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# Women's Attitudes toward Complementary and Integrative Therapies and Resilience during COVID-19: A Cross-Sectional Study

## Kadınların COVID-19 Sürecinde Tamamlayıcı ve İntegratif Tedavilere Yönelik Tutumları ve Kendini Toparlama Gücü: Kesitsel Bir Çalışma

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**ABSTRACT Objective:** The study aimed to investigate what kind of complementary and integrative therapies (CITs) women who tested positive for coronavirus disease-2019 (COVID-19) turned to and the relationship between their attitudes toward using CITs and their resilience. **Material and Methods:** This cross-sectional study was conducted between the dates December 1st, 2022, and June 1st, 2023. The study sample comprised 271 women who had tested positive for COVID-19. Data were gathered online using a personal information form, the Attitude towards Using Complementary Treatments Scale, and the Brief Resilience Scale. The data were analyzed using the Mann-Whitney U test, Kruskal-Wallis test, and Spearman's correlation coefficients. **Results:** Seven in ten participants used CITs when they had COVID-19. They mostly consumed vitamin supplements and herbal teas. Participants turned to CITs because they believed that CITs constituted natural and safe approaches capable of enhancing their overall quality of life. Most participants believed that CITs helped them recover from COVID-19. Participants who used CITs had more positive attitudes toward using CITs than those who did not use them ($p<0.05$). Participants who were vaccinated against COVID-19, especially those who got more than two shots, had more positive attitudes toward using CITs than those who were not ($p<0.05$). A positive and weak correlation existed between participants' attitudes toward CITs and their resilience during COVID-19 ($r=0.146$; $p=0.016$). **Conclusion:** Most participants used CITs to recover from COVID-19, which positively affected their resilience.

**Keywords:** Complementary therapies; COVID-19; cross-sectional study; resilience; women

**ÖZET Amaç:** Bu çalışmada, koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] geçirmiş kadınların hangi tamamlayıcı ve integratif tedaviler (TİT) kullandığı ve TİT kullanmaya yönelik tutumları ile kendini toparlama gücü arasındaki ilişkinin incelenmesi amaçlanmıştır. **Gereç ve Yöntemler:** Kesitsel tipteki bu çalışma, 1 Aralık 2022-1 Haziran 2023 tarihleri arasında yürütülmüştür. Araştırmanın örneklemini COVID-19 geçirmiş 271 kadın oluşturmuştur. Veriler kişisel bilgi formu, Tamamlayıcı Tedavileri Kullanmaya Yönelik Tutum Ölçeği ve Kendini Toparlama Gücü Ölçeği-Kısa Formu kullanılarak çevrim içi olarak toplanmıştır. Veriler Mann-Whitney U testi, Kruskal-Wallis testi ve Spearman korelasyon katsayıları kullanılarak analiz edilmiştir. **Bulgular:** On katılımcıdan yedisi COVID-19 geçirdikleri süreçte TİT kullanmıştır. Katılımcılar en sık olarak vitamin takviyeleri ve bitki çayları tüketmiştir. Katılımcılar TİT yaşam kalitelerini artıran doğal ve güvenli yöntemler içerdiğine inandıkları için tercih etmişlerdir. Çoğu katılımcı TİT'in COVID-19'dan iyileşmeye yardımcı olduğunu düşünmektedir. TİT kullanan katılımcıların kullanmayanlara göre TİT kullanmaya yönelik tutumları daha olumludur ($p<0,05$). COVID-19 aşısı olan katılımcıların, özellikle de ikiden fazla aşı olanların, aşı olmayanlara göre TİT kullanmaya yönelik tutumları daha olumludur ($p<0,05$). Katılımcıların COVID-19 sürecinde TİT kullanmaya yönelik tutumları ile kendini toparlama gücü arasında pozitif yönlü zayıf bir korelasyon bulunmaktadır ($r=0,146$; $p=0,016$). **Sonuç:** Çoğu katılımcı COVID-19'dan iyileşmek için TİT kullanmıştır ve bu durum kendini toparlama güçlerini olumlu yönde etkilemiştir.

