Središnja medicinska knjižnica

Abstract

We examined and compared the relationship between religiosity and symptom severity in patients with major depressive disorder (MDD; rated by the Hamilton Depression Rating Scale) and schizophrenia (Positive and Negative Syndrome Scale). Duke University Religion index, Santa Clara Strength of Religious Faith (SCSORF) questionnaire and Brief Religious Coping scale scores were similar between MDD (n=50) and schizophrenia (n=50) patients. In MDD patients, higher organized religious activity (ORA) (estimate=2.28, 95%CI 0.37, 4.19; P=0.020) and higher negative religious coping (estimate=0.43, 95%CI 0.03, 0.84; P=0.037) were independently associated with more severe symptoms. In schizophrenia patients, higher ORA was associated with lower negative symptoms (estimate=-1.99, 95%CI -3.94, -0.03; P=0.046). Higher SCSORF was associated with lower ORA in both patient subsets, and thus indirectly with milder symptoms in MDD patients and with more severe negative symptoms in schizophrenia patients. The relationship between religiosity and symptom severity apparently differs in patients with MDD and schizophrenia.

Key words: Religiosity, Religious coping, Major depressive disorder, Schizophrenia

Introduction

There is a considerable body of evidence that spirituality, religious beliefs and practices may be important resources for coping with stress, somatic and mental illnesses (Koenig, 2009; Bonelli & Koenig, 2013; Aldwin et al., 2014). In health care research, spirituality and religiousness are commonly used complementarily or synonymously to depict a multidimensional construct of addressing the transcendent (Koenig, 2009), although the two concepts differ in that religiousness is depicted by specific behavioural and social elements such as religious service attendance and affiliation, while spirituality refers to feelings of self-transcendence and subjective experiences that do not necessarily need to be related to any religious denomination (Aldwin et al., 2014).

In respect to mental health, higher level of religiosity is generally considered beneficial, as it is associated with increased life satisfaction, happiness, higher morale and positive mood (Moreira-Almeida et al., 2006). A systematic review of quantitative research published in the top 25% psychiatry journals between 1990 and 2010 concluded that there was good evidence for a conclusion that higher spirituality/religiousness was associated with lower prevalence of depressive disorders in general population or in medically ill patients, as well as with less severe symptoms in patients suffering from depressive disorders (Bonelli & Koenig, 2013). In respect to psychotic disorders, however, the relationship seems to be a more complex one. A rather high proportion of patients with schizophrenia experience religious delusions and/or hallucinations. Their prevalence and content may greatly vary across specific cultural, social and religious settings, and may be associated with a poorer prognosis (Koenig, 2009; Grover et al., 2014). High quality studies are considerably fewer than those pertaining to depression. Some have indicated a greater risk of transient psychotic disorders in subjects with

intensive religious experiences, while others (albeit not all) reported an association between a greater religious involvement and better treatment compliance or higher well-being in patients with schizophrenia (Bonelli & Koenig, 2013). Data also suggests that higher religiosity is associated with a lower level of smoking and other substance abuse in these patients (Borras et al., 2008; Huguelet et al., 2009), and that in many patients with schizophrenia, spirituality/religiosity might be effectively used to cope with the illness and to improve quality of life (Grover et al., 2014).

To the best of our knowledge, no study comparatively evaluated religiosity in patients with major depressive disorder (MDD) and patients with schizophrenia. We aimed to investigate the relationship between religiosity/positive and negative religious coping and symptom severity in inpatients with MDD and inpatients with schizophrenia "sampled" from the same cultural and social context and assessed within the same time-frame, and to explore potential differences between the two disorders in the relationships between symptom severity and specific religious domains, such as positive and negative religious coping, organizational and non-organizational religious activity, intrinsic religiosity and the strength of religious faith.

Patients and methods

Study design and flow

This cross-sectional study was performed at the Department of Psychiatry, University Hospital Center Zagreb, Croatia. It was approved by the institutional Ethics Committee and by the Ethics Committee of the Zagreb University School of Medicine. After confirmation of the respective diagnosis (MDD, or schizophrenia) and assessment of symptom severity by two independent licensed psychiatrists (researchers MŠ and AMP;

certified for the use of the employed instruments), patients were evaluated for several aspects of religiosity by a third investigator (LK).

Patients

Consecutive patients were diagnosed according to the DSM-IV criteria using the Structured Clinical Interview for Mental Disorders (SCID 1.0) and were included in the study if aged 18-65 years and had provided a written informed consent. Exclusion criteria were: a) intellectual disability, dementia or other cognitive disorder; b) past or current diagnosis of post-traumatic stress disorder; c) severe symptoms which would hinder conduction of the interview (e.g., catatonia, aggressive behavior); d) substance dependence or abuse within the past three months (except for nicotine and caffeine); e) any severe comorbid somatic/neurological disorder (uncontrolled hypertension, history of or present symptomatic coronary / peripheral artery disease, stroke or transitory ischemic attack, malignancy, chronic heart or renal failure, HIV, hepatitis, or any neurodegenerative disease); f) for patients with MDD – presence of psychotic symptoms (by SCID), for patients with schizophrenia – comorbid affective disorders (by SCID), religious delusions or first-episode psychosis.

Measures of psychopathology

Patients with MDD were evaluated using the Hamilton Rating Scale for Depression-17 item version (HAM-D) (Hamilton et al., 1967). It is a clinician-rated instrument designed to quantify severity of depressive symptoms over the past week. Higher scores indicate more severe symptoms (minimum =0, maximum=50) (Hamilton et al., 1967). It is one of the most widely used rating scales for depression, and has been extensively used in Croatian population (e.g., Šagud et al., 2018).

Patients with schizophrenia were assessed by a structured interview for the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). It is a 30-item clinician-rated instrument that quantifies the severity of psychopathology. Each item is rated from 1 to 7, and higher score=more severe psychopathology: 7 items rate positive symptoms and 7 rate negative symptoms (minimum=7, maximum=49 for each symptom subset), and 16 items rate general psychopathology (minimum=16, maximum=112) (Kay et al., 1987). PANSS is the most established instrument for quantification of symptoms in patients with schizophrenia, and is commonly used in Croatian patients as well (e.g., Vlatković et al., 2018).

