Article:
Johnson, MI, Paley, CA orcid.org/0000-0002-6335-2666 and Jones, G (2023) Has long-standing uncertainty about the clinical efficacy of TENS finally been resolved? Pain Management, 13 (4). pp. 201-204. ISSN 1758-1869

https://doi.org/10.2217/pmt-2023-0029

Has long-standing uncertainty about the clinical efficacy of TENS finally been resolved?

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Article Type: Invited Editorial

Journal: Pain Management

Running header: TENS Efficacy

FUNDING: There was no external funding associated with this article
ETHICAL APPROVAL: N/A
COMPETING INTERESTS: In the previous 5 years, Mark I. Johnson's employer has received income for expert consultancy activities from GlaxoSmithKline, TENSCare, and LifeCare Ltd. that lie outside of the submitted work. Mark I. Johnson declares book royalties from Oxford University Press. All other authors declare no conflicts of interests.
ACKNOWLEDGEMENTS: None

Instructions/Invitation
Having read your recent work and considering that you are an expert in the area, I would like to invite you to contribute an editorial article on the topic "Long-term uncertainty about TENS" to be considered for publication in Pain Management (MEDLINE, Emerging Sources Citation Index [ESCI], Web of Science, EMBASE/Excerpta Medica and EMCare). There is plenty of flexibility regarding the title of the piece. The article should be 1500 words with a limit of 20 references and would have a provisional submission deadline of 28-Apr-2023; however, I am more than happy to extend the deadline should you be interested in writing for the journal. I am happy for you to work with any co-authors you feel necessary. Please let me know as soon as possible if you will be able to accept my invitation. If you are unable to submit at this time, I would appreciate you recommending another expert author.

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Introduction

In 2017, we published an editorial in *Pain Management* stating "Practitioners should be mindful that recommendations not to offer transcutaneous electrical nerve stimulation (TENS) are based on a paucity of evidence on which to make a judgment rather than evidence of inferiority or equivalence to placebo" [1].. In 2022, our team published the largest meta-analysis on TENS to date which provides moderate-certainty evidence that pain intensity is lower during or immediately after TENS compared with placebo [2]. This editorial explores whether our meta-analysis will end speculation about the efficacy of TENS.

The efficacy impasse for TENS

During TENS, pulsed electrical current is delivered across the intact surface of the skin to stimulate peripheral nerves. Generally, TENS generates a strong comfortable sensation (electrical paraesthesiae) within, or close to, the site of pain for symptomatic relief. TENS can be tried on any type of pain and in any setting, and has a favourable safety profile compared with medication (see [3] for details).

In 1974 Long et al. published the first case series on TENS for persistent pain and concluded "the initial success that we have gained to date suggests that cutaneous electrical stimulation will be a significant advance in our ability to treat chronic pain … The possibility of placebo effect must be evaluated," [4]. In 2001, Carroll et al. published the first Cochrane review of randomised controlled trials (RCTs) on TENS for persistent pain stating "there is insufficient evidence to draw any conclusions about the effectiveness of TENS for the treatment of chronic pain in adults . . . Large multi-centre randomised controlled trials of TENS in chronic pain are urgently needed"[5]. In 2019, Gibson et al. published the first overview of eight Cochrane reviews on TENS for chronic pain stating "We were therefore unable to conclude with any confidence that, in people with chronic pain, TENS is harmful, or beneficial for pain control, disability, health-related quality of life, use of pain-relieving medicines, or global impression of change," [6]. "Given the resources allocated to TENS for the treatment of chronic pain in many countries there is an urgent need to undertake large RCTs to examine its effectiveness"[6].

The situation has been similar for acute pain. In 1996, Carroll et al. published a systematic review on TENS for post-operative pain and concluded "*we judged there to be no benefit of TENS compared with placebo*"[7]. In 2003, a meta-analysis by Bjordal et al. provided evidence that TENS "can significantly reduce analgesic consumption for postoperative pain"[8]. In 2009, Walsh et al. published the first Cochrane review on TENS for acute pain which was updated in 2015 by Johnson et al. stating "*The analysis provides tentative evidence that TENS reduces pain intensity over and above that seen with placebo (no current) TENS.*" [9, 10]

Thus, five decades of research comprising over 350 randomised controlled trials and 150 systematic reviews failed to determine whether TENS alleviates pain to a clinically meaningful extent [11]. Inconclusive evidence contributes to inconsistent and contradictory recommendations by clinical guideline panels. For example, in 2008 and 2014 , the National Institute for Health and Care Excellence (NICE) in the U.K. recommended that "Healthcare professionals should consider the use of TENS as an adjunct to core treatment for pain relief" for osteoarthritis [12, 13]. However, this decision was reversed in 2022 to "*do not offer any of the following electrotherapy treatments to people with osteoarthritis because there is insufficient evidence of benefit: TENS"* [14]. Interestingly, RCT evidence had differed little between 2014 and 2022. The NICE does not recommend TENS for chronic primary pain, non-specific low back pain or intrapartum care [15],[16],[17]. The NICE recommends TENS for rheumatoid arthritis "Adults with RA should have access to specialist physiotherapy, with periodic review, to: … learn about the short-term pain relief provided by methods such as TENS*."* [18]

