Annals of Behavioral Medicine, 2022, **XX**, 1–9
https://doi.org/10.1093/abm/kaac059
Advance access publication 10 April 2023
Regular Article

OXFORD

Support-Giving Is Associated With Lower Systemic Inflammation

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Abstract

Background Support-giving has emerged as a health-relevant social behavior, such that giving more support is associated with better physical health. However, biological mechanisms by which support-giving and health are linked remain unclear. Whether support-giving uniquely relates to health relative to other psychosocial factors is also an open research question.

Purpose Two studies test the hypothesis that support-giving is uniquely (over-and-above other psychosocial factors) related to lower systemic inflammation, a biological correlate of health.

Methods Cross-sectional associations of support-giving with markers of systemic inflammation (i.e., interleukin-6 [IL-6], C-reactive protein [CRP]) were examined in two independent samples of midlife adults (Study 1, n = 746; Study 2, n = 350).

Results Consistent with hypotheses, giving to more social targets (to family and friends, and also volunteering for various causes), but not receiving support from similar targets, was associated with lower IL-6. In conceptual replication and extension with a different measure of support-giving, higher frequency of support-giving behavior was associated with lower IL-6, even after adjusting for social network size and individual differences in social desirability. There were no associations between support-giving and CRP in either sample.

Conclusions Future research needs to establish causality and directly test mechanistic pathways, but together, findings reaffirm the health-relevance of support-giving behavior and shed light on a promising biological mechanism by which such effects may occur.

Lay Summary

Support-giving behavior and health are linked such that more support-giving is related to better health and longevity for the person giving. How such a link occurs, however, is an open question for research. Two cross-sectional studies test the hypothesis that support-giving behavior relates to lower systemic inflammation, a potential biological pathway linking supportive behavior with health. Results of Study 1 show that giving to more social targets (to family and friends, and also volunteering) is associated with lower inflammation. Receiving support was not associated with inflammation. In a replication and extension, Study 2 shows that a greater frequency of giving is also related to lower systemic inflammation, over and above the size of one's social network and individual differences in reporting socially desirable responses. Although more research is needed to establish whether support-giving causes systemic inflammation to change, the current findings highlight a promising pathway by which support-giving behavior benefits health.

Keywords Social support · Prosocial behavior · Altruism · Volunteering · Inflammation

Support-giving—such as giving advice or comfort to a friend, helping around the house, or volunteering at a local nonprofit—is a prevalent social behavior with relevance to the health of the giver. Indeed, individual differences in support-giving behavior relate to health such that higher reports of giving are associated with better physical health (e.g., lower indices of risk for cardiovascular disease [1, 2]) and greater longevity [3, 4]. Why, when, and especially how giving to others is health-promoting, however, remain open research questions [5]. The current studies, therefore, assess how support-giving and health relate by testing cross-sectional associations between two different measures of support-giving—one focused on giving to multiple different social targets (Study 1) and the other focused on the frequency of giving (Study 2)—and markers of systemic inflammation.

Why Support-Giving and Health?

There are compelling theoretical reasons why support-giving might relate to health. Supportive behavior, including behavior

intended to help or address the needs of others (close others, acquaintances, but also strangers or more abstract causes), appears daily throughout the lifespan [6, 7]. The prevalence of such "everyday" supportive behaviors suggests that humans might be predisposed to give [8–10], perhaps even engaging in support-giving behavior in a reflexive manner [11, 12]. That is, support-giving can occur without external reinforcement or direction. The ubiquity of support-giving behavior suggests there may be benefits, including health benefits, for the giver. Consistent with this possibility, random assignment to support-giving (vs. control conditions) increases positive social and emotional outcomes [13, 14] and reduces physiological responding to acute stress [15]. Continuing to engage in supportive behavior over time may then lead to better physical health [4]. If true, support-giving behavior may be an understudied contributor to the large-scale findings linking social ties and health [16].

Despite propositions that support-giving could be health protective, lingering questions remain. For instance, other factors that characterize the quantity and quality of social relationships also relate to health (e.g., social network size; received support), and may be confounded with support-giving behavior. The extent to which support-giving relates to health, separate from these other social factors, is unclear. A second question is about the nature of the supportive behavior that is most health-protective. Previous findings suggest that giving to a single, identifiable target, can be the most beneficial for well-being [13, 17]. In practice, however, one might encounter multiple identifiable targets within their social network who need support. Likewise, one might identify specific needs, such as a need for donations or volunteers, that could be addressed by support-giving behavior. Whether giving to more targets and needs relates to worse (e.g., giving becomes a burden) or better (e.g., giving increases connection to others) outcomes is unknown. Finally, the biological correlates of supportive behaviors are largely understudied, despite the fact that identifying biological correlates of support-giving could shed light on the mechanisms through which giving might promote health.

