Original Research Article

Title:

Traditional medicine and Modern Medicine: knowledge, attitude, and practice of medical students and their mothers in Tabuk city, Saudi Arabia.

Running Title: Traditional Medicine, Modern Medicine and KAP

Abstract:

Background:

Traditional remedies are mostly used as auto-medications for the treatment of physical diseases not only in Saudi Arabia but also worldwide. The traditional preparations are also prescribed by practitioners to patients who seek their consultation.

Objective:

The objective of this descriptive, cross-sectional study was to assess knowledge, attitude and practice (KAP) of medical students and their mothers towards traditional medicine (TM) and modern medicine (MM) in Tabuk city.

Methods:

A cross-sectional survey of purposefully selected University Preparatory Program (UPP) students (n=147) for health specialties and their mothers (n=61) was conducted to examine their KAP of TM and MM at the University of Tabuk and mothers' homes. A self-designed, self-administered questionnaire with 10-item to be answered mostly by "yes" or "no" was used in this research.

Results:

There were no significant differences of opinion between students and their mothers on items of TM safety, efficacy, rapid cure, cost, and use in various mild diseases and cosmetic conditions. However, mothers' views differed significantly as regard self-use of herbal medicines for skin diseases and TM being primitive mode of treatment compared to students.

Conclusion: The preliminary findings of this survey suggest that the participants differentially preferred the use of both TM and MM in the treatment of various physical conditions as well as for cosmetic purposes. Further research is needed to comparatively explore medical student-mother KAP regarding TM and MM in Saudi Arabia.

Keywords: Traditional medicine, modern medicine, knowledge, attitude, practice.

Introduction

The use of traditional medicine (TM) also called complementary and alternative medicine (CAM) related to unorthodox medical systems is increasing worldwide with a focus to balance mind-body-spirit paradigm of a whole person with or without disease [1-2]. For example, the globally reported prevalence of CAM use among people with chronic diseases ranges between 17%-72.8% and the most commonly used CAM therapies were dietary interventions and non-vitamin/non-mineral dietary supplements, nutritional supplements, herbal medicines, spiritual healing, naturopathy, manipulative-body based therapy, energy therapy, and relaxation techniques [3-6]. This increase could be attributed to a variety of reasons such as dissatisfaction with modern medicine (MM) especially medications that are associated with major side effects and high cost [7]. Other relevant factors that urge patients to use CAM therapies include CAM therapies being safer, having relatively less side-effects, self-care paradigm, and modern medications being less effective in the cure of chronic conditions, promotion of health and general wellbeing and also difficulty in accessing physicians in hospitals.

The World Health Organization (WHO) defined TM as 'the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses"[8,9]. Notably, the terms complementary/alternative/non-conventional medicine are used interchangeably with TM in many countries [8]. Traditional medicine, accepted for its role in the maintenance of health and the treatment of physical and psychological diseases [9] is based on indigenous theories, beliefs, attitude, knowledge and experiences that are handed down from generation to generation [10]. In other words, WHO described TM as including "diverse health practices, approaches, knowledge and beliefs incorporating plant, animal, and/or mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness" [11].

TM is an ancient medical practice that existed in human societies long before the inception of MM and over the last few decades, public interest in TM has re-emerged, and likely to be continued with a greater pace and scientific rigor. This is because of multiple

reasons for example a portion of the people in many countries often seeks consultation from CAM practitioners for alternative approaches to maintain a good health status [8] and also self-manage chronic diseases such as type 2 diabetes mellitus (T2DM) with CAM therapies based on their knowledge, practice and attitude towards CAM [12]. Obviously, public demands for TM and its growing economic importance, have led to increased interest shown by governments and academic communities worldwide in CAM [3].

Practices of TM vary greatly across the world, as they are influenced by local culture, history, personal attitudes and philosophy. In many cases, their theory and applications are quite different from those of MM [6]. Despite CAM popularity and extensive use reflecting its increasing prevalence during the last couple of decades [3, 11], TM has not been officially recognized and regulated in most countries of the world and similarly the research in holistic system approaches remained poorly organized [13, 14]. As a corollary, education, training and research in this area have not received due attention and support [8]. However, this dismal scenario of CAM is undergoing rapid changes globally as a result of widespread support from public, medical communities and academicians, research institutions, international health organizations, and strong political support and governments' policies in favour for CAM worldwide, with more focus on training, research and regulatory measures [15-18].

