. The optimal

application of menthol requires further investigation, including the merits of co-administration with established cooling techniques.

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Conflict of interest:

Owen Jeffries and Mark Waldron have no conflicts of interest directly relevant to its contents.

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Figure legends

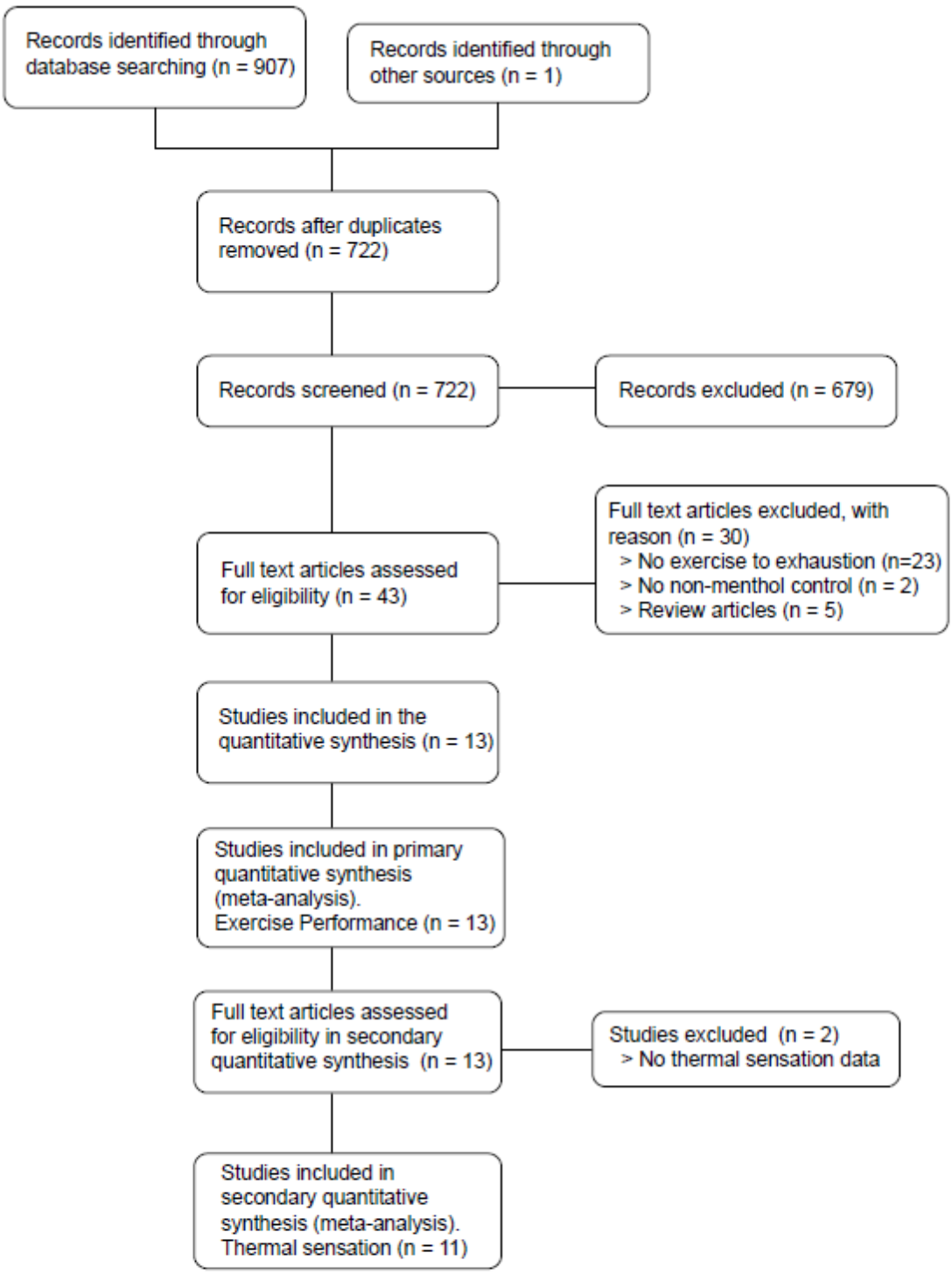
Figure 1. PRISMA flow diagram summarizing study selection for inclusion in the final meta-analysis.

