# Meta-analysis of the Efficacy of Magnetic Stimulation for Female Stress Urinary Incontinence

Kai Sun<sup>1</sup>, Gang Wu<sup>1</sup>, Jipeng Wang<sup>1</sup>, Tianqi Wang<sup>1</sup>, Dongxu Zhang<sup>1</sup>, Yuanshan Cui<sup>1</sup>, and Jitao Wu<sup>1</sup>

<sup>1</sup>Affiliation not available

July 20, 2020

#### Abstract

ABSTRACT Objective: Female stress urinary incontinence is one of the common diseases in menopausal women, which brings great inconvenience to life. We conducted a meta-analysis to evaluate the efficacy of magnetic stimulation (MS) in treating female stress urinary incontinence (SUI). Methods: The electronic databases (E-DB) MEDLINE, EMBASE and Cochrane Controlled Trial Registry system was used to retrieve the randomized controlled trials (RCTs) which recorded MS as a remedy to female SUI. Reference lists of related papers were carefully studied. Results: Six RCTs exploring the effect of MS in the treatment of female SUI were studied. We found that the MS group enjoyed a higher quality of life (QoL) (MD of 0.59, 95% CI of 0.23 to 0.95, P=0.001) and lower International Consultation on Incontinence Questionnaire (ICIQ) scores (MD of -3.93, 95% CI of -5.86 to -2.01, P<0.0001) and provided a higher objective cure rate (odds ratio [OR] of 8.49, 95% CI of 3.08 to 23.37) compared with the placebo group. Apart from this, MS treatment reduced the number of episodes of urinary incontinence (MD of -1.42, 95% CI of -2.24 to -0.59, P=0.0007) and urine loss on pad test (MD of -4.67 and 95% CI of -8.05 to -1.28, P=0.007). No significant treatment-related adverse reactions were reported. Conclusion: MS treatment showed a positive effect in the treatment of SUI and further trials are required to specify the best protocol to optimize the effect.

## Meta-analysis of the Efficacy of Magnetic Stimulation for Female Stress Urinary Incontinence

## ABSTRACT

**Objective:**Female stress urinary incontinence is one of the common diseases in menopausal women, which brings great inconvenience to life. We conducted a meta-analysis to evaluate the efficacy of magnetic stimulation (MS) in treating female stress urinary incontinence (SUI).

**Methods:** The electronic databases (E-DB) MEDLINE, EMBASE and Cochrane Controlled Trial Registry system was used to retrieve the randomized controlled trials (RCTs) which recorded MS as a remedy to female SUI. Reference lists of related papers were carefully studied.

**Results:** Six RCTs exploring the effect of MS in the treatment of female SUI were studied. We found that the MS group enjoyed a higher quality of life (QoL) (MD of 0.59, 95% CI of 0.23 to 0.95, P=0.001) and lower International Consultation on Incontinence Questionnaire (ICIQ) scores (MD of -3.93, 95% CI of -5.86 to -2.01, P<0.0001) and provided a higher objective cure rate (odds ratio [OR] of 8.49, 95% CI of 3.08 to 23.37) compared with the placebo group. Apart from this, MS treatment reduced the number of episodes of urinary incontinence (MD of -1.42, 95% CI of -2.24 to -0.59, P=0.0007) and urine loss on pad test (MD of -4.67 and 95% CI of -8.05 to -1.28, P=0.007). No significant treatment-related adverse reactions were reported.

**Conclusion:** MS treatment showed a positive effect in the treatment of SUI and further trials are required to specify the best protocol to optimize the effect.

Keywords: Stress urinary incontinence, Meta-analysis, Randomized controlled trials, Magnetic stimulation

## INTRODUCTION

Urinary incontinence (UI), thought as urinate involuntarily by the International Continence Society (ICS) and International Urogynecological Association, is a common, chronic and distressing circumstance which lessens quality of life (QoL), somewhat alike to some grievous chronic diseases<sup>1-3</sup>. (Horng, Huang et al. 2013)Three main types of UI were identified by Standardization Steering Committee and one of the most common is SUI<sup>4</sup>. Though the incidence varies from place to place, it is generally increasing year by year, which brings significant negative impact on families and great burdens to the society<sup>5,6</sup>.

