



Effects of religiosity and religious coping on medication adherence and quality of life among people with epilepsy

Chung-Ying Lin^a, Mohsen Saffari^b, Harold G. Koenig^{c,d,e}, Amir H. Pakpour^{f,g,*}

^a Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hung Hom, Hong Kong

^b Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^c Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA

^d King Abdulaziz University, Jeddah, Saudi Arabia

^e Ningxia Medical University, Yinchuan, China

^f Social Determinants of Health Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

^g Department of Nursing, School of Health and Welfare, Jönköping University, Jönköping, Sweden

ARTICLE INFO

Article history:

Received 14 June 2017

Revised 23 September 2017

Accepted 7 October 2017

Available online 22 November 2017

Keywords:

Coping

Epilepsy

Medication adherence

Quality of life

Religious

ABSTRACT

The epidemiologic information demonstrates the importance of caring people with epilepsy (PWE). Indeed, the impaired quality of life (QoL) and medication nonadherence rate among PWE have been reported. However, religiosity and religious coping could be potential factors for clinicians to foster appropriate intervention on epileptic care. This study investigated two models to further understand the relationships between religiosity, religious coping (including positive and negative coping), medication adherence, and QoL in an Iranian sample with epilepsy. Eligible PWE ($n = 760$) completed the religiosity scale (Duke University Religion Index; DUREL) at baseline; the religious coping scale (Brief Religious Coping Scale; Brief RCOPE) one month later; the medication adherence scale (Medication Adherence Report Scale; MARS-5) two months later; and the QoL scale (Quality of Life in Epilepsy; QOLIE-31) twelve months later. Their antiepileptic drug serum level was measured during the period they completed the MARS. Through structural equation modeling (SEM), we found that religiosity directly correlated with negative religious coping and medication adherence, and indirectly correlated with medication adherence through negative religious coping. Both positive and negative religious coping directly correlated with medication adherence and QoL. Therefore, religiosity and religious coping may be determinants of medication adherence and QoL in PWE; health professionals may consider asking PWE if religion is important to them and how they use it to cope with their epilepsy.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Epilepsy is an important problem in developing countries because of the high incidence (~10 to 19 per 10,000 person-year) [1] and the negative impact of epileptic symptoms on quality of life (QoL) [2,3]. A recent review analyzed 45 articles [4] and concluded that Iran has a high prevalence of epilepsy (5% in central Iran; 1% in northern Iran; 4% in eastern Iran). As antiepileptic drugs (AEDs) have controlled symptoms [5] and QoL has improved [6,7], medication adherence is a key factor

in the lives of people with epilepsy (PWE). Unfortunately, the poor adherence to medication is a problem among PWE: medication nonadherence rates range between 30 and 50% [8–10]. Hence, improving medication adherence in this population should be a top priority.

In order to address medication adherence, we thought that religiosity and religious coping in Iran could be important determinants. Religiosity is a multidimensional concept, including personal religious beliefs (intrinsic religiosity), individual involvement in public religious activities (organizational religiosity), and private religious practices such as praying and reading religious texts (nonorganizational religiosity) [11, 12]. Moreover, the link between religiosity and epilepsy has been demonstrated among PWE (e.g., Wise-Knut) [13]; indeed, approximately 4% of PWE reported religious premonitory symptoms or auras [14]. An underlying mechanism also has been proposed: religious cognition is related to specific brain regions and people with brain disorder (e.g., PWE) may have neuropsychological processes that predispose them to greater religiosity [15]. Although to our knowledge, no studies have examined whether religiosity is positively related to medication

Abbreviations: Quality of life, QoL; People with epilepsy, PWE; Antiepileptic drugs, AEDs; Duke University Religion Index, DUREL; Brief Religious Coping Scale, Brief RCOPE; Five-item Medication Adherence Report Scale, MARS-5; Quality of Life in Epilepsy, QOLIE-31; structural equation modeling, SEM; Comparative fit index, CFI; Tucker–Lewis index, TLI; Root mean square of error approximation, RMSEA; Standardized root mean square residual, SRMR.

* Corresponding author at: Social Determinants of Health Research Center (SDH), Qazvin University of Medical Sciences, Shahid Bahonar Blvd, Qazvin 3419759811, Iran.

E-mail address: apakpour@qums.ac.ir (A.H. Pakpour).

adherence among PWE, studies on people with HIV/AIDS show a positive relationship [16,17]. Therefore, we hypothesized that religiosity may be positively associated with medication adherence in PWE in Iran.

In addition to the direct relationship, religious coping could be a mediator in the relationship between religiosity and medication adherence. Religious coping is different than coping in general. According to the religious coping theory proposed by Pargament et al. [18], religious coping involves finding meaning, gaining control, gaining comfort, gaining intimacy with others and closeness to God, and achieving life transformation through religious methods. More general forms of coping do not usually include such methods. Religious beliefs and activities have been reported to be important strategies for coping with many diseases including cardiovascular diseases [19]. A relationship between religious coping and medication adherence has been found: negative religious coping was negatively related to self-reported medication adherence in people with inflammatory bowel disease [20]. Thus, we hypothesized that religiosity may affect medication adherence through religious coping.

We assume that religiosity, spirituality, and mood interact with one another. Pargament et al. [18] have defined spirituality as the key function of religion, and Koenig et al. [21] indicate that spirituality may (or may not) lead to or arise from the development of religious rituals. Moreover, the relationship between religiosity and psychiatric symptoms was found to be similar to, but not the same as the relationship between spirituality and psychiatric symptoms [22]. Other studies have found that mood is associated with religiosity/spirituality [23,24]. Therefore, we assumed that religiosity, spirituality, and mood are three related factors, while religiosity and spirituality are similar but different concepts.

