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Acute Patient Distress Is Associated With Poorer Caregiver Health Independent of Stroke Severity

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Abstract

Purpose. We examined how quality of life, distress and burden evolve jointly in stroke survivors and caregivers over the first year after stroke, and whether their associations depend on neurological severity.

Methods. Prospective single-center cohort of stroke patient-caregiver dyads assessed at baseline, 3 and 12 months, with control dyads without recent stroke assessed once, using the SF-36, Distress Thermometer and Zarit Burden Interview. Dyadic associations were examined with Spearman correlations (bootstrap confidence intervals), and caregiver trajectories with linear mixed models. Benjamini-Hochberg-adjusted p values (q) were computed within planned comparison groups.

Results. Twenty stroke and 17 control dyads were analyzed. After correction, patients and caregivers differed only in SF-36 Role Limitations-Physical at 12 months. In the stroke group, greater acute patient distress was associated with poorer caregiver general health (rho = -0.76, 95% CI -0.93 to -0.42, q = 0.034, n = 17); it persisted after adjustment for stroke severity (partial rho = -0.77) and was absent in controls (rho = +0.40; between-group q = 0.049). Caregiver distress declined nominally (-0.14 points/month, 95% CI -0.28 to -0.01) whereas burden did not (+0.17, 95% CI -0.14 to +0.47); 8 of 18 caregivers worsened and 8 improved in burden.

Conclusion. Greater acute patient distress was associated with poorer caregiver general health, not explained by stroke severity in this predominantly mild cohort. Caregiver burden was stable at group level despite marked individual variation. These findings suggest assessing caregiver health when patients report high acute distress and reassessing burden during follow-up.

Plain English summary

A stroke changes life for the person affected and for the supporting caregiver. We followed twenty stroke survivors and their main caregivers over the first year after stroke and compared them with 17 pairs without a recent stroke. Both members of each pair answered questionnaires on quality of life, distress and caregiver burden shortly after the stroke and again after 3 and 12 months. Shortly after the stroke (median 4 days, interquartile range 3–6 days), caregivers tended to report more distress than the patients themselves (median 7 versus 4 on a scale from 0 to 10). When patients were more distressed, their caregivers reported poorer general health, independent of stroke severity (median score 1 on a scale from 0 to 42, indicating mostly mild strokes). Caregivers' distress decreased within one year, while the average burden remained constant. Our findings suggest that the health and burden of caregivers should be assessed early after a stroke and again a few months later, so that caregivers who need support can be identified early.

Introduction

Cerebrovascular disease is among the leading causes of acquired disability; in Switzerland it affects approximately 21,000 people per year [1,2]. A stroke can abolish speech, orientation or walking within minutes and leave the survivor dependent on others. That dependence reaches beyond the patient: the informal caregiver's living conditions change with it [3].

The World Health Organization defines quality of life (QoL) as an individual's perception of their position in life in relation to their goals, expectations, standards and concerns [4]. Caregiver mental health and QoL after stroke are impaired across healthcare settings and can remain so for years [5–10]; low income, poor caregiver health, patient unemployment, cohabitation with the patient and long hospitalization have been reported as determinants [5].

Longitudinal studies have increasingly examined stroke survivors and their caregivers. QoL has been assessed in both members of the dyad over time [11–13], and changes in a survivor's

physical functioning have been associated with QoL in both survivors and caregivers [14], indicating interdependence between patient and caregiver outcomes.

Nevertheless, important questions remain. Measures of neurological deficit and functional impairment do not fully capture the impact of stroke on either member of the dyad: difficulty resuming everyday activities is reported even after transient ischemic attack with complete recovery on neurological testing [15], while some patients with residual deficits report preserved QoL. It remains unclear how patient and caregiver wellbeing evolve over the first year after stroke compared with unaffected dyads; previous studies have compared caregivers to non-caregivers [16], examined stroke and control dyads only in long-term follow-up [17] or assessed them at one specific time point (9 months after stroke) [18]. Further, it remains unclear whether and how the correlation between patient and caregiver wellbeing depends on neurological severity, the primary metric used to organize clinical follow-up after stroke.

We assessed QoL, psychological distress, and caregiver burden in stroke dyads over 12 months, alongside control dyads without recent stroke or disability, assessed once. We aimed at determining whether patient and caregiver wellbeing are coupled, and if this association is driven by stroke severity. We hypothesized that outcomes are correlated within dyads, and that wellbeing depends on patient- and caregiver-specific factors and not only on stroke severity.

Methods

Study design and setting

CODE-QoL (Cerebrovascular Disease: Quality of Life) is a prospective, single-center, observational cohort study conducted at the Stroke Center of the University Hospital Zurich, Switzerland, with enrollment from June 2023 to March 2026. The study is reported in accordance with the STROBE statement [19] (checklist in Supplementary Table S15). This report presents a

planned interim analysis of the ongoing study, based on a data lock from April 7, 2026. Additional measures and biomarker data collected in CODE-QoL will be reported separately.

Participants

Stroke survivor group. Inclusion criteria for stroke dyads required the patient to have a diagnosis of transient ischemic attack, ischemic stroke or intracerebral hemorrhage, with enrollment occurring within 28 days of the event. Each patient was enrolled together with one informal caregiver: the person nominated by the patient as their primary provider of unpaid support in daily life.

Control group. We recruited a control group with no previous stroke, or with a minor stroke occurring more than three years ago showing no functional disability (modified Rankin Scale [mRS] 0 or 1). Each participant was enrolled together with a close relative who completed the caregiver assessments. Control dyads were assessed once with the same instruments; without an index event, they were not followed over time.

In both groups, both members of the dyad had to be able to give informed consent and complete the self-report questionnaires; age, language, aphasia, neglect or cognitive impairment were no exclusion criteria. Individuals receiving steroid hormones within the preceding three months were excluded, because systemic glucocorticoids could confound hair-cortisol, one of the endpoints of CODE-QoL that is not reported here.

Assessments and instruments

Stroke dyads were assessed at baseline, at 3 and 12 months after stroke. Each visit recorded QoL (SF-36), neurological function and independence (National Institutes of Health Stroke Scale, NIHSS [20], mRS [21], Barthel Index [22], ECOG/Karnofsky performance status [23,24]), psychological distress (Distress Thermometer, DT) and caregiver burden (Zarit Burden Interview, ZBI).