All patients were rated by the Clinical Global Impression – Severity (CGI-S). It is a clinician-rated (from 1=patient is not at all ill, to 7=among most extremely ill patients) assessment of the overall severity of the disease (Guy et al., 1976). This scale has been commonly used in daily practice and for research purposes in Croatian patients (e.g., Vuksan-Ćusa et al, 2018).

Measures of religiosity

All patients were assessed using three self-reporting instruments: Duke University Religion index (DUREL) (Koenig & Bussing 2010), Santa Clara Strength of Religious Fate (SCSORF) questionnaire (Plante & Boccaccini 1997) and brief Religious Coping (RCOPE) scale (Pargament et al., 1998).

DUREL is a 5-item scale that quantifies three aspects of religiosity (higher scores indicate higher religious involvement): a) "organizational" religious activity (one question, scored 1-6), ORA, b) "non-organizational" religious activity, NORA (one question, scored 1-6), c) intrinsic religiosity (IR) (three questions, each scored 1-5), for a total score range 5-27. It has been used for investigative purposes in different

populations, including psychiatric patients (Koenig & Bussing 2010). Croatian version of DUREL has already been published (Mihaljević et al., 2016).

SCSORF is a 10-item scale (each rated 1-4) that assesses strength of religious faith regardless of religious denomination (higher score=stronger religious faith) (Plante & Boccaccini 1997). Croatian version of SCSORF has already been published (Aukst-Margetić et al., 2015).

Brief RCOPE is a 14-item instrument that quantifies the level of religious coping with major life stressors. It assesses two patterns of religious coping, positive (RCOPE-P; refers to seeking spiritual support, religious forgiveness, spiritual connection collaborative religious coping and purification, benevolent religious reappraisal and focus) and negative (RCOPE-N; refers to spiritual and interpersonal religious disconnect, punishing God reappraisals, demonic reappraisal and reappraisal of God's power), each assessed through 7 items (each rated 1-4), for a minimum of 7 and a maximum of 28 points, where higher score means a higher positive/negative coping pattern (Pargament et al., 1998). Croatian version of RCOPE has been published (Mihaljević et al., 2012).

Outcome measures

We used total HAM-D score as a measure of depressive symptoms, total PANSS and separately positive and negative symptom scores as measures of psychotic symptoms, DUREL subscales (ORA, NORA, IR) individually, SCSORF score and RCOPE-P and RCOPE-N scores. For an approximate comparison of disease severity between MDD and schizophrenia patients, HAM-D and PANSS scores were projected to a 0-100 scale by linear transformation. Standardized scores (mean=0, standard deviation=1) were used in some analyses either as adjustments or as a dependent variable.

Statistical analysis

Considering the cross-sectional design and exploratory nature of the study, we performed several analyses: a) relationships between measures of religiosity/religious coping were assessed by partial correlations; b) differences between MDD and schizophrenia patients in measures of religiosity were assessed as unadjusted differences and as adjusted differences in a multivariate analysis of variance; c) to explore the relationship in a "reverse" direction, measures of religiosity were considered as independents in a logistic model fitted to the binary outcome "diagnosis"; d) to evaluate the relationship between measures of religiosity and symptoms severity general linear models were fitted separately in MDD patients (to HAM-D) and in schizophrenia patients (to total PANSS and separately to positive and negative symptom scores). Since different associations were observed in the two diseases, models were re-fitted to standardized symptom scores and included the interaction terms between diagnosis and religiosity measures; e) based on the above analyses, we generated hypotheses about specific mediated associations between SCSORF and symptom severity that were tested by mediation analysis. We used SAS 9.4 for Windows (SAS Inc., Cary, NC, USA) software for data analysis.

Results

Patient characteristics

A total of 50 MDD patients (moderately depressed, median HAM-D score 17) and 50 patients with schizophrenia (moderate symptoms, median PANSS score 119, similar for positive and negative symptoms) were enrolled (Table 1). Their sociodemographic characteristics were generally typical for the two diseases, virtually all declared

themselves as practicing Catholics, and raw scores indicated no major difference in any of the measures of religiosity between the two patient subsets (Table 1).

Relationships between measures of religiosity and religious coping

As illustrated by partial correlations (adjusted for age, sex, history of disease/treatment, history of suicidal thoughts/attempts and symptom severity), the relationships between measures of religiosity and measures of religious coping were closely similar in MDD and schizophrenia patients (Table 2): DUREL subscales (ORA, NORA and IR) were positively correlated with each other, but were inversely correlated with SCSORF and positive RCOPE, with no clear association with the negative RCOPE score (Table 2); SCSORF was positively correlated with positive RCOPE and weakly (low coefficients) with negative RCOPE, while positive and negative RCOPE were positively correlated to each other (Table 2).

Relationship between measures of religiosity/religious coping and diagnosis

There was no independent association between the diagnosis and any of the measures of religiosity/religious coping as indicated by no relevant overall difference and no difference in any of the religiosity measures between MDD and schizophrenia patients in multivariate analysis of variance (Table 3, Model 1), and no association between the religiosity measures and probability of MDD in a "reverse" analysis (logistic regression) (Table 3, Model 2).

Relationship between measures of religiosity/religious coping and disease severity

Four general linear models with religiosity measures as independents (with further adjustments for age, sex, history of disease and whether living alone) were fitted to symptom scores: one in MDD patients (to HAM-D score) and three in schizophrenia patients (to total PANSS score, to positive and to negative symptoms scores) (Table 4):

a) in MDD, higher ORA and higher negative RCOPE scores were independently associated with higher HAM-D scores; b) no such associations were observed in schizophrenia patients regarding total PANSS and positive symptoms scores, while higher ORA was associated with lower negative symptom scores (Table 4). The same models re-fitted to standardized HAM-D and total or negative symptoms PANSS scores, with diagnosis as an additional independent and with interaction terms between measures of religiosity and diagnosis (Table 5) formally demonstrated that the association between ORA and symptom severity was conditional on diagnosis (significant diagnosis*ORA interaction). The interactions between diagnosis and RCOPE-N were not statistically significant, however higher RCOPE-N was associated with higher symptom score in MDD patients, while no association was observed in schizophrenia patients (Table 5).