Because better medication adherence is related to higher level of QoL [25,26], we additionally postulated that religiosity and religious coping may be indirectly correlated with QoL through medication adherence. However, research is mixed with regard to support of this proposition. Giovagnoli et al. [27] found a positive relationship between religiosity and QoL, whereas Tedrus et al. [12] reported no relationship between religiosity and QoL. Because mediated effects are usually weak, some studies may detect such associations while others may not. Hence, we considered using a mediated model to better understand the relationship between religiosity, medication adherence, and QoL. As for the religious coping, we hypothesized that it might also have a direct association with QoL for PWE as demonstrated by Tedrus et al. [28].

We proposed two models to examine the relationships among religiosity, religious coping, medication adherence, and QoL in an Iranian sample of PWE. Specifically, Model 1 (Fig. 1) hypothesized that religiosity would be positively associated with positive religious coping and medication adherence, and be negatively associated with negative

religious coping; positive/negative religious coping would be positively/negatively associated with medication adherence; positive and negative religious copings would mediate the association between religiosity and medication adherence. Model 2 (Fig. 2) hypothesized that medication adherence would be positively associated with QoL and that positive and negative religious coping together with medication adherence would mediate the relationship between religiosity and QoL.

2. Methods

2.1. Participants

From 2015 to 2016, PWE were prospectively recruited from four neurology clinics in the cities of Tehran and Qazvin. Participants were included if they (a) were 18 years old or more, (b) had a diagnosis for epilepsy identified by the International League Against Epilepsy criteria [29]; and (c) had been prescribed antiepileptic drugs. Patients were excluded if they (a) were not able to provide consent or (b) had intellectual disability or cognitive impairment (as assessed using the minimal status examination: MMSE < 24 [30]). The study was approved by the Ethics Committee of Qazvin University of Medical Sciences, and all participants provided informed consent before enrolling in the study.

2.2. Measures

2.2.1. Religiosity: Duke University Religion Index (DUREL)

The DUREL, a five-item scale, was used to measure religiosity. The five items were made up of three dimensions: intrinsic religiosity (3 items), organizational religiosity (1 item), and nonorganizational religiosity (1 item). All items are rated on a five-point Likert scale [31]. As suggested by the developers, the three dimensions should not be summed to prevent effects canceling out each other [32]. Therefore, using latent construct to measure the religiosity seems most appropriate. In addition, the DUREL has been translated into Persian for use in Iranian populations using the standard translation process, cognitive debriefing, and psychometric testing. The internal consistency is high ($\alpha = 0.87$ and 0.92), the test–retest reliability is excellent (intraclass correlation coefficient = 0.96 to 0.99), and the concurrent validity is based on strong high correlations with the Santa Clara Strength of Religious Faith Questionnaire ($r = 0.62$ to 0.79) [33].

2.2.2. Religious coping: Brief Religious Coping Scale (Brief RCOPE)

The 14-item brief RCOPE measures positive (7 items) and negative religious coping (7 items). Positive religious coping emphasizes connections with a transcendent force and belief in a benevolent higher power;

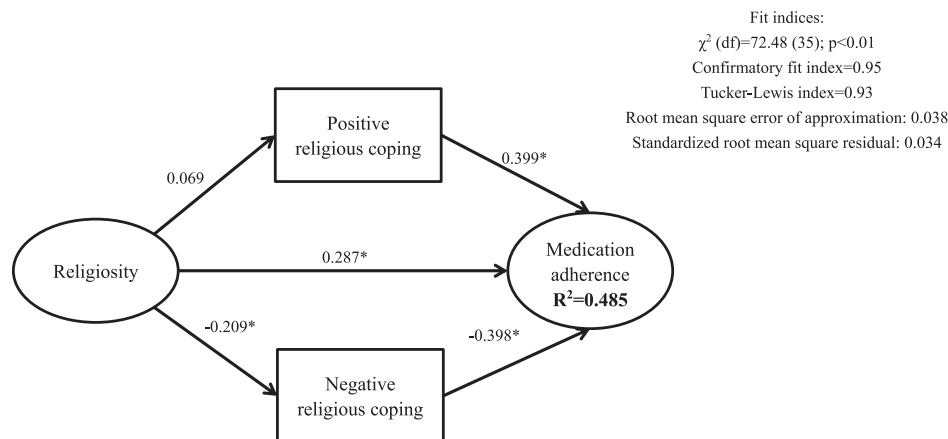


Fig. 1. Model 1: relationships between religiosity, religious coping, and medication adherence. Religiosity was composed of intrinsic, organizational, and nonorganizational religiosity; medication adherence included antiepileptic drug serum level and Medication Adherence Report Scale (MARS) score. Age, gender, duration of illness, and education were adjusted for in the model. * $p < 0.001$.