How Support-Giving Relates to Health: Systemic Inflammation

Inflammation is widely recognized as one pathway by which socio-emotional experiences and health are linked [18–20]. Thus, elevated circulating markers of C-reactive protein (CRP) and proinflammatory cytokines, such as interleukin-6 (IL-6), may confer future health risk. With regard to inflammation and support-giving, one study in adolescents (10th graders) showed that a volunteering intervention decreased circulating levels of IL-6 and CRP compared to a wait-list control condition [21]. Similarly, engaging in everyday forms of support-giving (described as "acts of kindness, generosity, and thoughtfulness") for 4 weeks reduces proinflammatory gene expression [17]. However, another study conducted on middle-aged women found no association between support-giving and circulating inflammation (i.e., IL-6, CRP was not assessed [22]). And, in situations involving protracted support-giving (i.e., caring for an ill loved one), the association described above reverses, such that chronic caregiving is associated with elevated levels of IL-6 [23] and CRP [24]. Despite these mixed findings, previous experimental evidence suggests that support-giving conditions (vs. control conditions in which no support is given) reduce sympathetic nervous system (SNS)-related responding [15, 25]. Given that SNS-activity enhances inflammation [26], it is possible that support-giving may also dampen systemic inflammation. Therefore, the current studies examined associations between support-giving and markers of systemic inflammation.

Current Studies

The current studies examine when and how support-giving and inflammation relate. To test study aims, we conducted secondary data analysis of survey and biomarker data from two separate samples of midlife adults: Midlife in the United States Series (MIDUS; Study 1) and Adult Health and Behavior Project, phase-II (AHAB-II; Study 2). In Study 1, support-giving measures focused on the number of social targets given to over the past month. Study 2 extends the measure of support-giving from Study 1 by assessing the frequency of supportive behavior. To assess the specificity of associations with support-giving, additional relationship and individual difference factors previously shown to correlate with inflammation (i.e., received support, social network size) or that might theoretically relate to the reporting of support-giving behavior (individual differences in reporting socially desirable responses) were also evaluated. Based on previous findings (reviewed in Ref. [9]), we hypothesized that support-giving, independent from these other factors, would be associated with inflammation.

Study 1

Methods

For Study 1, we conducted secondary data analyses on the publicly available dataset, Midlife in the United States (MIDUS Refresher): Biomarker Project, 2012–2016 [27]. For the Refresher Biomarker Project, assessments were completed during an overnight stay at one of the regional Clinical Research Units. On Day 1, participants completed several psychosocial questionnaires including questions assessing supportive behavior toward a number of possible social targets. On Day 2, blood was collected following overnight fasting between the hours of 6:30 and 7:00 AM and then stored at −60°C to −80°C until shipment to the MIDUS Biocore Lab for IL-6 and CRP assays [28].

Participants

Seven hundred forty-six participants from the full MIDUS Refresher sample had both support measures and inflammatory marker data (M_{age} = 51.62, 49.9% female, see Table 1 for additional demographic information). Of these 746 participants, 39 were removed from analyses with CRP (see below). Therefore, analyses with CRP are based on a sample of 707 participants.

Measures

Support-giving

In MIDUS, support-giving questions focused on the number of hours participants spent engaged in supportive behaviors over the past month (i.e., retrospective reporting). Thus, questions focused on the number of hours participants spent giving informal emotional support (e.g., comforting, listening

Table 1 Demographic Information for Studies 1 and 2

	Study 1 (MIDUS)	Study 2 (AHAB-II)
N	863	490
Excluded *n*	117	140
Analytic *n*	746	350
Age	51.62 (13.60) Range 25–76	43.46 (7.23) Range 30–54
% Female	49.9	53.1
BMI	29.97 (7.41)	27.32 (5.40)
% Hispanic/Latinx	3.7	1.4
Race		
% Native American/Alaska Native	1.9	0
% Asian/Asian American	1.3	0.6
% Black/African American	7.0	18.0
% Native Hawaiian/Pacific Islander	0.3	0
% White	70.0	80.3
% Multi/other	6.2	1.2
% Missing	13.4	0
Education		
High school diploma or less	14.2	7.4
Associate's or technical degree	10.5	14.0
Some college, no degree	18.1	10.9
Bachelor's degree	29.9	35.7
Master's degree or higher	27.2	32.0
Not reported	0.1	0
Individual income		
<$10,000	14.9	2.0
$10–14,999	3.2	5.1
$15–24,999	9.4	9.4
$25–34,999	11.5	16.0
$35-49,999	12.2	24.6
$50–64,999	13.4	18.3
$65–79,999	9.7	9.4
$80–94,999	5.2	6.0
$95–109,999	3.9	3.7
$110–124,999	2.5	1.4
$125–139,999	4.6	1.1
$140–154,999	1.2	0
$155–169,999	1.5	0.6
$170–185,000	0.5	0
>$185,000	2.4	2.3
Not reported	3.9	0