Conservative treatment and surgical treatment are the main treatment methods. Burch and urethral sling procedures are regarded as primary surgical procedure with high cure rate of 70% to 90%<sup>7</sup>. Nevertheless, owing to complications caused by the invasive procedures, such as pelvic pain and difficulty urinating, surgeries are increasingly not accepted by patients. On the basis of the 2017 European Association of Urology guidelines on the therapy of UI, pelvic floor muscle training (PFMT), bladder training (BT), electrical stimulation (ES) and magnetic stimulation (MS) are available for SUI<sup>8</sup>. PFMT has been nominated as the initial therapy of choice for SUI by AUA and SUFU, and has reported to be meaningful in previous randomized controlled trials<sup>9-12</sup>. Although it has been reported that the improvement of SUI after PFMT ranges from 50% to 70%, the cure rate of SUI is not exceeding 15%-30% mainly because of poor compliance<sup>13,14</sup>. It is said that ES does have success ratio of 48% to 70%, which is thought to be a replacement therapy<sup>15</sup>. The employ of this conservative therapy, however, has been restricted, given the discomfort or pain caused by high intensity percutaneous currents<sup>16-20</sup>. The United States Food and Drug Administration has ratified MS as an original method to SUI since 1998<sup>21</sup>. From then on, MS has captured great attention for recognized security, automatic contraction, no malaise from probe insertion and facilitation to administer.

There are certain clinical trials on the employ of MS to ameliorate female SUI, and the results are positive. Two meta-analyses<sup>22,23</sup> and one systematic review<sup>21</sup> both mentioned the effect of MS on the treatment of SUI, but they had some deficiencies in the number of included RCTs, the analysis of outcome indicators, and the treatment mechanism of MS. In addition, if the only source of literature search is limited to the English could potentially miss a lot of researches. Females are more prone to SUI due to special reasons such as childbirth, and the study subjects in the published RCTs are also women. Therefore, we intended to conduct a meta-analysis to more fully assess the impact of MS on SUI in women.

## MATERIALS AND METHONDS

#### 2.1 Search strategy

The methodology for this meta-analysis was performed in accordance with the preferred reporting items of the system review and meta-analysis (PRISMA) list<sup>24</sup>. Two authors did their best to conduct all RCTs independently published until March 1, 2020, regarding the association between SUI and MS. Designed to determine appropriate trials, the dominating search was processed in the E-DB MEDLINE, EMBASE, and the Cochrane Controlled Trials Register, using various combinations of Medical Subject Headings (MeSH) terms. The search terms that we used were "magnetic stimulation", "stress urinary incontinence" and "RCTs". Repeated studies were excluded. Third person evaluated any disputes. No language restriction system review process applied.

## 2.2 Inclusion criteria and trial selection

If RCT lived up to the following criterion, it would be absorbed: (1) Evaluation of the curative effect of therapy of female SUI in a patient: the activity of MS and MS false; (2) Text involving full content and relevant data was capable of being acquired; (3) The data deserving research are authentic, chiefly incorporating the sum of subjects and the meritorious consequences of each index. Provided the same outcomes were issued in various magazines or at diverse times, the updated research results would be absorbed in this meta-analysis. Considering the identical body of researchers looked into one subject group in numerous experiments, each study would be absorbed. Selection and elimination PRISMA flowchart is presented in Fig 1.

## 2.3 Quality assessment

Use the Jadad score and the Cochrane bias risk assessment tool to evaluate the methodological quality of all RCTs<sup>25,26</sup>. Not only generation of randomization sequences but also incomplete outcome data were involved in the quality standards. It also involves blinding, allocation concealment, along with freedom from selective reporting and other biases. The results of assessment were presented in Table 1.

#### 2.4 Data extraction

Two reviewers used predefined data extraction forms to extract data independently. Any disagreement was resolved by the senior author trial. The data include the following contents: (a) year of publication, first author's name, and motherland; (b) remedy that subjects got access to; (c) therapy plan; (d) results of SUI; (e) duration of follow up; (f) capacity of sample. These data had clinico-implications for making a measurable effectiveness on participants. Our research need not ethical consent.

## 2.5 Statistical analysis

Review Manager version 5.3.0 (Cochrane Collaboration, Oxford, UK) was appropriate for computing the data. Fixed or random effect models were suitable for appraising indicators. We applied mean difference (MD) to interpret continuous data. Odds ratio (OR) for dichotomous outcomes coupling with 95% CI<sup>27</sup>. Given the result showed P value was greater than .05, the study was thought to be homogeneous. And fixed effect model was applied to assess the data. The effect of heterogeneity on the results of meta-analysis is evaluated by I-square (I<sup>2</sup>) test. Provided the results where the I<sup>2</sup> value was greater than 50%, random effect model would be used. Sensitivity analysis or subgroup analysis were used flexibly to analyze the sources of heterogeneity. In case of the P value was < .05, results were reputed statistically significant.

#### RESULTS

## 3.1 Characteristics of the trials

In line with inclusion and exclusion criteria, 352 articles were found. 89 articles were excluded by going over all abstracts and titles. In the absence of available data, 25 articles were excluded of the remaining 32 articles. Two reviewers separately rated the absolute papers and selected in accordance with the criteria. Finally, seven articles containing six RCTs were included in our study to analyze the efficacy of MS in female patients with SUI for two articles shared the same study population<sup>28-34</sup>. The characteristics of the studies are rendered in Table 1. The risk of bias graph and summary are elucidated in Fig. 2.