We used the validated German version of the SF-36 [25,26] comprising eight subscales, each scored from 0 to 100, with higher scores indicating better health (listed in Table 3) [25]. Subscale scores were computed with the RAND-36 algorithm [27], which differs from the original SF-36 scoring only for Bodily Pain and General Health. Norm-based Physical and Mental Component Summary (PCS, MCS) scores were derived from the eight subscale scores with the standard US 1990 scoring coefficients [26]. Specifically, PCS comprises Physical Functioning (PF), Role Limitations-Physical (RP), Bodily Pain (BP) and General Health (GH); MCS includes Energy / Vitality (VT), Social Functioning (SF), Role Limitations-Emotional (RE) and Emotional Well-Being (Mental Health, MH) [28].

The DT [29] is a single-item scale from 0 (no distress) to 10 (extreme distress), originally developed and validated in oncology. While a score of 4 or higher conventionally indicates clinically relevant distress, this cut-off has not been formally validated in stroke and serves here solely as a descriptive reference.

Caregiver burden was measured with the 22-item ZBI (ZBI-22) [30]. Items are scored from 0 (never) to 4 (nearly always), yielding a total score between 0 and 88, with higher scores indicating greater burden. Burden was analyzed as a continuous outcome, because the conventional severity bands have not yet been validated in Switzerland.

Endpoints

The primary endpoint was QoL (SF-36) in stroke patients and their caregivers; secondary endpoints included psychological distress, neurological function and independence, and caregiver burden. The planned primary comparison evaluated patient versus caregiver SF-36 scores at each timepoint. All dyadic correlations, the exploratory models, and the component-summary analysis were secondary and hypothesis generating.

Statistical analysis

To ensure comparability across all timepoints without bias from changing cohort compositions, analyses were restricted to complete cases. Baseline dyadic correlations and the mixed models were repeated with all available data as sensitivity analyses (Supplementary Table S16).

Baseline characteristics of stroke patients, controls and their respective caregivers are summarized as frequencies and percentages for categorical variables and medians and interquartile ranges for continuous features.

Outcome measures are reported as medians with 2,000-replicate bootstrap percentile 95% confidence intervals at each timepoint and for each group. Inferential analysis was planned and grouped into six families: (A) Within-dyad comparison: patient versus caregiver at each timepoint using a Wilcoxon signed-rank test for paired samples (effect size: matched-pairs rank-biserial r), with bootstrap 95% CIs of the median paired difference (Supplementary Table S17); (B) Longitudinal pairwise changes: The within-subject change from baseline was assessed at timepoints 3 and 12 months using a Wilcoxon signed-rank test; (C) Longitudinal differences: Overall differences in outcomes across the three timepoints within each role (Friedman test); (D) Group comparisons: stroke versus control group at baseline (Mann-Whitney U test); (E) Dyadic baseline correlations: Spearman's rho with 20,000-replicate bootstrap percentile 95% confidence intervals; and (F) Longitudinal trend: Linear mixed models estimating monthly change in caregiver distress and burden, with time in months as a fixed effect and a subject-specific random intercept.

Multiple testing correction

Benjamini-Hochberg false discovery rate (FDR) correction [31] was applied within each analysis family, and both the uncorrected p-value and the FDR-adjusted q-value are reported for families A to E. Correction covered the nine outcomes per timepoint in family A, each role in families B to D (family D: nine patient and ten caregiver outcomes) and all 90 patient–caregiver outcome pairs

in family E; it was not applied across families or to the mixed models. Exploratory, hypothesis-generating analyses included univariable Spearman correlations (Benjamini-Hochberg correction within outcome; Supplementary Table S1); linear regression of caregiver outcomes on patient DT, mRS and caregiver sex (uncorrected; Supplementary Table S2); partial Spearman correlations adjusted for NIHSS, mRS or patient age (Supplementary Table S9); bootstrap comparison of each correlation between stroke and control dyads (Benjamini-Hochberg correction across the 90 pairs; Supplementary Tables S8 and S11); and Mann-Whitney U or Fisher's exact tests for attrition and kinship.

Hierarchical SF-36 component testing

Because the eight SF-36 subscales load onto two higher-order components [28], the PCS and MCS were used as omnibus measures in a hierarchical testing procedure for families A to D. Within each comparison, the PCS and MCS were tested at a Bonferroni-adjusted α of 0.025; to control the family-wise error rate, the four subscales of each component were tested only if that component was significant, applying a Holm adjustment at the same α (Supplementary Table S14). Because the US coefficients were derived for the original SF-36 scoring [26], these analyses were repeated with the BP and GH subscales rescored using the original algorithm as a sensitivity analysis.

Sample size sensitivity

No a priori power calculation was recorded in the study protocol for this interim analysis. We therefore estimated the minimum detectable effect sizes: with 80% power at a two-sided α of 0.05, the analyzed samples could detect correlations of |rho| 0.59 to 0.65, and a standardized within-dyad difference (paired Cohen’s d) of 0.68 with 19 pairs.

Analyses were performed in R version 4.6.1. The lme4 and lmerTest packages were used to fit the linear mixed models with restricted maximum likelihood (REML), with Wald 95% confidence

intervals and Satterthwaite-approximated p-values (Supplementary Table S6). To ensure reproducibility, bootstrap resampling procedures used fixed random seeds.

Ethics and registration

The study was approved by the Ethics Committee of the Canton of Zurich, Switzerland (KEK-2023-00224), and all participants gave written informed consent before any study procedure. It was registered at ClinicalTrials.gov (NCT06443268).

Results

Participant flow and sample

Of 180 individuals screened, 118 were enrolled, yielding 42 stroke dyads and 17 control dyads (Figure 1); two stroke-arm caregivers provided no baseline assessment. At the data lock, 22 stroke dyads were not included in the final outcome analyses: 14 had terminated early and 8 were still in follow-up.

[Insert Figure 1. here]

Comparison of dyads with and without complete follow-up

To assess attrition bias, we compared baseline characteristics and outcome measures of the 20 dyads with complete follow-up with those of the 14 dyads that terminated early (Supplementary Table S7). No characteristic differed after Benjamini-Hochberg correction; the largest difference was a lower caregiver PCS in dyads that terminated early (median 48.7 vs 54.7; $p = 0.018$, $q = 0.163$), and stroke severity was similar (median NIHSS 1 in both). Extending the comparison to all 22 dyads not included in the final outcome analyses gave the same result (smallest $p = 0.094$).