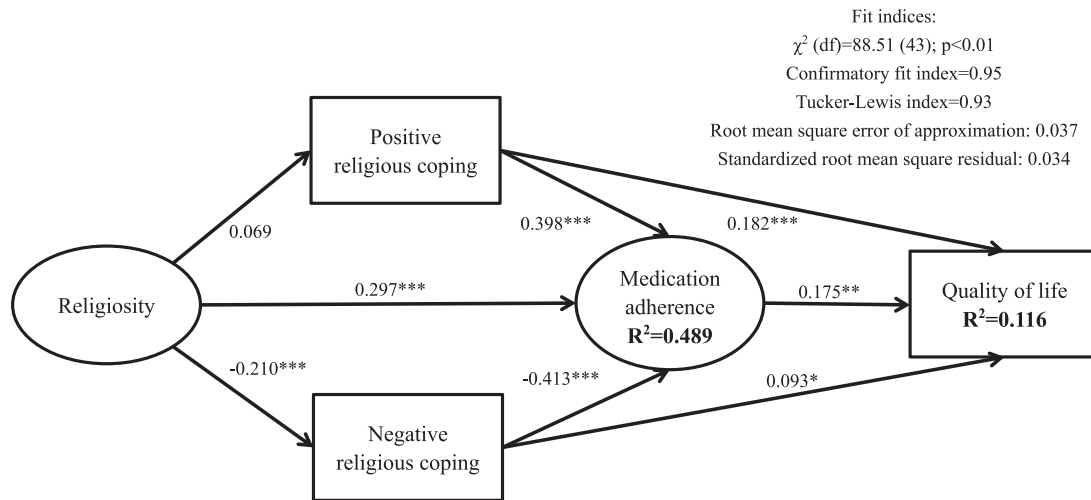


Fig. 2. Model 2: relationships between religiosity, religious coping, medication adherence, and quality of life (QoL). Religiosity was composed of intrinsic, organizational, and nonorganizational religiosity; medication adherence included antiepileptic drug serum level and Medication Adherence Report Scale (MARS) score; QoL was measured using the Quality of Life in Epilepsy. Age, gender, duration of illness, and education were adjusted for in the model. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

negative religious coping emphasizes spiritual tension, spiritual doubting, and negative reappraisals of the divine [34,35]. Examples of items on the positive religious coping subscale include “Looked for a stronger connection with God” and “Sought God’s love”. Sample items on the negative religious coping subscale include “Wondered whether be abandoned by God” and “Felt punished by God because of the lack of devotion” [34]. All items are listed in Table 1.

2.2.3. Medication adherence

Medication adherence was assessed using the five-item Medication Adherence Report Scale (MARS-5); in addition, antiepileptic drug serum levels were measured. The MARS-5 contains five items that ask about medication adherence, all rated on a five-point Likert scale. A higher score indicates better medication adherence. The MARS-5 has satisfactory internal consistency ($\alpha = 0.78$) [36] and concurrent validity ($r = 0.50$ with adherence ratings by healthcare providers) [37]. Although the psychometric properties of the MARS-5 Persian version have not been examined previously, its linguistic validity has been demonstrated [38].

Before participants took their next dose of drug (i.e., AEDs), blood samples were obtained to determine antiepileptic drug serum levels using a microparticle enzyme immunoassay (Abbott AxSYM®, Abbott Laboratories, Abbott Park, IL, USA), align with suggested procedure [39]. Based on the recommendations [40], we classified all the data into three categories: below, within, or above the therapeutic range.

Table 1
 Items in Brief Religious Coping Scale (Brief RCOPE).

Item
1. Looked for a stronger connection with God
2. Sought God’s love and care
3. Sought help from God in letting go of my anger
4. Tried to put my plans into action together with God
5. Tried to see how God might be trying to strengthen me in this situation
6. Asked forgiveness for my sins
7. Focused on religion to stop worrying about my problems
8. Wondered whether God had abandoned me
9. Felt punished by God for my lack of devotion
10. Wondered what I did for God to punish me
11. Questioned God’s love for me
12. Wondered whether my church had abandoned me
13. Decided the devil made this happen
14. Questioned the power of God

2.2.4. Quality of life: Quality of Life in Epilepsy (QOLIE-31)

The QOLIE-31, a 31-item questionnaire, was used to assess the QoL. Of the 31 items, one item is rated using a visual analogue scale, a second item is assessed using a “face” scale, and the other 29 items are rated on Likert-type scales (from 4 to 6 points). Except for the item on visual analogue scale, the items make up the following seven domains: seizure worry (5 items), cognitive function (6 items), energy/fatigue (4 items), emotional well-being (5 items), social function (5 items), medication effects (3 items), and overall QoL (2 items). According to the developers [41] and the scoring manual [42], all seven domains can be transformed into a 0–100 scale with higher scores indicating better QoL. An overall QoL score can then be computed based on the transformed domain scores. The original English version of QOLIE-31 has acceptable psychometric properties (test–retest reliability, $r = 0.64$ to 0.89 ; internal consistency, $\alpha = 0.77$ to 0.93) [42], and the Persian version has been validated in Iran (test–retest reliability, $r = 0.68$; internal consistency, $\alpha = 0.90$) [43].

2.3. Procedure

Two trained research assistants screened patients for eligibility. Eligible patients were asked to attend a short education session on study aims and complete informed consent in a private clinic room. Of 922 approached patients, 812 (88%) participated in the education session. Fifty-two patients did not sign the informed consent form and were excluded from the study. Therefore, we analyzed the data of the retained 760 PWE. After signing the consent form, participants were asked to complete the religiosity scale and a sociodemographic measure (baseline assessment). Participants completed the measure of religious coping (brief RCOPE) at one month after the baseline assessment. Two months after the baseline assessment, participants were asked to complete the self-reported measure of medication adherence (MARS-5). The objective measure of AED adherence was assessed on the same day from blood samples. Twelve months after baseline assessment, participants were asked to complete the QoL measure (QOLIE-31).