A PubMed search of regional literature using keyword 'complementary and alternative medicine' retrieved more than a dozen of articles on CAM and these studies have explored public, medical students' and professionals' KAP towards CAM and its use in several health conditions in Saudi Arabia and other Gulf countries [5,6,12, 14, 19-31]. In these studies, up to 85% of respondents showed that the participants used CAM therapies especially green tea and other medicinal herbs, nutrition and food supplements, roqia, honey and bee products, wet cupping (hijama), prayers, black seed, myrrh, and cautery. The traditional practitioners were found to be spiritual healers, herbalists, providers of honeybee products and wet cupping therapists. Overall, there is scanty literature on traditional medicines in Arabian Gulf countries.

Aims of the study

This study comparatively assessed the knowledge, attitude and practice (KAP) of UPP students (first year medical students) and their mothers towards TM and MM.

Methods

Study design

This was a cross-sectional, quantitative university- and home-based survey of purposefully selected sample of UPP students enrolled for health speciality courses in Tabuk University and their mothers staying at home.

Setting

This study was conducted at Tabuk University in Tabuk city, during the year 2011. The university was established in year 2006. This university was selected because the researchers had easy access to her student colleagues and through them to their mothers, and hence ease of data collection from all the included participants. This university has no special clinics for TM and CAM curriculum, which are yet to be integrated into the main curriculum of the university.

Sample

The number of UPP students in Tabuk University is 430. The sample was comprised of first year medical students (n=200) and their mothers (n=200). The purposeful sample selection technique was used in this study. Notably, this is a unique sample comprising of first year medical students and their mothers.

Questionnaire

A pre-designed, structured questionnaire was used for the purpose of this study, which was developed in Arabic language after a literature review of the topic of research in a similar setting to tap the participants' KAP about TM and MM use in Tabuk city. The questionnaire was translated into English and then back into Arabic by two bilingual experts and one neutral expert to check its accuracy, with modifications applicable to the community of Saudi Arabia. This questionnaire comprised of 10 questions. For example, one of the questions was "does income impact choice of traditional 'alternative' medicine over modern medicine? Almost all questions need to be answered by participants in yes/no except two questions; do you prefer using alternative medicine for cosmetic purposes and are you one of those who use alternative medicine to treat skin disease without consultation were answered in yes/no/neutral. All the experts reached 98% agreement on all questions that were included in this questionnaire. This one-page questionnaire was pilot tested on a sample of 20 subjects for testing the logistics, suitability, and clarity of the data collection along with administration time. The students

suggested minor changes in Arabic version, and the modifications were made with the agreement of all the experts with regard to any question included in this questionnaire. The questions were rearranged for the sake of clear coding system and the data entry. Finally, all the experts reached consensus regarding this questionnaire, its English and Arabic versions. This developmental process and final selection of 10 questions based on bilingual experts' consensus may reflect acceptable psychometric properties especially reliability. English language version was necessary because many students requested it. Conversely, all mothers requested Arabic version (both versions are available upon request from EAAG).

Inclusion and exclusion criteria

The inclusion criteria were age 17 years and above who were able to give oral informed consent to participate in the study, and Saudi nationals who can understand at least Arabic language. The exclusion criteria were expatriates, age below 17 and those with intellectual disability, and those who cannot read or write Arabic.

Procedure

The participants were approached when they were not attending their classes. Mothers were approached by their daughters when they were free at home to fill out the questionnaire. The questionnaire was distributed by the first author to UPP students (n=200) in the class room who agreed to participate in the study. The researcher also requested these students to distribute this questionnaire to their mothers for filling it out completely after briefing them about the aims and purpose of this study. Those mothers (n=200) who agreed to participate were given this questionnaire. The daughters helped their mothers in case they need any clarification about any question. The researcher collected the duly filled questionnaires from students (n=147) immediately after they completed it. Students collected duly filled questionnaire from their mothers (n=61) after they completed it and returned all questionnaires to the researcher next day. The time taken to fill out the questionnaire was about 10 to 15 minutes. Notably, neither mothers nor students were exposed to formal courses of TM.