Baseline characteristics

Baseline characteristics are summarized in Tables 1 and 2; baseline assessment was performed within a median of 4 days (interquartile range 3–6) after the event. Patients in the stroke dyads were older than their caregivers (median 76 versus 64 years). Roughly three quarters of the caregivers were spouses or partners; the remaining caregivers were adult children. Strokes were predominantly ischemic and mild (median NIHSS 1, range 0 to 17), and 10 of the 19 patients with a recorded mRS score (52.6%) were functionally independent (mRS 0 or 1). Control patients and caregivers were of similar age and neurologically intact or minimally affected.

Table 1. Baseline demographic characteristics, by group and role.

Characteristic	**Stroke patients (n=20)**	**Stroke caregivers (n=20)**	**Control patients (n=17)**	**Control caregivers (n=17)**
n	20	20	17	17
Age, median [range]	76.0 [20, 87]	64.0 [20, 88]	73.0 [49, 89]	65.0 [42, 83]
Sex: Female	10 (50.0)	9 (45.0)	10 (58.8)	7 (41.2)
Education, n reported/N	18/20	18/20	12/17	12/17
Education: Compulsory school only	0 (0.0)	2 (11.1)	1 (8.3)	1 (8.3)
Education: Apprenticeship / vocational training	5 (27.8)	2 (11.1)	3 (25.0)	2 (16.7)
Education: Upper-secondary school (Matura)	1 (5.6)	1 (5.6)	1 (8.3)	1 (8.3)
Education: Higher vocational school	5 (27.8)	6 (33.3)	2 (16.7)	3 (25.0)
Education: University / university of applied sciences	7 (38.9)	7 (38.9)	5 (41.7)	5 (41.7)

Values are n (%) unless otherwise stated. Education percentages refer to participants with education recorded. Age was derived from the recorded age at baseline where available and otherwise from year of birth; age was available for all participants. The number of participants with education recorded is given as n/N.

Table 2. Baseline clinical characteristics of stroke and control patients.

Characteristic	Stroke patients (n=20)	Control patients (n=17)
n	20	17
NIHSS (at admission), median [range]	1.0 [0, 17] (n=20)	0.0 [0, 2] (n=14)
mRS, median [range]	1.0 [0, 4] (n=19)	0.0 [0, 1] (n=14)
mRS 0–1, n (%) of those rated	10 (52.6)	14 (100.0)
Type: Ischemic stroke	18 (90.0)	-
Type: Intracerebral hemorrhage	1 (5.0)	-
Type: Transient ischemic attack	1 (5.0)	-

NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale. Stroke subtype is not applicable to the control group. The single control patient with a non-zero NIHSS (score 2, mRS 1) had a minor stroke in 2019.

Quality of life, distress and burden in dyads over time

Patient and caregiver scores at baseline, 3 months and 12 months are given in Table 3, Figure 2 and Supplementary Figures S1–S9.

[Insert Figure 2. here]

Table 3. SF-36 subscale and component summary, DT and ZBI scores in the stroke longitudinal sample.

Outcome	Patient BL	Patient 3 m	Patient 12 m	Caregiver BL	Caregiver 3 m	Caregiver 12 m
Physical Functioning (PF) (0–100)	70.0 [55.0, 95.0] (n=19)	90.0 [65.0, 95.0] (n=19)	80.0 [70.0, 95.0] (n=19)	95.0 [95.0, 100.0] (n=19)	95.0 [95.0, 100.0] (n=19)	100.0 [90.0, 100.0] (n=18)
Role Limitations-Physical (RP) (0–100)	75.0 [25.0, 100.0] (n=19)	87.5 [37.5, 100.0] (n=18)	50.0 [25.0, 100.0] (n=19)	100.0 [75.0, 100.0] (n=19)	100.0 [100.0, 100.0] (n=19)	100.0 [100.0, 100.0] (n=18)
Role Limitations-Emotional (RE) (0–100)	100.0 [66.7, 100.0] (n=19)	100.0 [33.3, 100.0] (n=19)	66.7 [33.3, 100.0] (n=19)	100.0 [66.7, 100.0] (n=18)	100.0 [100.0, 100.0] (n=19)	100.0 [83.3, 100.0] (n=18)
Energy / Vitality (VT) (0–100)	65.0 [45.0, 90.0] (n=19)	65.0 [55.0, 75.0] (n=19)	60.0 [55.0, 75.0] (n=19)	70.0 [50.0, 75.0] (n=19)	65.0 [53.3, 73.3] (n=19)	62.5 [55.0, 80.0] (n=16)
Emotional Well-Being (MH) (0–100)	72.0 [64.0, 92.0] (n=19)	80.0 [68.0, 84.0] (n=18)	76.0 [60.0, 84.0] (n=19)	76.0 [68.0, 84.0] (n=19)	80.0 [72.0, 86.0] (n=18)	76.0 [72.0, 86.0] (n=16)

Social Functioning (SF) (0–100)	75.0 [50.0, 100.0] (n=19)	87.5 [75.0, 100.0] (n=19)	87.5 [62.5, 100.0] (n=19)	87.5 [75.0, 100.0] (n=19)	100.0 [100.0, 100.0] (n=19)	100.0 [87.5, 100.0] (n=18)
Bodily Pain (BP) (0–100)	90.0 [77.5, 100.0] (n=19)	100.0 [67.5, 100.0] (n=19)	100.0 [87.5, 100.0] (n=19)	90.0 [77.5, 100.0] (n=19)	100.0 [77.5, 100.0] (n=19)	77.5 [57.5, 100.0] (n=18)
General Health (GH) (0–100)	55.0 [45.0, 70.0] (n=19)	60.0 [45.0, 70.0] (n=19)	55.0 [50.0, 65.0] (n=19)	65.0 [55.0, 75.0] (n=19)	80.0 [55.0, 85.0] (n=19)	67.5 [52.5, 77.5] (n=18)
Physical Component Summary (PCS) (T-score, mean 50)	45.4 [41.3, 51.4] (n=19)	50.1 [43.4, 53.6] (n=17)	49.3 [42.4, 52.3] (n=19)	54.6 [51.4, 56.7] (n=18)	55.7 [52.4, 57.3] (n=18)	52.8 [48.6, 56.4] (n=16)
Mental Component Summary (MCS) (T-score, mean 50)	48.3 [43.2, 60.0] (n=19)	52.8 [42.2, 57.4] (n=17)	50.8 [42.2, 55.5] (n=19)	50.3 [42.7, 53.8] (n=18)	53.1 [49.4, 57.2] (n=18)	53.0 [48.8, 56.4] (n=16)
Distress Thermometer (DT) (0–10)	4.0 [3.0, 6.0] (n=17)	3.0 [2.0, 4.0] (n=13)	4.0 [2.0, 5.0] (n=15)	7.0 [4.0, 8.0] (n=15)	3.5 [0.5, 5.0] (n=12)	3.0 [2.5, 5.0] (n=16)
Zarit Burden Interview (ZBI) (0–88)	-	-	-	8.5 [4.5, 13.0] (n=18)	3.0 [2.0, 8.0] (n=19)	6.0 [3.0, 13.0] (n=19)

