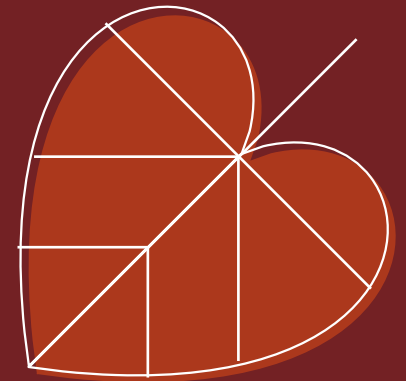


BALANCING THE  
MIND:INTEGRATIVE  
APPROACHES TO TREATING  
GENERALIZED ANXIETY  
DISORDER (GAD)

---

Rachel Eyma, MD, ABOIM



NO CONFLICT OF  
INTEREST TO DECLARE

---



# AGENDA

---

- 🕒 Diagnostic Criteria for GAD
- 🕒 Screening Tools
- 🕒 Formulating an Integrative Treatment Plan
- 🕒 Treatment Modalities
- 🕒 Summary



- 🕒 GAD and panic disorder are the most common anxiety disorders in adults<sup>3</sup>
- 🕒 In the U.S. the lifetime prevalence of GAD is 8%<sup>1</sup>
- 🕒 Peak onset late adolescence or early adulthood<sup>2</sup>
- 🕒 Lifetime rates of cardiovascular, respiratory, GI and other medical problems are disproportionately high in patients with anxiety<sup>4</sup>



# DSM V CRITERIA FOR GAD:

- ⌚ Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance)
- ⌚ The individual finds it difficult to control the worry
- ⌚ The disturbance is not attributable to the physiological effects of a substance (i.e. a drug of abuse, a medication) or another medical condition (i.e. hyperthyroidism)
- ⌚ The disturbance is not better explained by another mental disorder
- ⌚ The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

- ⌚ The anxiety and worry are associated with three or more of the following six symptoms (with at least some symptoms present for more days than not for the past six months:
  - Restlessness or feeling keyed up or on edge
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep

## GAD-7 Screening Tool for GAD

Over the past two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as though something awful might happen	0	1	2	3
<b>Total score:</b> _____ = _____ + _____ + _____ + _____				

**Note:** Total score for the seven items ranges from 0 to 21. Scores of 5, 10, and 15 represent cutoffs for mild, moderate, and severe anxiety, respectively. Although designed primarily as a screening and severity measure for GAD, the GAD-7 also has moderately good operating characteristics for panic disorder, social anxiety disorder, and posttraumatic stress disorder. When screening for anxiety disorders, a recommended cutoff for further evaluation is a score of 10 or greater.<sup>14</sup>

GAD = generalized anxiety disorder; GAD-7 = Generalized Anxiety Disorder 7-item screening tool.

*Adapted with permission from Spitzer RL, Williams JBW, Kroenke K, et al., with an educational grant from Pfizer Inc. GAD-7. Accessed August 9, 2021. [https://www.phqscreeners.com/images/sites/g/files/g10060481/f/201412/GAD-7\\_English.pdf](https://www.phqscreeners.com/images/sites/g/files/g10060481/f/201412/GAD-7_English.pdf), with additional information from reference 14.*

# TOOLS FOR ASSESSING SEVERITY IN GAD:

🕒 Hamilton Anxiety Rating Scale (HAM-A)

-<https://dcf.psychiatry.ufl.edu/files/2011/05/HAMILTON-ANXIETY.pdf>

🕒 Beck Anxiety Inventory

-<https://irp-cdn.multiscreensite.com/86f42237/files/uploaded/BAI.pdf>

🕒 Penn State Worry Questionnaire

-[http://caleblack.com/psy5960\\_files/PSWQ.pdf](http://caleblack.com/psy5960_files/PSWQ.pdf)





# INTEGRATIVE TREATMENT "CARE" PLAN

---

**C.. Collect**

**A.. Ask**

**R.. Reassure**

**E.. Engage**





# COLLECT

- Obtain patient history*
  - i.e. historical/present life circumstances, family/social history, (consider ACE screening)*
- Perform necessary diagnostic tests*