Data Management and Analysis

Statistical Package for Social Sciences (SPSS) Software Version.21 was used for data entry, coding, cleaning the data, data management and analysis. The results were described as

frequencies and percentages for all research variables. For continuous variables, mean and standard deviation were also calculated. The associations between both participants and their responses about TM and MM were determined using Pearson's Chi-square test. A p-value of ≤0.05 was considered significant. Yates correction test was used whenever necessary.

Ethical Considerations

The first author informed the concerned authorities of Tabuk University about this study. The permission was granted to her for conducting this study. Oral informed consent was taken from all participants prior to the distribution of questionnaire to them. The participants were clearly informed about the nature and objectives of the study. In addition, they were also informed that their anonymized data will be used only for research purpose and its confidentiality will be maintained. They can withdraw from this study and they can contact the study team for any query or to know the study results in the future. No incentives or rewards were given to the participants. Furthermore, this study did not involve any risk to the participants.

Results

There were 208 participants in this survey; 61 (29%) were mothers and 147 (71%) were university students, both living in Tabuk town. Their knowledge, attitude and practice about traditional medicine and modern medicine were assessed using a self-designed, structured questionnaire. Percentages were calculated using the total sample of mothers and students. The response rate of students was 73.5% whereas response rate of mothers was 30.5%. Some students (n=23, 11.5%) and mothers (n=45, 22.5%) withdrew from the study, and mothers were not able to read and write Arabic (n=51, 25.5%). Other reason for dropout was that students (n=30, 15%) and mothers (n=43, 21.5%) did not fill out questionnaires completely.

Among the respondents, 85% (n=176) preferred the use of MM while 15% (n=32) preferred traditional medicine when discussing their safety and rapid curative effect. Regarding cost, 43.3% (n=90) thought that income has substantial effect on selecting traditional medicine while 57.7% (n=118) disagreed on this point. Interestingly, 74% (n=153) of respondents reported no difference between traditional and modern medicine and 26% (n=55) perceived them different medical systems. Among participants, 14% (n=29) showed interest in traditional medicine, a primitive treatment preferred by tribal persons whereas 86%

(n=179) opted for modern medicine. Regarding herbal medicine, 29% of respondents (n=60) expressed they would prefer herbal preparations for the treatment of skin diseases, 32% of them (n=66) simply said no to use herbs and 39% of respondents (n=82) were neutral. For the treatment of simple illnesses like influenza, 59% of respondents (n=122) agreed about the use of traditional medicines, but 41% (n=86) disagreed with that practice. Notably, 69% of respondents (n=143) had used traditional medicine before for any kind of illness while 31% (n=65) of participants did not use traditional medicine for any disease in the past. Regarding the preference of traditional medicine use as cosmetics, 39% of participants (n=82) used TM for beauty purpose, 33% (n=68) of respondents preferred to use modern medicine and the rest (n=58, 28%) used neither of them. Traditional Medicine is preferred when Modern Medicine failed in treating diseases and preserving health, 97% of participants (n=201) agreed while 3% (n=7) disagreed. The use of Traditional Medicine in a scientific manner was assessed and 99% (n=207) of respondents agreed with this idea and only less than 0.5% (n=1) of respondent disagreed.

Table 1: Distribution of mothers (n=61) and students (N=147) responses by listed questionnaire variables

Variable	Mother	Student	Total	Exact P value
1. Cure and Safety				
Modern Medicine	50 (82%*)	126 (86%**)	176 (84.6%)	0.495
Traditional Medicine	11 (18%)	21 (14%)	32 (15.4%)	
2. Impact of income				
Yes	29 (48%)	61 (42%)	90 (43.3%)	0.423
No	32 (52%)	86 (58%)	118 (56.7%)	
3. Traditional and modern medicine are alike in efficacy				
Yes	43 (71%)	110 (75%)	153 (73.6%)	0.518
No	18 (29 %)	37 (25%)	55 (26.4%)	
4. Traditional medicine being primitive mode of treatment				
Yes	13 (21%)	16 (11%)	29 (13.9%)	0.048
NO	48 (79 %)	131 (89%)	179 (86.1%)	
5. Self-use of herbal medicines for skin diseases				
Yes	25 (41%)	35 (24%)	60 (28.8%)	0.004
No	22 (36%)	44 (30%)	66 (31.7%)	
Don't Know	14 (23%)	68 (46%)	82 (39.5%)	
6. Use of TM for the treatment of mild illnesses like common cold				
Yes	41 (67%)	81(55%)	122 (58.6%)	0.106
No	20 (33 %)	66 (45%)	86 (41.4%)	
7. Ever use of TM for the treatment of any form of illness				

