### Title

Outcomes of Randomized Clinical Trials of Interventions to Enhance Social, Emotional, and Spiritual Components of Wisdom




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# Outcomes of Randomized Clinical Trials of Interventions to Enhance Social, Emotional, and Spiritual Components of Wisdom
## A Systematic Review and Meta-analysis

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**IMPORTANCE** Wisdom is a neurobiological personality trait made up of specific components, including prosocial behaviors, emotional regulation, and spirituality. It is associated with greater well-being and happiness.

**OBJECTIVE** To evaluate the effectiveness of interventions to enhance individual components of wisdom.

**DATA SOURCES** MEDLINE and PsycINFO databases were searched for articles published through December 31, 2018.

**STUDY ELIGIBILITY CRITERIA** Randomized clinical trials that sought to enhance a component of wisdom, used published measures to assess that component, were published in English, had a minimum sample size of 40 participants, and presented data that enabled computation of effect sizes were included in this meta-analysis.

**DATA EXTRACTION AND SYNTHESIS** Random-effect models were used to calculate pooled standardized mean differences (SMDs) for each wisdom component and random-effects meta-regression to assess heterogeneity of studies.

**MAIN OUTCOMES AND MEASURES** Improvement in wisdom component using published measures.

**RESULTS** Fifty-seven studies (N = 7096 participants) met review criteria: 29 for prosocial behaviors, 13 for emotional regulation, and 15 for spirituality. Study samples included people with psychiatric or physical illnesses and from the community. Of the studies, 27 (47%) reported significant improvement with medium to large effect sizes. Meta-analysis revealed significant pooled SMDs for prosocial behaviors (23 studies; pooled SMD, 0.43 [95% CI, 0.22-0.3]; *P* = .02), emotional regulation (12 studies; pooled SMD, 0.67 [95% CI, 0.21-1.12]; *P* = .004), and spirituality (12 studies; pooled SMD, 1.00 [95% CI, 0.41-1.60]; *P* = .001). Heterogeneity of studies was considerable for all wisdom components. Publication bias was present for prosocial behavior and emotional regulation studies; after adjusting for it, the pooled SMD for prosocial behavior remained significant (SMD, 0.4 [95% CI, 0.16-0.78]; *P* = .003). Meta-regression analysis found that effect sizes did not vary by wisdom component, although for trials on prosocial behaviors, large effect sizes were associated with older mean participant age (β, 0.08 [SE, 0.04]), and the reverse was true for spirituality trials (β, −0.13 [SE, 0.04]). For spirituality interventions, higher-quality trials had larger effect sizes (β, 4.17 [SE, 1.07]), although the reverse was true for prosocial behavior trials (β, −0.91 [SE 0.44]).

**CONCLUSIONS AND RELEVANCE** Interventions to enhance spirituality, emotional regulation, and prosocial behaviors are effective in a proportion of people with mental or physical illnesses and from the community. The modern behavioral epidemics of loneliness, suicide, and opioid abuse point to a growing need for wisdom-enhancing interventions to promote individual and societal well-being.

Editorial

Supplemental content

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Wisdom has been discussed in religious and philosophical texts for centuries. The empirical study of wisdom began only 4 decades ago, but the number of research articles on wisdom has been growing. Vaillant's Harvard Study of Adult Development was the first to examine psychosocial and lifestyle factors associated with wisdom and well-being.[1] Baltes and Staudinger[2] defined wisdom as extensive pragmatic knowledge, focusing on the cognitive or intellectual aspect. Clayton and Birren[3] added reflective and affective components to the definition of wisdom. Sternberg[4] posited that wisdom resulted from an application of knowledge mediated by a balance of personal and societal interests. Ardelt[5] conceptualized wisdom as an integration of cognitive, reflective, and affective (or compassionate) personality qualities. Cloninger's research[6] highlighted the relevance of certain personality traits to well-being.

We previously reviewed the empirical literature on wisdom[7,8] and conducted a Delphi method study of consensus among international experts in wisdom,[7] as well as a mixed-methods qualitative-quantitative study of wisdom in an ancient religious document. These studies suggested that wisdom is a complex human trait with several specific components (ie, prosocial behaviors such as empathy and compassion, emotional regulation, spirituality, self-reflection, social decision-making or social advising, acceptance of uncertainty, and decisiveness). Wisdom is thought to be adaptive rather than fixed and can increase with age and personal experience. Blazer,[8] Williams et al,[9] Grossman,[10] and others have emphasized practical wisdom, considering the context that influences wise decision-making. Several investigations have reported that wisdom is associated with positive outcomes, including better overall physical and mental health,[11] well-being,[12] happiness,[13] life satisfaction,[14] and resilience,[15] as well as lower levels of loneliness.[15]

We also reviewed the literature on neurobiological basis of wisdom components and found that they seemed to share similar brain regions, specifically the prefrontal cortex (dorsolateral, ventromedial, and anterior cingulate) and limbic striatum.[16] Furthermore, we found a number of published case reports of damage to these areas that produced a loss of these components (eg, increased emotional lability, impulsivity, indecisiveness, lack of compassion) without affecting other cognitive abilities, such as in the case of Phineas Gage[17] and patients with frontotemporal dementia.[18] While there have been no prospective longitudinal studies of changes in wisdom with aging using standardized rating scales, older adults have been reported in multiple investigations to have greater emotional regulation,[19] positivity,[20] prosocial behaviors,[21] and self-reflection[19] compared with younger adults. Considerable empirical evidence indicating neuroplasticity of aging, especially in adults who are physically, cognitively, and socially active, supports the potential to modify wisdom-type traits in later life. Aging-associated brain adaptations, including reduced lateralization of functioning,[22] posterior-to-anterior shift in brain activity,[23] and diminished amygdala response to negative or stressful stimuli,[24] may facilitate wisdom-relevant brain function in later life. Distinct patterns of brain activation on functional magnetic resonance imaging (fMRI) in response to moral dilemmas have been observed in individuals with higher vs lower scores on a validated scale for assessing overall wisdom.[25]