Figure 2. Forest plot illustrating the effect of menthol on exercise performance. Squares indicate the individual study Hedges' g and the lines represent 95% CIs. The diamond represents the overall Hedges' g, with its width representing the 95% CIs. Data is displayed in subgroups representing internally applied menthol (1.1.1) (oral, drink, *n* = 6) and externally applied menthol (1.1.2) (spray, cream/gel, immersion, *n* = 7).

Figure 3. Forest plot illustrating the effect of menthol on thermal sensation during exercise. Squares indicate the individual study Hedges' g and the lines represent 95% CIs. The diamond represents the overall Hedges' g, with its width representing the 95% CIs. Data is displayed in subgroups representing internally applied menthol (1.2.1) (oral, drink, *n* = 5) and externally applied menthol (1.2.2) (spray, cream/gel, immersion, *n* = 6).

Figure. 4. Analysis of risk of bias according to the Cochrane Collaboration guidelines.

624 Figure 1



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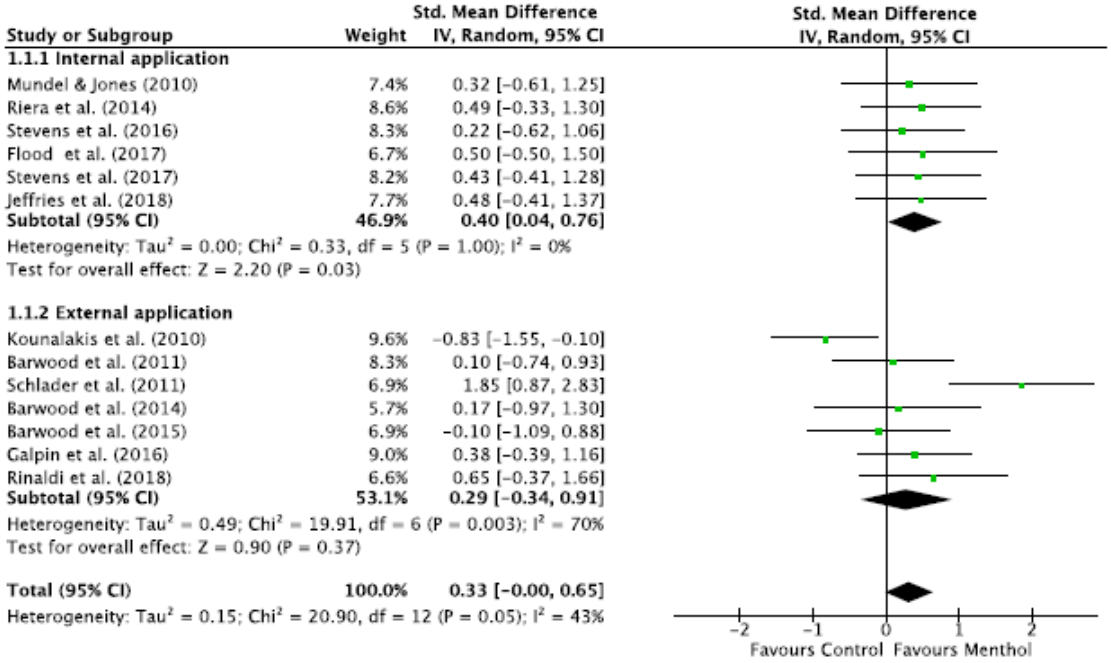
627 Figure 2