Yes	47 (77%)	96 (65%)	143 (68.7%)	0.096
No	14 (23 %)	51 (35%)	65 (31.3%)	
8. Use of TM for cosmetic purpose				
Yes	22 (36%)	60 (41%)	82 (39.5%)	0.417
No	24 (39%)	44 (30%)	68 (32.7%)	
Neither of them	15 (25%)	43 (29%)	58 (27.8%)	
9. Use of TM when Modern Medicine failed in treatment of pain				
Yes	58 (95%)	143 (97%)	201 (96.6%)	0.708#
No	3 (5%)	4 (3%)	7 (3.4%)	
10. Support TM use in a scientific manner				
Yes	60 (98%)	147 (100%)	207 (99.5%)	0.647#
No	1 (2 %)	0 (0%)	1 (0.5%)	

*Percentages calculated from 61 mother and** 147 student samples, # Yates correction

Group Comparison

For all 10-item, percentages were calculated using independent samples of mothers (n=61) and students (n=147) [Table 1]. With regard to safety and fast recovery, 86% of students (n=126) preferred modern medicine compared to 82% of mothers (n=50) while only 18% of mothers (n=11) preferred traditional medicine compared to 14% of students (n=21). Personal income can affect the choice of people buying and taking traditional medicines over modern medicine, and 48% of mothers (n=29) agreed to this view compared to 42% of students (n=61). Traditional medicine is alike modern medicine with regard to efficacy, 71% of mothers (n=43) agreed compared to 75% of students (n=110). Seeking consultation from healers and taking traditional therapies is considered primitive, 11% of students (n=16) thought so compared to 21% of mothers (n=13) [p=0.048]. Herbal preparations are commonly used by individuals for skin diseases without consultation of specialist doctor; 43% (n=25) of mothers said "yes" while similar response was given by 24% (n=35) of students [p=0.004]. Perceptions of participants about using traditional medicine in the treatment of mild illness like influenza revealed that 67% (n=41) of mothers agreed its usage compared to 55% (n=81) of students. Using traditional medicine in the treatment of any diseases or illnesses showed that 77% (n=47) of mothers has agreed its usage in any type of illness compared to 65% (n=96) students in the past. Regarding assessment of preference of Traditional Medicine or Modern Medicine for cosmetic purposes among the respondents; 36% (n=22) of mothers agreed to use traditional medicine compared to students, 41% (n=60). The choice of Traditional Medicine when Modern Medicine failed especially in the treatment

of pain was high among both respondents; 95% of mother (n=58) and 97% of students agreed (n=7). Majority of mothers (n=60, 98%) and students (n=147, 100%) agreed to use traditional medicine in scientific manner. Most of the participants agreed to use differentially TM and MM in many chronic diseases, though no statistically significant differences were observed between two groups except especially the use of herbal remedies and TM being primitive mode of treatment.

Discussion

This cross-sectional study explored the KAP of medical students and their mothers towards traditional medicine and modern medicine. According to this study, with regard to safety and cure, most participants perceived that MM is safe and rapidly cures human diseases compared to TM. However, other researches have documented the safety and efficacy of traditional therapies [32]. Regardless of disease severity and onset, traditional therapies are reported to be safe [32] and used effectively in many chronic conditions [33]. In these conditions, modern medicine is of little help and adjunctive use of traditional therapies is possibly of further advantages. Traditional remedies are often used effectively as complementary to modern medications in several chronic health conditions with good outcome, though research in holistic approaches remained poorly organized [13]. It is wise to realize that both modern and traditional therapies could cause potential harms to the patients [34, 35, 36].