Personality traits, such as resilience and optimism, have been shown to be moderately heritable (with estimates of 33%[26] to 52%[27]), suggesting they are also influenced by environmental factors. A recent investigation[28] reported 50% to 58% heritability of self-directedness, cooperativeness, and self-transcendence in a large, population-based study that was replicated in multiple samples. These components overlap with those in our definition of wisdom. Several recent studies have reported increases in resilience and optimism with behavioral interventions.[29,30] While acknowledging their limitations, these findings support the possibility that positive personality traits can be enhanced through psychosocial interventions and thereby potentially lead to improvement of health and well-being. Yet we found no published reviews of interventions for increasing wisdom or its components; thus, it was unclear whether such interventions were effective. Therefore, we conducted a systematic review with meta-analysis and meta-regression analysis of randomized clinical trials (RCTs) intended to enhance one of the specific components of wisdom.

### Key Points

**Question** How effective are interventions to enhance individual components of wisdom?

**Findings** Despite heterogeneity of studies and publication bias, this meta-analysis and meta-regression found that interventions to enhance prosocial behaviors, emotional regulation, and spirituality were generally effective, especially among older participants.

**Meaning** Per this analysis, interventions to enhance prosocial behaviors, emotional regulation, and spirituality are effective in a proportion of individuals with mental or physical illnesses and people from the community.

## Methods

### Procedures

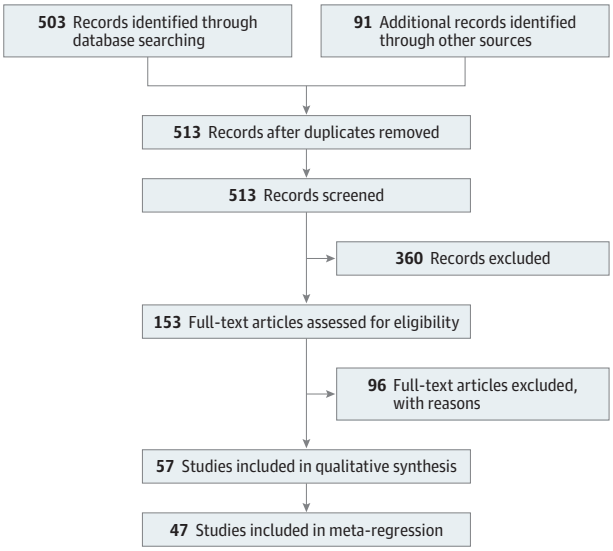
We conducted a literature search for interventions targeting wisdom components, as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (**Figure 1**). To identify articles for review, we surveyed the MEDLINE and PsycINFO online databases through December 31, 2018, with the following criteria: any study that (1) included one of the wisdom components listed above, (2) was published in English, (3) was an RCT, (4) had a minimum sample size of 40 participants, (5) included a published assessment tool to measure that component before and after the intervention, and (6) presented data that enabled computation of the intervention's effect size for enhancing the wisdom component.

The following MEDLINE search terms were used: "((Intervention [Title/Abstract] OR Interventions [Title/Abstract])

AND (wisdom[Title] OR pro-social[Title] OR empathy[Title] OR compassion[Title] OR emotion regulation[Title] OR emotional regulation[Title] OR spirituality[Title] OR self-reflection[Title] OR decisiveness[Title] OR social advising-[Title] OR altruism[Title]) AND ("0001/01/01"[PDat]: "2018/12/31"[PDat]) AND English[lang])." The following search terms were used in the PsycINFO database: "(ti(interventions OR intervention) OR ab(interventions OR intervention)) AND ti(wisdom OR pro-social OR empathy OR compassion OR self-reflection OR emotion regulation OR emotional regulation OR spirituality OR decisiveness OR social advising OR altruism))," with the additional limits of English language and publication prior to December 31, 2018.

This search yielded 513 articles of potential interest after the removal of duplicates, of which 153 were deemed relevant based on a review of their abstracts. At least 2 authors (of a group of 4: E.E.L., J.A.A., B.H., and G.E.) independently examined each full-text journal article for defined eligibility criteria. The κ statistic for study selection was 0.97. Disagreements on inclusion criteria were settled by a third author from the same group of 4. The final search resulted in 57 studies reported in 54 articles.

Figure 1. PRISMA Flow Diagram for Literature Review




## Statistical Analysis

For the meta-analysis, outcome data (assessment of wisdom component) were extracted from each study, including means, SDs, and sample sizes for the intervention and control groups. Data extraction was conducted by several authors in duplicate (E.E.L., M.R., and B.H.). The standardized mean differences (SMDs) for each RCT and the pooled SMD for each wisdom component were calculated using a random-effects model, given the heterogeneity of the interventions and outcome measures. Pooled SMDs were interpreted as small (0.2≤SMD<0.5), medium (0.5≤SMD<0.8), and large (0.8≤SMD).[31]

The quality of these studies was evaluated using a modified Scale for Assessing Scientific Quality of Investigations (SASQI).[32,33] Thirteen original items were retained in the modified version; the 3 excluded items referred to educational interventions that used technology.