Higher SCSORF score is indirectly associated with lower HAM-D score in MDD patients and with higher negative symptom score in schizophrenia patients

We considered strength of religious faith as a trait that has its origins in the early(er) periods of life and could be viewed as an "inherent characteristic" that might drive other aspects of religious behavior, i.e., those captured by the DUREL index, as well as the abilities of positive or negative religious coping. Therefore, although SCSORF scores were not directly associated with symptom severity (Table 4), we hypothesized that SCSORF might be indirectly ("through" other manifestations of religiosity) associated with symptom severity in MDD patients as well as in schizophrenia patients, at least regarding negative symptoms (Figure 1, upper panel). To test the hypothesis, we performed mediation analyses separately in MDD patients and in schizophrenia patients: SCSORF score was considered an independent variable, ORA, NORA, IR and

RCOPE-P (all correlated with SCSORF, Table 2) were the assumed mediators and HAM-D / negative symptoms score were dependent variables (Figure 1). Adjustments in both models were the same (age, sex, disease duration/history, RCOPE-N and living in a family). In both MDD (Figure 1, Model 1) and schizophrenia patients (Figure 1, Model 2), higher SCSORF score was comparably associated with lower ORA, NORA and IR scores and with a higher RCOPE-P score, and had no direct associations with the severity of symptoms (Figure 1). In MDD patients (Figure 1, Model 1), higher ORA was associated with higher HAM-D score, and higher SCSORF was indirectly, "through" the association with lower ORA, associated with lower HAM-D scores (indirect effect=-0.24 [95% CI - 0.60, -0.02]). In patients with schizophrenia (Figure 1, Model 2), higher ORA was associated with lower PANSS negative symptoms score, and higher SCSORF was indirectly, "through" the association with lower ORA, associated with higher PANSS scores (indirect effect= 0.20 [95%CI 0.00, 0.72]). Hence, MDD and schizophrenia patients apparently differed in the direction of association between ORA and symptom severity, as well as in the direction of indirect (through ORA) association between SCSORF and symptom severity.

Discussion

It is difficult to compare findings about relationships between such complex constructs like religiosity/religious coping and symptom severity across studies pertaining to different psychopathology and conducted in different cultural and religious contexts since these factors are likely to limit the generalizability of the individual observations. Present study is specific insofar that it explored these relationships simultaneously in patients with two distinct disorders, i.e., clinically manifest major depressive disorder

(MDD) or schizophrenia. However, its cultural and religious context is also specific, since it was conducted in a Central/Eastern European country in which 85.3% of the population declare themselves as practicing Roman Catholics (Croatian Bureau of Statistics, 2017) – a proportion practically identical to the prevalence of Catholics in both patient subsets – and which has gone through complex religious changes in the post-Communist era (Marinović Jarolimov & Zrinščak, 2006). Generalizability of the present observations is further limited by a relatively small sample size, possible incomplete control for confounding in multivariate models (due to a limited sample size) and the fact that MDD patients had to be free of psychotic symptoms, while schizophrenia patients had to be free of affective disorders and religious delusions. This latter inclusion criterion, however, enabled a clearer insight into the evaluated relationships in a "pure" moderately severe depression and/or psychosis, and detection of possible differences between the two conditions.

The present observations are several-fold. There appeared no substantial difference between MDD patients and patients with schizophrenia in scores quantifying organizational (ORA), non-organizational (NORA) and intrinsic religiosity (IR) (elements of the DUREL index), strength of religious faith (SCSORF), and scores quantifying the level of religious coping (RCOPE), positive (positive religious coping, PRC) and negative (negative religious coping, NRC). The relationship between these measures and symptom severity, however, differed between the two diseases. As evidenced by the analysis separately in MDD and in schizophrenia patients, as well as by the analysis in all patients that formally tested moderation by diagnosis, higher ORA was associated with more severe symptoms in MDD and with less severe negative symptoms in schizophrenia; higher level of NRC was associated with more severe symptoms in MDD,

while no association with symptom severity was observed in schizophrenia. No other measure of religiosity/religious coping was associated with severity of symptoms in either disorder. To the best of our knowledge, there have been no reports on the relationship between ORA and symptom severity in patients hospitalized for MDD. Studies in somatically ill patients with no clinical depression reported either no association between ORA and depressive symptoms (Lee et al., 2017), or higher ORA was associated with less depression (Freire de Madeiros et al., 2017). Present data suggest that MDD patients with more severe symptoms might be more engaged in religious services, presumably seeking comfort and hope. The association between higher ORA and lower PANSS negative symptoms was observed also in patients with schizophrenia in remission (Triveni et al., 2017). In this population with very mild symptoms, however, higher scores on other DUREL subscales were also associated with lower total PANSS and negative symptoms (Triveni et al., 2017). On the other hand, in a sample of patients with various conditions (mood disorders without psychosis, different psychotic disorders, religious delusions, substance abuse), higher NORA and IR were associated with worse symptoms (i.e., delusions and hallucinations) (AbdelGawad et al., 2017). Taken together, the present and published data indicate that the relationship between DUREL subscales and symptom severity in psychotic patients may depend on (co)morbidity and severity of the disease. Due to the cross-sectional study design, it remains unclear whether our patients with more severe negative symptoms attended religious services less frequently due to a lack of motivation/social withdrawal, or whether participation in such services had alleviated their symptoms.