#### 3.2 QoL scores

QoL scores were supplied by six articles enrolling 336 participators (174 in MS group and 162 in sham group). Using random effect model to evaluate these RCT, but I<sup>2</sup> test implied heterogeneity (Fig. 3a). We have made it clear through a succeeding influence detection that the study carried out by Lim, et al.<sup>31</sup> had the greatest effect. Removing this study and using fixed effect model remarkably reduced the I<sup>2</sup> to 39%. The MD was 0.59 while the 95% CI was 0.23 to 0.95 (P=0.001) (Fig. 3b), and the data were still statistically significant. We performed a subgroup analysis of the location of magnetic stimulation to understand the impact on QoL scores, showing the MD was 0.59 while the 95% CI was 0.15 to 5.25 (P=0.04) in pelvic floor (Fig. 3c).

## 3.3 Pad test

Five RCTs with a sample of 197 participators (107 in MS group and 90 in sham group) had data on pad test. Statistical heterogeneity was not satisfactory,  $I^2$  of 47% (P=0.42) (Fig. 4a). Considering the high heterogeneity between studies, sensitivity analysis was carried out. Manganotti, et al.<sup>28</sup> was the only cross-sectional trails removed through it. After omission of the study, it showed MD of -4.67 and 95%CI of -8.05 to -1.28 (P=0.007), and no heterogeneity (Fig. 4b).

## 3.4 Leaks

Three articles containing 127 patients (72 in MS group and 55 in sham group) devoted to the effectiveness of MS on female SUI in the sum of leaks/a week through a voiding diary. Fixed effect model was selected for analysis. Compared with the sham group, the MS group had a valid decline (MD of -1.42; 95% CI of -2.24 to -0.59; P=0.0007), and there was no heterogeneity (Fig. 4c).

#### 3.5 ICIQ scores

The pooled RCTs involving 185 patients (101 in MS group and 84 in sham group) had data on ICIQ scores. Fixed effect model was introduced to rate these RCTs, the MD was -3.93 and 95% CI was -5.86 to -2.01 (P< 0.0001) (Fig. 4d).

#### 3.6 Objective cure rate

The pooled RCTs containing data for objective cure (leakage less than 1gram on the 1-hour pad test) rate were aimed to evaluate the improvement in incontinence symptoms. Patients treated with MS have a higher objective cure rate when evaluated using the pad test (odds ratio [OR] of 8.49; 95% CI of 3.08 to 23.37; P<0.0001) (Fig. 4e).

## DISCUSSION

Despite the small sample sizes and the majority of the test non-uniform treatment regimens, when compared to the sham group, pooled analysis of the data showed that women with SUI combined with MS treatment were superior to women without MS treatment in terms of overall effectiveness.

QoL scores, as the most popular used indicator to evaluate the treatment of female SUI, has been improved greatly in the MS group compared with the sham group in this meta-analysis. All of the articles we included assessed the QoL and the results were encouraging. A research did by Hoşcan et al.<sup>35</sup> concluded that the mean score in QoL was increased from 61.6 to 75.4 after MS (p = 0.003). Lo et al.<sup>36</sup> used the Urge-Urinary Distress Inventory (U-UDI) to measure QoL and observed an improvement in the total UDI-6 scores. The King's Health Questionnaire (KHQ) is also popular with researchers to compute QoL<sup>37</sup>. Voorham et al.<sup>38</sup>confirmed progress in the 'role limitations' domain of the KHQ. To sum up, no matter which questionnaire is used to evaluate QoL, the results tend to be positive. ICIQ score is another questionnaire highly recommended by the 6th ICI and more and more recognized and used by scholars<sup>39</sup>. As more and more in-depth and precise experiments are carried out, more meaningful data will emerge, which will enhance our judgment on the efficacy of MS.

Though Gilling et al.<sup>33</sup> and Yamanishi et al.<sup>30</sup> did not report effective results and the result concluded by Manganotti et al.<sup>28</sup> showed high heterogeneity, the pooled data reported a huge improvement in urine loss on pad test. One paper covered deteriorative outcomes in 35.5% of SUI women based on pad tests<sup>40</sup>. However, that study lacked motivation and possessed a dropout rate of 35.4%. Another study concluded that 24-hour pad test had no advantage in predicting the conditions of prognosis of SUI<sup>41</sup>. On the contrary, the good news came from Hoşcan et al.<sup>35</sup> that they found pad weight was reduced from  $14.4\pm10.7$  to  $6.5\pm5.1$  grams at 3 months in MS group. Pad test has many detection schemes which may lead to deviation of measurement results. Pad test performance is described thoroughly in the literature, and it is usually the researchers that do not comply the rules, which inspires us to follow the rules more strictly to get more accurate results.