BMI, body mass index.

to problems, or giving advice) and giving unpaid assistance (help around the house, transportation, childcare) to each of the following: (a) spouse/partner, (b) parents, (c) in-laws, (d) children/grandchildren, (e) other family members or close friends, (f) anyone else. A similar set of questions asked about formal volunteering in various contexts: (g) hospital, nursing home, or other health-care-oriented work, (h) school or other youth-related causes, (i) political organizations or causes, (j) any other organization, cause, or charity.

Received support

Received support may also relate to health [29]. Therefore, received support was evaluated as an additional covariate. Participants were asked how many hours per month they received emotional support and unpaid assistance from the following social targets: (a) spouse/partner, (b) parents, (c) in-laws, (d) children/grandchildren, (e) other family members or close friends, (f) anyone else, (g) community volunteers, (h) religious groups, (i) any other nongovernmental organization, case, or charity, (j) any government group or agency. Note that some wording is not parallel between the questions regarding support-giving and receiving (i.e., support-giving targets include those that one might volunteer for such as a hospital or nursing home, but there were no questions about receiving support from hospitals). For the exact wording of the support-giving and received support questions from MIDUS, see Supplemental Material.

The range of reported hours for support-giving and received support questions was 0–744 h. However, the modal response for both support-giving and received support was 0 h, regardless of social target. Retrospective reporting of hours of supportive behavior over a month is (arguably) difficult to accurately report and thus, difficult to interpret. The data also showed a highly skewed distribution (skewness range from 4.857 to 24.496, kurtosis range from 32.925 to 631.985), violating a primary assumption of hypothesis testing with frequentist statistics. With these issues in mind, rather than focusing on the number of hours given to or received from each target, responses to each question were recoded into dichotomous responses such that 0 = zero hours reported (i.e., no support exchanged between the participant and the target(s)), and 1 = one or more hours of support exchanged between the targets over the past month. Dichotomous coding alters the interpretation of the questions from "how many hours over the past month" to "did you give to/receive from the following social target: yes or no." After dichotomizing responses for each social target, participants reported giving support to five targets (M = 5.00, SD = 2.26, *range* = 0–10; $\propto$ = .77) and receiving support from three targets (M = 3.56, SD = 2.20, *range* = 0 – 10; $\propto$ = .81) on average. Support-giving and received support were positively correlated (r = .676, p <. 001, bias corrected and accelerated [BCa] 95% confidence interval [CI] = [0.626 to 0.725]). We note the range of potential targets is the same for support-giving and received support.

IL-6 and CRP

Prior work has shown that circulating levels of IL-6 and CRP (to a marginal degree) showed a reduction following random assignment to a support-giving intervention ([21], no other markers were reported in this study). In addition, IL-6 and CRP share a physiological relationship (IL-6 can stimulate the production of CRP). Therefore, analyses were constrained to these two markers of inflammation.

IL-6 assays were conducted using Quantikine High Sensitivity ELISAs (R&D Systems, Minneapolis, MN). The assay sensitivity was 0.156 pg/mL, and the inter-assay coefficients of variability (CV) was 15.66%. CRP levels were measured using an immunonepholometric assay. The assay sensitivity was 0.164 ug/mL, and the inter-assay CV ranged from 1.08% to 4.3%. Samples that fell below the lower limit of detection with these assay methods were assayed again using a high sensitivity immunoelectrochemiluminescence

assay (Meso Scale Diagnostics #K151STG). The assay sensitivity was 0.01 ug/mL, and the inter-assay CV ranged from 4.72% to 5.16%. CRP values greater than 10 ug/mL may reflect acute infection rather than systemic inflammation [30]. Therefore, participants with raw values above 10 (n = 32) were removed from analyses with CRP. An additional seven participants were missing a CRP value. CRP analyses are based on 707 participants.