Although this was not formally tested, RCOPE-P scores in the present study were considerably higher than RCOPE-N scores in both MDD and schizophrenia patients

suggesting that they both used more PRC than NRC methods, an observation reported also by others in a number of different settings (Braam et al., 2014; Koenig et al., 2014; Nurasikin et al., 2012; Pargament et al., 1998). The association between higher NRC and more severe symptoms in MDD or in bipolar disorder has been reported from other cultural/religious settings, as well (Amadi et al., 2016; Bosworth et al., 2003; Dew et al., 2010; Rosmarin et al., 2014). It was also observed in somatically ill patients and/or their caregivers (Amadi et al., 2016; Hebert et al., 2009; Ng et al., 2017; Pargament et al., 1998; Park and Dornelas, 2011; Vitorino et al., 2017; Vitorino et al., 2018), and across different religious denominations (Braam et al., 2010; Pirutinsky et al., 2011). Several (Braam et al., 2014; Garcia et al., 2018; Krumrei et al., 2011), but not all (Bosworth et al., 2003) longitudinal studies have suggested a bi-directional relationship between NRC and depression. NRC, often referred to as spiritual struggle (Rosmarin et al., 2013) deserves particular attention in patients with MDD. Namely, NRC can "feed" the negative content of rumination –contrary to what happens in PRC (Garcia et al., 2018). More severely depressed patients have the feeling that "the God has left them" and consider their disease as a punishment for something they have done or have failed to do. There is evidence that clinical interventions might alleviate such spiritual struggles (Bay et al., 2008; Bolens et al., 2012; Revheim et al., 2010), and, importantly, improve NRC (Cronjé et al., 2017). The presently observed lack of association between PRC and severity of depression in MDD patients is in agreement with reports in MDD patients with a similar disease severity (Amadi et al., 2016; Koenig et al., 2014; Rosmarin et al., 2014). On the other hand, in patients who were mainly in remission (Bosworth et al., 2013), higher PRC was associated with lower depressive difficulties. Combined, data suggest that PRC might be protective in MDD patients during remission (Bosworth et al., 2003), but that

this relationship might be lost when symptoms become more pronounced (Koenig et al., 2014; Rosmarin et al., 2014; the current study) and patients begin perceiving their disease as a punishment or abandonment. The observed lack of association between either PRC or NRC and symptom severity in schizophrenia patients is in line with the observations in clinically manifest patients with schizophrenia, schizoaffective disorder or mood disorder with psychotic features (Rosmarin et al., 2013). The observed difference in NRC - symptom severity relationship in MDD and schizophrenia patients is likely due to the absence of psychotic symptoms in the present MDD sample. Psychotic (as were the current schizophrenia patients) patients do not have an insight into their illness, lack the sense of being ill and therefore have no reason to consider themselves punished (Misiak et al., 2016). In turn, they may gain the insight as psychotic symptoms improve (Misiak et al., 2016) and might be prone to NRC in remission (Triveni et al., 2017). As in MDD, PRC might be protective in remitted patients with schizophrenia (Triveni et al., 2017), while this association might not hold in the acute exacerbation of psychosis (Rosmarin et al., 2013). Actually, religiosity may not be a fixed concept for a given individual. For example, religiousness has changed in about a third of the patients with schizophrenia during a three-year period, where some patients experienced positive and some experienced negative changes (Mohr et al., 2010).

Finally, to our knowledge, no study so far assessed the relationship between strength of religious faith (SCSORF questionnaire) and symptom severity in acute MDD or schizophrenia patients. We observed no direct association between SCSORF scores and severity of symptoms, but mediation analysis (limited by the cross-sectional study design) suggested that strength of religious faith might be associated with disease severity indirectly, through its associations with other manifestations of religiosity (in

the present study, *via* ORA). In both diseases, higher SCSORF scores were associated with higher RCOPE-R scores (partial correlations, regressions), but only weak (correlation) or none (regressions) association was observed with RCOPE-N scores. It appears counterintuitive that SCSORF score was inversely associated with ORA, NORA and IR scores (correlations, regressions) in both MDD and schizophrenia patients, since positive correlations were reported in oncology patients and healthy subjects (Sherman et al., 2001). At least in part, this might be due to the specific cultural and religious context of the study. While religion (Catholicism) played an important role in preservation of the separate national identity (of Croatians) during the Communist era in the former country (Yugoslavia), the social role of religion has dramatically changed over the past 25 years and a number of dilemmas and debates have been raised about the "appropriate" role of religion in the modern society (Marinović Jerolimov & Zrinščak, 2006). However, the present observations clearly emphasize the need for further evaluation of this tool in psychiatric patients.

Conclusions

Despite certain limitations, the present study in a sample of adult inpatients with MDD and schizophrenia, almost exclusively practicing Catholics, suggests different relationships between organizational religious activity and negative religious coping and severity of depressive/psychotic symptoms in the two diseases. Longitudinal studies are needed to evaluate the relationship between religiosity and psychopathology in different stages of MDD and schizophrenia. Given the importance of religion and spirituality for many patients, better understanding of these relationships might eventually contribute to improved disease outcomes.

References

AbdelGawad N, Chotalia J, Parsaik A, Pigott T, Allen, M (2017) Religiosity in Acute
Psychiatric Inpatients: Relationship With Demographics, Clinical Features, and Length
of Stay. *J Nerv Ment Dis* 205(6):448-452.

Aldwin CM, Park CL, Jeong YL, Nath R (2014) Differing pathways between religiousness,
spirituality, and health: a self-regulation perspective. *Psychology of Religion and
Spirituality* 6(1):9-21.

Amadi KU, Uwakwe R, Odinka PC, Ndukuba AC, Muomah CR, Ohaeri, JU (2016) Religion,
coping and outcome in out-patients with depression or diabetes mellitus. *Acta Psychiatr
Scand* 133(6):489-496.

Aukst-Margetić B, Jakovljević M, Margetić B, Bišćan M, Šamija M. Religiosity, depression and
pain in patients with breast cancer. *Gen Hosp Psychiatry* 27(4):250-255.

