



## Literature Review

## PROGRESSIVE MUSCLE RELAXATION THERAPY TO RELIEVE DENTAL ANXIETY

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### Abstract

**Background:** Dental anxiety is complex phenomenon which is associated with the thought of visiting the dentist for therapeutic or care. It may be either physical, mental or social anxiety. The most common causes of anxiety in dental patients is fear of injections, fear of choking or gagging and fear of blood. It can be shown as fear, anxiety, phobia, stress, shivering, sweating, crying during or before dental treatment. Sympathetic nervous system is activated during dental anxiety and there is provoke of fight or flight response. This causes changes in various physiological activities such as reduction in pain threshold, increase in treatment complications, post-treatment pain, late healing. Identifying anxiety in dental patient is the first and foremost step in determining the type of treatment and schedule of appointments. Progressive muscle relaxation is one such technique a where muscles and body are allowed to relax after they are tensed.

**Materials and methods:** PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

**Results:** Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 73 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 34 articles were included for full text. This review aims at detailing progressive muscle relaxation technique, a non-pharmacological, economical approach to relieve dental anxiety.

**Keywords:** Dental Anxiety, Progressive muscle relaxation therapy, Non-Pharmacological

### INTRODUCTION

Dental anxiety is complex phenomenon which is associated with the thought of visiting the dentist for therapeutic or care. It may be either physical, mental or social anxiety. It can be shown as fear, anxiety, phobia, stress, shivering, sweating, crying during or before dental treatment.<sup>1</sup> This dental anxiety is shown to delay or cancel appointments and can even cause behavioral issues leading to stressful and unpleasant experience for practitioner and the patient. These consequences of dental anxiety can further cause pain, poor dental health complicating the treatment. The most common causes of anxiety in

dental patients is fear of injections, fear of choking or gagging and fear of blood.<sup>2</sup>

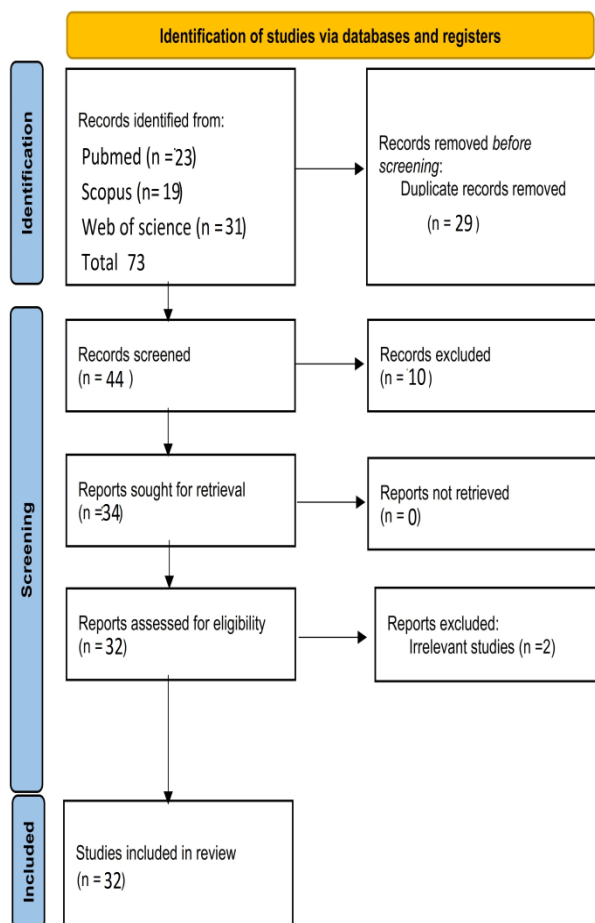
Agras et al in a study has found out that dental anxiety is one of the top ten causes of anxiety in general public.<sup>3</sup> A Canadian survey found out that 5.5 % of respondents were very afraid or terrified” of dental visits whereas 9.8% were somewhat afraid.<sup>4</sup> Studies have shown that dental anxiety in adult patients is 20 % with 5-7% having high anxiety. A study done by Santuchi et al has reported that patients with periodontal problems had higher dental anxiety due to their inflamed gingiva and bleeding gums.<sup>5</sup> As already mentioned earlier that etiology of dental anxiety is usually not single and is

multifactorial, no monotherapy for this anxiety is not promising.