2.4. Data analysis

All the demographics and clinical characteristics were analyzed using mean (SD) for continuous variables and n (%) for categorical variables. We used structural equation modeling (SEM) to examine our proposed models. It is a statistical analysis that includes two major

components: a measurement component that estimates the factor loadings and a structural component that estimates the path coefficients (i.e., the regression coefficients) and correlations (similar to Pearson correlation) [44]. Therefore, based on SEM, we can simultaneously obtain different statistical values, including factor loading, R^2 , and path and correlation coefficients.

In our proposed models, Model 1 (Fig. 1) examined the associations among religiosity, positive and negative religious copings, and medication adherence; Model 2 (Fig. 2) examined the associations between QoL and the four aforementioned factors. To further examine the association between religiosity and QoL, Model 3 (Fig. 3) based on Model 2 was constructed. All models controlled the demographics of age, gender, duration of illness, years of education. In addition, religiosity (included intrinsic, organizational, and nonorganizational religiosity) and medication adherence (included MARS-5 score and AED serum levels) were constructed as latent variables. Directional instead of reciprocal associations were assumed in the two models because we collected the data in a certain sequence across time (religiosity at baseline; religious coping at one-month follow-up; medication adherence at two-month follow-up; QoL at twelve-month follow-up). These directional effects were based on the literature [16,17,19,20,25,26]. Moreover, we assessed constructs at different follow-up times, assuming that QoL changes more slowly in people with chronic epilepsy with religious coping and medication adherence preceding those changes. The literature suggests that religiosity leads to religious coping, which leads to medication adherence, which leads to QoL [16,17,19,20,25,26]. Therefore, we believe that the time sequence of assessments during follow-up was appropriate.

The measurement part of the SEM models (i.e., whether the three domain scores loaded on the religiosity domain; whether MARS-5 and serum level loaded on the medication adherence domain) was examined in addition to the structural part (i.e., the paths among factors) of the models. Specifically, we hypothesized that religiosity and religious coping were directly associated with medication adherence, and medication adherence and religious coping were directly associated with QoL. We also hypothesized that positive and negative religious coping were mediators in the relationship between religiosity and medication adherence, and that both religious coping and medication adherence were mediators in the relationship between religiosity and QoL.

Both SEM models were estimated using the maximum likelihood method, and the missing values were treated using the full information

maximum likelihood estimator. Before testing the path coefficient and mediated effects, we used four indices to determine acceptable model fit for both models: comparative fit index (CFI) and Tucker–Lewis index (TLI) were set at 0.9 or above; root mean square of error approximation (RMSEA) and standardized root mean square residual were set at 0.08 or below [45–47]. After ensuring model fit, we examined whether the measurement part of both models were acceptable; acceptable measurement should have all factor loadings >0.3 . Finally, we used Sobel tests to test the significance level of each of the mediated effects [48].

Data were analyzed using SPSS 23.0 (for descriptive analyses of demographics and clinical characteristics) and R software with Lavaan package (for model testing and mediated effects of the two SEM models) [49].

3. Results

Table 2 demonstrates the characteristics of participants ($n = 760$), including religiosity, religious coping, medication adherence, and QoL. Participants were relatively young (mean age = 36.19; SD = 13.13). Nearly half (45.5%) were male, and most were currently married (76.2%). Mean duration of illness was 6.86 years (SD = 4.54). The most common diagnosis was symptomatic partial epilepsy (45.7%), followed by idiopathic generalized epilepsy (30.7%), and cryptogenic partial epilepsy (23.7%). At the two-month follow-up, slightly more than half of the participants had AED serum levels in the recommended therapeutic range (52.6%).

All proposed models (Figs. 1–3) had acceptable fit, except for the significant χ^2 . In Model 1, fit indices were CFI = 0.95, TLI = 0.93, RMSEA = 0.038, and SRMR = 0.034; in Model 2, they were CFI = 0.95, TLI = 0.93, RMSEA = 0.037, and SRMR = 0.034; and in Model 3, they were CFI = 0.95, TLI = 0.92, RMSEA = 0.038, and SRMR = 0.034. With regard to the measurement part of both models, intrinsic (factor loading = 0.71), organizational (factor loading = 0.72), and nonorganizational religiosity (factor loading = 0.36) loaded strongly on the latent construct of religiosity (all p -values <0.001); MARS-5 (factor loading = 0.87) and antiepileptic serum level (factor loading = 0.37) also loaded acceptably on the latent construct of medication adherence (both p -values <0.001). In terms of the structural part of both models, all paths were significant except for the path between religiosity and positive religious coping (standardized coefficient = 0.069 and $p = 0.12$ in both models).