Values are median [2,000-replicate bootstrap percentile 95% confidence interval] with the analyzable n in parentheses. BL, baseline. The possible score range of each scale is given in parentheses. The analyzable n is below 19 for the DT and the ZBI because of item-level missingness. PCS and MCS scores are norm-based T-scores (US 1990 general population mean 50, standard deviation 10) and are undefined when any subscale is missing.

To evaluate whether stroke affected both members of a dyad similarly, we compared patients with their caregivers at each timepoint. At baseline, caregivers reported more distress than the patients themselves (median DT 7 vs 4; p = 0.023, q = 0.117, r = 0.69), whereas patients scored lower on PF (median 70 vs 95; p = 0.026, q = 0.117, r = 0.61). Neither difference remained significant after correction across the nine outcomes (Table 4). Across all three timepoints, a single patient versus caregiver comparison remained significant after correction: RP at 12 months (median 50 vs 100; p = 0.003, q = 0.027, r = 0.92; Supplementary Table S4).

Next, we compared the component summaries hierarchically (Supplementary Table S14). Patients scored numerically lower than their caregivers on the PCS at baseline (median 45.5 vs 54.6; p = 0.031), at 3 months (48.4 vs 55.7; p = 0.026) and at 12 months (46.3 vs 52.8; p = 0.049), but no comparison reached the Bonferroni-adjusted α of 0.025, so no subscale was tested. The MCS did not differ between roles at any timepoint (p ≥ 0.088), and neither component changed within either role (p ≥ 0.084).

Table 4. Patient versus caregiver at the baseline (acute) assessment.

Outcome	n pairs	Median patient	Median caregiver	r	p	q
Physical Functioning (PF) (0–100)	19	70.0	95.0	0.61	0.026	0.117
Role Limitations-Physical (RP) (0–100)	19	75.0	100.0	0.35	0.220	0.496
Role Limitations-Emotional (RE) (0–100)	18	100.0	100.0	0.04	0.905	0.972
Energy / Vitality (VT) (0–100)	19	65.0	70.0	0.07	0.793	0.972
Emotional Well-Being (MH) (0–100)	19	72.0	76.0	0.22	0.419	0.658
Social Functioning (SF) (0–100)	19	75.0	87.5	0.24	0.439	0.658
Bodily Pain (BP) (0–100)	19	90.0	90.0	0.01	0.972	0.972
General Health (GH) (0–100)	19	55.0	65.0	0.54	0.058	0.175
Distress Thermometer (DT) (0–10)	15	4.0	7.0	0.69	0.023	0.117

Wilcoxon signed-rank test for paired samples with matched-pairs rank-biserial r; n is the number of dyads with both values available; Benjamini-Hochberg FDR applied across the nine outcomes within the baseline timepoint. Higher SF-36 scores indicate better health; higher DT and ZBI scores indicate more distress and greater burden. No comparison remained significant after correction at baseline. The ZBI is caregiver-only and is therefore not compared between roles.

Next, we examined change within each role. Patients showed no significant change on any SF-36 domain or on distress between baseline and 12 months (all uncorrected p > 0.2; Supplementary Table S12).

Caregiver distress declined nominally, mostly within the first three months (median change -4 points; p = 0.012, q = 0.117), and remained lower at 12 months (p = 0.019, q = 0.186; Supplementary Table S12). Distress also differed across the three timepoints (Friedman p =

0.042; Supplementary Table S5) and declined in the mixed model (-0.14 points per month, 95% CI -0.28 to -0.01, p = 0.046; Supplementary Table S6), but neither the Friedman nor the pairwise result remained significant after correction.

Caregiver burden, by contrast, did not change on average (Friedman p = 0.632; mixed-model slope +0.17 points per month, 95% CI -0.14 to +0.47, p = 0.286). Among the 18 caregivers assessed at all three timepoints, 8 worsened at 12 months, 8 improved and 2 remained unchanged (median change 0.0 points, interquartile range -2.5 to +2.8; Figure 3); the mean absolute change was 5.8 points and the largest 25 points. Rank order was preserved across the year (Spearman rho = 0.61, p = 0.008), and improvement and deterioration occurred in spouses or partners and adult children alike (p = 0.429). With all available observations (35 caregivers), the mixed-model slopes were similar for distress (-0.16 points per month, 95% CI -0.29 to -0.04) and burden (+0.02, 95% CI -0.30 to +0.34; Supplementary Table S16).

[Insert Figure 3. here]

Comparison of quality of life, distress and burden between stroke and control dyads at baseline

To test for differences from unaffected dyads, both roles were compared at baseline. No SF-36 domain differed between stroke and control dyads in either role (Supplementary Table S13). Median PF and RP were numerically lower in stroke patients (70 versus 85 and 75 versus 100), and median caregiver burden was more than twice as high in the stroke arm (ZBI 8 versus 3; all p ≥ 0.075). Neither component summary differed between stroke and control dyads in either role (smallest p = 0.105; Supplementary Table S14).

Dyadic baseline correlations

To test whether patient and caregiver wellbeing are coupled, each baseline patient outcome was correlated with each baseline caregiver outcome (90 pairs; Supplementary Table S3); the eight

strongest by uncorrected p are given in Table 5 and the leading association in Figure 4. One correlation remained significant after correction: greater patient acute distress was associated with poorer caregiver GH (Spearman rho = -0.76, bootstrap 95% CI -0.93 to -0.42, $p < 0.001$, $q = 0.034$, n = 17 dyads). It extended to the caregiver PCS, to which GH contributes (rho = -0.57, 95% CI -0.84 to -0.10, p = 0.020, n = 16), and was weaker for the MCS (rho = -0.39, 95% CI -0.81 to +0.18, p = 0.139). In all 33 stroke dyads with baseline data, the association with caregiver GH was weaker (rho = -0.31, 95% CI -0.61 to +0.05, p = 0.083), and it was -0.49 (95% CI -0.79 to -0.07, n = 23) after excluding dyads that terminated early (Supplementary Table S16).

