Religiosity and telomere length: One step forward, one step back

Tyler J. VanderWeele [a, *], Alexandra E. Shields [b]

[a] Harvard T.H. Chan School of Public Health, Department of Epidemiology, Program on Integrative Knowledge and Human Flourishing, Harvard University, National Consortium on Psychosocial Stress, Spirituality, and Health, United States
[b] Harvard Medical School, Harvard/MGH Center on Genomics, Vulnerable Populations, and Health Disparities, National Consortium on Psychosocial Stress, Spirituality, and Health, United States

ARTICLE INFO

Hill et al. (2016) report a positive association between religiosity (a summary measure of service attendance, frequency of prayer, and religious identity) and telomere length. Their results, if replicated in other studies with more rigorous designs, might account for one mechanism through which religious participation affects longevity. As the authors note, research on religiosity and telomere length is still in its infancy, with prior research employing only one small convenience sample study using a religiosity measures similar to that of Hill et al. (Koenig et al., 2016). There have been, however, other previous studies linking forms of religious (e.g., Buddhist) meditation and other spiritual practices with cellular aging. Randomized controlled trials have shown various forms of meditation (Jacobs et al., 2011; Lavretsky et al., 2013) and Qi Gong (Ho et al., 2012) to be associated with increased telomerase activity. Loving-kindness meditation (Hoge et al., 2013) has also been associated with increased relative leukocyte telomere length. Despite the Hill et al. (2016) study's cross-sectional design, it does provide additional evidence for an association between their particular measures of religiosity and telomere length, and thus moves us one step forward.

Although the Hill et al.'s (2016) study constitutes a step forward concerning evidence for an association, it also represents a step back for the field of religion/spirituality (R/S) and health research in terms of the study design used and subsequent quality of evidence for causality or for identifying underlying mechanisms. Much of the early R/S and health literature came under attack for its preponderance of cross-sectional study designs and inadequate control for confounding (Sloan et al., 1999). Cross-sectional designs can contribute little evidence for causality; lack of confounding control for baseline health and other variables compromises evidence even within longitudinal studies. The field has advanced considerably over the last two decades, with a number of high quality longitudinal studies on various outcomes (e.g., mortality, depression, suicide) now available (Hummer et al., 1999; Strawbridge et al., 2001; Gillum et al., 2008; Schnall et al., 2010; Balbuena et al., 2013; Kleinman and Liu, 2014; Li et al., 2016a, b; VanderWeele et al., 2016a, b; See VanderWeele (2016) for a recent review). While such studies have begun to set a new standard for the field, it is still the case that the vast majority of studies within R/S and health research are cross-sectional (Koenig et al., 2012). For health outcomes for which several good longitudinal studies are now available, cross-sectional analyses effectively contribute no additional evidence for causality. Since there have yet to be any longitudinal studies of religiosity and telomere length, the present study by Hill et al. does make a contribution to the field by documenting an association in a population-based sample. However, analyses of the relationship between R/S variables and telomere length conducted within a rigorous prospective study design are needed if R/S research is to keep pace with other fields of inquiry.

A second important point in interpreting the results of Hill et al. (2016) concerns power and sample size. At 1252 participants, their study is not small, but nor is it particularly large. In discussing potential mechanisms for the association between religiosity and telomere length, the investigators claim that none of the potential mediators (i.e., depression, smoking, heavy drinking, or allostatic

* Corresponding author. Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, 02115, United States.
E-mail address: tvanderw@hsph.harvard.edu (T.J. VanderWeele).

load) was significant. This claim is somewhat problematic from two perspectives: first, study design requirements to assess mediation and mechanisms are in general even more stringent than for assessing total causal effects (VanderWeele, 2015). As noted above, cross-sectional analysis is very limited in its ability to establish causation, and thus also very limited in its ability to assess mechanisms of any purported causal effect. Second, significant mediating relationships may not have been identified due to inadequate power to detect these associations, and, in fact, at least depression seems to be borderline statistically significant (the coefficient estimate is 0.027 and approximately twice its standard error of 0.013). Although the confidence interval would include 0, the estimate for the proportion mediated by depression is $(0.38-0.31)/0.38 = 18.4\%$, nearly one-fifth. Their summary, "we can conclude… that no mediation processes are present in our data," is thus premature. A much larger study, with longitudinal design, would be needed to come to this conclusion (and may very well come to a different conclusion). Indeed, it would be surprising if the association between religious participation and telomere length (or other health outcomes) were entirely unmediated. Smoking, depression, stress, and possibly a sense of meaning and purpose, all seem likely, plausible, mechanisms through which religiosity might affect telomere length.