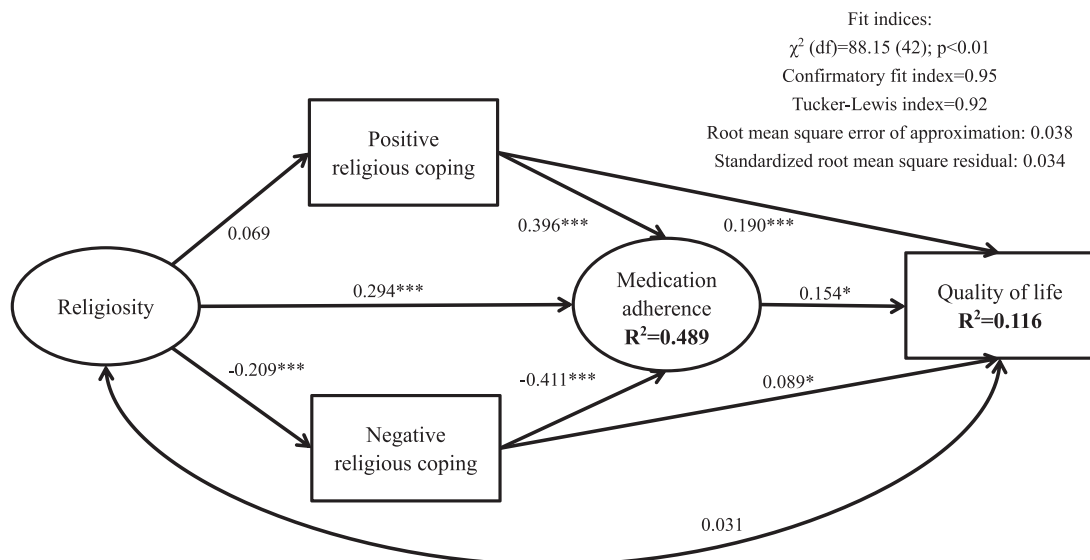


Fig. 3. Model 3: religiosity measured by intrinsic, organizational, and nonorganizational indicators; medication adherence assessed by antiepileptic drug serum level and Medication Adherence Report Scale (MARS) score; and quality of life measured using the Quality of Life in Epilepsy Scale. Age, gender, duration of illness, and education were adjusted for in the model. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 2
Participants' characteristics.

Characteristics	n (%) or M (SD)
Baseline	
Age (year)	36.19 (13.13)
Gender (male)	346 (45.5%)
Years of education	8.88 (5.11)
Marital status	
Single	162 (21.3%)
Married	579 (76.2%)
Widowed	18 (2.4%)
Missing	1 (0.1%)
Duration of illness (year)	6.86 (4.54)
Type of epilepsy	
Generalized	233 (30.7%)
Focal	527 (69.3%)
Age at the seizure onset	29.33 (12.83)
Surgical intervention (yes)	160 (21.1%)
Type of AED	
Monotherapy	343 (45.1%)
Polytherapy	417 (54.9%)
MMSE	28.0 (2.2)
Type of lesions ^a	
DNET	30 (16.7%)
Ganglioglioma	23 (12.8%)
traumatic brain injury	60 (33.3%)
Acute cerebrovascular accident	22 (12.2%)
Unknown	45 (25.0%)
Religiosity	
Intrinsic	9.14 (4.87)
Organizational	3.75 (1.88)
Non-organizational	3.91 (2.00)
One month after baseline	
Positive religious coping	18.05 (7.51)
Negative religious coping	13.33 (7.31)
Two months after baseline	
Medication Adherence Report Scale	13.46 (6.52)
Antiepileptic drug serum level	
Below therapeutic range	360 (47.4%)
Within therapeutic range	298 (39.2%)
Above therapeutic range	102 (13.4%)
One year after baseline	
Quality of Life in Epilepsy	68.82 (20.34)

DNET = Dysembryoplastic neuroepithelial tumor; MMSE = mini-mental status examination.

^a With missing values.

Negative associations were found between negative religious coping and both religiosity and medication adherence; all other associations were positive.

Religiosity, positive religious coping, and negative religious coping together explained a substantial proportion of variance of medication adherence (48.5% in Model 1 and 48.9% in Model 2). The explained variance for QoL, however, was only modest in Model 2 (11.6%). Model 3 was similar to Model 2, although religiosity was not significantly correlated with QoL in that model (Fig. 3). In addition to the direct effects shown in Models 1 and 2, Sobel tests revealed several significant mediated effects (Table 3) as follows: negative religious coping in the relationship between religiosity and medication adherence (standardized coefficient = -0.060 ; $p < 0.001$); medication adherence in the relationship between religiosity and QoL (standardized coefficient = 0.052 ; $p = 0.01$); and negative religious coping together with medication adherence in the relationship between religiosity and QoL (standardized coefficient = 0.015 ; $p = 0.02$).

4. Discussion

We found that religiosity directly correlated with negative religious coping and medication adherence, and indirectly correlated with medication adherence through negative religious coping. Both positive and negative religious copings directly correlated with medication

Table 3

Mediated effects in the relationship between religiosity and medication adherence (Model 1), and between religiosity and quality of life (Model 2).

Mediator(s)	Coefficient (SE)/standardized coefficient	
	Model 1	Model 2
Positive religious coping	0.466 (0.310)/0.020**	0.190 (0.129)/0.013
Negative religious coping	$-1.387 (0.392)/-0.060^{***}$	$-0.296 (0.157)/-0.019^{\#}$
Medication adherence	–	0.788 (0.304)/0.052*
Positive religious coping and medication adherence	–	0.073 (0.053)/0.005
Negative religious coping and medication adherence	–	0.230 (0.097)/0.015*

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

$p = 0.06$.

adherence and QoL. Thus, religiosity was indirectly correlated with QoL through medication adherence and negative religious coping.