[Insert Figure 4. here]

The association linked the patient's distress with the caregiver's health and was specific to caregiver GH. Patient distress was not associated with caregiver distress (rho = +0.09, p = 0.747, n = 15), caregiver distress was not associated with the caregiver's own GH (rho = -0.12, p = 0.660, n = 16), and patient GH was not associated with caregiver GH (rho = +0.21, p = 0.387, n = 19); the reverse pairing, caregiver distress with patient GH, was weaker, with a confidence interval including zero (rho = -0.44, 95% CI -0.80 to +0.10, p = 0.103, n = 15).

The association was little changed by adjustment for stroke severity or age (partial rho -0.74 to -0.77). Neurological severity was not associated with QoL or distress in either role, and in the adjusted models, patient distress remained the only correlate of caregiver GH and PCS (PCS beta -1.32, 95% CI -2.51 to -0.13, p = 0.033), but not of the MCS (p = 0.377; Supplementary Tables S1, S2 and S9). No corresponding negative association was observed in control dyads (rho = +0.40, 95% CI -0.24 to +0.90, p = 0.199, n = 12); the between-arm difference (-1.16, bootstrap 95% CI -1.71 to -0.45, $p < 0.001$) was the largest of the 90 pairs and the only one significant after correction ($q = 0.049$; Supplementary Tables S8 and S11; Supplementary Figure S10). The association was not detectable at 3 months (rho = -0.16, n = 13) or 12 months (rho =

+0.02, n = 15), and the other seven strongest baseline pairs attenuated in parallel (Supplementary Table S10; Supplementary Figure S11).

Table 5. Dyadic baseline correlations in the stroke dyad sample (n = 20 dyads): the eight strongest associations by uncorrected p.

Patient outcome	Caregiver outcome	n	rho	95% CI	p	q
Distress Thermometer (DT) (0–10)	General Health (GH) (0–100)	17	-0.76	[-0.93, -0.42]	<0.001	0.034
Distress Thermometer (DT) (0–10)	Role Limitations-Physical (RP) (0–100)	17	-0.62	[-0.83, -0.27]	0.007	0.332
Distress Thermometer (DT) (0–10)	Social Functioning (SF) (0–100)	17	-0.60	[-0.84, -0.19]	0.011	0.332
Physical Functioning (PF) (0–100)	Bodily Pain (BP) (0–100)	19	-0.51	[-0.80, -0.08]	0.026	0.585
Distress Thermometer (DT) (0–10)	Zarit Burden Interview (ZBI) (0–88)	17	0.50	[0.05, 0.79]	0.042	0.627
Role Limitations-Physical (RP) (0–100)	Role Limitations-Physical (RP) (0–100)	19	-0.44	[-0.78, 0.01]	0.058	0.627
Social Functioning (SF) (0–100)	Distress Thermometer (DT) (0–10)	15	-0.49	[-0.81, -0.00]	0.063	0.627
Role Limitations-Physical (RP) (0–100)	Zarit Burden Interview (ZBI) (0–88)	18	-0.44	[-0.77, 0.05]	0.067	0.627

Spearman rho with 20,000-replicate bootstrap percentile 95% confidence intervals; n is the number of dyads with both values available. Benjamini-Hochberg FDR applied across all 90 patient-outcome by caregiver-outcome pairs tested; the full matrix is Supplementary Table S3. Only the first row remained significant after correction.

Discussion

The principal finding of this prospective dyadic study was that greater patient distress in the acute phase was associated with poorer caregiver GH. The association extended to the PCS and was not explained by the severity of the neurological deficit.

The association ran between partners: neither the caregiver's own distress nor the patient's own GH was associated with caregiver GH.

These findings are compatible with a dyadic model of stroke recovery in which the patient's psychological state and the caregiver's perceived GH are linked in the acute phase. Previous dyadic studies have reported cross-partner associations between psychological distress and QoL after stroke, with varying direction and outcomes [32,33]. Our finding extends this to the acute phase. That the association was not explained by neurological severity is consistent with the limited predictive value of initial stroke severity for caregiver health-related QoL [34], although the narrow severity range of our cohort limits this inference. Caregivers' perceived GH should therefore warrant assessment when patients report high acute distress, irrespective of apparent neurological severity. Early identification would allow support before poor caregiver health and distress become sustained [6–8]. The direction of the association remains open, because it was observed only at baseline, when both were measured simultaneously: distressed patients may burden their caregivers, caregivers in poor health may be less able to buffer patient distress, or a shared context may drive both.

Caregiver distress and burden followed different trajectories: distress declined nominally over the first year, mostly within the first three months, whereas burden remained unchanged. This dissociation is compatible with early psychological adjustment in the caregiver alongside care demands that do not diminish, as reported in caregiver cohorts followed for 12 months and beyond [7,8,35].

In individual caregivers, burden improved as often as it worsened, leaving the group median unchanged (Figure 3); earlier longitudinal work likewise found that burden changes in some caregivers and remains stable in many [36].

These findings and earlier longitudinal caregiver studies [6–8,36] suggest that burden follows individual courses and may warrant sustained monitoring. Caregiver psychological distress, by contrast, appears most pronounced early after stroke and may call for support in the acute phase [37]. Beyond the acute phase, international studies have reported anxiety, physical symptoms,

reduced social life, moderate to severe burden and socioeconomic and health-related determinants of QoL among stroke caregivers [5,9,38]. Which baseline characteristics predict individual burden trajectories, particularly deterioration, remains to be determined.

Patients' physical component scores were numerically lower than their caregivers', but no component summary differed after correction. The single domain-level difference that remained significant, RP at 12 months, is the anticipated consequence of stroke; no longitudinal recovery signal was detectable in patients. Caregivers reported nominally higher early distress than patients, in line with earlier reports of caregiver distress soon after stroke [6,10,37]; at about 9 months, survivors reported more depressive symptoms than caregivers, although both exceeded matched controls [18]. In patients, the component summaries warrant cautious interpretation. Their scaling assumptions were not satisfied in one stroke sample [39]. In a Swedish sample assessed 2–3 weeks after discharge, all subscales were reliable, but BP correlated more closely with the mental component, although the standard scoring counts it towards the PCS [40].

Strengths and limitations

The main strengths of our study are the prospective dyadic design, with paired patient and caregiver assessment from the acute phase to 12 months, and the concurrently recruited control group of dyads. Longitudinal caregiver studies have often begun months after the stroke [6], when early distress may already have subsided.