Sympathetic nervous system is activated during dental anxiety and there is provoke of fight or flight response. This causes changes in various physiological activities such as reduction in pain threshold, increase in treatment complications, post-treatment pain, late healing. Evoking physical, emotional, behavioral and cognitive responses can make treatment more challenging and stressful to dentists.<sup>6</sup>

**Materials and methods:** PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

**Results:** Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 73 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 34 articles were included for full text (fig.1).



**Figure 1.** Prisma flow chart

This review aims at detailing progressive muscle relaxation technique, a non-pharmacological, economical approach to relieve dental anxiety.

**Types of dental anxiety**

Four types of dental anxiety have been identified and is shown below in table format. Please have a look.<sup>7</sup>

**Table 1. Types of dental anxiety and management strategies**

SNO	Type of dental anxiety	Characteristics
1.	Fearful of specific stimuli	These can be easily identified and the stimuli include injections, pain associated with dental treatment, sound, smell or sight of drill/ handpiece. Management includes, relaxation strategies and gradual systematic desensitization.
2.	Fearful of medical catastrophe	These individuals are afraid that treatment may cause medical emergency. They complain of allergy due to latex or anesthesia, shortness of breath, palpitations etc. management includes medical history, gradual exposure to dental treatment etc.
3.	Generalized dental anxiety	These individuals have generalized anxiety and its difficult to identify one aspect. Relaxation strategies can help and gradual exposure can also help the patient to gain a sense of mastery.
4.	Distrustful of dental personnel	They complain that the treatment procedure was not under their control i.e., the dentist just pulled out a tooth without his/her notice. These patients should be clearly explained before starting a procedure.

The major disadvantage of dental anxiety is it affects proper dental treatment by delaying the appointments and increased pain after treatment causing delay in recovery. This anxiety is associated with avoidance of dental care and oral health, postponement of dental treatment leading to mental anxiety and decreased quality of life.<sup>8</sup>

Therefore, to improve the quality of life and provide a better dental treatment with lesser appointments, reducing anxiety during dental procedures is a must. This requires proper evaluation by identifying the source and level of anxiety.<sup>9</sup> Anxiety can be triggered

by clinic ambience, interaction with receptionist and even while scheduling the appointments. Anxiety in a dental patient can be identified by psychophysiological responses such as muscle tightness, restlessness, clearing the throat, stiff posture, holding things tightly, hands unsteady, sweating of palms, forehead, frequent urination etc. In children, behavioral and emotional responses include panicky, hyperactivity, nervousness, sitting on the edge of the chair, leaning forward, inattentiveness, excessive worrying, poor memory, getting tongue tangled etc. Once a dentist or clinician identifies these responses, he/she should attempt to reduce the anxiety by anxiolysis, later start the treatment.<sup>10</sup>

Anxiolysis is a procedure which helps in decreasing the anxiety by different techniques either pharmacological or non-pharmacological. American dental association has made it mandatory to use anxiolytic methods in patients with dental anxiety. During ancient times, plants such as papaver and somniferum were used to reduce anxiety. Other methods included incubation which is physiological healing process through sleep. To induce sedation and anesthesia, ancients used Aleppo sponge which is a combination of mandragora, cannabis, hyoscyams, opium, black night shade.<sup>11</sup>

Now a days, pharmacological methods are being used to reduce dental anxiety by inhalation or injective sedatives with benzodiazepines, nitrous oxide and general anesthesia, but the risk of side effects, higher cost and need for trained personnel have limited their use. The major side effects with sedatives include increased time of absorption, gastro-intestinal disorders, respiratory depression, nausea, vomiting and allergic reactions.<sup>12</sup> Therefore, drug free methods have been implemented in reducing the dental anxiety or before the treatment. Anxiolysis through pharmacological methods will not affect respiratory and cardiac functions while putting the patient respond to verbal instructions. Cognition and coordination are impaired slightly.