Bay PS, Beckman D, Trippi J, Gunderman R, Terry C (2008) The effect of pastoral care
services on anxiety, depression, hope, religious coping, and religious problem solving
styles: a randomized controlled study. *J Relig Health* 47(1):57-69.

Bonelli RM, Koenig, HG (2013) Mental disorders, religion and spirituality 1990 to 2010: a
systematic evidence-based review. *J Relig Health* 52(2):657-673.

Borras L, Mohr S, Brandt PY, Gillieron C, Eytan A, Huguelet P (2008) Influence of spirituality
and religiousness on smoking among patients with schizophrenia or schizo-affective
disorder in Switzerland. *Int J Soc Psychiatry* 54(6):539-549.

Bosworth HB, Park KS, McQuoid DR, Hays JC, Steffens DC (2003) The impact of religious
practice and religious coping on geriatric depression. *Int J Geriatr Psychiatry*
18(10):905-914.

Braam AW, Schaap-Jonker H, van der Horst MH, Steunenberg B, Beekman AT, van Tilburg W, Deeg DJ (2014) Twelve-year history of late-life depression and subsequent feelings to God. *Am J Geriatr Psychiatry.* 22(11):1272-1281.

Braam AW, Schrier AC, Tuinebreijer WC, Beekman AT, Dekker JJ, de Wit MA (2010) Religious coping and depression in multicultural Amsterdam: a comparison between native Dutch citizens and Turkish, Moroccan and Surinamese/Antillean migrants. *J Affect Disord.* 125(1-3):269-278.

Croatian Bureau of Statistics (2017) Statistical Yearbook of the Republic of Croatia, pp. 112. available at: https://www.dzs.hr/Hrv_Eng/ljetopis/2017/sljh2017.pdf, accessed August 04, 2018),

Cronjé FJ, Sommers LS, Faulkner JK, Meintjes WA, Van Wijk CH, Turner RP (2017) Effect of a Faith-Based Education Program on Self-Assessed Physical, Mental and Spiritual (Religious) Health Parameters. *J Relig Health* 56(1):89-108.

Dew RE, Daniel SS, Goldston DB, McCall WV, Kuchibhatla M, Schleifer C, Triplett MF, Koenig HG (2010) A prospective study of religion/spirituality and depressive symptoms among adolescent psychiatric patients. *J Affect Disord* 120(1-3):149-155.

Freire de Medeiros CM, Arantes EP, Tajra RD, Santiago HR, Carvalho AF, Libório A (2017) Resilience, religiosity and treatment adherence in hemodialysis patients: a prospective study. *Psychol Health Med* 22(5):570-577.

García FE, Cova F, Páez D, Miranda F (2018) Brooding as moderator of depressive symptoms after a work accident: A longitudinal study. *Scand J Psychol* 59(2):236-242.

Grover S, Davuluri T, Chakrabarti S (2014) Religion, Spirituality and Schizophrenia: A Review, *Indian Journal of Psychological Medicine* 36(2):119-124.

Guy W (1976) ECDEU Assessment Manual for Psychopharmacology —Revised (DHEW Publ No ADM 76–338). Rockville, MD, U.S. Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, NIMH Psychopharmacology Research Branch, Division of Extramural Research Programs 218–222.

Hamilton M (1967) Development of a rating scale for primary depressive illness. *British J Soc Clin Psychol* 6:278–296.

Hebert R, Zdaniuk B, Schulz R, Scheier M (2009) Positive and NRC and well-being in women with breast cancer. *J Palliat Med* 12(6):537-545.

Huguelet P, Borras L, Gillieron C, Brandt PY, Mohr S (2009) Influence of spirituality and religiousness on substance misuse in patients with schizophrenia or schizo-affective disorder. *Subst Use Misuse* 44(4):502-513.

Kay Sr, Fiszbein A, Opler, LA (1987) The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 13:261-276.

Koenig HG (2009) Research on religion, spirituality, and mental health. *Can J Psychiatry* 54(5):283-291.

Koenig HG, Büssing A (2010) The Duke University Religion Index (DUREL): A Five-Item Measure for Use in Epidemological Studies. *Religions 1*(1):78-85.

Koenig HG, Berk LS, Daher NS, Pearce MJ, Bellinger DL, Robins CJ, Nelson B, Shaw SF, Cohen HJ, King MB (2014) Religious involvement is associated with greater purpose, optimism, generosity and gratitude in persons with major depression and chronic medical illness. *J Psychosom Res* 77(2):135-143.

Krumrei EJ, Mahoney A Pargament KI (2011) Spiritual stress and coping model of divorce: a longitudinal study. *J Fam Psychol* 25(6):973-985.

Lee SA, Ryu HU, Choi EJ, Ko MA, Jeon JY, Han SH, Lee GH, Lee MK, Jo KD (2017) Associations between religiosity and anxiety, depressive symptoms, and well-being in Korean adults living with epilepsy. *Epilepsy Behav* 75:246-251.

Marinović Jerolimov D, Zrinščak S (2006) Religion within and beyond borders: the case of Croatia. *Social Compass* 53:279-290.

Mihaljević S, Aukst-Margetić B, Karničnik S, Vuksan-Ćusa B, Milošević M (2016) Do spirituality and religiousness differ with regard to personality and recovery from depression? A follow-up study. *Compr Psychiatry* 70:17-24.

Mihaljević S, Aukst-Margetić B, Vuksan-Ćusa B, Koić E, Milošević M (2012) Hopelessness, suicidality and religious coping in Croatian war veterans with PTSD. *Psychiatr Danub* 24(3):292-297

Misiak B, Frydecka D, Beszłej JA, Moustafa AA, Tybura P, Kucharska-Mazur J, Samochowiec A, Bieńkowski P, Samochowiec J (2016) Effects of antipsychotics on insight in schizophrenia: results from independent samples of first-episode and acutely relapsed patients. *Int Clin Psychopharmacol* 31(4):185-191.