On whether or not family or personal income impacts use of traditional remedies, both participants were equally divided in their opinions. However, there is converging evidence that traditional therapies are cost-effective, and cheaper, and drive poor people and under-served communities to seek help from traditional healers and practitioners [33, 37]. Factors that support such TM help-seeking trend include, modern medicines being too expensive, physicians not easily accessible, and chronic diseases not fully cured by modern drugs, which also have potentially dangerous adverse effects [1, 35, 36]. At global level, people use out-of-pocket money in billions of US dollars on traditional remedies, most of which unlike modern therapies are not covered by insurance companies [24, 38]. This huge financial investment in traditional therapies by clients unsatisfied with modern medications invigorated public and governments' interest to frame policies that support research funding and the use of traditional remedies around the world [9-11, 15, 18, 39].

According to this study, mothers and their daughters held the view that TM is similar to MM in effectiveness. Both medical systems produce similar results in health conditions. This belief is often challenged by the opponents of traditional system simply because traditional therapies lack research support, researches based evidence and are not effective in many diseases. Notably, to gather evidence-based data several international health organizations and research institutions supported research, practice and training on traditional therapies across the world [15, 34]. Furthermore, the mechanisms of traditional therapies underlying their therapeutic effects are not clear and need to be further elucidated [40]. This is possible through conducting basic research in traditional therapies. Comparative studies are also needed to clarify which medical system and its products are more effective and produce better outcomes in human diseases. Over the past 15 years, researches with rigor methodologies are beginning to address these loopholes of traditional therapies [41-44]. It is expected that the research evidence to support the use of traditional therapies globally will continue to emerge and will bridge this knowledge gap in traditional medicine.

Evidently, a large number of clients tend to seek consultation from faith healers for the promotion of health and treatment of a variety of illnesses [9-11,13]. However this health seeking pathway is considered primitive approach of treating health conditions and is not justifiable in the present state of affairs. In fact, no doubt that the traditional therapies were used by ancient people as remedy for diseases, but presently modern people extensively use them for health promotion and for prevention and treatment of common diseases [4, 34, 35,38]. Furthermore, the increasing global prevalence of traditional therapies use is strong evidence against the aforesaid view [34, 35,36]. According to the present study, most mothers significantly supported the aforesaid view compared to their daughters which could be due to mother' sustained old beliefs in traditional medicine being ancient and primitive. Currently, traditional therapies which are diverse in numbers [1,2] are used as adjunctive or alternative to modern therapies. The traditional therapies are also integrated with modern medicine and this system is referred to as "integrative medicine" [45, 46]. The underlying philosophy of integrative medicine is holistic and the optimum use of both MM and TM in the management of physical and psychological disorders [47-49]. The integrative medicine paradigm tends to bring equilibrium between mind, body and spirit.

Herbal preparations are commonly used by individuals for skin diseases [40, 50-52]. These herbs may include but not limited to garlic, onion, neem, prickly chaff flower, beetroot, red cabbage, Barbados aloe, marigold, green tea, charas (marijuana), orchid tree,

298 saffron, turmeric, carrot, purple cone flower, eucalyptus (camphor oil), fig, lavender, henna,
299 tomato, mango, chamomile, bitter gourd, peach, rosemary, Ashoka and thyme. These herbs
300 are used in rashes, viral infections, bacterial infections, parasitic infection, fungal infections,
301 pigmentation disorders, cancers and tumors, trauma, and other conditions including wrinkles
302 [50]. Patients not only with skin disorders but also other diseases auto-medicate themselves
303 with phytomedicines without consultation of specialist doctor [53]. However, traditional
304 healers and allopathic physicians also reported to prescribe herbal medicines to patients with
305 dermal problems [50]. According to this research, mothers significantly supported this view
306 compared to their daughters. Women frequently use herbal preparations in the treatment of
307 skin disorders including breast cancer [54,55] and hence they supported the aforesaid view.
308 Conversely, their daughters who are medical students believe in modern medications being
309 the best treatment for multiple health problems [53]. What are the views of other researchers
310 on this mother-daughter paradigm and use of TM and MM is not known. This is because of
311 CAM researches yet to recruit mother-daughter sample to explore their KAP towards
312 traditional medicine including herbal preparations in various diseases including skin
313 problems.