Data analysis

IL-6 and CRP values were natural log-transformed prior to analysis to adjust for positive skew. Body mass index (BMI) was positively correlated with IL-6 (r =.436, p < .001, BCa 95% CI = [0.361 to 0.512]) and CRP (r = .496, p < .001, BCa 95% CI = [0.421 to 0.568]) as was age (IL-6: r = .256, p < .001, BCa 95% CI = [0.194 to 0.317]; CRP: r = .079, p = .032, BCa 95% CI = [0.010 to 0.150]). Women had higher levels of CRP than men ($t(737)$ = 3.573, p < .001, BCa 95% CI = [−.208 to −.060]) and reported receiving more support than men ($t(737)$ = 2.551, p =.011, BCa 95% CI = [−.716 to −.106]), but no sex differences emerged for IL-6 ($t(737)$ = 0.032, p = 0.975, BCa 95% CI = [−.105 to .101]) or support-giving ($t(737)$ = 1.885, p = .060, BCa 95% CI = [−.659 to 0.008]). 70.9% of the sample endorsed current use of prescription medication at the time of the blood draw. It is likely that prescription medication and the conditions they treat alter systemic inflammation. Therefore, prescription medication use was included as a covariate. Reported associations also adjust for BMI, age, and sex following recommended best practices for analyses with inflammation [31].

Data were evaluated for potential violations of model assumptions, but no violations were identified. Specifically, the data met the assumption of collinearity (IL-6: Tolerance = 0.543, variance inflation factor (VIF) = 1.842, CRP: Tolerance = 0.544, VIF = 1.839), independent errors (Durbin-Watson values IL-6 = 1.937, CRP = 2.092), and the assumption that the data did not contain influential cases that could influence the model (Cook's Distance values for IL-6 and CRP all below 0.200). The scatterplots of standardized residuals likewise showed that the data met assumptions of homoscedasticity and the P-P plots suggested there were no violations to the assumption of normality of the residuals (i.e., data was close to the line).

Two-stage hierarchical multiple regressions were then run to evaluate associations between support-giving and inflammation (IL-6 and CRP separately), adjusting for BMI, age, sex, prescription medication use reported at the time of the blood draw, and received support. Significance was determined based on a p-value of .05, two-tailed, and a BCa bootstrap 95% CI excluding 0.

Exploratory analyses examining non-linear associations between support-giving and inflammation were tested by squaring the support-giving predictor and using it in identical regression models. Results of these analyses were not significant (ps ≥ .149).

Results

BMI, age, sex, prescription medication use, and received support accounted for 25.3% of the variance in IL-6 ($F(5, 734)$ = 49.751, p < .001). Adding support-giving to the model accounted for an additional 1.1% of the variance and this R^2 change was significant ($F(1, 733)$ = 10.538, p = .001, BCa 95% CI = [−0.069 to −.0.017]; Table 2). That is, giving support to more social targets was associated with lower levels of IL-6, even when accounting for other factors known to relate to inflammation (BMI, age, sex, prescription medications) and the number of targets one received support from. For associations broken down based on type of support-giving behavior (i.e., giving emotional support, giving unpaid assistance, formal volunteer work) see Supplemental Material.

Turning to associations with CRP, BMI, age, sex, prescription medication use, and received support, accounted for 25.0% of the variance in CRP ($F(5, 701)$ = 46.694, p < .001). Support-giving explained.4% of additional variance in CRP, but this R^2 change was not significant ($F(1, 700)$ = 3.406, p = .065, BCa 95% CI = [−0.036 to 0.001], Table S1 presented in Supplemental Material).

Discussion

Findings from Study 1 suggest support-giving relates to less IL-6, apart from received support and other factors known

Table 2 Summary of Hierarchical Regression Analysis for Association Between Support-Giving and IL-6, Apart From Other Variables (Study 1, N = 746, 49.9% Female)

Variable	β	BCa 95% CI	p	R	R^2	ΔR^2
Step 1				.503	.253	.253
BMI	0.041	[0.033 to 0.048]	<.001			
Age	0.012	[0.009 to 0.015]	<.001			
Sex	0.046	[−0.042 to 0.134]	.300			
Prescription medication	0.021	[−0.084 to 0.114]	.692			
Received support	−0.009	[−0.030 to 0.011]	.357			
Step 2				.514	.264	.011
BMI	0.041	[0.033 to 0.048]	<.001			
Age	0.013	[0.009 to 0.016]	<.001			
Sex	0.049	[−0.039 to 0.136]	.273			
Prescription medication	0.014	[−0.086 to 0.106]	.795			
Received support	0.020	[−0.008 to 0.049]	.137			
Support-giving	−0.043	[−0.069 to −0.017]	.001			

BMI, body mass index; *BCa*, bias corrected and accelerated; *CI*, confidence interval.

to relate to inflammation. The current study assessed the number of social targets supported over the past month, but this is only one facet of everyday supportive behavior. In addition, while results hold when adjusting for the use of prescription medication at the time of the blood draw, analyses did not account for the systematic screening for prior health conditions that might influence inflammation. Therefore, to conceptually replicate and extend the pattern of findings, secondary data analysis occurred on an independently collected sample of community-dwelling midlife adults from the AHAB-II which included a different measure of support-giving behavior. Participants in AHAB-II also underwent extensive, detailed screening for conditions and medication that might alter inflammation.