Mohr S, Borras L, Rieben I, Betrisey C, Gillieron C, Brandt PY, Perroud N Huguelet P (2010) Evolution of spirituality and religiousness in chronic schizophrenia or schizo-affective disorders: a 3-years follow-up study. *Soc Psychiatry Psychiatr Epidemiol* 45(11):1095-1103.

Moreira-Almeida A, Neto FL, Koenig HG (2006) Religiousness and mental health: a review. *Revista Brasileira de Psiquiatria* 28(3):242-250.

Ng GC, Mohamed S, Sulaiman AH, Zainal NZ(2017) Anxiety and Depression in Cancer

Patients: The Association with Religiosity and Religious Coping. *J Relig Health*

56(2):575-590.

Nurasikin MS, Khatijah LA, Aini A, Ramli M, Aida SA, Zainal NZ, Ng CG (2013) Religiousness,

religious coping methods and distress level among psychiatric patients in Malaysia. *Int J*

Soc Psychiatry 59(4):332-338.

Pargament KI, Smith BW, Koenig HG, Perez L (1998) Patterns of positive and negative

religious coping with major life stressors. *J Sci Study Relig* 37:710-724.

Park CL, Dornelas E (2012) Is religious coping related to better quality of life following

acute myocardial infarction? *J Relig Health* 51(4):1337-1346.

Pirutinsky S, Rosmarin DH, Pargament KI, Midlarsky E (2011) Does NRC accompany,

precede, or follow depression among Orthodox Jews? *J Affect Disord* 132(3):401-405.

Plante TG, Boccaccini M (1997) The Santa Clara Strength of Religious Faith Questionnaire.

Pastoral Psychology 45:375–387.

Revheim N, Greenberg, Citrome L (2010) Spirituality, schizophrenia, and state hospitals:

program description and characteristics of self-selected attendees of a spirituality

therapeutic group. *Psychiatr Q* 81(4):285-292.

Rosmarin DH, Bigda-Peyton JS, Öngur D, Pargament KI, Björgvinsson T (2013) Religious

coping among psychotic patients: relevance to suicidality and treatment outcomes.

Psychiatry Res 210(1):182-187.

Rosmarin DH, Malloy MC, Forester BP (2014) Spiritual struggle and affective symptoms

among geriatric mood disordered patients. *Int J Geriatr Psychiatry* 29(6):653-660.

Šagud M, Petrović B, Vilibić M, Mihaljević-Peleš A, Vuksan-Ćusa B, Radoš I, Gres A, Trkulja V (2018) The relationship among psychopathology, religiosity, and nicotine dependence in Croatian war veterans with posttraumatic stress disorder. *Croat Med J* 59(4):165-77.

Sherman AC, Simonton S, Adams DC, Latif U, Plante TG, Burns SK, Poling T (2001) Measuring religious faith in cancer patients: reliability and construct validity of the Santa Clara Strength of Religious Faith questionnaire. *Psycho-oncol* 10:436-443

Triveni D, Grover S, Chakrabarti S (2017) Religiosity among patients with schizophrenia: An exploratory study. *Indian J Psychiatry* 59(4):420-428.

Vitorino LM, Marins LS, Granero Lucchett, AL, Oliveira Santos AE, Cruz JP, Oliveira Cortez PJ, Lucchetti G (2018) Spiritual/religious coping and depressive symptoms in informal caregivers of hospitalized older adults. *Geriatr Nurs* 9(1):48-53.

Vitorino LM, Soares RCES, Santos AEO, Lucchetti ALG, Cruz JP, Cortez PJO, Lucchetti G (2017) Two Sides of the Same Coin: The Positive and Negative Impact of Spiritual Religious Coping on Quality of Life and Depression in Dialysis Patients *J Holist Nurs* in press

Vlatković S, Šagud M, Švob Štrac D, Sviben M, Živković M, Vilibić M, Vuksan-Ćusa B, Mihaljević-Peleš A, Pivac N (2018) Increased prevalence of Toxoplasma gondii seropositivity in patients with treatment-resistant schizophrenia. *Schizophr Res* 93:480-81.

Vuksan Ćusa B, Klepac N, Jakšić N, Bradas Z, Božičević M, Palac N, Šagud M (2018) The Effects of Electroconvulsive Therapy Augmentation of Antipsychotic Treatment on Cognitive Functions in Patients With Treatment-Resistant Schizophrenia. *J ECT* 34(1):31-4.

Zimmerman M, Martinez JH, Young D, Chelminsko I, Dalrymple K (2013) Severity

classification on the Hamilton Depression Rating Scale. *J Affect Dis* 150(2):384-388.

Figure 1 Indirect (mediated) association between the strength of religious faith (Santa Clara Strength of Religious Faith, SCSORF, score) and severity of symptoms in patients with major depressive disorder (MDD) (Hamilton Depression Rating Scale, HAM-D, score) and severity of negative symptoms in patients with schizophrenia (SCH) (Positive And Negative Syndrome Scale, PANSS, negative symptom score). Upper panel illustrates the hypothesis, middle panel (Model 1) summarizes results of mediation analysis in major depression patients and lower panel (Model 2) summarizes results of mediation analysis in schizophrenia patients. All direct (full arrows) and indirect (dashed arrows) associations are adjusted for the same covariates, hence all are independent. All associations are depicted by true regression coefficients (95% CI) (black arrows and numbers if different from zero, gray otherwise), while P-values and covariate effects are omitted for clarity. ORA - organizational religious activity, NORA – non-organizational religious activity, IR – intrinsic religiosity, RCOPE-N – negative religious coping, RCOPE-P – positive religious coping. ORA, NORA and IR are subscales of the Duke University Religiosity index (DUREL).

Table 1 Patient characteristics overall and by diagnosis – major depressive disorder (MDD) or schizophrenia (SCH). Data are median (range) or count (percent), and differences (MDD-SCH) are median or proportion differences with 95% confidence intervals (CI).