# ASK

- Underlying medical conditions*
- Current meds/supplements*
- Environmental factors*
- Substance use/abuse*



# REASSURE

- Anxiety is a normal emotion*
- Discuss treatment options*
- Review risks, benefits, alternatives, and potential side effects*



# ENGAGE

- Discuss goals of treatment*
- Shared decision making*

# TREATMENT MODALITIES:



- 1. Lifestyle Modifications**
- 2. Pharmaceuticals**
- 3. Botanicals/Supplements**
- 4. Mind Body Therapies**
- 5. Additional Therapies**

# I. LIFESTYLE MODIFICATIONS:

## 1. MOVEMENT

- 🕒 Physical activity reduces the symptoms of anxiety
- 🕒 Some studies have shown aerobic exercise programs seem to have produced a larger effect compared to weight training and flexibility regimes although all appear effecting for improvement in mood<sup>5</sup>
- 🕒 Consider patients level of fitness, interests in specific physical activities and concerns (i.e time constraints, environmental safety, social influences, etc)





## 2. NUTRITION

- 🕒 **Diet-** Observational studies have shown an association between lower anxiety symptom severity or disorder prevalence and "healthy" diet patterns (i.e. higher intake of vegetables, fruits, whole grains, fish, legumes and unprocessed meats)<sup>8</sup>
- 🕒 **Omega 3 fatty acids-** Levels of polyunsaturated fats and cholesterol metabolism influence neuronal tissue synthesis, membrane fluidity, and serotonin metabolism<sup>7</sup>



- 🕒 **Caffeine-** Long term use has been linked to anxiety and depression<sup>9</sup>
- 🕒 **Alcohol-** Has been found to diminish levels of serotonin and dopamine<sup>10</sup>
- 🕒 **Gut microbiome-** Interventions aimed at increasing microbiome diversity or addition of fermented foods or fiber were associated with decreased anxiety symptom severity<sup>8</sup>



### 3. SLEEP

- 🕒 Maintain a regular sleep-wake schedule, even on weekends
- 🕒 Develop a soothing evening ritual as a bridge to sleep
- 🕒 Go to bed only when tired
- 🕒 Keep the bedroom cool (68 degrees or less), dark and quiet
- 🕒 Remove electric clocks and other devices away from your head and bed

## II. PHARMACEUTICALS:

### SSRI's/SNRI's

- first line medication treatment
- recommendation is to take for 6-12 months to minimize risk of relapse<sup>11</sup>
- recent meta analysis found that escitalopram, duloxetine and venlafaxine appear to be the most effective and well tolerated<sup>12</sup>

### Buspirone

- agonist of the serotonin receptor subtype 5-hydroxytryptamine 1-A
  - RCT evidence exists for its usefulness as an adjunct to 1st line treatment with antidepressants in the case of partial response<sup>13</sup>

## 🕒 **Tricyclic Antidepressants (TCA's)**

- non selective antagonists of the serotonin and norepinephrine receptors
- associated with a broad range of adverse side effects including weight gain, sedation, orthostatic hypotension, and dizziness

## 🕒 **Anti epileptics (i.e pregabalin, gabapentin)**

- GABA analogs
- effective for treatment of GAD but may cause weight gain and sedation
- risk of misuse/abuse

## 🕒 **Benzodiazepines (i.e. alprazolam, klonazepam, diazepam, etc)**

- promote the binding of GABA to GABA subunit receptors (GABA-A)
- short term use recommended
- quick onset of action (dose response relationship associated with tolerance, sedation, confusion and increased mortality)

## 🕒 **Antihistamines (i.e. hydroxyzine)**

- comparable efficacy to buspirone and benzodiazepines for the treatment of GAD<sup>13</sup>

## **Antipsychotics**

-off label use- NOT FDA approved for treatment of GAD due to concerns about significant cardiovascular and metabolic risks.