Study 2

Methods

AHAB-II comprises a registry of behavioral and biological measurements for the study of individual differences. For detailed information about recruitment, eligibility, and the AHAB-II protocol, see previously published findings [32–34]. The current findings are the first from AHAB-II to examine a relationship of support-giving with systemic inflammation and have not been published elsewhere.

In AHAB-II, participants fasted overnight, avoided exercise for 12 h and alcohol for 24 h before visiting the laboratory to have blood drawn for plasma IL-6 and CRP assays. Appointment times ranged from 7:30 AM to 12:35 PM (M = 9:16 AM ± 0:54 min), and appointments were rescheduled if participants reported symptoms of an acute infection. Blood was collected in citrated tubes, with harvested plasma frozen at −80°C until batch analysis. At this visit, a registered nurse completed a medical history and medication use interview, and measured height and weight to determine BMI in kg/m^2. During the same visit, participants completed psychosocial measures including the Social Network Index (SNI) [35]. At a separate visit, participants completed additional psychosocial measures, including the Self-Reported Altruism Scale (SRA; [36]) and Marlowe-Crowne Social Desirability Questionnaire (MCSD) [37].

Participants

Four hundred ninety individuals participated in AHAB-II between 2008 and 2011. One hundred forty of these participants were excluded for one or more of the following reasons: did not complete the SRA only because the instrument was added to the protocol ~7 months after the start of the study (n = 78), an invalid or missing IL-6 measure (n = 21), history of asthma (n = 22), history of medical condition potentially impacting immune function (n = 2), using inhaled corticosteroids (n = 10), steroid medication (n = 2), immunosuppressant (n = 1), antihistamines (n = 22), cold/allergy medication (n = 1), and/or antibiotic (n = 5).

The final analytic sample included 350 participants (M_{age} = 43.46, 53.1% female, see Table 1 for additional demographic information). Of these 350 participants, 33 additional participants were removed for reasons related to the CRP measure just for analyses with CRP (see below). CRP analyses are based on a sample of 317 participants. Participants provided written informed consent and procedures were run under the oversight of the University of Pittsburgh's Institutional Review Board.

Measures

Support-giving

Participants completed the 20-item SRA Scale, which assesses the frequency of engaging in a range of supportive behaviors [36]. The scale items are well-suited to the current purposes as the questionnaire asks about frequency of giving to a range of potential targets (strangers, acquaintances, charities), though is notably different from the support-giving measure from Study 1 in that there are no questions about behavior toward close others. Instructions asked participants to rate the frequency with which they engaged in the behaviors on a never (1), once (2), more than once (3), often (4), and very often (5) scale. Higher numbers on the SRA indicate more support-giving (M = 63.19, SD = 10.32, range = 33–92 out of a total possible range of 20–100, $\propto$ = .85.).

Covariates: social network size and social desirability

Associations between support-giving and health could be attributed to other individual difference or social factors. Social integration has already been related to health [16], and separately, also related to lower IL-6 [38]. It could be that the current measure of support-giving behavior reflects the degree to which one is socially integrated, rather than anything specific about support-giving behavior per say. Further, support-giving is generally perceived to be a behavior that one "should" endorse with some level of frequency (i.e., a socially desirable behavior). To address these alternative explanations, participants' score on the SNI [35] and the MCSD Questionnaire [37] were evaluated as covariates.

The SNI measures the total number of people in one's social network from a list of 12 social role categories (spouse, parent, daughter/son, daughter/son-in-law, relative, friend, church member, student, employee, neighbor, volunteer, other group member), accounting for the frequency of contact. In other words, only network members who participants see or talk to at least once every 2 weeks are included in the network measure. Controlling for scores on the SNI thus allows us to examine support-giving's potentially unique association with inflammation, apart from the availability of social targets in the network. The total number of people in the network was summed across roles (M = 21.69, SD = 9.00, range from 2 to 53) to provide a measure of overall social network size. Scores on the SRA (support-giving) and social network size were positively related (r = .318, p < .001).

Individual differences in the extent to which participants over-report socially desirable behaviors, including support-giving behaviors, were assessed with the MCSD (M = 19.26, SD = 5.31, range from 1 to 32, $\propto$ = .78). In this questionnaire, participants read 33 items and decide whether each statement is true or false as it pertains to them. Affirmative responses reflect the desire to respond in socially desirable ways. Frequency reporting for some of the support-giving behaviors, as measured by the SRA (described above), could reflect individual differences in such motivations. Indeed, higher scores on the SRA were associated with higher scores on the MCSD (r = .118, p = .027).