However, the sample is small and the strokes were predominantly mild, which limits both power and generalizability to moderate and severe stroke; the narrow severity range limits the test of whether severity explains the dyadic coupling. With twenty dyads and ceiling effects in caregiver scores, only large differences were detectable, so the absence of a difference is not evidence of equivalence. The analyses are best read as effect-size estimates for a larger study.

The complete-case design is vulnerable to attrition bias, as fewer than half of the enrolled stroke dyads were included in the analyses. Dyads that terminated early did not differ at baseline after correction (Supplementary Table S7), but their caregivers had a lower PCS at the uncorrected level, which would bias the analyzed sample towards healthier caregivers; this comparison could detect only large differences and cannot exclude bias on unmeasured characteristics. In all stroke dyads with baseline data, the dyadic association was weaker (rho = -0.31; Supplementary Table S16). Item-level missingness further reduced the sample for the outcomes that carry the main finding, which rests on 17 of the 20 dyads. Education and relationship status were incomplete, particularly in the control group (education unrecorded for 5 of 17 in each role).

Correction for multiplicity was applied only within test families, so the overall false-positive rate may exceed the within-family rate. The exploratory models are hypothesis-generating. The component summaries rest on US scoring coefficients that may not be optimal for a Swiss sample. In comparisons involving patients, subscales were tested only when their component summary was significant, although these summaries are of uncertain validity after stroke [39,40]; differences in patient subscales may therefore have been missed, whereas caregiver analyses were unaffected. Because some control participants had chronic illness, ZBI scores in control relatives may reflect burden from that illness, not from stroke-related physical disability.

The DT has not been validated in stroke. This is a single-center Swiss cohort, so both the absolute levels of caregiver burden and the healthcare context may differ elsewhere.

The control dyads were assessed once by design, so the stroke specificity of the association is established at baseline only; stability of control scores over the year was assumed from the measurement properties of the instruments rather than observed. The association was the strongest of 90 pairs, so its size is probably overestimated. Its absence at 3 and 12 months is compatible with regression to the mean. The findings are preliminary and need confirmation in a larger cohort.

Conclusion

Even after a predominantly mild stroke, caregivers reported high distress in the acute phase. Greater acute patient distress was associated with poorer caregiver general health, which was not explained by neurological severity and remained significant after correction for multiple comparisons. Caregiver distress declined nominally over the first year, whereas burden was unchanged at group level while moving in both directions within individual caregivers.

Family caregivers provide most of the care for stroke survivors at home, and caregiver stress is a leading cause of survivor institutionalization [41]; which dyads need support, and when, remains insufficiently characterized. Our findings suggest that patient distress and caregiver general health merit systematic assessment from the acute phase and over at least the following year, to identify dyads that need support before distress or ill health becomes established. Confirmation in larger cohorts should precede routine implementation.

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Statements and Declarations

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Ethics approval

The study was approved by the Ethics Committee of the Canton of Zurich, Switzerland (KEK-2023-00224) and was conducted in accordance with the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Author contributions

All listed authors meet the four ICMJE criteria for this manuscript. Contributions are given using the CRediT taxonomy.

Anton Schmick: conceptualization, methodology, investigation, funding acquisition, project administration, data curation, formal analysis, validation, visualization, writing - original draft, writing - review and editing.

Pascal Sommerhalder: investigation, software, writing - review and editing

Lisa Herzog: formal analysis, validation, data curation, writing - review and editing

Simone K. Huber: investigation, project administration, writing - review and editing

Jonathan Amstutz: investigation, writing - review and editing

Stefanie Reichlin: investigation, writing - review and editing

Lukas Otto: investigation, writing - review and editing

Roland von Känel: conceptualization, writing - review and editing

Susanne Wegener: conceptualization, resources, methodology, supervision, writing - review and editing.

Competing interests

Roland von Känel received consulting fees from Heel GmbH, Germany, book royalties from Kohlhammer and Springer, Germany, and research funding from the Swiss National Science Foundation. The other authors declare that they have no competing interests.

Data availability

CODE-QoL is an ongoing study and the data reported here are those available at the data lock of 7 April 2026. Individual participant data are not available. The consent obtained from participants and the approval granted by the Ethics Committee of the Canton of Zurich do not provide for the transfer of individual participant data outside the study team, and no public or on-request deposition of individual data is planned. Aggregate results beyond those reported here may be requested from the corresponding author; any release would require a separate application to the Ethics Committee. The analysis code used to produce the reported results may be made available from the corresponding author on reasonable request.

Figure legends

Figure 1. Participant flow chart. Screening, enrollment, early termination, and derivation of the analysis samples. Participant numbers are reported as *n*, with the corresponding number of dyads shown in parentheses. The 118 enrolled participants formed 59 patient–caregiver dyads: 42 in the stroke arm and 17 in the control arm. Two stroke-arm caregivers consented but provided no baseline assessment. Consequently, the assessed stroke-arm sample comprised 82 rather than

84 participants and 40 rather than 42 caregivers. The dyad sample included 20 stroke dyads in which the patient completed all three assessments; the longitudinal sample was nested within this group and included the 19 dyads in which both members completed all three assessments. Of the 22 stroke dyads not included in the final outcome analyses, 14 terminated before the 12-month assessment, including one following patient death, and eight remained within the follow-up period. At the participant level, 29 stroke-arm participants from 15 dyads recorded an early-termination event; the additional dyad reflects one caregiver who withdrew while the corresponding patient completed the full protocol.

Figure 2. Overview of SF-36 subscales, Distress Thermometer and Zarit Burden Interview by role and timepoint. Box plots (median, interquartile range, 1.5 x IQR whiskers) with individual data points; blue, patient; orange, caregiver. Stroke longitudinal sample (n = 19) at baseline, 3 and 12 months, with the cross-sectional control group to the right of the dotted line. Higher SF-36 scores indicate better health; higher Distress Thermometer and Zarit scores indicate more distress and greater burden. The bracket marks the single comparison that remained significant after FDR correction, the patient deficit in Role Limitations-Physical at 12 months.