	All	MDD	SCH	MDD–SCH (95% CI)
N	100	50	50	
Disease duration (years)	10 (0.1-58)	9 (0.1-58)	10 (0.1-36)	1.8 (-2.0, 5.0)
Age (years)	47.5 (20-86)	56 (22-86)	35 (20-60)	19 (14, 23)
Men	45 (45.0)	13 (26.0)	32 (64.0)	-38.0 (-54.4, -18.8)
Never married	34 (34.0)	7 (14.0)	27 (54.0)	-40.0 (-55.6, -22.1)
Live alone (vs. family/other)	22 (22.0)	16.0 (32.0)	6 (12.0)	20.0 (3.8, 35.8)
Unemployed (vs. employed/retired/study)	24 (24.0)	7 (14.0)	17 (34.0)	-20.0 (-36.2, -3.2)
Education ≤ elementary	15 (15.0)	8 (16.0)	7 (14.0)	2.0 (-12.6, 16.7)
Religious denomination				
None - Atheist	9 (9.0)	5 (10.0)	4 (8.0)	2.0 (-10.4, 14.7)
Catholic	87 (87.0)	43 (86.0)	44 (88.0)	-2.0 (-16.1, 12.0)
Other (non-Muslim)	4 (4.0)	2 (4.0)	2 (4.0)	0.0
HAM-D	---	17 (2-31)	---	---
PANSS - total	---	---	119 (74-168)	---
PANSS – positive	---	---	28 (17-39)	---
PANSS – negative	---	---	29 (10-44)	---
HAM-D/PANSS transformed	40 (3.8-77)	33 (3.8-60)	49 (24-77)	-16.6 (-21.0, -12.0)
CGI-S	5 (3-7)	4.5 (3-6)	5 (3-7)	0.0 (-1.0, 0.0)
Suicidal thoughts/attempts				
Never	42 (42.0)	22 (44.0)	20 (40.0)	4.0 (-15.2, 23.0)
Have had thoughts	31 (31.0)	12 (24.0)	19 (38.0)	-14.0 (-31.5, 4.3)
Attempted suicide	27 (27.0)	16 (32.0)	11 (22.0)	10.0 (-7.6, 27.2)
DUREL - ORA	4 (1-6)	3 (1-6)	4 (1-6)	0.0 (-1.0, 0.0)
DUREL - NORA	2 (1-6)	1 (1-6)	3 (1-6)	0.0 (-1.0, 0.0)
DUREL - IR	7 (3-15)	7 (3-15)	7 (3-15)	0.0 (-2.0, 1.0)
SCSORF	28.5 (10-40)	32 (10-40)	26 (10-40)	4.0 (-1.0, 9.0)
RCOPE - positive	21 (7-28)	21 (7-28)	18 (7-28)	1.5 (-1.0, 5.0)
RCOPE - negative	10 (7-25)	10 (7-25)	10 (7-22)	0.0 (-1.0, 2.0)

CGI-S – clinical global impression – status, DUREL – Duke University religion Index (ORA – organizational religious activity, NORA – non-organizational religious activity, IR – intrinsic religiosity subscores); HAM-D – Hamilton Depression Rating Scale; PANSS – Positive and Negative Syndrome Scale; RCOPE – religious coping scale; SCSORF – Santa Clara Strength of Religious Faith Questionnaire

Table 2 Partial correlations (adjusted for age, sex, history of disease/treatment, history of suicidal thoughts/attempts and symptom severity) between measures of religiosity (DUREL subscales ORA, NORA, IR and SCSORF) and religious coping (RCOPE, positive [P] or negative [N]) by diagnosis (major depression, MDD; or schizophrenia, SCH). Correlation coefficients are given with P-values (in brackets).

	ORA	NORA	IR	SCSORF	RCOPE-P	RCOPE-N
MDD patients						
ORA	---	0.705 (<0.001)	0.658 (<0.001)	-0.731 (<0.001)	-0.645 (<0.001)	-0.302 (0.044)
NORA	0.705 (<0.001)	---	0.674 (<0.001)	-0.851 (<0.001)	-0.769 (<0.001)	-0.155 (0.308)
IR	0.658 (<0.001)	0.674 (<0.001)	---	-0.796 (<0.001)	-0.703 (<0.001)	-0.210 (0.167)
SCSORF	-0.731 (<0.001)	-0.796 (<0.001)	-0.796 (<0.001)	---	0.918 (<0.001)	0.220 (0.146)
RCOPE-P	-0.645 (<0.001)	-0.703 (<0.001)	-0.703 (<0.001)	0.918 (<0.001)	---	0.304 (0.042)
RCOP-N	-0.302 (0.044)	-0.155 (0.308)	-0.210 (0.167)	0.220 (0.146)	0.304 (0.042)	---
SCH patients						
ORA	---	0.588 (<0.001)	0.586 (<0.001)	-0.600 (<0.001)	-0.523 (<0.001)	-0.026 (0.863)
NORA	0.588 (<0.001)	---	0.711 (<0.001)	-0.876 (<0.001)	-0.798 (<0.001)	-0.195 (0.198)
IR	0.586 (<0.001)	0.711 (<0.001)	---	-0.714 (<0.001)	-0.651 (<0.001)	-0.099 (0.519)
SCSORF	-0.600 (<0.001)	-0.876 (<0.001)	-0.714 (<0.001)	---	0.903 (<0.001)	0.327 (0.028)
RCOPE-P	-0.523 (<0.001)	-0.798 (<0.001)	-0.651 (<0.001)	0.903 (<0.001)	---	0.463 (0.001)
RCOP-N	-0.026 (0.863)	-0.195 (0.198)	-0.099 (0.519)	0.327 (0.028)	0.463 (0.001)	---

DUREL – Duke University Religiosity Index (ORA – organizational religious activity, NORA – non-organizational religious activity, IR – intrinsic religiosity subscores); HAM-D – Hamilton Depression Rating Scale; PANSS – Positive and Negative Syndrome Scale; RCOPE – religious coping scale; SCSORF – Santa Clara Strength of Religious Faith Questionnaire

Table 3 Assessment of independent associations between diagnosis (major depressive disorder, MDD or schizophrenia, SCH) and measures of religiosity (DUREL subscales ORA, NORA, IR and SCSORF) and religious coping (RCOPE, positive [P] or negative [N]). **Model 1** –measures of religiosity and religious coping were simultaneous dependent variables in a multivariate analysis of variance to determine differences between MDD and SCH patients (adjusted for age, sex, history of disease/treatment, history of suicidal thoughts/attempts, living alone and disease severity [standardized HAM-D and total PANSS scores]). **Model 2** – a logistic model was fitted to diagnosis as a binary dependent variable to evaluate whether any of the measures of religiosity/religious coping was associated with the diagnosis (same adjustments as above). Effects are adjusted odds ratios (OR).