IL-6 and CRP

IL-6 was determined by a high-sensitivity quantitative sandwich enzyme immunoassay kit (R&D Systems, Minneapolis, MN, standard range = 0.156–10 pg/mL) run by the University of Pittsburgh's Behavioral Immunology Laboratory. IL-6

levels were extrapolated from a standard curve with linear regression from a log-linear curve. IL-6 samples were run twice (average CV = 6.67%).

High-sensitivity CRP was measured by the Laboratory for Clinical Biochemistry Research at the University of Vermont with a BNII nephelometer utilizing a particle-enhanced immunonephelometric assay (Dade Behring, Deerfield, IL). The detection range for this assay is 0.15–1100 mg/L, and the routine inter-assay CV is 5% at the University of Vermont. As in Study 1, CRP values greater than 10 ug/ml were removed from analyses (n = 5) because such values may reflect acute infection rather than systemic inflammation [30]. An additional 28 participants were removed from analyses with CRP (27 = below the lower limit of detection of 0.16, 1 = sample lost). Analyses with CRP in Study 2 are based on a sample of 317 participants.

Data analysis

Both IL-6 and CRP values were natural log-transformed to adjust for skewness prior to analysis. IL-6 was positively correlated with BMI (r =.387, p < .001, BCa 95% CI = [0.287 to 0.475]) and age in AHAB-II (r = .149, p = .005, BCa 95% CI = [0.0422 to 0.252]). CRP was also positively correlated with BMI (r = .345, p < .001, BCa 95% CI = [0.251 to 0.428]), but not with age (r = .082, p = .143, BCa 95% CI = [–0.028 to 0.200]). There were no sex differences on IL-6, CRP, support-giving, the SNI, or the MCSD (ps ≥.110). However, sex, as well as BMI, and age, were included as covariates following recommended best practices for analyses with inflammation [31].

Data met the assumption of collinearity (IL-6: Tolerance = 0.838, VIF = 1.193, CRP: Tolerance = 0.861, VIF = 1.161), independent errors (Durbin-Watson values IL-6 = 1.945, CRP = 2.055), and the assumption that the data did not contain influential cases that could influence the model (Cook's Distance values for IL-6 and CRP below 0.050). The scatterplots of standardized residuals likewise showed that the data met assumptions of homoscedasticity and the P-P plots suggested there were no violations to the assumption of normality of the residuals.

Following checks on model assumptions, hierarchical regressions were run to assess associations between the SRA and circulating inflammatory markers (IL-6 and CRP separately). BMI, age, sex, social network size, and individual differences in social desirability were entered at Step 1 followed by the SRA at Step 2. Significance was determined based on a p-value of .05, two-tailed, and a BCa bootstrap 95% CI excluding 0.

As in Study 1, exploratory analyses probed for non-linear associations with inflammation. Results of these additional regression analyses were not significant (ps ≥ .344).

Results

Higher frequency of support-giving behaviors was associated with lower IL-6: BMI, age, sex, social network size, and individual differences in social desirability accounted for 16.7% of the variance in IL-6 (F(5, 343) = 13.737, p < .001). Adding support-giving to the model explained an additional 1.2% of the variance (F(1, 342) = 5.102, p = .025, BCa 95% CI = [–0.006 to –0.001], Table 3).

BMI, age, sex, social network size, and social desirability explained 14.2% of the variance in CRP (F(5, 310) = 10.250, p < .001), but as in Study 1, adding support-giving to the model only explained an additional 0.1% of the variance (F(1, 309) = .435, p = .510, BCa 95% CI = [–0.007 to 0.003], Table S2 found in Supplemental Material). Thus, support-giving was not related to CRP.

Discussion

In conceptual replication and extension of findings from Study 1, more support-giving was related to lower levels of IL-6, even after adjusting for demographic factors known to relate to systemic inflammation, an indicator of the size of one's social network, and individual differences in socially desirable reporting. Study 2 addressed some of the limitations of Study 1, namely intensive and detailed screening for medication and the use of established, validated scales.

General Discussion

How support-giving behaviors relate to health and well-being remains an open question for research. The current studies take a preliminary step toward addressing this question by quantifying associations between support-giving and systemic inflammation in two different samples of midlife adults.

Table 3 Summary of Hierarchical Regression Analysis for Association Between Support-Giving and IL-6, Apart From Other Variables (Study 2, N = 350, 53.1% Female)

Variable	β	BCa 95% CI	p	R	R^2	ΔR^2
Step 1				.408	.167	.167
BMI	0.021	[0.016 to 0.026]	<.001			
Age	0.004	[0.000 to 0.008]	.037			
Sex	0.027	[–0.031 to 0.089]	.360			
Social network size	0.002	[–0.001 to 0.004]	.343			
Social desirability	–0.002	[–0.008 to 0.004]	.461			
Step 2				.423	.179	.012
BMI	0.021	[0.016 to 0.026]	<.001			
Age	0.005	[0.001 to 0.010]	.010			
Sex	0.025	[–0.032 to 0.084]	.391			
Social network size	0.003	[0.000 to 0.006]	.111			
Social desirability	–0.002	[–0.007 to 0.004]	.504			
Support-giving	–0.003	[–0.006 to –0.001]	.025			

BMI, body mass index; *BCa*, bias corrected and accelerated; CI, confidence interval.