Resolving the efficacy impasse for TENS

We argued that a meta-analysis irrespective of type of pain would be valuable because it would capture the status of all available pain intensity data [1, 19]. In 2022, our team published a systematic review of 381 studies with a meta-analysis of pain data irrespective of diagnosis that met 'rule of thumb' standards for pooling data (i.e. >500 participants per trial arm) [2]. Grading and Recommendations, Assessment, Development and Evaluation (GRADE) judged there to be moderate-certainty evidence that pain intensity is lower during or immediately after TENS compared with placebo with a mean difference of approximately 20mm on a 100mm visual analogue scale (i.e., clinically meaningful). This finding is ecologically valid because it related to measures of pain during or immediately after TENS (i.e., pain in-the-moment) which is of primary importance to TENS users. We found no serious adverse events during TENS.

Will the answer be accepted?

Undoubtably guideline panels will continue to call for 'larger multicentred trials' to raise the certainty of evidence of benefit from moderate to high. We advocate an enriched enrolment with randomized withdrawal study that includes a 'run-in phase' that can remove people not wishing to use TENS and tailor treatment protocols to individual need prior to allocation to active and placebo TENS interventions [19, 20]. We argue that our meta-analysis provides sufficient evidence to offer TENS as an option to soothe pain in the moment.

Guideline panel recommendations influence who covers the costs of TENS treatment, although history suggests that people will try TENS irrespective of the viewpoints of clinicians, policy makers, funders or guideline panel recommendations. It is general knowledge that TENS may soothe pain, costs compare favourably with other treatments and is easy to use without the need for clinical supervision, although clinical input is preferable at the start [21-23]. An advantage of TENS is the ability to precisely control the characteristics of currents to optimise the pleasantness of TENS sensation according to need. Smart electrodes integrated with wi-fi and Bluetooth technology can overcome the inconvenience of lead wires and smart phone technology can optimise treatment algorithms. Future research should focus on how best to integrate TENS into pain management strategies, including development of interactive educational packages to support self-treatment [24].

Research waste and long-standing uncertainty is not unique to TENS

Our analysis of published research on TENS revealed research waste and long-standing uncertainty about analgesic efficacy, something that is common for non-pharmacological agents. For example, NICE guidelines for management of non-specific low back recommended acupuncture in 2009 but reversed this decision in updated guidelines in 2016 [16, 25]. Yet, in 2021 the NICE recommended acupuncture for the management of chronic primary pain in which non-specific low back is a sub-category [15]. The quantity and quality of RCT evidence depends on the priorities of research funders, both from public and private sectors, and this determines whether an evidence base is sufficiently robust. We advocate a shift in language used by guideline panels from 'insufficient evidence of benefit' to 'insufficient evidence to judge'.

Uncertainty and low quality RCT evidence extends to pharmacological interventions. Recently, Moore et al. stated "Frequent and clear warnings over the past 30 yr appeared to have been ignored. Clinical research in pain and anaesthesia has yet fully to address the major problems of research quality, research waste, and research integrity that threaten scientific and clinical advances" [26] . In 2015, the editor of the Lancet stated "*much of the scientific literature, perhaps half, may simply be untrue*" [27] ,also cited in [26]. Recent books which include the illusion of

evidence based medicine and *science fictions: exposing fraud, bias, negligence and hype in science* reflect this crisis in confidence [28, 29].

Pain is a subjective phenomenon that sits uncomfortably in the objective world of biomedical research. Outcomes for pain are 'noisy' because they rely on the self-report of a complex, dynamic and multidimensional sensory, affective and cognitive experience. The illusion of objectivity is created by collapsing the self-report of this complex experience into individual attributes that are then quantified and statistically analysed. Subjective pain experience is susceptible to socio-ecological (contextual) factors in the past, present (moment-to-moment), and anticipated future. This is one of many confounders to the precision and stability of data used in statistical analysis. Perhaps we should not be surprised of inconsistent findings, inconclusive evidence, and long-standing uncertainty about the efficacy of interventions to alleviate pain.

Summary and Conclusion

It will be fascinating to see whether our meta-analysis resolves long-standing uncertainty about the clinical efficacy of TENS. We believe it should. However, we will not be surprised if it does not, because the aspiration is for high-certainty evidence, resulting in a perpetual efficacy-impasse. Perhaps we should concede that moderate-certainty evidence may be the best we can achieve, and start to pay more attention to the insidious forces motivating the publication of research that is 'flawed, futile and fabricated' [26].