The frequency of incontinence is a vital objective indicator to assess the ability of the MS treatment. Although our meta-analysis included only three RCT, the pooled data concluded that the reduction in frequency of SUI was statistically significance. Galloway et al.<sup>42</sup> found a significant reduction in leakage events, which is the same as our results and proves the effectiveness of MS.

It is reported that a large proportion of patients with moderate and below SUI are mostly manifested as external urethral sphincter (EUS) and pelvic floor muscle weakness<sup>43</sup>. EUS, which has complete neuromuscular innervation, answers to movement by boosting its bulk and strength<sup>44</sup>. Eddy currents can be induced by transcutaneous magnetic stimulation (MS) in the pelvis and flow into tissues, which can depolarize axons.

Given it was a peripheral motor nerve axon, the impulse to spread would pass to the motor endplate, causing the mandatory release of acetylcholine. The homologous muscle fibers would depolarize and contract<sup>42,45</sup>. MS may modify the activity in pelvic floor muscle groups, as well as the discharge pattern and frequency of the motor nerve fibers responsible for the resting tension of the pelvic floor and sphincter. MS leads to a significant increase in bladder volume, which may be due to the acute activation of the inhibitory detrusor reflex pathway after stimulation of the pudendal afferent nerve. Both Fujishiro et al.<sup>34</sup> and Tsai et al.<sup>32</sup> noticed changes in bladder volume and maximum urethral closure pressure after MS treatment. The bladder capacity in MS group was significantly higher than that in sham operation group. Determination of maximum urethral closure pressure, however, didn't draw a same conclusion. It was found that the maximum urethral closure pressure did not increase obviously by Fujishiro et al.<sup>34</sup> but Tsai et al.<sup>32</sup> concluded that it did. This may have something to do with the two sides' different methods of measurement.

The thing really troubles us is the low level of standardization of MS protocol. Different studies used different stimulus intensities, frequencies, locations and durations. Until now, the optimal frequency and duration of the pulse have always been controversial. It is reported that frequencies of 20–50 Hz are effective for SUI and good pelvic floor contraction in the treatment of SUI need a higher dose of 50  $Hz^{46,47}$ . As a result, the treatment may not be as effective as expected in three RCTs using stimuli at frequencies ranging from 5 to 15 Hz. A subgroup analysis of QoL scores was conducted for the two different stimulation sites of sacral roots and pelvic floor, and the results showed little difference between the two groups, which could conclude preliminarily that the stimulation site might affect the therapeutic effect and the pelvic floor may enjoy a better reaction. However, there is no valid report on the effect of differentiating the stimulus sites so far, which is deserved to explore further. This also suggests that it is worth exploring whether the outcome indicators can be improved by stimulating other parts apart from sacral roots and pelvic floor. The duration of treatment and follow up varies from study to study, which inevitably led to differences in outcomes. Galloway et al.<sup>48</sup> concluded that active MS of the pelvic floor twice a week for six weeks dramatically improved SUI, which remained effective after three months. Previous researches have reported that the benefits of MS have worsened over time<sup>42,48,49</sup>, perhaps because of the treatment regimen. And if we want to improve the effective rate of MS treatment and promote MS in clinical treatment widely, an appropriate MS protocol needs to be developed.

We calculated the objective cure rate and the results showed that patients who received MS therapy possessed a higher objective cure rate. A study once pointed out that the cure rate and improvement rate after EMS treatment were not much better than that after PFMT treatment<sup>44</sup>. Hoscan et al.<sup>35</sup> asserted 29.7% cure rate. And after 3 months, 48.1% improvement rate, as well as an extraordinary improvement in QoL. Suzuki et al.<sup>50</sup> found a cure rate of 20% in the MS group after the active treatment. But the results cannot be used to disparage MS treatment for the patients were all non-responders to PFMT or to drug therapy. The potential explanation is that active contractions produced by PFMT exercise muscle strength better than passive contraction induced by MS. Moreover, since MS has not yet explored an appropriate treatment system, the therapeutic effect cannot reach the best.

In articles not included in this meta-analysis, only one reported side effects including lower limbs, abdominal and back pain, etc. But they were not serious and life-threatening<sup>40</sup>. Less side effects of MS were obtained in the included articles, suggesting that it is relatively safe and tolerable.

However, some of the limitations in our meta-analysis should be recognized. We note that the quality of these studies is flawed, basically in terms of study design, patient selection, blinding, publication bias, and outcome data. Our results are based on unadjusted estimates; more accurate results will come from adjustments to other confounders, such as gender, body mass index, lifestyle, age, etc. So, an ocean of RCTs including abundant sample size and statistics are needed to validate our findings. Additional superb RCTs with matching data should apply to further indagations for the purpose of ascertaining the virtue and defect of MS in treating female SUI.