Model 1 (overall diagnosis effect P=0.807)	MDD – SCH (95% CI)	P
ORA	0.35 (-0.42, 1.13)	0.368
NORA	-0.23 (-1.20, 0.74)	0.642
IR	-0.02 (-1.98, 1.94)	0.982
SCSORF	1.33 (-3.73, 6.38)	0.604
RCOPE-P	1.00 (-2.43, 4.23)	0.563
RCOP-N	0.46 (-1.93, 2.84)	0.703
Model 2 (probability of diagnosis=MDD)	OR (95% CI)	P
ORA	1.48 (0.88-2.50)	0.138
NORA	0.90 (0.48-1.71)	0.752
IR	1.02 (0.80-1.30)	0.869
SCSORF	1.04 (0.86-1.26)	0.680
RCOPE-P	1.00 (0.81-1.25)	0.975
RCOP-N	1.01 (0.88-1.14)	0.927

DUREL – Duke University Religiosity Index (ORA – organizational religious activity, NORA – non-organizational religious activity, IR – intrinsic religiosity subscores); HAM-D – Hamilton Depression Rating Scale; PANSS – Positive and Negative Syndrome Scale; RCOPE – religious coping scale; SCSORF – Santa Clara Strength of Religious Faith Questionnaire

Table 4 Assessment of independent associations between measures of religiosity – organizational (ORA) and non-organizational (NORA) religious activity, intrinsic religiosity (IR), strength of religious faith (SCSORF) and positive (P) or negative (N) religious coping (RCOPE) – and severity of symptoms (HAM-D score) in patients with major depressive disorder (MDD) and in patients with schizophrenia (SCH) (total PANSS score, positive and negative symptoms scores). A separate general linear model was fitted to each of the four measures of symptom severity (further adjustments for age, sex, history of disease/treatment and whether living alone).

	MDD: HAM-D score		SCH: total PANSS score		SCH: positive symptoms		SCH: negative symptoms	
	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P
SCSORF (by 1 point)	0.26 (-0.36, 0.88)	0.408	-0.53 (-2.42, 1.35)	0.570	-0.26 (-0.75, 0.23)	0.292	-0.31 (-0.98, 0.35)	0.346
ORA (by 1 point)	**2.28 (0.37, 4.19)**	**0.020**	-2.84 (-8.37, 2.70)	0.306	-0.39 (-1.83, 1.05)	0.587	**-1.99 (-3.94, -0.03)**	**0.046**
NORA (by 1 point)	-0.41 (-2.35, 1.53)	0.671	3.00 (-4.36, 10.4)	0.414	0.74 (-1.17, 2.66)	0.437	0.49 (-2.12, 3.09)	0.707
IR (by 1 point)	-0.02 (-0.82, 0.78)	0.958	0.73 (-1.68, 3.10)	0.545	-0.27 (-0.90, 0.36)	0.395	0.75 (-0.10, 1.60)	0.082
RCOPE-P (by 1 point)	-0.09 (-0.84, 0.65)	0.802	1.27 (-1.03, 3.57)	0.272	0.40 (-0.20, 1.00)	0.182	0.52 (-0.30, 1.33)	0.206
RCOPE-N (by 1 point)	**0.43 (0.03, 0.84)**	**0.037**	0.54 (-1.25, 2.32)	0.548	0.02 (-0.44, 0.49)	0.927	0.12 (-0.51, 0.75)	0.699

HAM-D – Hamilton Depression Rating scale; PANSS – Positive and Negative Syndrome Scale

Table 5 Association of organizational religious activity (ORA) and of negative religious coping (RCOPE-N) with symptom severity is conditional on diagnosis (major depressive disorder or schizophrenia). Models from Table 4 were re-fitted to standardized HAM-D and total or negative PANSS scores considering all patients, with diagnosis as an additional independent and with interaction terms between diagnosis and each of the indicators of religiosity/religious coping. Estimates are shown only for diagnosis*ORA and diagnosis*RCOPE-N interactions. In line with models fitted separately to MDD and schizophrenia patients (Table 4), no other associations were observed.

Model 1 - standardized HAM-D and total PANSS	Estimate (95% CI)	P
Diagnosis*ORA interaction	0.52 (0.12, 0.91)	0.011
ORA in major depressive disorder patients	0.35 (0.05, 0.66)	---
ORA in schizophrenia patients	0.17 (-0.16, 0.51)	---
Diagnosis*RCOPE-N interaction	0.04 (-0.06, 0.15)	0.397
RCOPE-N in major depressive disorder patients	0.06 (0.00, 0.12)	---
RCOPE-N in schizophrenia patients	0.02 (-0.06, 0.09)	---
Model 2 - standardized HAM-D and PANSS negative symptoms		
Diagnosis*ORA interaction	0.64 (0.26, 1.03)	0.001
ORA in major depressive disorder patients	0.35 (0.05, 0.66)	---
ORA in schizophrenia patients	-0.29 (-0.54, -0.05)	---
Diagnosis*RCOPE-N interaction	0.05 (-0.05, 0.15)	0.331
RCOPE-N in major depressive disorder patients	0.06 (0.00, 0.12)	---
RCOPE-N in schizophrenia patients	0.01 (-0.07, 0.09)	---

HAM-D – Hamilton Depression Rating scale; PANSS – Positive and Negative Syndrome Scale