Figure 3. Caregiver burden (Zarit Burden Interview) from baseline to 12 months. (A) Zarit Burden Interview trajectories for the 18 caregivers assessed at baseline, 3 and 12 months (thin lines, one per caregiver) with the group median superimposed (thick line). (B) Change in Zarit score from baseline to 12 months, one mark per caregiver, sorted by change. Eight caregivers worsened, eight improved and two were unchanged, giving a median change of 0.0 points despite a mean absolute change of 5.8 points; baseline and 12-month scores remained correlated (Spearman rho = 0.61, p = 0.008). Burden was stable at group level but changed in both directions in individual caregivers. Higher scores indicate greater burden.

Figure 4. Dyadic association between patient acute distress and caregiver general health. Baseline patient Distress Thermometer score against caregiver SF-36 General Health, one

marker per dyad (n = 17). Larger markers denote coincident dyads with identical values, each representing two dyads. Line, least-squares fit; shaded band, 4,000-replicate bootstrap percentile 95% confidence band. Spearman rho = -0.76, 95% CI -0.93 to -0.42, $p < 0.001$, $q = 0.034$. Higher patient distress was associated with poorer caregiver general health. The dotted vertical line is drawn at 3.5, so that scores at or above the conventional Distress Thermometer cut-off of 4 fall to its right.

Figures

Figure 1. Participant flow chart.

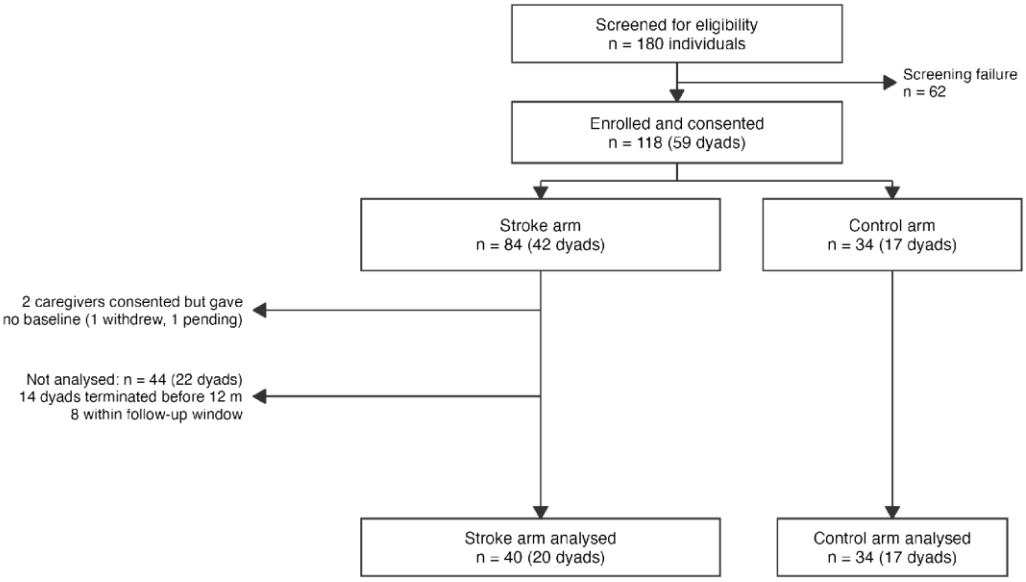
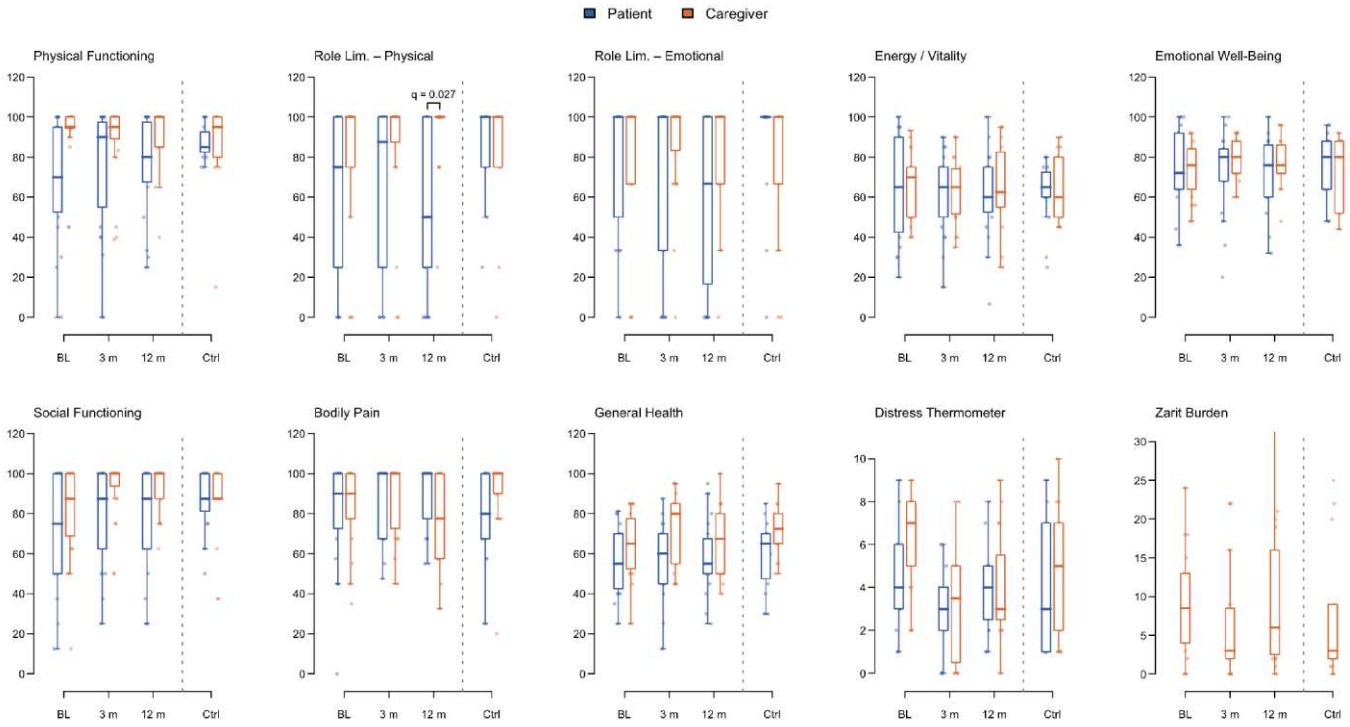
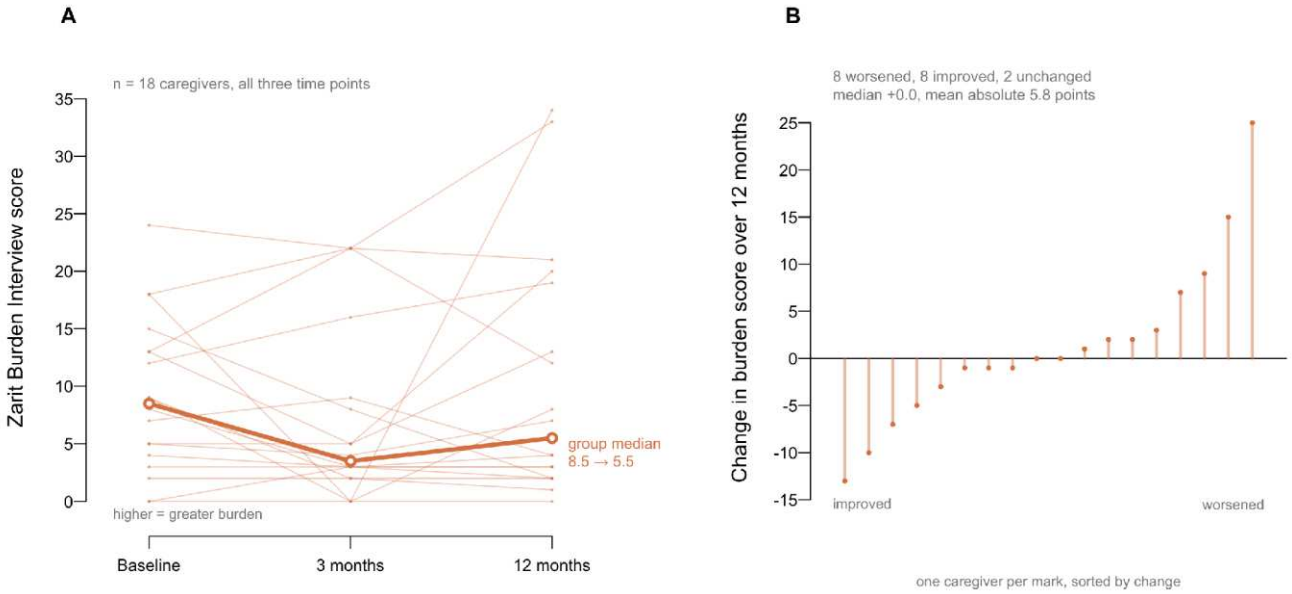