The finding of positive relationship between religiosity and medication adherence supported our hypothesis and is consistent with studies on people with HIV/AIDS [16,17]. However, the results here on religious coping and medication adherence are inconsistent with studies on people with inflammatory bowel disease [20]. Although results from both Freitas et al. [20] and us indicate that negative religious coping has a negative relationship with medication adherence, the significant relationship found between positive religious coping and medication adherence contrasts with the nonsignificant finding reported by Freitas et al. [20].

Three possible reasons may explain differences between the results of Freitas et al. [20] and ours. First, the populations were different. Freitas et al. [20] examined a Brazilian sample, while we studied an Iranian sample. Because these ethnic groups may vary in their religious beliefs, the effects of religious coping may differ as well. Second, Freitas et al. [20] adopted a cross-sectional design to test the relationship between religious coping and medication adherence, while we collected the information on religious coping (one month after baseline) and medication adherence (two months after baseline) at different time points. It is possible that negative religious coping may have earlier effects than positive religious coping on medication adherence does. Third, Freitas et al. [20] only used a subjective report of medication adherence, whereas we used both subjective and objective measures. The different adherence measures, then, could account for the different findings.

Future studies are needed to determine the validity of the speculations. However, the relationship between negative religious coping and medication adherence in both the present study and Freitas et al. [20] suggests that health professionals in epileptic care should consider addressing negative religious coping among PWE to increase their medication adherence. In addition, some may question whether different measures of AED adherence (i.e., MARS-5 vs. AED serum levels) may vary in their correlation with religiosity, positive religious coping, and negative religious coping. Given that this was not the primary purpose of this study, we constructed another SEM model that did not combine MARS-5 and serum levels as a latent construct to address this. Those results showed that MARS-5 ($R^2 = 0.31$), compared with AED serum level ($R^2 = 0.07$), had a stronger correlation with religiosity, positive religious coping, and negative religious coping. Future studies may wish to replicate these findings.

The relationship between religiosity and QoL shown in Model 2 suggests that these two factors are only weakly correlated, and a similar finding has been found in patients undergoing hemodialysis in Iran [50]. The weak and mediated associations help to explain why some investigators found a significant relationship between religiosity and QoL [27], while others have not [28]. We found that religiosity was associated with QoL only when mediated by medication adherence. In addition,

the mediated effects were relatively weak ($B = 0.052$ through medication adherence; $B = 0.015$ through negative religious coping and medication adherence). Indeed, the explained variance for QoL in the entire model was quite low (11.6%). The direct relationship between religious coping and QoL and that between medication adherence and QoL are consistent with previous studies on PWE [25–28]. The nonsignificant correlation between religiosity and QoL indicated in Model 3 suggests that religiosity might not have a direct association with QoL. Instead, religiosity is likely related with QoL through other mediators (e.g., religious coping and medication adherence).

Based on our findings, we propose two recommendations for health professionals when providing epileptic care. First, we recommend that providers encourage PWE to use positive religious coping. Among PWE who are using negative religious coping, health professionals should consider referring them to pastoral care providers (chaplains, pastoral counselors, and other trained clergy) to address their religious coping struggles [51]. Second, we recommend that integrating patients' religious beliefs into counseling may enhance its effectiveness. Indeed, a meta-analysis has confirmed the positive effects of religious interventions on both biological and psychological outcomes for oncology patients [52]. We believed that such interventions might have similar effects in PWE.

4.1. Limitations

There are several limitations to the study. First, it is unclear whether these results can be generalized to other ethnicities because of their varying religious beliefs. For example, all of our participants were Muslim, and it is unclear whether the effects of religious beliefs in Muslim are similar to those with other religion beliefs (e.g., Buddhists and Christians). Second, although we applied a longitudinal design to investigate the relationships among religiosity, religious coping, medication adherence, and QoL for PWE, this is essentially a cross-sectional analysis; and we did not control for outcomes at baseline. That is, we did not measure baseline medication adherence and QoL. Therefore, we cannot conclude that changes in religious coping affect change of medication adherence or QoL. Third, our measures on medication adherence may be affected by (1) previous studies showing that MARS-5 correlated poorly with medication refills [53], and (2) half of our participants had low AED serum levels; such low levels could be due to inadequate prescribing, time of testing (hours postdose), or poor adherence.

Fourth, we did not control for mood or seizure frequency, two potentially important confounders in our proposed model [23,24,54]. We recommend that future studies that seek to replicate our findings control for both mood and seizure frequency. Mood, anxiety, or other psychological symptoms may influence and interact with general coping and QoL. Furthermore, seizure frequency may be correlated with drug-resistance and medication adherence, and the AED regimen may affect cognitive functions and daily activities. Given that AED treatment consisted of 45.1% monotherapy and 54.9% polytherapy, we speculate that our sample was evenly distributed between mild and severe epilepsy.

Fifth, incomplete information on brain lesion, lesion location and laterality in nearly half of the sample, and such factors may affect cognition and coping behavior, particularly if the lesion involves the frontal or mesial temporal lobe or other limbic structures. Future studies attempting to replicate our findings should collect such information.

Sixth, the measures used in this study, such as the RCOPE and the MARS-5 (our primary measure of drug adherence) may also have limitations. The RCOPE likely has some overlap with the DUREL, in that those who are more religious are likely to use religion in coping. The reliability of MARS-5 (our primary measure of drug adherence), in turn, is not well-established. Lastly, we did not collect information on how PWE think about their bodies. Some pious people may wish to keep their bodies pure and free from medication, and some may believe that seizures are their destiny (a concept that is very important in Islam).

Therefore, religiosity may result in both poorer adherence and better adherence, issues that future psychological and philosophical studies will need to address.