## CONCLUSION

In conclusion, our meta-analysis, MS may be beneficial for management of female SUI. The encouraging improvement of indicators implied that MS is a breathtaking and hopeful nonsurgical alternative for sufferers who do not eager to surgery. And more trials are needed to determine the appropriate protocol to optimize the therapeutic effect.

## AUTHORS' CONTRIBUTIONS

KS and GW were responsible for designing the research, analyzing the extractable data and writing the first draft. JPW, TQW and DXZ was responsible for searching the literature, extracting and analyzing the data. JTW was in charge of analyzing data, reviewing the manuscript and providing critical scientific input. YSC was responsible for resolving discrepancies about the quality of the included studies and providing critical scientific input. All authors made contribution to this article and confirmed the final version.

# CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## REFERENCE

1. Bo K, Frawley HC, Haylen BT, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for the conservative and nonpharmacological management of female pelvic floor dysfunction. *Neurourol Urodyn*.2017;36(2):221-244.

2. Horng SS, Huang N, Wu SI, Fang YT, Chou YJ, Chou P. The epidemiology of urinary incontinence and it's influence on quality of life in Taiwanese middle-aged women. *Neurourol Urodyn*.2013;32(4):371-376.

3. Shulz SE, Kopec JA. Impact of chronic conditions. *Health Rep.*2003;14(4):41.

4. Health NCCFWSS. Urinary Incontinence in Women: The Management of Urinary Incontinence in Women. London; Royal College of Obstetricians and Gynaecologists (UK). 2013;60(8):906-911.

5. Irwin DE, Mungapen L, Milsom I, Kopp Z, Reeves P, Kelleher C. The economic impact of overactive bladder syndrome in six Western countries. *BJU Int.* 2009;103(2):202-209.

6. Subak LL, Goode PS, Brubaker L, et al. Urinary incontinence management costs are reduced following Burch or sling surgery for stress incontinence. Am J Obstet Gynecol. 2014;211(2):171 e171-177.

7. Bergman A, Koonings PP, Ballard CA. Primary stress urinary incontinence and pelvic relaxation: prospective randomized comparison of three different operations. Am J Obstet Gynecol. 1989; 161(1): 97-101.

8. Lucas MG, Bosch RJ, Burkhard FC, et al. [European Association of Urology guidelines on assessment and nonsurgical management of urinary incontinence]. Actas Urol Esp. 2013;37(4):199-213.

9. Bo K, Talseth T, Holme I. Single blind, randomised controlled trial of pelvic floor exercises, electrical stimulation, vaginal cones, and no treatment in management of genuine stress incontinence in women. *BMJ*. 1999;318(7182):487-493.

10. Felicissimo MF, Carneiro MM, Saleme CS, Pinto RZ, da Fonseca AM, da Silva-Filho AL. Intensive supervised versus unsupervised pelvic floor muscle training for the treatment of stress urinary incontinence: a randomized comparative trial. *Int Urogynecol J.*2010;21(7):835-840.

11. Gormley EA, Lightner DJ, Faraday M, Vasavada SP, American Urological A, Society of Urodynamics FPM. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol.* 2015;193(5):1572-1580.

12. Takahashi S, Takei M, Nishizawa O, et al. Clinical Guideline for Female Lower Urinary Tract Symptoms. Low Urin Tract Symptoms.2016;8(1):5-29.

13. Elia G, Bergman A. Pelvic muscle exercises: when do they work? Obstet Gynecol. 1993;81(2):283-286.

14. Klarskov P, Belving D, Bischoff N, et al. Pelvic floor exercise versus surgery for female urinary stress incontinence. *Urol Int*.1986;41(2):129-132.

15. Miller K, Richardson DA, Siegel SW, Karram MM, Blackwood NB, Sand PK. Pelvic floor electrical stimulation for genuine stress incontinence: who will benefit and when? *Int Urogynecol J Pelvic Floor Dysfunct*. 1998;9(5):265-270.

16. Yokoyama T, Nishiguchi J, Watanabe T, et al. Comparative study of effects of extracorporeal magnetic innervation versus electrical stimulation for urinary incontinence after radical prostatectomy. *Urology*. 2004;63(2):264-267.

17. Correia GN, Pereira VS, Hirakawa HS, Driusso P. Effects of surface and intravaginal electrical stimulation in the treatment of women with stress urinary incontinence: randomized controlled trial. *Eur J Obstet Gynecol Reprod Biol.* 2014;173:113-118.