Figure 2. Overview of SF-36 subscales, Distress Thermometer and Zarit Burden Interview by role and timepoint.



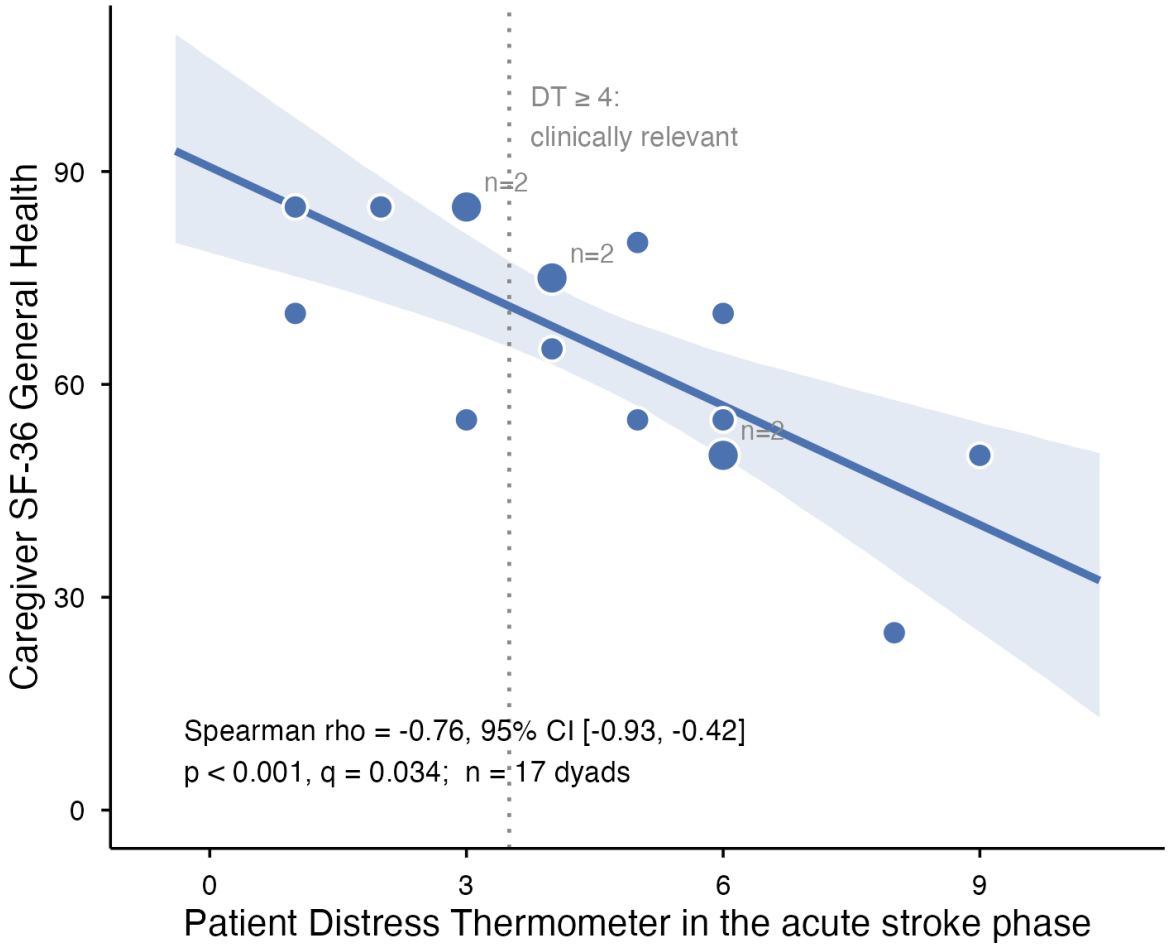
SF-36 score / DT score / ZBI score by panel; higher SF-36 = better, higher DT/ZBI = worse
q = Benjamini–Hochberg FDR across the nine domains at that time point; only the 12-month Role Limitations–Physical comparison survived.

633 **Figure 3. Caregiver burden (Zarit Burden Interview) from baseline to 12 months.**



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Figure 4. Dyadic association between patient acute distress and caregiver general health at baseline.



Supplementary Files

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