The $I^2$ statistic was used to assess statistical heterogeneity of the study outcomes, with the following interpretation about its importance: low (0%-40%), moderate (30%-60%), substantial (50%-90%), and high (75%-100%).[34] Publication bias was assessed using the Egger test (a measure of the asymmetry of the funnel plot),[35] as well as the Duval and Tweedie trim-and-fill procedure[36] to adjust the funnel plot and pooled SMD for missing studies.

To perform meta-regression analyses, we first converted different types of effect sizes into $\eta^2$ and logit-transformed $\eta^2$ to remove range restriction. We then performed a meta-regression model using the generalized estimating equation, weighted by sample size of each study.[37] This led to models with the following factors included: type of patient (community based vs physically ill vs psychiatrically ill), mean age of participants, percentage of female participants, intervention format (individual vs group), number of sessions, length of individual sessions (minutes), and SASQI score (with the median split into 2 levels). The variance inflation factor was calculated to detect potential multicollinearity.[38] Additional factors included interaction terms: mean age by wisdom component, SASQI median split by wisdom component, and length of sessions by wisdom component based on variance inflation factor analyses. Significance was defined as an α less than .05 (2-tailed) for all analyses. All analyses were conducted using RevMan version 5.3 (Cochrane Reviews) and R version 3.6.1 (R Foundation for Statistical Computing).

# Results

## Study Characteristics

Of the 57 intervention studies that met our review criteria (**Table 1**; eTable 1 in the Supplement), 29 focused on prosocial behaviors[39-65] (eg, empathy, compassion, altruism), 13 on emotional regulation,[66-77] and 15 on spirituality.[78-92] We did not find any published RCTs for self-reflection, social decision-making or social advising, acceptance of uncertainty, and decisiveness.

Forty-five studies[43-52,55-60,62-65,67,70,71,73,74,76-92] included only adult participants. Twenty-nine reports[39,41-46,51,53,54,56-67,70,72,79,89,92] had community-based participants, 19 reports[40,47-49,52,55,68,69,71,73-78,81,90,91] included persons with psychiatric illnesses or behavioral problems, and 9 had participants with physical illnesses.[50,80,82-88] Forty interventions[39,42-44,46,49,50,53,54,56-62,64-68,71-76,80,81,83,84,86,87,89-92] took place in a group setting. Across the wisdom components, the interventions varied in length, duration, and outcome measures used (eTable 1 in the Supplement). The mean (SD) intervention duration was 748 (753) minutes. Study quality was generally high because of the criteria for selecting reports for this review, with mean (SD) modified SASQI scores of 10.44 (1.7; possible range, 0-13; observed range, 5-13; eTable 2 in the Supplement). Compared with control

Table 1. Summary of Intervention Characteristics[a]

| Characteristic | Wisdom component, No. | | |
|---|---|---|---|
| | Prosocial behaviors | Emotional regulation | Spirituality |
| Randomized clinical trial | | | |
| With inert control group | 17 | 8 | 8 |
| With active control group | 9 | 5 | 7 |
| Age groups | | | |
| Child/adolescent | 6 | 5 | 0 |
| Adult | 20 | 8 | 15[a] |
| Sample characteristics | | | |
| Community based | 18 | 5 | 3 |
| Physically ill | 1 | 0 | 8 |
| Psychiatrically ill | 7 | 8 | 4 |
| Intervention format | | | |
| Group | 19 | 10 | 10 |
| Individual | 7 | 3 | 5 |
| Sample size, mean (SD), No. | 116.1 (115.0) | 130.9 (115.0) | 143.3 (116.6) |
| Age, mean (SD), y | 28.7 (13.9) | 28.2 (13.7) | 42.2 (16.1) |
| Women, mean (SD), % | 58.9 (23.1) | 60.2 (38.1) | 72.0 (20.7) |
| Sessions, mean (SD), No. | 8.8 (8.6) | 10.0 (4.6) | 5.6 (3.7) |
| Length of sessions, mean (SD), min | 123.8 (102.3) | 87.3 (24.8) | 102.5 (102.8) |
| SASQI score, mean (SD) | 10.0 (2.0) | 10.9 (1.3) | 10.3 (1.5) |

Abbreviations: SASQI, Scale for Assessing Scientific Quality of Investigations (modified version).

[a] One study[78] included both adolescents and young adults (aged 13-25 years).

groups, 27 RCTs (47%) reported significantly improved wisdom components with a medium to large effect size.[39,45,47,49-51,55-57,59,60,62-65,67,69,70,72,74,77,82-84,88,90,92]

The proportion of trials with medium to large effect sizes did not differ across the 3 components: prosocial behaviors (15 of 29 studies[39,45,47,49-51,55-57,59,60,62,63,65]), emotional regulation (6 of 13 studies[67,69,70,72,74,77]), and spirituality (6 of 15 studies[82-84,88,90,92]). Among the prosocial behavior RCTs, the trials with medium to large effect sizes had older mean participant ages ($t_{20}$ = −3.59; $P$ = .002; $d$, −1.57). Among the emotional regulation studies, the interventions with medium to large effect sizes were more likely to occur within individual-based formats (3 of 3[69,70,77]) compared with group settings (3 studies[67,72,74] of 10 studies[66-68,71-76]) ($\chi^2_1$ = 4.55; $P$ = .03).