-limited evidence for use

-a meta analysis in 2016 found quetiapine to be efficacious as a monotherapy for GAD at doses between 50-100mg daily, with discontinuation and drop out rates similar to those in clinical trials of anti depressants<sup>14</sup>

# III. BOTANICALS/SUPPLEMENTS:

## KAVA (Piper Methysticum)-

-mechanism of action seems to be similar to that of benzodiazepines (binding to GABA receptors)

-anxiolytic, analgesic, and muscle relaxant properties

-inhibits the cytochrome p450 system

-onset of action 20-45 minutes

-A meta analysis of RCT's showed that kava is consistently better compared to placebo in producing modest reductions in anxiety symptoms<sup>15</sup>

Dosing:

Standardized extract: 250-500mg QD  
(standardized to 30% kava lactones)

Decoction: 1.5-3g of the dried rhizome QD

-avoid in patients with Parkinsons dz, regular ETOH use, liver dz, pregnancy and breastfeeding





## **ASHWAGANDHA (Withania somnifera)-**

**Root extract in capsules 300-500mg PO TID  
(mac 3000mg QD)**

**-mechanism of action is through modulation of the HPA axis**

**-anti inflammatory, immunomodulating, provides cognitive support**

**-anxiolytic- calming, slightly sedative effect**

**-best dosed in evening**

**Dosing:**

**Standardized extract-Sensoril (standardized to 2.5% withanolides) 500mg PO QD-BID**

**KSM66 (standardized to >5% withanolides) 300mg PO BID**



## **LAVENDER (Lavendula angustifolia)-**

**-Mechanism of action is through inhibition of voltage gated calcium channels, reduction of 5HT1A receptor activity and increased parasympathetic tone<sup>16</sup>**

**-effective in reducing anxiety, restlessness, agitation, disturbed sleep and nervousness**

**-use with caution in children (several case report of prepubertal gynecomastia in boys associated with TOPICAL use)**

### **Dosing:**

**Silexan (WS1265-proprietary lavender oil)  
80-160mg PO QD**

**1 tsp of lavender flowers per 8oz of water  
(infuse for 15 min) QD-TID**

**Topical lavender essential oil-few drops  
diluted in carrier oil applied to wrists, nape of  
neck or behind ears**



## **INOSITOL-**

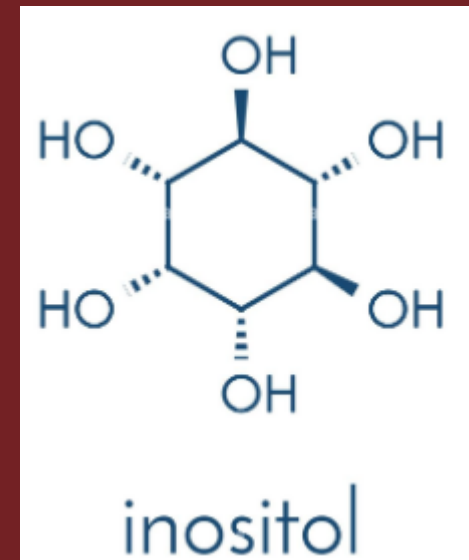
**-type of sugar naturally found in plants/ foods**

**-plays a role in cell signal transduction, cell membrane formation, insulin regulation, and management of neurotransmitter levels<sup>17</sup>**

**-in a RCT comparing inositol with fluvoxamine in patients with panic disorder inositol was superior to placebo and had comparable effects (compared to fluvoxamine) in terms of reduction of panic attack frequency and intensity, anxiety score scales and clinical global improvement scores<sup>18</sup>**

**Dosing:**

**12-18 grams QD**



## **MAGNESIUM-**

**-Mechanism of action is through modulation of the HPA axis**

**-Reduces central ACTH<sup>19</sup> and peripheral cortisol levels<sup>20</sup>**

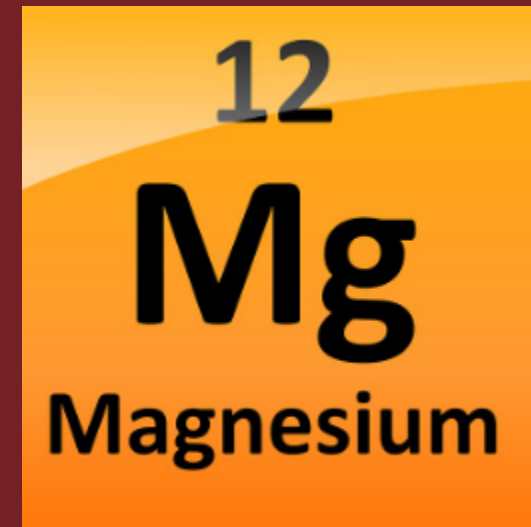
**-anxiolytic, muscle relaxation effects**