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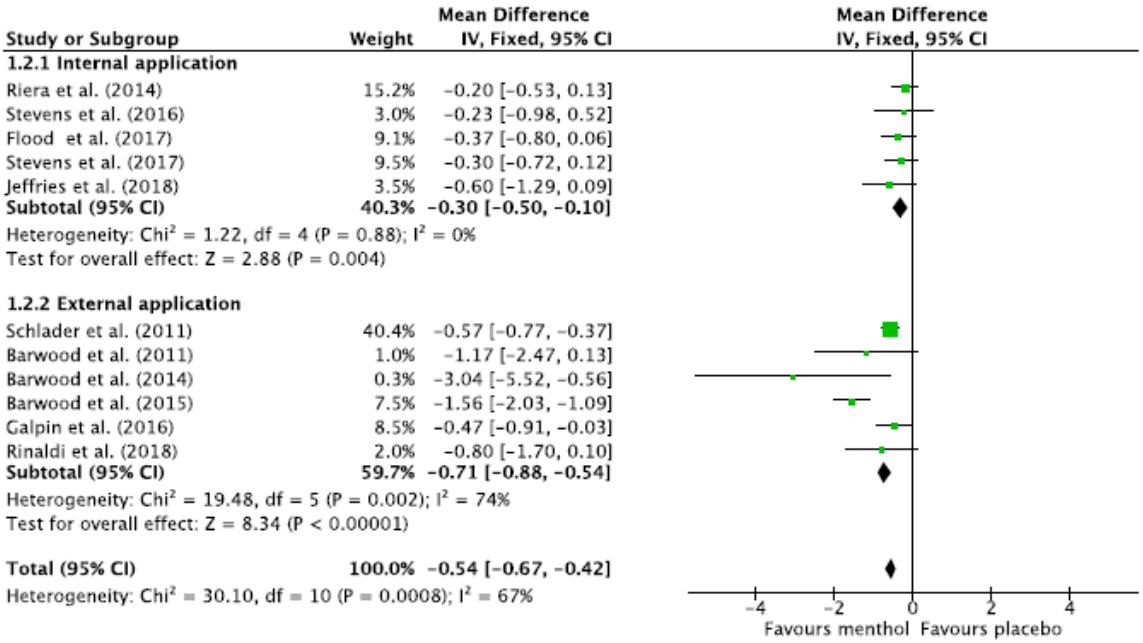
631 Figure 3



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634 Figure 4

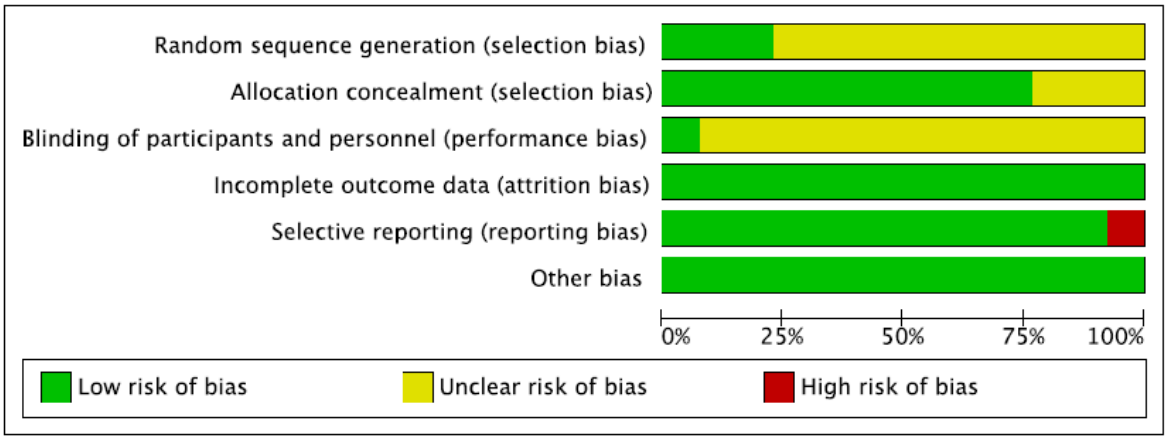

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Table 1. Summary of studies included in the meta-analysis for the effects of menthol on exercise performance and thermal sensation