**Anahtar Kelimeler:** Tamamlayıcı terapiler; COVID-19; kesitsel çalışmalar; dirençlilik; kadınlar

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The coronavirus disease-2019 (COVID-19) initially surfaced in China and was subsequently designated a pandemic by the World Health Organization in 2020.[1] Owing to the swift global dissemination of COVID-19 and the absence of a conclusive curative approach, the conclusion of October 2020 witnessed a tragic toll of 1.2 million fatalities linked to the disease.[2] Extended limitations enforced throughout the pandemic have impeded access to healthcare facilities. Consequently, people who tested positive for COVID-19 turned to complementary and integrative therapies (CITs) as a means to manage symptoms.[3,4] A range of CITs employed to alleviate COVID-19 symptoms encompass vitamin-mineral supplements, botanical compounds, targeted dietary strategies, methodologies from mind-body medicine, and more.[5] They preferred CITs that are likely to interact with the treatment received in COVID-19 therapy, mainly because of their easy accessibility and applicability.[6] In addition, the utilization of CITs exhibits diversity contingent upon people's perceptions of the ailment, their stance towards the disease and therapeutic approaches, as well as factors such as age and gender.[7,8] Research shows that women use CITs more than men.[4,6,9-11] This is several reasons. First, women exhibit help-seeking behaviors more frequently than men. Second, women have more unmet health needs than men because they are more vulnerable than men.[6,11]

COVID-19 diminishes an individual's bodily resilience and adversely affects their overall well-being.[12] Resilience is characterized as an individual's capacity to consistently renew their physical and psychological state when confronted with significant adverse life events.[13] COVID-19 patients exhibit notably diminished resilience. The foremost elements contributing to this decline encompass COVID-19-related apprehension, depression, anxiety, and stress.[14] Research has also shown that women experienced higher levels of stress, depression, and anxiety than men during the COVID-19 pandemic.[15,16] In addition, in Türkiye, where gender inequality is deeply felt, women were more affected by the negative consequences of the pandemic than men.[17] Therefore, women were also more vulnerable than men during the pandemic in Türkiye. Furthermore, considering that women's resistance may be lower than the male population during the pandemic period, it was thought that they may resort to CITs to reduce their symptoms.

Only a few researchers have explored the effect of CITs on resilience.[18,19] There is no study on this subject in Turkish population, where women both use CITs frequently and have low resilience.[19-21] Furthermore, there has been a lack of attention from researchers toward understanding how CITs influence the resilience of women specifically in pandemic. Do women with lower resilience levels than men see CITs as a coping mechanism in a stressful period such as the pandemic? Therefore, this study aimed to investigate the types of CITs employed by women who tested positive for COVID-19 and to discern the influence of these therapies on their resilience.

***Research questions***

**$Q_1$.** What types of CITs use women who tested positive for COVID-19?

**$Q_2$.** Is there a relationship between attitudes towards using CITs and resilience of women who tested positive for COVID-19?

## MATERIAL AND METHODS

### DESIGN

This cross-sectional study was conducted between December 1, 2022, and June 1, 2023, in Türkiye.

### STUDY GROUP

The study population comprised all Turkish women who tested positive for COVID-19. A power analysis (G*Power 3.1) was performed to calculate the sample size. Küçükkaya and Işık's study, and Öztürk et al. study, these studies on the use of CITs, carried out only with women, web-based and cross-sectional in Türkiye.[22,23] The power analysis results based on these studies' finding, indicated that a sample of 210 participants would be large enough to detect significant differences (0.25 effect size, with a 5% margin of error, 95% confidence interval, 95% power, and 0.05 significance). The sample consisted of 271 participants. Participants were recruited using convenience sampling.[24] The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.[25]

The inclusion criteria were (1) being a woman older than 18 years of age, (2) having tested positive for COVID-19 at least once, (3) being literate in Turkish, and (4) being able to use a smartphone or fill out online surveys. The exclusion criteria were (1) having a psychiatric illness or cognitive impairment, and (2) failing to complete the online surveys.

### DATA COLLECTION

#### Personal Information Form

The form was prepared by the researchers.[4-6,26,27] It comprised 16 items on sociodemographic characteristics (age, marital, education, employed and economic status, longest residential area, having a health-related job and chronical disease), COVID-19 characteristics (vaccinated and dose of vaccination against COVID-19, COVID-19 symptoms) and CITs characteristics (used CITs during COVID-19, information resources on CITs, reasons for choosing the use of CITs, benefits of CITs use, the harms of the CITs used).