4.2. Conclusion

In conclusion, the present findings suggest that religiosity and religious coping may be determinants of medication adherence and QoL in PWE. Higher level of religiosity may lead to less negative religious coping, and the less use of negative religious coping may help to increase medication adherence. Since higher positive religious coping was associated with greater medication adherence, health professionals may consider asking PWE if religion is important to them and how they use it to cope with their epilepsy. If religion is important to them and they use it to cope, then encouraging positive forms of religious coping may be considered. Among those who are using negative religious coping, referral to religious professionals who are trained on how to address these issues (pastoral counselors, chaplains) may be warranted.

Conflict of interest

All the authors have no conflict of interests.

References

- [1] Sander JW. The epidemiology of epilepsy revisited. *Curr Opin Neurol* 2003;16:165–70.
- [2] Ettinger AB, Ottman R, Lipton RB, Cramer JA, Fanning KM, Reed ML. Attention-deficit/hyperactivity disorder symptoms in adults with self-reported epilepsy: results from a national epidemiologic survey of epilepsy. *Epilepsia* 2015;56:218–24.
- [3] Ottman R, Lipton RB, Ettinger AB, Cramer JA, Reed ML, Morrison A, et al. Comorbidities of epilepsy: results from the epilepsy comorbidities and health (EPIC) survey. *Epilepsia* 2011;52:308–15.
- [4] Sayemiri K, Tavan H, Sayemiri F, Mohammadi I, Carson KV. Prevalence of epilepsy in Iran: a meta-analysis and systematic review. *Iran J Child Neurol* 2014;8:9–17.
- [5] Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med* 2000;342:314–9.
- [6] Eatock J, Baker GA. Managing patient adherence and quality of life in epilepsy. *Neuropsychiatr Dis Treat* 2007;3:117–31.
- [7] Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: surveys of patients with epilepsy and physicians. *Epilepsy Behav* 2008;13:316–22.
- [8] Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimens. *Seizure* 1997;6:87–93.
- [9] Dilorio C, Shafer PO, Letz R, Henry TR, Schomer DL, Yeager K. Project EASE: a study to test a psychosocial model of epilepsy medication management. *Epilepsy Behav* 2004;5:926–36.
- [10] Pakpour AH, Gholami M, Esmaeili R, Naghibi SA, Updegraff JA, Molloy CJ, et al. A randomized controlled multimodal behavioral intervention trial for improving antiepileptic drug adherence. *Epilepsy Behav* 2015;52:133–42.
- [11] Ellison CG, Levin JS. The religion-health connection: evidence, theory, and future directions. *Health Educ Behav* 1998;25:700–20.
- [12] Tedrus GM, Fonseca LC, Fagundes TM, da Silva GL. Religiosity aspects in patients with epilepsy. *Epilepsy Behav* 2015;50:67–70.
- [13] Brodtkorb E, Nakken KO. The relationship between epilepsy and religiosity illustrated by the story of the visionary mystic Wise-Knut. *Epilepsy Behav* 2015;46:99–102.
- [14] Devinsky O, Lai G. Spirituality and religion in epilepsy. *Epilepsy Behav* 2008;12:636–43.
- [15] Johnstone B, Holliday G, Cohen D. Heightened religiosity and epilepsy: evidence for religious-specific neuropsychological process. *Ment Health Relig Cult* 2016;19:704–12.
- [16] Raghavan R, Ferlic-Stark L, Clarke C, Rungta M, Goodgame R. The role of patient religiosity in the evaluation and treatment outcomes for chronic HCV infection. *J Relig Health* 2013;52:79–90.
- [17] Simoni JM, Frick PA, Huang B. A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy. *Health Psychol* 2006;25:74–81.
- [18] Pargament KI, Koenig HG, Perez LM. The many methods of religious coping: development and initial validation of the RCOPE. *J Clin Psychol* 2000;56:519–43.
- [19] Najafi Ghezjelteh T, Emami A. Strategies for recreating normal life: Iranian coronary heart disease patients' perspectives on coping strategies. *J Clin Nurs* 2014;23:2151–60.
- [20] Freitas TH, Hyphantis TN, Andreoulakis E, Quevedo J, Miranda HL, Alves GS, et al. Religious coping and its influence on psychological distress, medication adherence, and quality of life in inflammatory bowel disease. *Rev Bras Psiquiatr* 2015;37:219–27.
- [21] Koenig HG, McCullough ME, Larson DB. *Handbook of religion and health*. New York: Oxford University Press; 2001.