Findings show that more support-giving is related to lower levels of the circulating inflammatory marker IL-6, but not CRP. Associations were found with two different support-giving measures, across a range of social targets (close others, acquaintances, strangers, organizations) and participant age ranges (25–76 years), apart from other well-known psychosocial predictors of health (e.g., social network size, received social support). Associations are consistent with the hypothesis that support-giving behavior can be good for health and illuminate avenues for future directions in this line of research.

Results of the current studies suggest that everyday types of supportive behavior, including giving emotional support to close others, volunteering or giving to charity, or helping a stranger with an immediate need, might be health-relevant. Giving to more social targets (Study 1) and giving with a greater frequency (Study 2) both related to lower IL-6, apart from potential predictors of support-giving (social desirability) and IL-6 (social network size [39]). Support-giving was not, however, related to CRP. This could be because, relative to IL-6, CRP is a more stable, chronic measure of inflammation that is potentially less sensitive to social experiences like support-giving [18]. Regardless, the association between support-giving and IL-6 point to the possibility that frequently giving to a variety of social targets (up to 10 were measured in Study 1) may be health-protective. Future intervention or experimental research could manipulate the frequency or number of targets one supports to evaluate the causal contribution of such factors on support-giving and health and may clarify when support-giving is health-protective.

Despite the trend that giving more support relates to better markers of health, a notable exception outside of these findings comes from the vast literature on caregiving, where one engages in dedicated and prolonged support-giving and care of an ailing close other (e.g., spouse, parent, child). Caregiving can be related to higher IL-6 [40], which departs from the patterns shown in the current studies. However, experiences of caregiving and experiences of support-giving, as conceptualized in the current manuscript, are not necessarily related. That is, there are many important psychological and structural differences between the experience of caregiving and the support-giving assessed in the current studies. For example, caregiving can involve prolonged periods of giving while witnessing a close loved one deteriorate while also becoming increasingly more socially isolated [41]. This is in contrast to support-giving, as assessed in the current studies, which might involve supporting an otherwise healthy individual with an immediate need, or giving to address a more abstract need or cause (e.g., a charity, political organization). It is likely that the pathways contributing to caregiver health and those of the "everyday" support-giving behavior assessed in the current studies diverge and need to be developed separately. Regardless, an important direction for future research is to better understand the threshold at which support-giving associations with inflammation reverse and/or identify which features make caregiving detrimental [42], or protective [43], for health. Such future research may clarify links between support-giving behavior and health, as assessed in the current studies, and caregiving and health.

A goal of the current studies was to clarify *how* support-giving might be related to better health—that is, the mechanisms by which support-giving and health are linked. Although this remains an open question for research, our theoretical model [5, 9] and previous findings suggest that neurobiological mechanisms that reinforce continued care as well as those that reduce stress might lead to the longer-term health benefits of support-giving. For example, brain imaging research in humans shows that giving to others is related to less activity in neural regions (e.g., the anterior insula, anterior cingulate cortex, and amygdala; [44]) that have previously been related to increased inflammation and related-SNS responding [45]. Consistent with this observation, random assignment to support-giving conditions (vs. conditions in which no support is given) reduces sympathetic-related physiological responding [15, 25, 46] and markers of systemic inflammation [17, 21, 22]. Thus, findings from the current studies provide additional support for neurobiological models of support-giving and health to also include inflammation as a promising pathway by which support-giving can relate to better health. Future research aiming to understand biological mechanisms linking support-giving and health would benefit from an experimental design with manipulations of support-giving behavior, guided by the operationalization of support-giving in Study 1 (e.g., adapting a paradigm by which participants give to more vs. less targets) or Study 2 (e.g., random assignment to frequent everyday support-giving behavior vs. control conditions without support-giving) before and after the measurement of IL-6. Such study designs could inform existing mechanistic models by which support-giving and health are linked and clarify mechanistic links [8, 9].