18. Wang S, Lv J, Feng X, Lv T. Efficacy of Electrical Pudendal Nerve Stimulation versus Transvaginal Electrical Stimulation in Treating Female Idiopathic Urgency Urinary Incontinence. *J Urol*.2017;197(6):1496-1501.

19. Yamanishi T, Kaga K, Fuse M, Shibata C, Uchiyama T. Neuromodulation for the Treatment of Lower Urinary Tract Symptoms. Low Urin Tract Symptoms. 2015;7(3):121-132.

20. Yamanishi T, Kamai T, Yoshida K. Neuromodulation for the treatment of urinary incontinence. Int J Urol. 2008;15(8):665-672.

21. Lim R, Lee SW, Tan PY, Liong ML, Yuen KH. Efficacy of electromagnetic therapy for urinary incontinence: A systematic review. *Neurourol Urodyn.* 2015;34(8):713-722.

22. He Q, Xiao K, Peng L, et al. An Effective Meta-analysis of Magnetic Stimulation Therapy for Urinary Incontinence. *Sci Rep.*2019;9(1):9077.

23. Peng L, Zeng X, Shen H, Luo DY. Magnetic stimulation for female patients with stress urinary incontinence, a meta-analysis of studies with short-term follow-up. *Medicine (Baltimore)*.2019;98(19):e15572.

24. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-1012.

25. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials.* 1996;17(1):1-12.

26. Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev.*2019;10:ED000142.

27. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-188.

28. Manganotti P, Zaina F, Vedovi E, et al. Repetitive magnetic stimulation of the sacral roots for the treatment of stress incontinence: a brief report. *Eura Medicophys*.2007;43(3):339-344.

29. Lim R, Liong ML, Leong WS, Karim Khan NA, Yuen KH. Pulsed Magnetic Stimulation for Stress Urinary Incontinence: 1-Year Followup Results. *J Urol.* 2017;197(5):1302-1308.

30. Yamanishi T, Suzuki T, Sato R, Kaga K, Kaga M, Fuse M. Effects of magnetic stimulation on urodynamic stress incontinence refractory to pelvic floor muscle training in a randomized sham-controlled study. *Low Urin Tract Symptoms.* 2019;11(1):61-65.

31. Lim R, Liong ML, Leong WS, Khan NAK, Yuen KH. Effect of pulsed magnetic stimulation on quality of life of female patients with stress urinary incontinence: an IDEAL-D stage 2b study. *Int Urogynecol J.* 2018;29(4):547-554.

32. Tsai PY, Wang CP, Hsieh CY, Tsai YA, Yeh SC, Chuang TY. Long-term sacral magnetic stimulation for refractory stress urinary incontinence. Arch Phys Med Rehabil. 2014;95(12):2231-2238.

33. Gilling PJ, Wilson LC, Westenberg AM, et al. A double-blind randomized controlled trial of electromagnetic stimulation of the pelvic floor vs sham therapy in the treatment of women with stress urinary incontinence. *BJU Int.* 2009;103(10):1386-1390.

34. Fujishiro T, Enomoto H, Ugawa Y, Takahashi S, Ueno S, Kitamura T. Magnetic stimulation of the sacral roots for the treatment of stress incontinence: an investigational study and placebo controlled trial. *J Urol.* 2000;164(4):1277-1279.

35. Hoscan MB, Dilmen C, Perk H, et al. Extracorporeal magnetic innervation for the treatment of stress urinary incontinence: results of two-year follow-up. *Urol Int.* 2008;81(2):167-172.

36. Lo TS, Tseng LH, Lin YH, Liang CC, Lu CY, Pue LB. Effect of extracorporeal magnetic energy stimulation on bothersome lower urinary tract symptoms and quality of life in female patients with stress urinary incontinence and overactive bladder. J Obstet Gynaecol Res. 2013;39(11):1526-1532.

37. Kelleher CJ, Cardozo LD, Khullar V, Salvatore S. A new questionnaire to assess the quality of life of urinary incontinent women. Br J Obstet Gynaecol. 1997;104(12):1374-1379.

38. Voorham-van der Zalm PJ, Pelger RC, Stiggelbout AM, Elzevier HW, Lycklama a Nijeholt GA. Effects of magnetic stimulation in the treatment of pelvic floor dysfunction. *BJU Int.* 2006;97(5):1035-1038.

39. Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. *Neurourol Urodyn.* 2004;23(4):322-330.

40. Ismail SI, Forward G, Bastin L, Wareham K, Emery SJ, Lucas M. Extracorporeal magnetic energy stimulation of pelvic floor muscles for urodynamic stress incontinence of urine in women. *J Obstet Gynaecol.* 2009;29(1):35-39.