- [22] King M, Marston L, McManus S, Brugha T, Meltzer H, Bebbington P. Religion, spirituality and mental health: results from a national study of English households. *Br J Psychiatry* 2013;202:68–73.
- [23] Stroppa A, Moreira-Almeida A. Religiosity, mood symptoms, and quality of life in bipolar disorder. *Bipolar Disord* 2013;15:385–93.
- [24] Szczesniak RD, Zou Y, Dimitriou SM, Quittner AL, Grosseohme DH. Use of daily phone diary to study religiosity and mood: convergent validity. *J Health Care Chaplain* 2017;23:67–85.
- [25] Lin C-Y, Burri A, Fridlund B, Pakpour AH. Female sexual function mediates the effects of medication adherence on quality of life in people with epilepsy. *Epilepsy Behav* 2017;67:60–5.
- [26] Lin C-Y, Chen H, Pakpour AH. Correlation between adherence to antiepileptic drugs and quality of life in patients with epilepsy: a longitudinal study. *Epilepsy Behav* 2016;63:103–8.
- [27] Giovagnoli AR, Meneses RF, da Silva AM. The contribution of spirituality to quality of life in focal epilepsy. *Epilepsy Behav* 2006;9:133–9.
- [28] Tedrus GM, Fonseca LC, De Pietro Magri F, Mendes PH. Spiritual/religious coping in patients with epilepsy: relationship with sociodemographic and clinical aspects and quality of life. *Epilepsy Behav* 2013;28:386–90.
- [29] Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia* 2010;51:676–85.
- [30] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
- [31] Koenig H, Parkerson GR, Meador KG. Religion index for psychiatric research. *Am J Psychiatry* 1997;154:885–6.
- [32] Koenig HG, Büssing A. The duke university religion index (DUREL): a five-item measure for use in epidemiological studies. *Religions* 2010;1:78–85.
- [33] Saffari M, Zeidi IM, Pakpour AH, Koenig HG. Psychometric properties of the Persian version of the Duke University Religion Index (DUREL): a study on Muslims. *J Relig Health* 2013;52:631–41.
- [34] Pargament K, Feuille M, Burdzy D. The Brief RCOPE: current psychometric status of a short measure of religious coping. *Religions* 2011;56:51–76.
- [35] Mohammadzadeh A, Najafi M. Factor analysis and validation of the Brief Religious Coping Scale (Brief-RCOPE) in Iranian university students. *Ment Health Relig Cult* 2016;19:911–9.
- [36] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67–74.
- [37] Jónsdóttir H, Opjordsmoen S, Birkenaes AB, Engh JA, Ringen PA, Vaskinn A, et al. Medication adherence in outpatients with severe mental disorders: relation between self-reports and serum level. *J Clin Psychopharmacol* 2010;30:169–75.
- [38] Lin C-Y, Updegraff JA, Pakpour AH. The relationship between the theory of planned behavior and medication adherence in patients with epilepsy. *Epilepsy Behav* 2016;61:231–6.
- [39] Tomson T, Dahl ML, Kimland E. Therapeutic monitoring of antiepileptic drugs for epilepsy. *Cochrane Database Syst Rev* 2007;2:CD002216.
- [40] Affolter N, Krähenbühl S, Schlienger RG. Appropriateness of serum level determinations of antiepileptic drugs. *Swiss Med Wkly* 2003;133:591–7.
- [41] Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translation of a 31-item quality of life inventory. *Epilepsia* 1998;39:81–8.
- [42] Vickery BG, Perrine KR, Hays RD, Hermann BP, Cramer JA, Meador KJ, et al. Scoring manual for the Quality of Life in Epilepsy-31 (QOLIE-31, version 1). St Monica: RAND; 1993.
- [43] Mohammadi N, Kian S, Davoudi F, Nia SM, Nojomi M. Psychometric evaluation of the Persian version of the quality of life in epilepsy inventory-31. *Iran J Neurol* 2013;12:144–8.
- [44] Hox JJ, Bechger TM. An introduction to structural equation modeling. *Fam Sci Rev* 1998;11:354–73.
- [45] Cheng C-P, Luh W-M, Yang A-L, Su C-T, Lin C-Y. Agreement of children and parents scores on Chinese version of pediatric quality of life inventory 4.0: further psychometric development. *Appl Res Qual Life* 2016;11:891–906.
- [46] Tsai M-C, Strong C, Lin C-Y. Effects of pubertal timing on deviant behaviors in Taiwan: a longitudinal analysis of 7th- to 12th-grade adolescents. *J Adolesc* 2015;42:87–97.
- [47] Wu T-H, Chang C-C, Chen C-Y, Wang J-D, Lin C-Y. Further psychometric evaluation of the self-stigma scale-short: measurement invariance across mental illness and gender. *PLoS One* 2015;10:e0117592.
- [48] Sobel ME. Asymptotic confidence intervals for indirect effects in structural equation models. In: Leinhardt S, editor. *Sociological methodology*. Washington DC: American Sociological Association; 1982. p. 290–312.
- [49] Rosseel Y, Oberski D, Byrnes J, Vanbrabant L, Savalei V, Merkle E, et al. Package 'lavaan'. URL: <https://cran.r-project.org/web/packages/lavaan/lavaan.pdf>; 2015. [accessed 05.11.17].
- [50] Saffari M, Pakpour AH, Naderi MK, Koenig HG, Baldacchino DR, Piper CN. Spiritual coping, religiosity and quality of life: a study on Muslim patients undergoing haemodialysis. *Nephrol Ther* 2013;18:269–75.
- [51] Hebert R, Zdaniuk B, Schulz R, Scheier M. Positive and negative religious coping and well-being in women with breast cancer. *J Palliat Med* 2009;12:537–45.
- [52] Kaplar M, Wachholtz A, O'Brien W. The effect of religious and spiritual interventions on the biological, psychological, and spiritual outcomes of oncology patients: a meta-analytic review. *J Psychosoc Oncol* 2004;22:39–44.
- [53] Tommelein E, Mehuy E, Van Tongelen I, Brusselle G, Boussey K. Accuracy of the Medication Adherence Report Scale (MARS-5) as a quantitative measure of adherence to inhalation medication in patients with COPD. *Ann Pharmacother* 2014;48:589–95.
- [54] Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. *Epilepsia* 2002;43(5):535–8.