#### Attitude towards Using Complementary Treatments Scale

The scale was developed by Bilge et al. in 2018.[28] It has 13 items rated on a four-point Likert-type scale. Item 9 is reverse scored. The total score ranges from 0 to 39, with higher scores indicating more positive attitudes toward CITs. The scale has a Cronbach's alpha score of 0.79, which was 0.83 in this study.[28]

#### Brief Resilience Scale

The scale was developed by Smith et al. in 2008.[29] It consists of six items rated on a five-point Likert-type scale. Three items (2, 4, and 6) are reverse scored. The total score of the scale is at least 6 and at most 30, with higher scores indicating more resilience. The instrument was adapted to Turkish by Haktanir et al. in 2016.[30] The Turkish version has a Cronbach's alpha score of 0.82, which was 0.81 in this study.[30]

#### Procedure

The study was conducted online. The data were collected using an e-survey [Google Forms (Google, USA)] prepared by the researchers. The data were collected on social media platforms (WhatsApp, Instagram, Facebook, etc.).

### ETHICAL CONSIDERATIONS

The study was approved by Ankara Yıldırım Beyazıt University Ethics Board (date: November 03, 2022, no: 17). The study adhered to the Declaration of Helsinki. Participation was voluntary. All women were briefed on the research purpose and procedure. Informed consent was obtained from all participants.

### DATA ANALYSIS

The data were analyzed in SPSS (SPSS, IBM version 26, USA). Numbers and percentages were used for categorical variables, while means and standard deviations were used for numerical variables. The Kolmogorov-Smirnov test was used for normality. The data were non-normally distributed. Therefore, they were analyzed using the Mann-Whitney U test, Kruskal-Wallis test, and Spearman correlation coefficients.

## RESULTS

### PARTICIPANTS AND COVID-19

The sample consisted of 271 women. Participants had a mean age of 34.6±8.8 years (min=18, max=66). Most participants were 25 to 44 years of age (72.7%). More than half of the participants were married (66.4%). Most participants had bachelor's or higher degrees (86.3%). More than half of the participants were employed (74.5%). Over half of the participants had neutral incomes (income=expense) (52%). Most participants lived in cities (95.9%). More than a quarter of the participants had health-related jobs (33.9%). Less than a quarter of the participants had chronic diseases (23.2%) (Table 1).

Most participants were vaccinated against COVID-19 (87.1%). Over a quarter of the participants were vaccinated more than three times (28.8%). The most common COVID-19 symptoms were fatigue (21.1%), muscle and joint pain (17.6%), and headaches (14.6%) (Table 2).

### CITS USE AND COVID-19

More than half of the participants used CITs when they had COVID-19 (69.4%) (Table 3). The most common CITs participants used were vitamin supplements (40.2%), herbal teas (26.6%), and mineral

**TABLE 1:** Distribution of participants by characteristics (n=271).

| Characteristics | n | % |
|---|---|---|
| Age, years ($\bar{X}$±SD=34.6±8.8) | | |
| 18-24 | 44 | 16.2 |
| 25-44 | 197 | 72.7 |
| 45-64 | 28 | 10.3 |
| 65 and ↑ | 2 | 0.7 |
| Marital status | | |
| Married | 180 | 66.4 |
| Single | 91 | 33.6 |
| Education status | | |
| Primary school ↓ | 13 | 4.8 |
| High school | 24 | 8.9 |
| Bachelor or ↑ | 234 | 86.3 |
| Employed | | |
| Yes | 202 | 74.5 |
| No | 69 | 25.5 |
| Economic status | | |
| Low income | 61 | 22.5 |
| Neutral income | 141 | 52.0 |
| High income | 69 | 25.5 |
| Longest residential area | | |
| Urban | 260 | 95.9 |
| Rural | 11 | 4.1 |
| Had a health-related job | | |
| Yes | 92 | 33.9 |
| No | 179 | 66.1 |
| Chronical disease | | |
| Yes | 63 | 23.2 |
| No | 208 | 76.8 |

SD: Standard deviation.