41. Henderson JW, Kane SM, Mangel JM, et al. A Randomized Comparative Study Evaluating Various Cough Stress Tests and 24-Hour Pad Test with Urodynamics in the Diagnosis of Stress Urinary Incontinence. J Urol. 2018;199(6):1557-1564.

42. Galloway NT, El-Galley RE, Sand PK, Appell RA, Russell HW, Carlin SJ. Update on extracorporeal magnetic innervation (EXMI) therapy for stress urinary incontinence. *Urology*. 2000;56(6 Suppl 1):82-86.

43. Hunskaar S, Arnold EP, Burgio K, Diokno AC, Herzog AR, Mallett VT. Epidemiology and natural history of urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2000;11(5):301-319.

44. Fowler SB. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Clin Nurse Spec.* 2011;25(5):226-227.

45. Quek P. A critical review on magnetic stimulation: what is its role in the management of pelvic floor disorders? *Curr Opin Urol*.2005;15(4):231-235.

46. Janez J, Plevnik S, Suhel P. Urethral and bladder responses to anal electrical stimulation. J Urol. 1979;122(2):192-194.

47. Yamanishi T, Yasuda K, Suda S, Ishikawa N, Sakakibara R, Hattori T. Effect of functional continuous magnetic stimulation for urinary incontinence. *J Urol.* 2000;163(2):456-459.

48. Galloway NT, El-Galley RE, Sand PK, Appell RA, Russell HW, Carlan SJ. Extracorporeal magnetic innervation therapy for stress urinary incontinence. *Urology*. 1999;53(6):1108-1111.

49. Yokoyama T, Fujita O, Nishiguchi J, et al. Extracorporeal magnetic innervation treatment for urinary incontinence. Int J Urol.2004;11(8):602-606.

50. Suzuki T, Yasuda K, Yamanishi T, et al. Randomized, double-blind, sham-controlled evaluation of the effect of functional continuous magnetic stimulation in patients with urgency incontinence. *Neurourol Urodyn.* 2007;26(6):767-772.

## **Figure Legends**

Figure 1. Flowchart of the study selection process. RCT, randomized controlled trials.

Figure 2. (a) Risk of bias summary: review authors' judgements about each risk of bias item for each included study. (b) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Forest plot comparing the change in (a) the QoL scores, (b) the QoL scores after omitting study, (c) the QoL scores in the subgroup analysis of the location of magnetic stimulation between the active and sham groups.

Figure 4. Forest plot comparing the change in (a) the pad test, (b) the pad test after omitting study, (c) NO. of leaks, (d) the ICIQ scores, (e) the objective cure rate between the active and sham groups.

## Table

Table 1. The details of included studies. LUTS, lower urinary tract symptoms; SUI, stress urinary incontinence; QoL, quality of life; PFR, peak flow rate; PVR, post void residual; POP, pelvic organ prolapse; PFM, pelvic floor muscle; UPP, urethral pressure profile; U-UDI, Urge-Urinary Distress Inventory; OAB-q, Overactive Bladder Questionnaire; ICIQ, International Consultation on Incontinence Questionnaire; ICIQ-UI SF, ICIQ for Urinary Incontinence-Short Form; ICIQ-LUTSqol, ICIQ-Lower Urinary Tract Symptoms Quality of Life; UI, urinary incontinence; MS, magnetic stimulation; PMS, pulsed magnetic stimulation; PGI-I, Patient Global Impression of Improvement; NA, not available; PFMT, pelvic floor muscle training; ALPP, abdominal leak point pressure.



Yamanishi 2017 ه	Tsai 2014	Manganotti 2007	Lim 2017	Gilling 2009	Fujishiro 2000	
•	+	••	•	•	?	Random sequence generation (selection bias)
••	+	••	•	•	••	Allocation concealment (selection bias)
•	••		•	••		Blinding of participants and personnel (performance bias)
••	+	••	•	•	••	Blinding of outcome assessment (detection bias)
•	•	••	•	•	•	Incomplete outcome data (attrition bias)
•	••	•	•	••	•	Selective reporting (reporting bias)
						Other bias