**-magnesium taurate and glycinate have the most research supporting their effects on anxiety<sup>21</sup>**

## **Dosing:**

**——Magnesium glycinate 70-360mg PO QD**

**Magnesium taurate 375-500mg PO QD**





## ADDITIONAL BOTANICALS:

---

- 🕒 **German Chamomile**  
(*Matricaria recutita*)
- 🕒 **Passion Flower** (*Passiflora incarnata*)
- 🕒 **Lemon Balm** (*Melissa officinalis*)
- 🕒 **Valerian Root** (*Valeriana officinalis*)

## **IV. MIND BODY THERAPIES:**

- 🕒 Defined as practices that focus on the interactions of the brain, mind, body, and behavior, with the intent of using the mind to alter physical function and promote overall health. <sup>22</sup>**
- 🕒 In a recent review of high quality studies evaluating mind body interventions for anxiety the highest-quality data existed for yoga, mindfulness-based interventions, and applied relaxation for anxiety disorders. <sup>23</sup>**

# 1. PSYCHOTHERAPY



- ⌚ Includes relaxation techniques, cognitive restructuring (i.e. cognitive behavioral therapy-CBT) and exposure therapy
  - ⌚ As effective as pharmacotherapy for treatment of GAD<sup>24</sup>
  - ⌚ Evidence is strongest for CBT
  - ⌚ CBT focuses on identifying and challenging thought patterns while gradually facing worries in a controlled way
- \*Woebot app

## 2. MINDFULNESS



- 🕒 Practice of bringing all your attention to the present moment without judgement
- 🕒 Has similar effectiveness to traditional CBT or other behavior therapies<sup>25</sup>

### A. Meditation

-A practice in which an individual uses a technique to train attention and awareness

\*Insight timer, Calm, Headspace apps





## **B. Mindfulness Based Stress Reduction (MBSR)**

-8 week evidence based program that uses a combination of mindfulness meditation, body awareness, yoga, and exploration of patterns of behavior, thinking, feeling, and action

\*Palouse mindfulness online program

## **C. Breathwork**

-controlled conscious breathing increases oxygenation, relaxation, body awareness and mindfulness<sup>26</sup>

\*4-7-8 breath, box breathing, calm strips, etc



## D. Yoga

-a group of physical, mental, and spiritual disciplines with the intention of creating union of the body/mind/spirit

-studies have shown yoga may be more effective at reducing anxiety symptoms compared with no treatment<sup>27</sup>

## E. Grounding

-technique used to connect the physical body to the earth's electrical energy (i.e forest bathing, gardening, etc)

## 3. BIOFEEDBACK



- ⌚ Uses monitors and sensors to identify and control the body's reactions to certain stimuli through monitoring of heart rate, breathing patterns, temperature and muscle responses
- ⌚ Designed to teach the patient how to manage their responses to things like stress and pain
- ⌚ Effects in reduction of symptoms seen after 4 weeks of training<sup>28</sup>

\*Heartmath

## 4. PRAYER AND SPIRITUALITY



- ⌚ Prayer is one of the most prevalent complementary therapies in the U.S.
- ⌚ 56% of adults have stated that faith has helped them recover from illness, injury or disease<sup>29</sup>
- ⌚ Every illness is a potential spiritual crisis and may have deep spiritual dimensions for the patient
- ⌚ Spiritual distress can be experienced physically and emotionally
- ⌚ Spiritual beliefs can be an important part in medical decision making for patients