The outcome measures used varied across the reports (eTable 3 in the Supplement). Forty-eight of 57 studies[41-52,54-62,65,70-75,77-92] (84%) used self-rated measures. Ten trials (17.5%) used objective outcomes: 5 on prosocial behaviors (3 task-based,[53,63,64] 1 researcher-rated,[39] and 1 parent-rated[40]), and 5 on emotional regulation in 4 studies (teacher-rated or parent-rated).[66-69]

## Prosocial Behavior Interventions

Twenty-nine RCTs focused on prosocial behaviors of empathy, compassion (including self-compassion), and altruism.[39-65] Twenty-three studies[39,43-52,55-60,62-65] included adults. Eight trials[40,47-49,52,55] included persons with psychiatric or behavioral problems, 1 trial[50] included people with physical illness (diabetes mellitus), and 21 were community based.[41-46,51,53,54,56-65] While empathy and compassion were hypothesized to reduce cyberbullying[41,54] and aggression[61] and improve grades and learning[53] in young people, self-compassion was hypothesized to decrease distress and improve well-being.[50,62]

The meta-analysis calculations for these interventions were based on 23 RCTs from 21 articles,[39-41,43,45-47,49,50,52-62,65] with a pooled SMD of 0.43 (95% CI, 0.22-0.3; $P$ = .01; **Figure 2**). Heterogeneity of the studies was considerable ($I^2$ = 84%; $P$ < .001). Altogether, the interventions had a statistically significant but modest association with prosocial behaviors.

## Emotional Regulation Interventions

There were 13 studies (in 12 articles[66-77]) of emotional regulation interventions in either psychiatrically ill or community-based populations, with 10 using group settings.[66-68,71-76] These RCTs sought to improve binge-eating behaviors,[71] behavioral problems,[69] test anxiety,[72] and family relationships.[67]

The meta-analysis calculations for these interventions were based on 12 studies from 11 published RCTs,[66,67,69-77] with a pooled SMD of 0.67 (95% CI, 0.21-1.12; $P$ = .004; **Figure 3**). Heterogeneity of study outcomes was considerable ($I^2$ = 93%; $P$ < .001). Altogether, the interventions had a statistically significant, medium-sized association with emotional regulation outcomes.

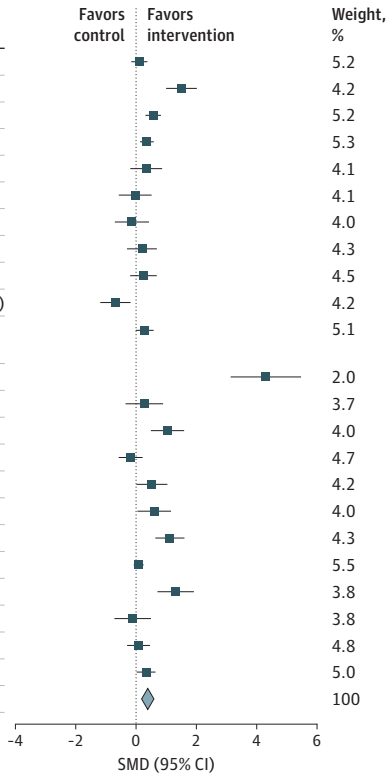
## Spirituality Interventions

There were 15 spirituality-focused RCTs,[78-92] all in adults, and 8 of these[80,82-88] were in people with serious and/or terminal medical illnesses. Four RCTs included psychiatric samples: patients with opiate use disorders stabilized with methadone maintenance,[90] adults with depression/anxiety,[78,81] and women with eating disorders.[91] Ten interventions were conducted in group settings[80,81,83,84,86,87,89-92] and 2 drew from specific religions (Buddhist teachings[80] or Islamic traditions[82]).