0	MS		Sham		Mean Difference	Mean Difference
a Study or Subaroup	Mean SD	Total Mean	SD Tota	Weight	IV Fixed 95% CI	IV Fixed 95% CI
Euiishiro 2000	0.9 1.47	31 02	1 15 3	17 1%	0 70 [0 04 1 36]	
Gilling 2009	27 4 47	35 11	5.64 3	5 1.3%	1 60 [-0 78 3 98]	
Lim 2017	8 74 1 25	60 41	1.08 60	12 3%	4 64 [4 22 5 06]	
Manganotti 2007	0.14 1.23	10 03	0.55 10	24.3%	0 10 [-0.45, 0.65]	
Tani 2014	1 56 0.90	10 0.3	1.09 1.	10.24.370	1 12 [0.45, 0.05]	
Vemenieki 2017	1.00 0.09	20 0.44	1.20 14	12.3%	1.12 [0.34, 1.90]	
ramanishi 2017	1.00 3.23	16 0.25	1.30	2.0%	1.41 [-0.27, 3.09]	
Total (95% CI)		174	163	100.0%	2 30 [2 03 2 58]	•
Heterogeneity: Chi <sup>2</sup> =	214 55 df = 5	(P < 0.00001)	l <sup>2</sup> = 98%			
Test for overall effect	7 = 16.61 (P	< 0.00001)	- 5070			-4 -2 0 2 4
rescion overall effect	2 - 10.01 (1	< 0.00001)				Favours MS Favours Sham
h	MS		Sham		Mean Difference	Mean Difference
Study or Subgroup	Mean SD	Total Mean	SD Tota	Weight	IV. Fixed, 95% CI	IV. Fixed, 95% Cl
Eulishiro 2000	0.0 1 47	31 0.2	1 15 2	20.7%	0.70 0.04 1.201	
Cilling 2000	0.9 1.47	31 0.2	1.10 3	29.7%	1.60 [ 0.79, 2.09]	
Gilling 2009	2.7 4.47	35 1.1	0.64 3	2.3%	1.00 [-0.78, 3.98]	
wanganotti 2007	0.4 0.7	10 0.3	0.55 10	42.1%	0.10[-0.45, 0.65]	Γ
Tsal 2014	1.56 0.89	20 0.44	1.28 14	21.3%	1.12 [0.34, 1.90]	
Yamanishi 2017	1.66 3.23	18 0.25	1.36 12	4.6%	1.41 [-0.27, 3.09]	
Total (95% CI)		114	102	100.0%	0.59 [0.23, 0.95]	◆
Heterogeneity: Chi <sup>2</sup> =	6.54 df = 4 (F	$P = 0.16$ ): $I^2 = 39$	9%		-	
Test for overall effect	7 = 3.22 (P =	0.001)				-4 -2 0 2 4
	L 0.LL (/	0.001)				Favours MS Favours Sham
с	MS	S	ham		Mean Difference	Mean Difference
Study or Subgroup	Mean SD	Total Mean	SD Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI
2.1.1 sacral floor						
Euiishiro 2000	09 147	31 0.2	1 15 31	17.5%	0 70 [0 04 1 36]	
Manganotti 2007	04 07	10 0.3	0.55 10	17.6%	0 10 [-0 45 0 65]	+
Tsai 2014	1.56 0.89	20 0.44	1.28 14	17.3%	1 12 [0 34, 1 90]	
Subtotal (95% CI)	1.00 0.00	61	55	52.4%	0.59 [0.00, 1.18]	◆
Heterogeneity: Tau <sup>2</sup> =	0.16 Chi <sup>2</sup> = 4	81 df = 2 (P = )	$0.09$ ): $l^2 = 58$	%		
Test for overall effect:	7 = 1.98 (P = 1)	0.05)				
		,				
2.1.2 pelvic floor						
Gilling 2009	2.7 4.47	35 1.1	5.64 35	14.1%	1.60 [-0.78, 3.98]	
Lim 2017	8.74 1.25	60 4.1	1.08 60	17.7%	4.64 [4.22, 5.06]	-
Yamanishi 2017	1.66 3.23	18 0.25	1.36 12	15.8%	1.41 [-0.27, 3.09]	
Subtotal (95% CI)		113	107	47.6%	2.70 [0.15, 5.25]	
Heterogeneity: Tau <sup>2</sup> =	4.39; Chi <sup>2</sup> = 1	8.73, df = 2 (P <	0.0001); l <sup>2</sup> =	= 89%		
Test for overall effect:	Z = 2.07 (P =	0.04)				
Total (95% CI)		174	160	100.0%	1 60 [ 0 36 3 57]	
10tal (95% CI)		1/4	162	100.076	1.00 [-0.30, 3.57]	
Hetereesity T2-	E 60. Ohi2 - 0	14 EE # - E /D	< 0.000041	12 - 0.00/		
Heterogeneity: Tau <sup>2</sup> =	5.63; Chi <sup>2</sup> = 2	14.55, df = 5 (P	< 0.00001);	l² = 98%		-4 -2 0 2 4
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:	5.63; Chi <sup>2</sup> = 2 Z = 1.60 (P = 1	14.55, df = 5 (P 0.11)	< 0.00001);	l² = 98%		-4 -2 0 2 4 Favours MS Favours Sham



## Hosted file

Table 1 The details of included studies..doc available at https://authorea.com/users/344321/ articles/470896-meta-analysis-of-the-efficacy-of-magnetic-stimulation-for-female-stressurinary-incontinence