## V. ADDITIONAL THERAPIES:

🕒 Traditional Chinese Medicine

-acupuncture, cupping, Chinese herbal medicine, qi gong, tai chi, etc

🕒 Progressive Muscle Relaxation

🕒 Aromatherapy

🕒 Sound/Music therapy

🕒 Massage therapy

# SUMMARY:

- 🕒 Anxiety disorders are very common with a wide reaching impact in the lives of thousands of adults, adolescents and children
- 🕒 Integrative treatment of generalized anxiety disorder has the potential to benefit many people by offering expanded treatment options
- 🕒 **Considerations for treatment:**
  - patient cultural/personal/spiritual beliefs
  - treatment preferences
  - financial/time constraints
  - access to appropriately trained providers

THANK YOU



*Rachel Eyma MD ABOIM*

*Rachel.eyma@halifax.org*

# REFERENCES

1. Kessler RC, Petukhova M, Sampson NA, et al. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res.* 2012;21(3):169-18
2. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, et al. Anxiety disorders in older adults. *Depress Anxiety.* 2010;27(2):190-211
3. Love AS, Love R. Anxiety disorders in primary care settings. *Nurs Clin North Am.* 2019;54(4):473-493
4. Meuret AE, Tunnell N, Roque A, et al. Anxiety disorders and medical comorbidity. *Adv Exp Med Biol.* 2020;1191:237-261
5. Rebar AL, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C. A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. *Health Psychol Rev.* 2015;9(3):366-78.
6. Weiss F, Porrino LJ. Behavioral neurobiology of alcohol addiction: recent advances and challenges. *J Neurosci.* 2002 May 1;22(9):3332-7
7. Su KP, Tseng PT, Lin PY, Okubo R, Chen TY, Chen YW, Matsuoka YJ. Association of Use of Omega-3 Polyunsaturated Fatty Acids With Changes in Severity of Anxiety Symptoms: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2018 Sep 7;1(5):e182327
8. Aucoin M, LaChance L, Naidoo U, Remy D, Shekdar T, Sayar N, Cardozo V, Rawana T, Chan I, Cooley K. Diet and Anxiety: A Scoping Review. *Nutrients.* 2021 Dec 10;13(12):4418.
9. Poole R, Kennedy OJ, Roderick P, Fallowfield JA, Hayes PC, Parkes J. Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ.* 2017;359:5024.



10. Weiss F, Porrino L. Behavioral neurobiology of alcohol addiction: Recent advances and challenges. *J Neurosci* 2002;(22):3332-3337

11. Van Leeuwen E, van Driel ML, Horowitz MA, et al. Approaches for discontinuation versus continuation of long-term antidepressant use for depressive and anxiety disorders in adults. *Cochrane Database Syst Rev*. 2021(4):CD013495.

12. Slee A, Nazareth I, Bondaronek P, et al. Pharmacological treatments for generalised anxiety disorder [published correction appears in *Lancet*. 2019; 393(10182):1698]. *Lancet*. 2019;393(10173):768-777

13. Guaiana G , Barbui C , Cipriani A : Hydroxyzine for generalised anxiety disorder . *Cochrane Database Syst Rev* 2010. ; 12 : CD006815

14. Maneeton N , Maneeton B , Woottitluk P , et al. : Quetiapine monotherapy in acute treatment of generalized anxiety disorder: a systematic review and meta-analysis of randomized controlled trials . *Drug Des Devel Ther* 2016. ; 10 : 259 - 276

15. Pittler MH, Ernst E. Kava extract for treating anxiety. *Cochrane Database Syst Rev*. 2002;(2):CD003383. doi: 10.1002/14651858.CD003383. Update in: *Cochrane Database Syst Rev*. 2003;(1):CD003383. doi: 10.1002/14651858.CD003383. PMID: 12076477

16. Malcolm BJ, Tallian K. Essential oil of lavender in anxiety disorders: Ready for prime time? *Ment Health Clin*. 2018 Mar 26;7(4):147-155. doi: 10.9740/mhc.2017.07.147. PMID: 29955514; PMCID: PMC6007527.