**TABLE 2:** Distribution of participants by COVID-19-related characteristics (n=271).

| Characteristics | n | % |
|---|---|---|
| Vaccinated against COVID-19 | | |
| Yes | 236 | 87.1 |
| No | 35 | 12.9 |
| Dose of vaccination against COVID-19 | | |
| 0 | 35 | 12.9 |
| 1 | 6 | 2.2 |
| 2 | 75 | 27.7 |
| 3 | 78 | 28.8 |
| 4 | 52 | 19.2 |
| 5 | 22 | 8.1 |
| 6 | 3 | 1.1 |
| COVID-19 symptoms* | | |
| Fatigue | 235 | 21.1 |
| Muscle and joint pain | 196 | 17.6 |
| Headache | 162 | 14.6 |
| Cough | 144 | 12.9 |
| Sore throat | 141 | 12.7 |
| Loss of taste and smell | 125 | 11.2 |
| Fiber | 97 | 8.7 |
| Hoarseness | 3 | 0.3 |
| Postnasal drip | 3 | 0.3 |
| Dyspnea | 3 | 0.3 |
| Nausea | 2 | 0.2 |
| Waist and back pain | 1 | 0.1 |

*Percentages were given over the total number of symptoms.

supplements (23.2%) (Figure 1). More than a quarter of the participants learned about CITs from their spouses, friends, neighbors, or relatives (35.6%). Four in ten participants preferred CITs because they believed that they were natural and safe (40.3%). More than a quarter of the participants preferred CITs because they believed that they improved their quality of life (27.4%). Participants believed that the CITs they used to help them relax (18.3%), recover fast (13.4%), and cough less (13.4%). They also reported liver toxicity (1.0%), low blood pressure (1.0%), and pyrosis (1.0%) after using the CITs (Table 3).

Participants who used CITs had a significantly higher mean Attitude towards Using Complementary Treatments Scale (ACTS) score than those who did not (p<0.001). Participants who were not vaccinated against COVID-19 had a significantly higher mean ACTS score than those who were (p<0.001). Participants who were vaccinated more than twice had a significantly higher mean ACTS score than those who were vaccinated less than twice (p=0.002). Table 4 shows the distribution of ACTS scores by some variables.

### ATTITUDE TOWARD USING CITS AND RESILIENCE DURING COVID-19

Participants had a mean ACTS score of 19.1±7.0 (min=3, max=36). They had a mean Brief Resilience Scale (BRS) score of 18.1±5.1 (min=6, max=30). There was a weak and positive correlation between ACTS and BRS scores (r=0.146; p=0.016).

## DISCUSSION

This study had two objectives: (1) investigating what kind of CITs women who tested positive for COVID-19 turned to and (2) investigating the relationship between their attitudes toward CITs and their resilience.

**TABLE 3:** Distribution of participants by characteristics regarding the used CITs during COVID-19 (n=271).

| Characteristics | n | % |
|---|---|---|
| Used CITs during COVID-19 | | |
| Yes | 188 | 69.4 |
| No | 83 | 30.6 |
| Information resources on the use of CITs | | |
| Spouse, friends, neighbors, or relatives | 133 | 35.6 |
| Radio, television, or internet | 114 | 30.5 |
| Healthcare professionals | 109 | 29.1 |
| Scientific publications | 18 | 4.8 |
| Reasons for choosing the CITs | | |
| Natural and safe | 122 | 40.3 |
| Improved the quality of life | 83 | 27.4 |
| Many sides effect of medical treatments | 80 | 26.4 |
| Believing that there is a direct solution | 14 | 4.6 |
| Supportive treatment | 4 | 1.3 |
| Benefits of CITs | | |
| Relaxation | 34 | 18.3 |
| Fast recovery | 25 | 13.4 |
| Reducing cough | 25 | 13.4 |
| Feeling fit | 23 | 12.4 |
| Increasing resilience | 21 | 11.3 |
| Decreasing pain | 14 | 7.5 |
| Decreasing fatigue | 14 | 7.5 |
| Spiritual well-being/placebo | 11 | 6.2 |
| Immunity boost | 7 | 3.5 |
| Alternative to anti-drug/vaccine | 3 | 1.5 |
| Increasing quality of life | 1 | 0.5 |
| The harms of the CITs | | |
| Liver toxicity | 2 | 1.0 |
| Low blood pressure | 2 | 1.0 |
| Pyrosis | 2 | 1.0 |
| Kidney toxicity | 1 | 1.0 |
| Impairment of liver functions | 1 | 0.5 |

CITs: Complementary and integrative therapies.