In addition to biological pathways, socioemotional pathways may link support-giving with health. Support-giving (vs. control conditions without giving) increases feelings of social connection [9], and separately, engaging in more support-giving relates to decreased loneliness over time [47]. Although these prior studies did not include measures of inflammation, experimentally induced inflammation is known to reduce feelings of social connection [45]. Likewise, cross-sectional findings show that lower feelings of social connection (i.e., loneliness) are related to higher levels of IL-6 [48]. Recent data also suggests that support-giving might decrease inflammation via increases in eudaimonic well-being, defined as a sense of purpose, meaning, and self-realization [49]. Whether the kinds of support-giving behavior measured in the current studies have similar effects on both eudaimonic well-being and social connection has yet to be tested, but could be promising pathways to probe in future research.

Limitations and Future Directions

Despite the consistency of associations across Studies 1 and 2, the current findings remain correlational. Future research that establishes causal direction is needed. In addition to the study designs noted above, random assignment to real-world support-giving behavior and assessment over longer periods of time would be a strong test of support-giving's potential causal effects on health and would help rule out other confounding factors (e.g., whether healthier people are giving more support). In the other direction, experimental inflammation is known to alter social behavior [45], and may, therefore, also influence support-giving behavior. Such changes may depend on the target in need of support [50].

Apart from BMI, sex, and age, Study 1 did not adjust for health status or health-related behavior that might influence the inflammatory measures. Although we addressed these limitations in Study 2, the inclusive approach of Study 1 should be noted. We also dichotomized the social support measures in Study 1 because the modal response for all supportive

behavior, regardless of target and regardless of whether one was reporting on support-giving or received support, was zero hours. However, such an approach may have masked other differences in those who reported very few hours per month as compared to those who reported hundreds of hours (up to 744). Additional research linking well-established, valid, reliable measures of support-giving with inflammation would help solidify claims that giving to multiple social targets relates to better health. The focus of the current research is on support-giving and systemic inflammation, but it is important to note that the additional variance explained by adding support-giving to models predicting IL-6 was relatively small for both Study 1 and 2. Finally, the demographics of Studies 1 and 2 are different than estimates from the 2019 U.S. Census (https://www.census.gov/quickfacts/fact/table/US/PST045219). Exploring support-giving in a nationally representative sample, but particularly in populations historically underrepresented in health research, is needed for generalizability.

In conclusion, results from two studies suggest support-giving is related to lower systemic inflammation and reaffirm perspectives proposing support-giving can be a beneficial, rather than solely detrimental, contributor to health.

Acknowledgments

We thank Anna Marsland for input on earlier drafts, and generosity with the AHAB-II inflammatory data. Study 1 (MIDUS) is funded by the John D. and Catherine T. MacArthur Foundation Research Network, National Institute on Aging (P01-AG020166), National Institute on Aging (U19-AG051426), and NIH National Center for Advancing Translational Sciences (NCATS) Clinical and Translational Science Award (CTSA) (1UL1RR025011). Study 2 (AHAB-II) was supported by National Institutes of Health grant P01 HL040962 to S.B.M. We gratefully acknowledge those involved in the data collection and processing efforts for MIDUS and AHAB-II.

Compliance With Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards: Authors Tristen K. Inagaki, Gabriella M. Alvarez, Edward Orehek, Rebecca A. Ferrer, Stephen B. Manuck, Nicole M. Abaya, and Keely A. Muscatell declare that they have no conflict of interest. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national).

Authors' Contributions: Tristen K. Inagaki served as a lead for conceptualization, formal analysis, and visualization, and writing—original draft, and writing—review and editing. Gabriella M. Alvarez served in a supporting role for formal analysis, writing—original draft, and writing—review and editing. Edward Orehek served in a supporting role for conceptualization, writing—original draft, and writing—review and editing. Rebecca A. Ferrer served in a supporting role for conceptualization, writing—review and editing. Stephen B. Manuck served as lead for resources, and a supporting role for conceptualization, writing—review and editing. Nicole M. Abaya contributed to writing—original draft, and writing—review and editing. Keely A. Muscatell served in a supporting role for conceptualization, formal analysis, writing—original draft, and writing—review and editing.

Study registration: To our knowledge, Study 1 (Midlife in the United States Series) was not registered. The full cohort for Study 2 (Adult Health and Behavior Project—II) was not registered.

Analytic plan preregistration: The analysis plan was not formally preregistered.

Analytic code availability: Analytic code used to conduct the analyses presented in this study are not available in a public archive. They may be available by emailing the corresponding author.

Materials availability: Study 1: Materials used to conduct the study are available in the same public archive as the data. Primary measures are also available in Supplementary Material associated with the present publication. Study 2: Materials used to conduct the study are not publicly available.

Data availability

Study 1: De-identified data from MIDUS are available in a public archive hosted by the University of Michigan's Institute for Social Research (ICPSR). Study 2: De-identified data from this study are not available in a public archive. De-identified data from this study will be made available for the purposes of replication by emailing the corresponding author.

Supplementary Material

Supplementary material is available at *Annals of Behavioral Medicine* online.

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