Issues of statistical power are also relevant in Hill et al.'s interaction analyses. A crude calculation, assuming equally sized groups (cf. VanderWeele, 2015), suggests that, even if the magnitude of the interaction were as large as the main effect of religiosity, the sample size required to detect the interaction with 80% power would be 6147 (i.e. much larger than that in the Hill et al. study). If the interaction were only half as large of the main effect, the sample size required for 80% power would be nearly 25,000 participants. Once again, their conclusion, "the results suggest that the positive association between religiosity and telomere length is comparable across levels of age, for women and men, and for non-Hispanic blacks and whites," is premature. Absence of evidence does not imply evidence of absence. A much larger study would be needed for such a conclusion.

Despite these limitations, Hill et al. make an important contribution in helping to bring R/S research more towards the current stream of cutting edge science. The challenge now is to push the field beyond merely documenting associations between R/S and various outcomes towards understanding the underlying biological pathways and mechanisms underpinning these relationships. Significantly advancing R/S research will require employing more rigorous, prospective study designs, with larger sample sizes, that can support more sophisticated analyses.

We believe the field of R/S and health research would benefit greatly by making more use of the resources provided by large prospective cohort studies. These cohort studies typically have the advantage of a very large sample size (often 50,000 or 100,000 or more), repeated measures of all variables, long-term follow-up, and extensive information on potential confounding and mediating variables. Most cohorts also collect biological specimens and biomarker data needed to pursue hypotheses regarding biological pathways or mechanisms. Many of these cohort studies already have some measures of religiosity and spirituality. Indeed, we have recently carried out analyses examining longitudinal associations between religious service attendance and other R/S measures and various health outcomes using both the Nurses' Health Study and the Black Women's Health Study (Li et al., 2016a, b; VanderWeele et al., 2016a, b). In the case of the Nurses' Health Study, repeated measurements of service attendance were available every four years, thereby also allowing for control of past exposure. Such longitudinal studies, allowing for control of past exposures and past outcomes, constitute one of the most powerful designs, short of a randomized trial, for contributing evidence for causality (VanderWeele et al., 2016c). Moreover, if efforts were made to incorporate additional measures of religion and spirituality into future waves of data collection for existing cohort studies, these cohorts would be yet more valuable for advancing R/S and health research.

Efforts are underway to expand capacity to conduct such R/S research through a consortium effort that builds on several national cohorts (http://cgvh.harvard.edu). This consortium effort will be conducting original research to evaluate which R/S measures seem to be the most useful to collect in the effort to understand the underlying biological pathways or mechanisms through which R/S likely affects human health, and thus to help cohort leaders prioritize future R/S data collection efforts in cohort studies. Collaborative efforts can build on the wealth of data, collected over decades by the dedicated cohort leaders and their study teams. These cohorts include rich biological, clinical, demographic, environmental, behavioral and psychosocial data, and also include some R/S measures, all of which can be leveraged now to advance knowledge regarding the various biological mechanisms and pathways through which R/S operates to affect human health and vulnerability to disease. As new biological markers strongly associated with R/S measures are collected by cohorts in the future, these data resources will become even more valuable in understanding the relationship between religion and spirituality, risk of disease (or protective effects), and human health.

References

Balbuena, L., Baetz, M., Bowen, R., 2013. Religious attendance, spirituality, and major depression in Canada: a 14-year follow-up study. Can. J. Psychiatry 58, 225—232.

Gillum, R.F., King, D.E., Obisesan, T.O., Koenig, H.G., 2008. Frequency of attendance at religious services and mortality in a U.S. national cohort. Ann. Epidemiol. 18 (2), 124—129.

Hill, T.D., Ellison, C.G., Burdette, A.M., Taylor, J., Friedman, K.L., 2016. Dimensions of religious involvement and leukocyte telomere length. Soc. Sci. Med. 163, 168—175.