Figure 2. Forest Plot for Interventions for Prosocial Behaviors

| Study or subgroup | Experimental Mean (SD) | Experimental Total | Control Mean (SD) | Control Total | SMD (95% CI) | Weight, % |
|---|---|---|---|---|---|---|
| DeSmet et al,[41] 2018 | 3.44 (0.53) | 96 | 3.38 (0.56) | 120 | 0.11 (-0.16 to 0.38) | 5.2 |
| Larti et al,[43] 2018 | 122.11 (12.05) | 36 | 105.02 (10.46) | 41 | 1.51 (1.00 to 2.02) | 4.2 |
| Sommers-Spijkerman et al,[45] 2018 | 54.5 (10.44) | 120 | 48.05 (12.11) | 122 | 0.57 (0.31 to 0.83) | 5.2 |
| Buffel du Vaure et al,[46] 2017 | 111.9 (10.6) | 155 | 107.7 (12.7) | 144 | 0.36 (0.13 to 0.59) | 5.3 |
| Westerhof-Evers et al,[47] 2017 | -13.3 (3) | 29 | -14.5 (4) | 27 | 0.34 (-0.19 to 0.86) | 4.1 |
| de Bruin et al,[49] 2016[a] | 4.32 (0.98) | 27 | 4.35 (1.12) | 25 | -0.03 (-0.57 to 0.52) | 4.1 |
| de Bruin et al,[49] 2016[b] | 4.21 (0.87) | 23 | 4.35 (1.12) | 25 | -0.14 (-0.70 to 0.43) | 4.0 |
| Friis et al,[50] 2016 | 3.21 (0.72) | 32 | 3.08 (0.59) | 31 | 0.19 (-0.30 to 0.69) | 4.3 |
| Toole et al,[52] 2016 | 2.95 (0.62) | 40 | 2.8 (0.59) | 40 | 0.25 (-0.19 to 0.69) | 4.5 |
| Flook et al,[53] 2015 | 5.13 (1.78) | 29 | 6.2 (1.33) | 37 | -0.69 (-1.19 to -0.18) | 4.2 |
| Garaigordobil and Martínez-Valderrey,[54] 2015 | 103.35 (19.09) | 93 | 98.08 (17.32) | 83 | 0.29 (-0.01 to 0.58) | 5.1 |
| Kelly and Carter,[55] 2015 | 3.58 (0.18) | 15 | 2.79 (0.18) | 26 | 4.30 (3.14 to 5.47) | 2.0 |
| Lor et al,[56] 2015 | 115.3 (11.9) | 20 | 112.2 (10.2) | 20 | 0.27 (-0.35 to 0.90) | 3.7 |
| Erogul et al,[57] 2014 | 3.7 (0.53) | 28 | 3.1 (0.6) | 30 | 1.04 (0.49 to 1.59) | 4.0 |
| Mantzios and Wilson,[58] 2014[a] | 87.38 (16.85) | 48 | 90.46 (17.32) | 50 | -0.18 (-0.58 to 0.22) | 4.7 |
| Mantzios and Wilson,[58] 2014[b] | 94.14 (13.55) | 27 | 87.92 (9.95) | 34 | 0.53 (0.01 to 1.04) | 4.2 |
| Smeets et al,[59] 2014 | 4.6 (0.72) | 27 | 4.11 (0.88) | 25 | 0.60 (0.05 to 1.16) | 4.0 |
| Yadavaia et al,[60] 2014 | 19.28 (2.92) | 34 | 15.26 (3.96) | 44 | 1.12 (0.64 to 1.61) | 4.3 |
| Castillo et al,[61] 2013 | 3.59 (0.57) | 361 | 3.54 (0.59) | 229 | 0.09 (-0.08 to 0.25) | 5.5 |
| Neff and Germer,[62] 2013 | 3.78 (0.6) | 25 | 2.93 (0.67) | 27 | 1.31 (0.71 to 1.92) | 3.8 |
| Wallmark et al,[65] 2012 | 9.8 (7.12) | 20 | 10.45 (4.18) | 22 | -0.11 (-0.72 to 0.50) | 3.8 |
| Solantaus et al,[40] 2010 | 7.06 (1.77) | 53 | 6.9 (2.02) | 53 | 0.08 (-0.30 to 0.46) | 4.8 |
| Bonvicini et al,[39] 2009 | 8.09 (2.36) | 80 | 7.38 (1.85) | 80 | 0.33 (0.02 to 0.65) | 5.0 |
| Total (95% CI) | | 1418 | | 1335 | 0.43 (0.22 to 0.63) | 100 |

Heterogeneity: $\tau^2 = 0.19$; $\chi^2_{22} = 137.69$, ($P < .001$); $I^2 = 84\%$
Test for overall effect: $z = 4.06$ ($P < .001$)




SMD indicates standardized mean differences.

Spirituality was hypothesized to reduce psychological suffering and improve quality of life.[78-92]

The meta-analysis calculations for these interventions were based on 12 studies from 12 published RCTs,[78-92] with a pooled SMD of 1.00 (95% CI, 0.41-1.60; $P = .001$; Figure 2C). Heterogeneity of study outcomes was considerable ($I^2 = 96\%$; $P < .001$). Altogether, the interventions had a statistically significant large-sized association with spiritual outcomes.

## Quality of Included Studies

The quality rating for each study is reported in eTable 2 in the Supplement, using the information from the modified SASQI scale. Overall, 29 studies[40-43,45,46,48,50,51,54,55,57,59,60,64,65,69,71,74-76,78,81,82,85,87-90] (51%) described the method used to randomize participants to the intervention vs control groups, 23 (40%) included an active control group,[40,44,47,49,51,54,58,59,61,63,66,68,74-76,79,82,85,87,88,91,92] and 21 (37%) examined whether participants who dropped out differed significantly from those who completed the study.[40,45,46,48-51,55,56,69,73-75,77,78,82,83,85,90,92] The lower-quality reports (those in the lower 50th percentile; 25 studies vs 32 higher-quality reports) were less likely to describe randomization methods (6 of 25 lower-quality studies vs 13 of 32 higher-quality studies), inclusion and exclusion criteria (14 lower-quality studies vs 30 higher-quality studies), withdrawals or dropouts (11 lower-quality studies vs 31 higher-quality studies), comparison of demographic variables between the control and intervention groups (18 lower-quality studies vs 31 higher-quality studies), and analytical plan to address differences between control vs intervention groups (15 lower-quality studies vs 29 higher-quality studies) and between participants who dropped out vs completed the study (0 lower-quality studies vs 29 higher-quality studies).

## Publication Bias

The Egger test indicated the presence of publication bias among the studies of prosocial behavior ($z$, 3.48; $P < .001$) and emotional regulation ($z$, 9.01; $P < .001$), but not the spirituality studies ($z$, 0.10; $P = .92$). Funnel plots using the trim-and-fill method[36] resulted in the following adjusted SMDs (prosocial behavior: SMD, 0.4 [95% CI, 0.16-0.78]; $P = .003$; emotional regulation: SMD, 1.26 [95% CI, -0.53 to 3.04]; $P = .17$; spirituality: SMD, 1.00 [95% CI, 0.46-1.54]; $P < .001$; eFigures 1, 2, and 3 in the Supplement).