**17. Concerto C, Chiarenza C, Di Francesco A, Natale A, Privitera I, Rodolico A, Trovato A, Aguglia A, Fisicaro F, Pennisi M, Bella R, Petralia A, Signorelli MS, Lanza G. Neurobiology and Applications of Inositol in Psychiatry: A Narrative Review. Curr Issues Mol Biol. 2023 Feb 20;45(2):1762-1778. doi: 10.3390/cimb45020113. PMID: 36826058; PMCID: PMC9955821.**

**18. Palatnik A, Frolov K, Fux M, Benjamin J. Double-blind, controlled, crossover trial of inositol versus fluvoxamine for the treatment of panic disorder. J Clin Psychopharmacol. 2001 Jun;21(3):335-9. doi: 10.1097/00004714-200106000-00014. PMID: 11386498.**

**19. Murck H, Steiger A. Mg<sup>2+</sup> reduces ACTH secretion and enhances spindle power without changing delta power during sleep in men -- possible therapeutic implications. Psychopharmacology (Berl). 1998 Jun;137(3):247-52. doi: 10.1007/s002130050617. PMID: 9683002.**

**20. Held K, Antonijevic IA, Künzel H, Uhr M, Wetter TC, Golly IC, Steiger A, Murck H. Oral Mg(2+) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans. Pharmacopsychiatry. 2002 Jul;35(4):135-43. doi: 10.1055/s-2002-33195. PMID: 12163983.**

**21. Uysal N, Kizildag S, Yuce Z, Guvendi G, Kandis S, Koc B, Karakilic A, Camsari UM, Ates M. Timeline (Bioavailability) of Magnesium Compounds in Hours: Which Magnesium Compound Works Best? Biol Trace Elem Res. 2019 Jan;187(1):128-136. doi: 10.1007/s12011-018-1351-9. Epub 2018 Apr 21. PMID: 29679349.**

**22. Mayden KD. Mind-body therapies: evidence and implications in advanced oncology practice. J Adv Pract Oncol. 2012 Nov;3(6):357-73. PMID: 25031967; PMCID: PMC4093363.**

23. Bandealy SS, Sheth NC, Matuella SK, Chaikind JR, Oliva IA, Philip SR, Jones PM, Hoge EA. Mind-Body Interventions for Anxiety Disorders: A Review of the Evidence Base for Mental Health Practitioners. *Focus (Am Psychiatr Publ)*. 2021 Jun;19(2):173-183. doi: 10.1176/appi.focus.20200042. Epub 2021 Jun 17. PMID: 34690580; PMCID: PMC8475909.
24. Cuijpers P, Gentili C, Banos RM, Garcia-Campayo J, Botella C, Cristea IA. Relative effects of cognitive and behavioral therapies on generalized anxiety disorder, social anxiety disorder and panic disorder: A meta-analysis. *J Anxiety Disord*. 2016 Oct;43:79-89. doi: 10.1016/j.janxdis.2016.09.003. Epub 2016 Sep 13. PMID: 27637075.
25. Khoury B, Lecomte T, Fortin G, Masse M, Therien P, Bouchard V, Chapleau MA, Paquin K, Hofmann SG. Mindfulness-based therapy: a comprehensive meta-analysis. *Clin Psychol Rev*. 2013 Aug;33(6):763-71. doi: 10.1016/j.cpr.2013.05.005. Epub 2013 Jun 7. PMID: 23796855.
26. Lothian JA. Lamaze breathing: what every pregnant woman needs to know. *J Perinat Educ*. 2011 Spring;20(2):118-20. doi: 10.1891/1058-1243.20.2.118. PMID: 22379360; PMCID: PMC3209750.
27. Saeed SA, Cunningham K, Bloch RM. Depression and Anxiety Disorders: Benefits of Exercise, Yoga, and Meditation. *Am Fam Physician*. 2019 May 15;99(10):620-627. PMID: 31083878
28. Blase K, Vermetten E, Lehrer P, Gevirtz R. Neurophysiological Approach by Self-Control of Your Stress-Related Autonomic Nervous System with Depression, Stress and Anxiety Patients. *Int J Environ Res Public Health*. 2021 Mar 24;18(7):3329. doi: 10.3390/ijerph18073329. PMID: 33804817; PMCID: PMC8036915.
29. McNichol T. The new faith in medicine. *USA Today Weekend*, April 5-7, 1996:4-5 (survey conducted February 1996 by ICR Research Group).