314 It is generally believed that traditional remedies are commonly used in the treatment of
315 mild illness like common cold; however their use is not supported by strong evidence [56].
316 These remedies may include herbal preparations Shuanghuanglian oral liquid, Xiaoer
317 Resuqing oral liquid and antiviral drugs [57]. Sometimes people with common cold do not
318 use any medications traditional or modern and wait for recovery with time, because of its
319 self-limiting nature [58]. One study reported that about up to 17% of adults and 33% of
320 children with common cold visit a physician and this consultation trend is associated with
321 huge direct and indirect costs [59]. The recommended interventions for common cold were
322 physical approaches like hand wash, and zinc supplement (some benefits), followed by
323 probiotics, ginseng, gargle, exercise, vitamin C supplement, vitamin D, garlic supplement,
324 homeopathy, and Echinacea (no benefits). According to this study, mothers and their
325 daughters supported the use of traditional medicines in common cold but with no significant
326 differences in their responses.

327 According to this study, most mothers and their daughters opined that traditional
328 therapies are used in the treatment of any form of illness. This finding is consistent with other
329 studies [60,61]. These two studies reported about CAM therapies used in different
330 departments of public and private Norwegian and Danish hospitals. The reported findings

were that traditional therapies especially acupuncture and art therapy and massage are used in a variety of disciplines and related diseases including psychiatric disorders, painful conditions, cancers, blood diseases, substance use disorders, palliative conditions, disabilities, surgical conditions, gynaecology diseases and rheumatology disorders. People suffering from any form of diseases tend to use one or more than one traditional therapies in their life time (62). Evidently, the use of traditional remedies in a variety of diseases including cancers is on the increase around the world [33, 35,61].

According to this research, about 40% of participants agreed that people use TM for cosmetic purposes or for improving their appearance while 28% of subjects reported that they use neither TM nor MM for this particular purpose. A large number of studies supported the use of TM especially herbal products for beauty [52,63]. Young girls tend to use natural herbal products for improving their appearance, hairs, skin colour and tattooing, and weight reduction, all this associated with considerable costs, and sometimes with adverse outcomes [64].

Modern Medicine is not panacea in all diseases. Notably, persons with certain diseases such as prostate and pancreatic cancers, musculoskeletal diseases such as rheumatoid arthritis, ankylosing spondylitis, fibromyalgia syndrome, infectious conditions such as resistant tuberculosis, psychiatric disorders such as depression and schizophrenia, dementias, hypertension and other chronic painful conditions fail to respond to modern medications. Some of them only respond partially and continue to suffer with poor quality of life. In some of these clinical scenarios, the role of traditional therapies as complementary therapy is suggested and consequently patients tend to have better outcome, with better quality of life [65, 66]. In such clinical scenarios, high quality randomized clinical trials need to be conducted in future. The present study suggested adding TM in those patients with painful conditions which fail to respond to modern medications.

Finally, majority of participants agreed to the idea that traditional therapies need to be used in scientific ways. This paradigm suggests that traditional therapies should have evidence-based data about their effectiveness, association with better outcomes and lack of any major adverse effects, as found in many studies. Traditional remedies, either alone or as adjunctive treatment, should also target correctly diagnosed diseases after proper laboratory investigations. Furthermore, a specific traditional therapy should have specific indications for its use. A fist does not fit all sizes should apply to the discipline of traditional medicine.

According to this review, Indigo Naturalis is a safe, inexpensive, and effective standalone topical treatment for skin and nail psoriasis [67]. The role of traditional therapies in the promotion of health and wellbeing and prevention of disease [68] also need to be emphasized when planning health intervention strategies.

There are some limitations of this study. This is a cross-sectional study and hence no cause and effect relationship could be determined. Moreover, the demographic details of the participants were not collected. This research is conducted in Tabuk University only and therefore its results are not generalizable to other academic settings. No scoring system was used to assess and compare the KAP of TM and MM between two participants, students and mothers. Nonetheless, this study produced some preliminary results that are meaningful and make some sense in the context of TM and MM.

In conclusion, this preliminary study suggested that the mothers and their daughters preferred the use of traditional medicine in the treatment of various physical conditions as well as for cosmetic purposes. Mothers' opinion differed significantly with regard to the self-use of herbal medicines for skin diseases and traditional medicine being primitive mode of treatment. Future research should assess comprehensively the KAP of medical students and their mothers towards modern medicine and complementary and alternative medicine across Saudi Arabia.

Conflicts of interest: None, and unfunded research

Author contribution: All authors contributed equally to this work

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