## Meta-regression Analysis

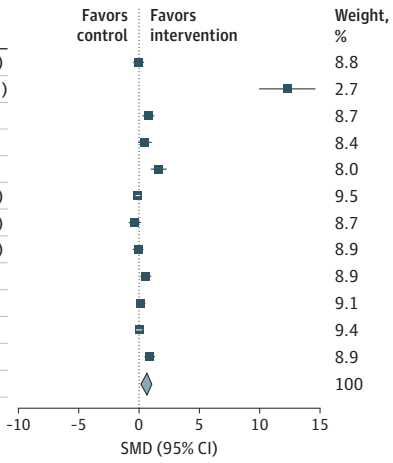
The meta-regression analyses found that effect sizes did not differ among different wisdom components. Among trials on prosocial behavior, sample populations with older mean ages had higher effect sizes (β, 0.08 [SE, 0.04]); for spirituality trials, sample populations with younger mean ages had higher effect sizes (β, −0.13 [SE, 0.04]) (**Table 2**). Among spirituality interventions, studies with higher SASQI scores had larger effect sizes (β, 4.17 [SE, 1.07]), while the reverse was true for prosocial behavior trials (β, −0.91 [SE, 0.44]).

Figure 3. Forest Plots for Interventions for Emotional Regulation and Spirituality

A Interventions for emotional regulation

| Study or subgroup | Experimental Mean (SD) | Experimental Total | Control Mean (SD) | Control Total | SMD (95% CI) |
|---|---|---|---|---|---|
| Ma et al,[70] 2018 | 93.88 (15.83) | 35 | 94.47 (17.35) | 41 | -0.04 (-0.49 to 0.42) |
| Rahmani et al,[71] 2018 | -64.5 (9.71) | 30 | -159.11 (4.61) | 30 | 12.29 (9.96 to 14.62) |
| Weiss et al,[69] 2018 | 2.16 (0.295) | 35 | 1.91 (0.344) | 33 | 0.77 (0.28 to 1.27) |
| Shahidi et al,[72] 2017 | 122.08 (13.43) | 25 | 115.32 (14.15) | 25 | 0.48 (-0.08 to 1.05) |
| Spidel et al,[73] 2017 | 15.8 (0.5) | 30 | 14.9 (0.6) | 20 | 1.64 (0.98 to 2.29) |
| Houck et al,[66] 2016 | 2.95 (0.59) | 222 | 3.01 (0.6) | 198 | -0.10 (-0.29 to 0.09) |
| Tornås et al,[74] 2016 | 53.97 (9.75) | 31 | 58.26 (14.11) | 34 | -0.35 (-0.84 to 0.14) |
| Ravindran et al,[67] 2015[a] | 4.81 (1.14) | 50 | 4.89 (0.89) | 34 | -0.08 (-0.51 to 0.36) |
| Ravindran et al,[67] 2015[b] | 5.5 (0.88) | 50 | 4.96 (1.06) | 34 | 0.56 (0.12 to 1.00) |
| Schuppert et al,[75] 2012 | 21.33 (6.54) | 54 | 20.27 (6.82) | 55 | 0.16 (-0.22 to 0.53) |
| Berking et al,[76] 2008 | 2.59 (63) | 90 | 2.51 (0.75) | 144 | 0.00 (-0.26 to 0.27) |
| Slee et al,[77] 2008 | -17.98 (8.51) | 42 | -25.41 (8.17) | 48 | 0.88 (0.45 to 1.32) |
| Total (95% CI) | | 694 | | 696 | 0.67 (0.21 to 1.12) |

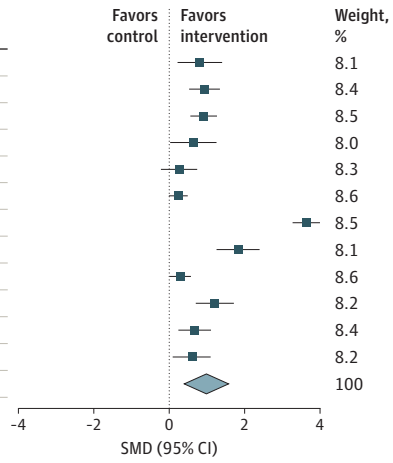
Heterogeneity: $\tau^2 = 0.56$; $\chi^2_{11} = 158.72$, ($P < .001$); $I^2 = 93\%$
Test for overall effect: $z = 2.88$ ($P = .004$)




B Interventions for spirituality

| Study or subgroup | Experimental Mean (SD) | Experimental Total | Control Mean (SD) | Control Total | SMD (95% CI) |
|---|---|---|---|---|---|
| Chimluang et al,[80] 2017 | 113.35 (7.41) | 23 | 102.64 (16.5) | 25 | 0.81 (0.22 to 1.40) |
| Sankhe et al,[81] 2017 | 33.8 (7.1) | 70 | 26.6 (8.5) | 40 | 0.94 (0.53 to 1.34) |
| Labelle et al,[83] 2015 | 35.35 (7.26) | 77 | 27.13 (10.71) | 61 | 0.91 (0.56 to 1.27) |
| Brown et al,[84] 2014 | 97.8 (13.8) | 21 | 87.5 (17.5) | 22 | 0.64 (0.03 to 1.25) |
| Breitbart et al,[85] 2012 | 2.72 (0.83) | 33 | 2.52 (0.68) | 34 | 0.26 (-0.22 to 0.74) |
| Chan et al,[85] 2012 | 37.07 (8.96) | 141 | 34.81 (9.81) | 110 | 0.24 (-0.01 to 0.49) |
| Chochinov et al,[87] 2011 | 33.97 (10.29) | 108 | 3.45 (7.25) | 218 | 3.63 (3.27 to 4.00) |
| Ando et al,[88] 2010 | 25.5 (4.9) | 34 | 13.8 (7.5) | 34 | 1.83 (1.25 to 2.40) |
| Bay et al,[89] 2010 | 104.9 (12.2) | 87 | 101 (13.9) | 112 | 0.29 (0.01 to 0.58) |
| Margolin et al,[90] 2006 | 5.6 (1.37) | 38 | 3.83 (1.53) | 34 | 1.21 (0.70 to 1.71) |
| Richards et al,[91] 2006 | 54.9 (5.8) | 43 | 47.7 (13.7) | 44 | 0.68 (0.24 to 1.11) |
| Wachholtz and Pargament,[92] 2005 | 64.4 (9.19) | 25 | 58.68 (9.76) | 43 | 0.60 (0.09 to 1.10) |
| Total (95% CI) | | 700 | | 777 | 1.00 (0.41 to 1.60) |