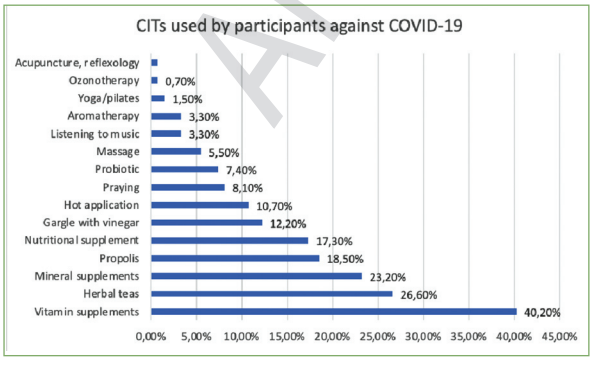


**FIGURE 1:** CITs methods used by participants against COVID-19.
CITs: Complementary and integrative therapies.

**TABLE 4:** Distribution of participants' ACTS scores by some variables (n=271).

| Characteristics | ACTS scores Median (Minimum-Maximum) | Analyses z/KW; p |
|---|---|---|
| Age, years | | |
| 18-24 | 17 (6-36) | 6.984; 0.072 |
| 25-44 | 19 (3-36) | |
| 45-64 | 18 (5-36) | |
| 65 and ↑ | 19 (5-36) | |
| Marital status | | |
| Married | 19 (5-36) | -0.597; 0.550 |
| Single | 18 (3-36) | |
| Education status | | |
| Primary school ↓ | 19 (14-36) | 1.491; 0.475 |
| High school | 20 (6-36) | |
| Bachelor or ↑ | 19 (3-36) | |
| Paid job | | |
| Yes | 19 (3-36) | -1.437; 0.151 |
| No | 20 (7-36) | |
| Economic status | | |
| Low income | 19 (6-36) | 0.830; 0.660 |
| Neutral income | 19 (5-36) | |
| High income | 19 (3-33) | |
| Had a health-related job | | |
| Yes | 17 (3-36) | -1.938; 0.053 |
| No | 19 (6-36) | |
| Longest residential area | | |
| Urban | 19 (3-36) | -0.181; 0.856 |
| Rural | 17 (9-33) | |
| Chronical disease | | |
| Yes | 19 (5-36) | 0,063; 0.949 |
| No | 19 (3-36) | |
| Used CITs during COVID-19 | | |
| Yes | 15 (0-39) | -6.588; <0.001* |
| No | 14 (0-39) | |
| Vaccinated against COVID-19 | | |
| Yes | 18 (3-36) | -3.346; <0.001* |
| No | 24 (10-33) | |
| Dose of vaccination against COVID-19 | | |
| 0 | 24 (6-36) | 69.703; 0.002** |
| 1 | 21 (10-32) | |
| 2 | 20 (6-36) | |
| 3 | 17 (3-36) | |
| 4 | 19 (8-36) | |
| 5 | 15 (5-36) | |
| 6 | 24 (10-33) | |

*p<0.001; **p<0.05; ACTS: The Attitude towards Using Complementary Treatments Scale; CITs: Complementary and integrative therapies; z: Mann-Whitney U; KW: Kruskal-Wallis tests.

## CITS AND COVID-19

The majority of our participants stated that they used CITs to alleviate COVID-19 symptoms, such as fa-

tigue, muscle and joint pain, and headaches. Mulder et al. and Kristoffersen et al. also reported that almost four out of five Norwegian and Dutch women used CITs to combat COVID-19 symptoms (77%).[9,20] A quarter of our participants took vitamin-mineral supplements and drank herbal teas. A recent study shows that most people who used CITs took vitamin-mineral supplements during the pandemic.[6] Moreover, women consumed vitamin-mineral supplements more than men.[4,20] In another recent study, it was noted that pregnant women particularly resorted to CITs during the pandemic to protect themselves from COVID-19, especially using garlic, turmeric, and ginger. Additionally, they stated that they found CITs to be safer than drug treatments and used them to increase their physical resistance.[31] Almost half of our participants believed that CITs were natural and safe. A quarter of our participants believed that CITs improved their quality of life. Mulder et al. also documented that people used CITs mostly because they believed that they improved their quality of life.[9] People believe that CITs have a high level of efficacy and few side effects.[9,20] Most of our participants noted that CITs helped them relax, recover faster, cough less, and feel energetic and strong. However, some participants stated that CITs caused liver toxicity, hypotension, and pyrosis. While certain researchers have documented the favorable impacts of CITs on alleviating COVID-19 symptoms, they have concurrently highlighted potential drug-drug and drug-nutrient interactions.[6,9] While certain countries have released guidelines pertaining to CITs amid the pandemic, a universally accepted, dependable guideline for global application remains elusive.[32,33] In addition, participants stated that they mostly obtained information about the CITs used from spouses, friends, neighbors, or through television and the internet, rather than from healthcare professionals. Similarly, a study conducted in Türkiye found that during the COVID-19 period, pregnant women obtained information on the use of herbal products more from the internet, social media, television and their surroundings rather than from healthcare professionals.[31] Especially in terms of preventing possible side effects in the using CITs or preventing drug-drug or drug-nutrient interaction or drug-herb interaction, it is among the issues that should be taken especially in situations where people have limited access to health, such as pandemics.