Psychotherapeutic techniques or Non-pharmacological methods are easy and don not have any side effects. These techniques include physical restraints, behavior modification techniques, communication and rapport building and cognitive behavior therapy. Other techniques to manage dental fear and anxiety include tell and do, audio analgesia or white noise, systematic desensitization, hypnosis, biofeedback and progressive muscle relaxation. These are conservative and non-invasive.<sup>13</sup>

#### **Progressive muscle therapy in dental practice**

Let us discuss more about progressive muscle relaxation therapy practiced during dental anxiety. Progressive muscle relaxation technique is a

systematic technique to relax the muscles and body which was developed several decades ago. This procedure was successful in managing variety of anxiety disorders and in managing dental anxiety.<sup>14</sup> Dental anxiety is usually stimulated by psychological and physiological response and thereby activate sympathetic nervous system. Muscle relaxation therapies help in reducing this activity of sympathetic nervous system. This in turn helps in lowering the heart rate, respiratory rate and blood pressure. This technique also regulates central and peripheral nervous system and eventually reduces stress, anxiety, depression leading to improved quality of life.<sup>15</sup>

The other process by which progressive muscle relaxation technique decreases dental anxiety is based on basic principle of physiology of muscle. When is muscle is tensed, releasing tension causes relaxation of muscle. Once the muscle is relaxed it does not return to pre-tension state, but becomes more relaxed when it is allowed to rest. Here, the patient is asked to focus on specific voluntary muscles by tensing them later relaxing. As the process of tensing and relaxing progresses, other physiological responses also gradually and naturally become slow. These responses include breathing which becomes slower and deeper, blood pressure and heart rate decreases, vasodilation in small capillaries of extremities resulting in subjective calmness and ease. The patient is trained for progressive muscle relaxation technique to practice at home for 1-2 weeks later used in clinics.<sup>16</sup>

Bernstein and Borkovec were the first to describe the procedure of progressive muscle relaxation technique this was used in many other studies.<sup>17</sup> Conrad A and Roth WT in their studies found out that progressive muscle relaxation techniques can help in decreasing generalized anxiety states and panic disorders.<sup>18</sup> Isa MR et al conducted a study among prostate cancer patients who were suffering from anxiety and depression. They recorded the anxiety using Depression Anxiety Stress Scale-21. The results showed significant improvement in anxiety levels in progressive muscle relaxation group.<sup>19</sup> Progressive muscle relaxation technique has thought to even reduce blood pressure, heart rate thereby reducing triglyceride levels, and total cholesterol as in a study conducted by Chaudari et al.<sup>20</sup>

Sabherwal et al in 2021 conducted a study on 60 children who were aged between 8-12 years and undergoing primary tooth extraction. He measures anxiety by Visual Facial Anxiety scale, partial pressure of oxygen, heart rate, blood pressure and pain using Wong-baker faces pain scale were recorded pre/post-operatively. The children were randomly allocated to hypnotic group and progressive muscle relaxation technique group. He

found out that both hypnotic therapy and progressive muscle relaxation therapy were equally effective for managing pain and anxiety in pediatric dental patients.<sup>21</sup>

#### **The technique of Progressive muscle relaxation**

Though there is limited literature in dentistry for managing dental anxiety, its technique and advantages make dental practitioners force to use progressive muscle relaxation to provide better treatment. Berggren et al in 2000 conducted a study on 112 patients with dental anxiety and evaluated the effect of progressive muscle relaxation technique. There was significant reduction in dental anxiety in progressive muscle relaxation technique group compared to cognitive therapy group.<sup>22</sup>

Park et al in 2019 conducted a study on dental anxiety patients and found out that progressive muscle relaxation therapy helped in reducing anxiety, depression, pulse rate and depression in patients undergoing periodontal surgery.<sup>23</sup> Miller et al in 1978 conducted a study on dental anxiety patients in which he recorded anxiety using dental anxiety scale. They found out that group receiving progressive muscle relaxation technique had less anxiety levels compared to corresponding control group.<sup>24</sup> Similarly, Lamb et al in 1980 also found out effectiveness of progressive muscle relaxation technique and reported that there was significant decrease in anxiety levels even in next dental appointment. Progressive Muscle Relaxation can decrease neuromuscular tension and help in alleviating anxiety during or before dental procedures.<sup>25</sup>

#### **Jacobson's technique of progressive muscle relaxation:<sup>26</sup>**

Another technique by Jacobson is also being used in dentistry to reduce dental anxiety. In this technique the patient is stimulated to reach a state of whole-body deep relaxation through voluntary and conscious tensing as well as relaxing of specific muscle groups. Individual muscle parts are tensed in specific order initially for 5-7 seconds, they are held for brief time and then released for 20 seconds. In this technique, there is continuous reduction in tension in individual muscle groups. Muscle parts which are tensed include toes, knees, heels, shoulders, elbows and facial muscles. 15-20 minutes of time is given to the patient to practice the relaxation technique. Repeated use of this technique helps in making the patient sensitive to the body and to feel even the slightest tension in order to know where to relax. This technique helps in successful management of dental anxiety.