Heterogeneity: $\tau^2 = 1.05$; $\chi^2_{11} = 283.61$, ($P < .001$); $I^2 = 96\%$
Test for overall effect: $z = 3.30$ ($P = .001$)




SMD indicates standardized mean differences.

## Discussion

Overall, our meta-analysis of RCTs supports significant increase in levels of the wisdom components with small to large effect sizes, with no difference among the 3 wisdom components. However, the studies had several limitations.

The large range of SMD values could reflect differing outcome measures, as well as variability in types of study participants, control conditions, and interventions. The meta-regression analysis took into account several variables listed in Table 2. The intervention methodology varied widely from cognitive behavioral therapy to mindfulness-based group therapies to spiritual counseling. Other participant characteristics and nuances in intervention type, adherence, and outcome measures that could not be assessed in this study might also affect SMD value.

### Importance of Participant Characteristics

Prosocial behavioral interventions conducted in samples with older mean ages had greater effect sizes. This finding is consistent with published cross-sectional studies reporting higher levels of certain wisdom components in participants of older age.[93-95] These include emotional regulation,[96-98] with decreased likelihood of using destructive strategies to manage conflict[99] and lower recall of negative emotional experiences.[100] Similarly, older adults exhibit greater emotional empathy (empathic concern)[101] and altruistic behavior,[21,102] despite deficits in cognitive empathy (accurate perceptions of others' feelings).[101]

The percentage of female participants varied across studies, and male and female participants had similar responses to interventions. However, women have been reported to have greater baseline empathy and compassion,[103] as well as different emotional neurocircuitry than men.[104-106] One study[67] of emotional regulation in family units found a medium to large

Table 2. Results of Meta-regression Analysis

| Characteristic | Multivariate model of all studies | | |
|---|---|---|---|
| | β (SE) | Wald statistic | *P* value |
| Intercept | −1.12 (0.80) | 1.93 | .17 |
| Wisdom component | | | |
| Emotional regulation (vs prosocial behaviors) | −0.12 (0.53) | 0.05 | .82 |
| Spirituality (vs prosocial behaviors) | −0.32 (0.42) | 0.57 | .45 |
| Participant type | | | |
| With physical illness (vs community based) | 0.59 (0.56) | 1.11 | .29 |
| With psychiatric illness (vs community based) | 0.09 (0.34) | 0.07 | .79 |
| Mean age, y | 0.08 (0.04) | 5.11 | .02 |
| Women, % | 0.003 (0.008) | 0.16 | .69 |
| Intervention format | | | |
| Individual (vs group) | 0.39 (0.42) | 0.87 | .35 |
| Sessions, No. | −0.02 (0.03) | 0.55 | .46 |
| Length of sessions, min | 0.002 (0.002) | 1.03 | .31 |
| SASQI | | | |
| Scores in top 50th percentile (vs bottom 50th percentile) | −0.91 (0.44) | 4.39 | .04 |
| Interaction terms | | | |
| Wisdom component (prosocial behavior) × mean age | 0.00 [Reference] | NA | NA |
| Wisdom component (emotional regulation) × mean age | −0.06 (0.04) | 2.18 | .14 |
| Wisdom component (spirituality) × mean age | −0.13 (0.04) | 9.64 | .002 |
| Wisdom component (prosocial behavior) × SASQI Score (top 50th percentile) | 0.00 [Reference] | NA | NA |
| Wisdom component (emotional regulation) × SASQI Score (top 50th percentile) | 0.78 (0.87) | 0.80 | .37 |
| Wisdom component (spirituality) × SASQI Score (top 50th percentile) | 4.17 (1.07) | 15.1 | <.001 |

Abbreviations: NA, not applicable; SASQI, Scale for Assessing Scientific Quality of Investigations (modified version).

effect size in mothers but not in fathers, which was attributed to greater caregiving roles taken by mothers and thus greater involvement with the intervention, which had relied heavily on home-based work. Further investigation of sex differences is needed to clarify the underlying neurobiological mechanisms of positive psychological traits.

## Features of Interventions

Intervention features, such as session length, frequency, and format, were not associated with outcomes in the meta-regression. While several interventions included home-based practice, such sessions had variable guidelines and adherence levels and therefore could not be included in the meta-regression. Informal skills practice may be essential to honing such traits and should be considered in developing future interventions for wisdom components. Of note, the comparison of trials with medium to large effect sizes with trials with small effect sizes showed that, among the emotional regulation interventions, individual-based interventions were more likely to have medium to large effect sizes than group-based interventions. This finding could partially reflect the fact that fewer RCTs used individual-based formats than group formats because of cost difference and potential gains from group-based settings (eg, social and peer support).