## ATTITUDES TOWARD USING CITS AND RESILIENCE DURING COVID-19

Attitude is characterized as an acquired and consistent emotional predisposition towards a given situation, indicating a state of preparedness to exhibit specific behaviors.[34] Put simply, individuals with positive attitudes towards a particular subject are more inclined to demonstrate behaviors that align with that subject. Our results also indicated that participants with more positive attitudes toward CITs used them to alleviate their COVID-19 symptoms. Moreover, participants who were vaccinated more than three times against COVID-19 had more positive attitudes toward using CITs. Nuraliyeva et al. further observed that nearly all women who had tested positive for COVID-19 (90%) had both received vaccinations and resorted to CITs.[36] Therefore, we can state that individuals who have taken precautions against the disease, including receiving the COVID-19 vaccine, tend to exhibit positive attitudes and behaviors when it comes to utilizing CITs.

Unforeseen events like the COVID-19 pandemic, characterized by an unknown treatment approach and resulting in social isolation, have profound impacts on individuals, families, and communities at large. In situations where access to healthcare services becomes challenging, individuals may grapple with not only the symptoms of the disease but also feelings of fear, anxiety, and depression stemming from uncertainty.[14] Duru et al. assert that the capacity to tolerate uncertainty assumes a significant role in elucidating resilience amid the COVID-19 pandemic. Hence, the pandemic exerts a detrimental effect on resilience, underscoring the influence of mental health in this context.[12] Sirois also contends that individuals capable of effectively managing everyday stressors tend to possess higher levels of resilience and are more inclined to engage in the use of CITs.[18] In a study examining multiple factors affecting COVID-19 in Italy, it was found that resilience is positively correlated with psychological well-being. It is suggested that these correlated fac-

tors could mitigate persistent negative psychological effects related to COVID-19, such as anxiety, intolerance of anxiety and resilience could alleviate the negative psychological impacts of the pandemic.[36] Our results also showed a significant, weak and positive correlation between participants' attitudes toward using CITs and resilience during COVID-19. The positive but weak correlation can be explained by the participants' using CITs against COVID-19 during the pandemic, which were primarily directed towards physical symptoms such as fatigue, muscle aches, and headaches rather than psychological symptoms. As a result, women with positive attitudes towards CITs may be inclined to use these methods, potentially enhancing their resilience.

### LIMITATIONS AND STRENGTHS

We recruited to women who used smartphones, had internet access and social media accounts because we conducted this study online. Therefore, women with high technology/digital literacy fill out the survey form. The high level of education of these women is also expected and a limitation of the study. Therefore, our results cannot be generalized to all Turkish women. This study has a high original value as it is the first study on this subject in our country.

## CONCLUSION

Considering that seven in every ten women used CITs when they had COVID-19, and a positive weak correlation existed between CITs and resilience; it is important to develop international and evidence-based CITs guidelines for diseases that threaten public health, such as COVID-19. These guidelines should be integrated into health services in primary health care organizations. Nurses should identify individuals resorting to CITs for mitigating COVID-19 symptoms and provide them with information regarding both the potential advantages and risks associated with such approaches. If necessary, nurses should provide individual counseling to those patients. This proactive communication can empower individuals to make informed decisions about their health management strategies. Researchers should conduct thorough investigations into the correlation between the utilization of CITs and resilience across diverse patient groups and various medical conditions. Such studies could shed light on the broader applicability and potential efficacy of CITs in fostering resilience within varying healthcare contexts.


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*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*


***Conflict of Interest***

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

***Authorship Contributions***

*All authors contributed equally while this study preparing.*



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