For example, the patient coming for a dental treatment will be asked to

STEP 1: Sit comfortably or Lie down in supine and

comfortable position with minimal distractions.

STEP 2: The patient is also asked to clench teeth and lips, held briefly and let go. Finally, the patient is asked to express how the muscles felt after exercise.

STEP 3: Press the tongue briefly to roof of the mouth and hold it for few seconds and let it drop loosely. Let the eyes screw them up a little, hold and let go.

STEP 4: Similarly frown the forehead a little, hold and let go.

STEP 5: Ask the patient to take deep breath through nose, held for few seconds and then breath out.

STEP 6: To pull toes near knees, gently pull shoulders towards ears, press elbows and upper arms towards body, gently clench hands, push head forward slightly, held briefly and let it go.

STEP 7: tense the muscles of stomach and chest, hips, buttocks

These all steps are held for 5 seconds and released slowly for 10 seconds. During the release the patient should experience the sense of relaxation.

Here, each muscle is tensed to 75% of full tension approximately, held for 5-10 seconds, and then relaxed for about 10 seconds focusing on tension and relaxation of specific muscles.

Note: The person performing this technique should be cautious not to tense the points which are in physical pain while taking slow, deep breaths throughout the exercise.<sup>27</sup>

#### **Progressive muscle relaxation technique for children**

In this technique, the child is asked to close his or her eyes and breath in and out i.e., inhale and exhale 5 times. This is followed by tensing and relaxing target muscle groups from tip to toe sequentially. This can include tighten and then relax the jaw, shoulders, stomach, chewing. Starching arms high above the ceiling and relaxing. Child is advised to imagine walking on the sand, squeezing toes and then relaxing. This technique is based on Karasu et al, 2009.<sup>28</sup>

Other combination techniques for progressive muscle relaxation include:

1. *Music therapy*: Music therapy is age old technique to relax the muscles and simultaneously anxiety. It helps in producing physiological arousal such as blood pressure, pulse rate, galvanic skin response and temperature resulting in simultaneous drop in psychological measures of anxiety. Progressive muscle relaxation technique is

combined with music therapy to relieve dental anxiety.<sup>29</sup> Stoudenmire found out in his research that listening to music and muscle relaxation were equally effective and reduced anxiety. Combination of both found to be even more effective.<sup>30</sup> A study done by Lahmann et al in 2008 found out that muscle relaxation technique was safe, effective and economically sound non-pharmacological approach in short term reduction of dental anxiety when compared to music distraction.<sup>31</sup>

2. *Deep breathing/Meditation:* Progressive relaxation technique is combined with deep breathing or meditation when a patient is called for a dental appointment. She/he is advised to meditate for 2 weeks prior to treatment along with practicing progressive muscle relaxation.<sup>32</sup>

## Conclusion

In order to improve oral health and an individual's general well-being, it is essential to identify and eliminate dental anxiety and phobia as these conditions can have detrimental effects on a person's quality of life. Excellent dental care is one of the fundamental principles in treating a patient with dental problems. Communication with patient can help in identifying the source of anxiety and fear while enabling to categorize the patient into mild, moderate and severe. Several methods can be employed to reduce the fear or anxiety gradually and help the patient to slowly get through while improving quality of life.

Patients who are under stress can benefit from therapy interventions that involve relaxation techniques. Progressive muscle relaxation technique is one such method to reduce the fear or anxiety

slowly and gradually. In progressive muscle relaxation, the muscles and body are tensed and gradually relaxed leading to decrease in stress and anxiety. Clinician can employ this technique to manage patients with anxiety as this method is easy, economical and doesn't require high equipment for employing.