References

1. Johnson MI, Jones G. Transcutaneous electrical nerve stimulation: current status of evidence. *Pain Manag* 7(1), 1-4 (2017).
2. Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults: a systematic review and meta-analysis of 381 studies (the meta-TENS study). *BMJ Open* 12(2), e051073 (2022).
3. Johnson M. *Transcutaneous electrical nerve stimulation (TENS). Research to support clinical practice*. Oxford University Press Oxford, UK. (2014).
4. Long DM. Cutaneous afferent stimulation for relief of chronic pain. *Clinical Neurosurgery* 21, 257-268 (1974).
5. Carroll D, Moore RA, Mcquay HJ, Fairman F, Tramer M, Leijon G. Transcutaneous electrical nerve stimulation (TENS) for chronic pain. *Cochrane Database Syst Rev* (3), CD003222 (2001).
6. Gibson W, Wand BM, Meads C, Catley MJ, O'connell NE. Transcutaneous electrical nerve stimulation (TENS) for chronic pain - an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2 CD011890 (2019).
7. Carroll D, Tramer M, Mcquay H, Nye B, Moore A. Randomization is important in studies with pain outcomes: systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. *British journal of anaesthesia* 77(6), 798-803 (1996).
8. Bjordal JM, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur J Pain* 7(2), 181-188 (2003).
9. Walsh DM, Howe TE, Johnson MI, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database Syst Rev* (2), CD006142 (2009).
10. Johnson MI, Paley CA, Howe TE, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database Syst Rev* 6 CD006142 (2015).
11. Paley CA, Wittkopf PG, Jones G, Johnson MI. Does TENS Reduce the Intensity of Acute and Chronic Pain? A Comprehensive Appraisal of the Characteristics and Outcomes of 169 Reviews and 49 Meta-Analyses. *Medicina (Kaunas)* 57(10), (2021).

12. National Institute for Health and Clinical Excellence. NICE clinical guideline 59 Osteoarthritis: the care and management of osteoarthritis in adults. doi:www.nice.org.uk 1-22 (2008).
13. National Institute for Health and Care Excellence. Osteoarthritis: care and management. NICE guidelines [CG177] doi:www.nice.org.uk 1-37 (2014).
14. National Institute for Health and Care Excellence. Osteoarthritis in over 16s: diagnosis and management. NICE guideline [NG226]. (2022).
15. National Institute for Health and Care Excellence. Chronic Pain (Primary and Secondary) in over 16s: Assessment of all Chronic Pain and Management of Chronic Primary Pain (NG193). 1–36 (2021).
16. Low back pain and sciatica in over 16s: assessment and management. Clinical guideline [NG59] https://www.nice.org.uk/guidance/ng59
17. National Institute for Health and Clinical Excellence. NICE clinical guideline 55 Intrapartum care: care of healthy women and their babies during childbirth. doi:www.nice.org.uk 1-65 (2007).
18. Rheumatoid Arthritis in Adults www.nice.org.uk/NG100 (17/10/2019).
19. Johnson MI. Resolving Long-Standing Uncertainty about the Clinical Efficacy of Transcutaneous Electrical Nerve Stimulation (TENS) to Relieve Pain: A Comprehensive Review of Factors Influencing Outcome. *Medicina (Kaunas, Lithuania)* 57(4), (2021).
20. Bennett MI, Hughes N, Johnson MI. Methodological quality in randomised controlled trials of transcutaneous electric nerve stimulation for pain: low fidelity may explain negative findings. *Pain* 152(6), 1226-1232 (2011).
21. Pivec R, Minshall ME, Mistry JB, Chughtai M, Elmallah RK, Mont MA. Decreased Opioid Utilization and Cost at One Year in Chronic Low Back Pain Patients Treated with Transcutaneous Electric Nerve Stimulation (TENS). *Surg Technol Int* 27 268-274 (2015).
22. Pivec R, Stokes M, Chitnis AS, Paulino CB, Harwin SF, Mont MA. Clinical and economic impact of TENS in patients with chronic low back pain: analysis of a nationwide database. *Orthopedics* 36(12), 922-928 (2013).
23. Woods B, Manca A, Weatherly H *et al*. Cost-effectiveness of adjunct non-pharmacological interventions for osteoarthritis of the knee. *PLoS One* 12(3), e0172749 (2017).
24. Gladwell PW, Cramp F, Palmer S. Foundational Research Could Improve Future Transcutaneous Electrical Nerve Stimulation Evaluations. *Medicina (Kaunas)* 58(2), (2022).
25. Low back pain in adults: early management https://www.nice.org.uk/guidance/cg88 (25/06/2019).
26. Moore A, Fisher E, Eccleston C. Flawed, futile, and fabricated-features that limit confidence in clinical research in pain and anaesthesia: a narrative review. *British journal of anaesthesia* doi:10.1016/j.bja.2022.09.030 (2022).
27. Horton R. Offline: What is medicine's 5 sigma? *The Lancet* 385 1380 (2015).
28. Jureidini J, Mchenry LB. *The illusion of evidence based medicine: Exposing the crisis of credibility in clinical researc.* Wakefield Press, Mile End, South Australia. (2020).
29. Ritchie S. *Science Fictions: Exposing Fraud, Bias, Negligence and Hype in Science*. Vintage, London. (2020).