Study	Design	Sample	Menthol application	Performance type	Ambient temperature	Exercise outcome	Thermal sensation outcome
Mundel & Jones. (2010)	Crossover, randomised	Healthy, males (*n* = 9). Age 25 ± 7 y	Oral mouth-rinse 25ml 0.01% (19 °C)	TTE at 65% Wmax	34 °C	9 % ↑ TTE	Not reported
Kounalakis et al. (2010)	Crossover, counterbalanced	Healthy, males (*n* = 16). Age 24 ± 3 y	Cream 4.6 % to whole body	Time to 38 °C Tre @ 60% of VO_{2max}	24 °C	26 % ↑ time to Tre = 38 °C	Not reported
Schlader et al. (2011)	Crossover, randomised	Healthy, physically active, males (*n* = 12). Age 23 ± 1 y.	Gel 8 % to full face ~0.5 g per 100 cm^2	Fixed-RPE protocol	20 °C	21 % ↑ total work completed (kJ)	0.6 pt ↓ TS across trial
Barwood et al. (2011)	Crossover, randomised, single-blind	Trained, non-acclimated, males (*n* =11). Age 30 ± 8 y	Spray 0.05 % in water (22 °C) full tee shirt	40-km TT - cycling	32 °C	NS 1 % ↑ TT	1.2 pt ↓ TS across trial
Barwood et al. (2014)	Crossover, single-blind, randomised	Healthy, males (*n* = 6). Age 21 ± 1 y	Spray 0.20 % in water (34 °C) full tee shirt	5-km TT - run	34 °C	NS 1 % ↑ TT	3.0 pt ↓ TS across trial
Riera et al. (2014)	Crossover, randomised	Trained, heat-acclimated males (*n* = 12). Age 42 ± 13 y	Drink 190 mL 0.01% (23 °C)	20-km TT - cycling	31 °C	6 % ↑ TT	0.2 pt ↓ TS at end exercise

Barwood et al. (2015)	Crossover, counter-balanced, double-blind	Healthy, males (*n* = 8). Age 21 ± 2 y	Spray 0.20 % in water (34 °C) full tee shirt	16.1-km TT cycling	34 °C	NS 1 % ↓ TT	1.6 pt ↓ TS at across trial
Galpin et al. (2016)	Crossover, randomised	Physically active, males (*n* = 13). Age 25 ± 5 y)	Spray 8 % neck	TTE at 30% PP	25 °C	11 % ↑ TTE	0.5 pt ↓ TS at across trial
Stevens et al. (2016)	Crossover, randomised	Moderately trained, males (*n* = 11). Age 29 ± 9 y	Oral mouth-rinse 25ml 0.01% (22 °C)	5-km TT - run	33 °C	3 % ↑ TT	0.2 pt ↓ TS at across trial
Stevens et al. (2017)	Crossover, randomised	Trained runners, male (*n* = 11). Age 30 ± 9 y	Oral mouth-rinse 25ml 0.01% (22 °C)	3-km TT - run	33 °C	4 % ↑ TT	0.3 pt ↓ TS at across trial
Flood et al. (2017)	Crossover, randomised, single-blind	Healthy, males (*n* = 8). Age 26 ± 5 y	Oral mouth-rinse 25ml 0.01% (20 °C)	Fixed-RPE protocol	35 °C	8 % ↑ TTE	0.4 pt ↓ TS at across trial
Rinaldi et al. (2018)	Crossover, randomised	Heat acclimated, males (*n* = 8). Age 24 ± 4 y	Immersion to shoulder, 0.1% (10 °C)	20-min TT - cycling	29 °C	15.6 % ↑ TT PO	0.8 pt ↓ TS across trial
Jeffries et al. (2018)	Crossover, randomised. single-blind	Healthy, males (*n* = 10). Age 33 ± 9 y	Oral mouth-rinse 25ml 0.01% (20 °C)	TTE at 70 % Wmax	35 °C	6 % ↑ TTE	0.6 pt ↓ TS at across trial

TT time-trial, TTE time-to-exhaustion, TS thermal sensation, NS non-significant, pt point (on thermal sensation scale), Wmax maximal power output achieved in incremental ramp test, RPE rating of perceived exertion, PO power output, Y years old.