## Study Quality

The modified SASQI scores (lower vs higher than the 50th percentile) reflect the quality of the included studies. While study quality did not differ among different wisdom components, less rigorous RCTs of prosocial behavior had larger effect sizes overall (ie, confounding factors could inflate differences found between the intervention and control group). Interestingly, specifically among spirituality interventions, higher-quality studies reported larger effect sizes. Interventions to improve spirituality may face the additional challenges of its broad definition, ranging from awareness of other powers or forces that influence the universe to living a spiritual life (which is more similar to religious ideals),[107,108] connection to personality traits,[6] and involvement of multiple brain regions.[69]

## Study Outcomes

Unsurprisingly, most of the studies used self-rated or subjective measures as outcomes. While there is great value in assessing the subjective experience of individuals for assessing personality traits such as wisdom, objective assessments should be encouraged. An example is a study by Bonvicini and colleagues[39] objectively assessing physician empathy based on audio recordings of patient-physician interactions.

## Future Directions

Future studies should be based on hypotheses generated from this review—for example, that (1) enhancement of wisdom components will contribute to improvement of overall wisdom, health, and well-being, and (2) older people are more likely to have improvements in wisdom components than younger persons. Exploratory analyses should include examination of

hedonic vs eudemonic well-being, interventions, sex differences in response to interventions, and validity of objective vs subjective ratings of wisdom components. Use of objective measures of wisdom components, techniques such as ecological momentary assessments, technology such as artificial intelligence, relevant biomarkers, and longer-term follow-ups are recommended.

We believe that the relevance of wisdom-associated interventions expands beyond the individual level to the societal level. Over the past 3 decades, annual rates of deaths from opioid overdose and suicides have been rising rapidly,[109,110] resulting in a decline in the mean American lifespan for the first time in half a century.[111] Loneliness and social isolation have been reported to lead to higher stress levels, as well as physical and psychiatric morbidity, including substance abuse and suicidal behavior.[112-115] These recent behavioral epidemics of loneliness, suicides, and opioid abuse[112-115] will require behavioral or psychosocial vaccines or antidotes. The strong inverse correlation between loneliness and wisdom found in a recent study[15] suggests that wisdom may be a remedy for behavioral toxins, such as loneliness.[116]

### Limitations

This review has several limitations. Improvement in individual components of wisdom is not the same as increase in overall wisdom. Studies focusing on wisdom as an entity are clearly warranted. We found only 1 RCT[117] with overall wisdom as an outcome measure, but it did not meet other selection criteria. However, a recently published study by Treichler and colleagues[118] showed increased overall wisdom using the San Diego Wisdom Scale with a 1-month group-based intervention in senior housing communities, which also reduced perceived stress and increased resilience without affecting overall well-being.

Next, search terms were limited to the specific wisdom components and thus did not include negative terms associated with lack of wisdom components (eg, impulsivity, selfishness), and may have missed some relevant studies. Outcomes were limited to the specific wisdom component, because many studies did not assess well-being or other health-associated measures. Most studies relied on self-report assessments of wisdom components, which have potential for bias because of socially desirable responses and problems with recall accuracy. Objective and technology-based measures (eg, reports by participants' close associates, ecological momentary assessments, and video game–based tasks) are warranted. Whether improvements in a wisdom component generalized to everyday life was not examined. Rationale for the study design, study participants' sociodemographic and clinical characteristics, trial methodology, outcomes evaluated, and statistics used varied across the RCTs, contributing to significant heterogeneity among studies, publication bias, and challenges in analyzing all the study features. Follow-up periods were often short, making longer-term efficacy of the interventions unknown. Another limitation pertains to exclusion of articles that were not in the English language. Also, we could not include distal outcomes that were sometimes the goals of the original RCTs (eg, reducing binge-eating behaviors, preventing cyberbullying),[41,55,81] because of marked heterogeneity. Finally, only a few trials were of pragmatic type (ie, combining efficacy with effectiveness, using manualized interventions, and ensuring implementation and dissemination potential in the real world).

Few studies used neurobiological assessments. One novel study, although it did not meet our selection criteria, represents the type of research required to improve our understanding of the neurobiological implications of wisdom-associated interventions. Klimecki and colleagues[119] used an fMRI socioaffective video task to analyze brain activation in women after compassion training compared with memory training and reported enhanced brain activation in anterior insula and anterior midcingulate cortex (regions associated with empathy), as well as the ventral striatum, anterior cingulate, and medial orbitofrontal cortex (regions identified in putative wisdom neurocircuitry).[16] Adding neurobiological assessments, such as regional brain activation on fMRI, with an emotion-based task (eg, seeing happy vs angry faces) would help broaden our knowledge of the brain-based mechanisms mediating improvements in wisdom or its components. Although a wisdom pill is unlikely in the near future, the next generation of advanced and targeted neurostimulation techniques could selectively activate or inhibit neurocircuits associated with components of wisdom.

## Conclusions

Basic research is needed to better understand the neurobiology of wisdom and develop new biologically oriented, wisdom-associated interventions. Eventually, development of wisdom-enhancing interventions at societal level will become a priority, although a number of steps are required to enable development and testing of effective large-scale community-wide interventions. Balancing these 2 priorities will require political wisdom on the part of health care leaders. Increased wisdom in both individuals and communities is likely to confer broad advantages in well-being and health that would ultimately improve survival and flourishing of the society as a whole.

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