Ho, R.T., Chan, J.S., Wang, C.W., Lau, B.W., So, K.F., Yuen, L.P., et al., 2012. A randomized controlled trial of qigong exercise on fatigue symptoms, functioning, and telomerase activity in persons with chronic fatigue or chronic fatigue syndrome. Ann. Behav. Med. 44, 160—170.

Hoge, E.A., Chen, M.M., Orr, E., Metcalf, C.A., Fischer, L.E., Pollack, M.H., et al., 2013. Loving-Kindness Meditation practice associated with longer telomeres in women. Brain Behav. Immun. 32, 159—163.

Hummer, R.A., Rogers, R.G., Nam, C.B., Ellison, C.G., 1999. Religious involvement and US adult mortality. Demography 36 (2), 273—285.

Jacobs, T.L., Epel, E.S., Lin, J., Blackburn, E.H., Wolkowitz, O.M., Bridwell, D.A., et al., 2011. Intensive meditation training, immune cell telomerase activity, and psychological mediators. Psychoneuroendocrinology 36, 664—681.

Kleinman, E.M., Liu, R.T., 2014. Prospective prediction of suicide in a nationally representative sample: religious service attendance as a protective factor. Br. J. Psychiatry 204, 262—266.

Koenig, H.G., King, D.E., Carson, V.B., 2012. Handbook of Religion and Health, second ed. Oxford University Press, Oxford, New York.

Koenig, H., Nelson, B., Shaw, S., Saxena, S., Cohen, H., 2016. Religious involvement and telomere length in women family caregivers. J. Nerv. Ment. Dis. 204, 36—42.

Lavretsky, H., Epel, E.S., Siddarth, P., Nazarian, N., Cyr, N.S., Khalsa, D.S., et al., 2013. A pilot study of yogic meditation for family dementia caregivers with depressive symptoms: effects on mental health, cognition, and telomerase activity. Int. J. Geriatr. Psychiatry 28, 57—65.

Li, S., Okereke, O.I., Chang, S.-C., Kawachi, I., VanderWeele, T.J., 2016a. Religious service attendance and lower depression among women - a prospective cohort study. Ann. Behav. Med. 176 (6), 777—785.

Li, S., Stamfer, M., Williams, D.R., VanderWeele, T.J., 2016b. Association between religious service attendance and mortality among women. JAMA Intern. Med. (in press).

Schnall, E., Wassertheil-Smoller, S., Swencionis, C., et al., 2010. The relationship between religion and cardiovascular outcomes and all-cause mortality in the

Women's Health Initiative Observational Study. Psychol. Health 25 (2), 249—263.

Sloan, R.P., Bagiella, E., Powell, T., 1999. Religion, spirituality, and medicine. Lancet 353 (9153), 664—667.

Strawbridge, W.J., Shema, S.J., Cohen, R.D., Kaplan, G.A., 2001. Religious attendance increases survival by improving and maintaining good health behaviors, mental health, and social relationships. Ann. Behav. Med. 23 (1), 68—74.

VanderWeele, T.J., 2015. Explanation in Causal Inference: Methods for Mediation and Interaction. Oxford University Press, New York.

VanderWeele, T.J., 2016. Religion and health: a synthesis. In: Balboni, M.J., Peteet, J.R. (Eds.), Spirituality, Religion and the Culture of Medicine. Oxford University Press.

VanderWeele, T.J., Li, S., Tsai, A., Kawachi, I., 2016a. Religious service attendance and suicide among U.S. women. JAMA Psychiatry. http://dx.doi.org/10.1001/jamapsychiatry.2016.1243 (in press).

VanderWeele, T.J., Yu, J., Cozier, Y.C., Wise, L., Rosenberg, L., Shields, A.E., Palmer, J.R., 2016b. Religious service attendance, prayer, religious coping, and religious-spiritual identity as predictors of all-cause mortality in the Black Women's Health Study. Am. J. Epidemiol. (in press).

VanderWeele, T.J., Jackson, J.W., Li, S., 2016c. Causal inference and time-varying exposures: a case study of religion and mental health. Soc. Psychiatry Psychiatric Epidemiol.