## DECLARATIONS

### *Conflicts of interest and financial disclosures*

None declared

### *Ethical approval*

Not applicable

## REFERENCES

1. Armfield JM, Stewart JF, Spencer AJ. The vicious cycle of dental fear: exploring the interplay between oral health, service utilization and dental fear. *BMC Oral Health*. 2007;7:1. doi: 10.1186/1472-6831-7-1.
2. Cohen SM, Fiske J, Newton JT. The impact of dental anxiety on daily living. *Br Dent J*. 2000;189(7):385–390. doi: 10.1038/sj.bdj.4800777.
3. Agras S, Sylvester D, Oliveau D. The epidemiology of common fears and phobia. *Compr Psychiatry*. 1969;10(2):151–156. doi: 10.1016/0010-440x(69)90022-4.
4. Chanpong B, Haas DA, Locker D. Need and demand for sedation or general anesthesia in dentistry: a national survey of the Canadian population. *Anesth Prog*. 2005 Spring;52(1):3-11. doi:10.2344/0003-3006(2005)52[3:NADFSO]2.0.CO;2.
5. Santuchi C.C., Cortelli S.C., Cortelli J.R., et al. Pre- and post-treatment experiences of fear, anxiety, and pain among chronic periodontitis patients treated by scaling and root planing per quadrant versus one-stage full-mouth disinfection: a 6-month randomized controlled clinical trial. *J Clin Periodontol*. 2015;42:1024–1031. doi: 10.1016/j.jds.2021.04.002
6. Gatchell RJ, Ingersoll BD, Bowman L, Robertson MC, Walker C. The prevalence of dental fear and avoidance: a recent survey study. *J Am Dent Assoc*. 1983;107(4):609–610. doi: 10.14219/jada.archive.1983.0285.

7. Appukkuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. *Clin Cosmet Investig Dent*. 2016 Mar 10;8:35-50. doi: 10.2147/CCIDE.S63626. doi: 10.2147/CCIDE.S63626.
8. Pohjola V, Lahti S, Vehkalahti MM, Tolvanen M, Hausen H. Association between dental fear and dental attendance among adults in Finland. *Acta Odontol Scand*. 2007;65(4):224–230. doi: 10.1080/00016350701373558.
9. Berggren U, Hakeberg M, Carlsson SG. No differences could be demonstrated between relaxation therapy and cognitive therapy for dental fear. *J Evid Based Dent Pract*. 2001;1(2):117–118.
10. American Dental Association (2019) Guidelines for the Use of Sedation and General Anesthesia by Dentists.
11. Crocq MA. A history of anxiety: from Hippocrates to DSM. *Dialogues Clin Neurosci*. 2015;17(3):319-25. doi: 10.31887/DCNS.2015.17.3/macrocq.
12. Farach FJ, Pruitt LD, Jun JJ, Jerud AB, Zoellner LA, Roy-Byrne PP. Pharmacological treatment of anxiety disorders: current treatments and future directions. *J Anxiety Disord*. 2012 Dec;26(8):833-43. doi: 10.1016/j.janxdis.2012.07.009.
13. Cottraux J. Nonpharmacological treatments for anxiety disorders. *Dialogues Clin Neurosci*. 2002;4(3):305-19. doi: 10.31887/DCNS.2002.4.3/jcottraux.
14. Sabherwal P, Kalra N, Tyagi R, Khatri A, Srivastava S. A conceptual review on pretreatment anxiety management in a dental setting using hypnosis and progressive muscle relaxation. *Archives of A conceptual review on pretreatment anxiety management in a dental setting using hypnosis and progressive muscle relaxation and Anxiety*. 2022;8(1):019-26. doi:10.17352/2455-5460.000070
15. Neacsu V, Sfeatcu IR, Maru N, Dumitrache MA. Relaxation and systematic desensitization in reducing dental anxiety. *Procedia-Social and Behavioral Sciences*. 2014;127:474-8. doi:10.1016/j.sbspro.2014.03.293
16. Tak GS, Maheshwari SK, Kaur M. Effectiveness of progressive muscle relaxation technique on anxiety among elderly. *Int J Ther Appl*. 2016; 32:48-54. doi:10.20530/IJTA\_32\_48-54
17. Bernstein DA, Borkovec TD. Progressive relaxation training: a manual for the helping professions. Champaign: IL Research Press; 1973. doi:https://doi.org/10.1016/0005-7967(82)90143-7
18. Conrad A, Roth WT. Muscle relaxation therapy for anxiety disorders: it works but how? *J Anxiety Disord*. 2007;21(3):243-64. doi: 10.1016/j.janxdis.2006.08.001.
19. Isa MR, Moy FM, Abdul Razack AH, Zainuddin ZM, Zainal NZ. Impact of applied progressive deep muscle relaxation training on the level of depression, anxiety and stress among prostate cancer patients: a quasi-experimental study. *Asian Pac J Cancer Prev*. 2013;14(4):2237-42. doi: 10.7314/apjcp.2013.14.4.2237.
20. Chaudhuri A, Ray M, Saldanha D, Bandopadhyay A. Effect of progressive muscle relaxation in female health care professionals. *Ann Med Health Sci Res*. 2014;4(5):791-5. doi:10.4103/2141-9248.141573.
21. Sabherwal P, Kalra N, Tyagi R, Khatri A, Srivastava S. Hypnosis and progressive muscle relaxation for anxiolysis and pain control during extraction procedure in 8-12-year-old children: a randomized control trial. *Eur Arch Paediatr Dent*. 2021;22(5):823-832. doi: 10.1007/s40368-021-00619-0.
22. Berggren U, Hakeberg M, Carlsson SG. Relaxation vs. cognitively oriented therapies for dental fear. *J Dent Res*. 2000;79(9):1645-51. doi: 10.1177/00220345000790090201.
23. Park ES, Yim HW, Lee KS. Progressive muscle relaxation therapy to relieve dental anxiety: a randomized controlled trial. *Eur J OralSci*. 2019;127(1):45-51. doi: 10.1111/eos.12585.
24. Miller AA. Psychological considerations in dentistry. *J Am Dent Assoc* 1970;81:941-46. doi: 10.14219/jada.archive.1970.0347.
25. Lamb DH, Strand KH. The effect of a brief relaxation treatment for dental anxiety on measures of state and trait anxiety. *J Clin Psychol*. 1980 Jan;36(1):270-4. doi: 10.1002/1097-4679(198001)36:1<270:aid-jclp2270360134>3.0.co;2-n.
26. Jacobson E (1938) Progressive Relaxation. Chicago: University of Chicago Press.
27. Armfield JM, Heaton LJ. Management of fear and anxiety in the dental clinic: a review. *Aust Dent J*. 2013;58(4):390–407. doi: 10.1111/adj.12118.
28. Karasu TB, Karasu SR. Psychoanalysis and psychoanalytic psychotherapy. In: Sadock BJ, Sadock VA, Ruiz P, editors. Kaplan &

- Sadock's Comprehensive Textbook of Psychiatry. 9. Philadelphia: Lippincott Williams & Wilkins; 2009;2787–88.
29. Bradt J, Teague A. Music interventions for dental anxiety. *Oral diseases*. 2018 Apr;24(3):300-6.doi: 10.1111/odi.12615
  30. Stoudenmire, J. (1975), A comparison of muscle relaxation training and music in the reduction of state and trait anxiety. *J. Clin. Psychol*,31:490-492. [https://doi.org/10.1002/1097-4679\(197507\)31:3<490::AID-JCLP2270310328>3.0.CO;2-E](https://doi.org/10.1002/1097-4679(197507)31:3<490::AID-JCLP2270310328>3.0.CO;2-E)
  31. Lahmann C, Schoen R, Henningsen P, Ronel J, Muehlbacher M, Loew T et al. Brief relaxation versus music distraction in the treatment of dental anxiety: a randomized controlled clinical trial. *J Am Dent Assoc* 2008;139(3):317-24.doi: 10.14219/jada.archive.2008.0161.
  32. Toussaint L, Nguyen QA, Roettger C, Dixon K, Offenbacher M, Kohls N, Hirsch J, Sirois F. Effectiveness of Progressive Muscle Relaxation, Deep Breathing, and Guided Imagery in Promoting Psychological and Physiological States of Relaxation. *Evid Based Complement Alternat Med*. 2021 2021:5924040. doi: 10.1155/2021/5924040.