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Depression as a Mediator between Disability and Health-Related Quality of Life in Stroke Survivors: A Causal Mediation Analysis

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Abstract

Background

Stroke disproportionately affects survivors in low-and middle-income countries, yet the pathway from disability to poor health-related quality of life (HRQOL) remains unquantified in Africa. Therefore, this study aimed to assess the extent to which depression mediates the relationship between disability and HRQOL among stroke survivors in Addis Ababa, Ethiopia.

Methods

A cross-sectional study was conducted among 364 stroke survivors at Zewditu Memorial Hospital and Yekatit 12 Medical College Hospital in Addis Ababa, Ethiopia. Disability was assessed using modified Rankin Scale. Depression was assessed using Patient Health Questionnaire-9 (PHQ-9), and HRQOL was assessed using the Stroke-Specific Quality of Life (SSQOL-49), dichotomized into poor and good HRQOL. Causal mediation analysis was used to assess the extent to which depression mediates the relationship of disability on HRQOL. Sensitivity analysis was conducted to assess the effect of unmeasured confounding.

Results

The prevalence of poor HRQOL was 60.7%, and 67% of survivors had minor to severe disability. All stroke survivors had minimal to severe depression. Depression, female sex, hypertension, cardiac disease and physical inactivity were factors associated with poor HRQOL. The proportion mediated was 39.1%. The total effect of disability on poor HRQOL was 0.223 (95% CI: 0.017–0.429, p = 0.004), the direct effect (average direct effect) of disability on poor HRQOL was 0.087 (95% CI: 0.019–0.214, p = 0.004) and the indirect effect average causal mediation effect was 0.136 (95% CI: 0.017–0.213, p = 0.004). The sensitivity analysis showed that unmeasured confounder needs a very strong correlation (ρ = 0.86) to nullify the indirect effect. The differences between subgroups were not statistically significant.

Conclusion

Depression mediated approximately two-fifths of the effect of disability on poor HRQOL of stroke survivors in Addis Ababa, Ethiopia. Sensitivity analysis indicated high robustness to unmeasured confounding (ρ = 0.86).

1. Introduction

Stroke is the second leading cause of death and the third leading cause of disability adjusted life years (DALYs) globally, accounting for 6.6 million death and 143 million DALYs annually [1]. The consequences

of stroke extend beyond physical impairment to a significant impact on psychological and social well-being that compromises health-related quality of life (HRQOL) [2]. The burden of stroke is disproportionately high in low and middle income countries (LMICs), with over 5.5 million stroke related death and over 127 million DALYs per year [3]. In Ethiopia stroke is a major growing public health concern causing 7% of total deaths[4].

Post stroke disabilities include hemiparesis, memory loss, shortened attention span, aphasia (speech, writing, and understanding difficulties), and severe fatigue. And disability after stroke is a significant predictor of poor HRQOL, and concomitantly declines in daily physical activity are commonly reported [5]. However, the way that disability significantly affects HRQOL is not fully understood. Post stroke depression is one of the most common experiences among stroke survivors which occurs approximately 1 in 3 survivors, may represent a critical pathway linking disability to poor HRQOL [6,7]. Post stroke disability affects biological (chronic pain, neuro-inflammation, and functional limitation), psychological (identity grief, cognitive appraisal, and learned helplessness), and social (social isolation, stigma and discrimination, financial strain, and loss of independence) which lowers HRQOL of stroke survivors [8].

Traditional regression analysis and causal steps method proposed by Baron and Kenny in 1986 was used to establish associations among disability, depression, and HRQOL[9]. However, these methods cannot quantify the extent to which depression mediates the relationship between disability and HRQOL. To address this gap, we employed causal mediation analysis. Causal mediation analysis is an approach based on the counterfactual framework that simulates potential outcomes, providing direct estimates and formal tests of the indirect effect through the Average Causal Mediation Effect (ACME) and the proportion mediated, thereby offering a more rigorous and causally interpretable quantification of mechanistic pathways[10], addressing the gap of traditional models.

Despite the high burden of stroke in LMIC, Africa suffers the vast majority burden of stroke mostly affecting the younger community directly impacting on the health system with an instantaneous impact leads to disabilities and functional limitations that compromises HRQOL of stroke survivors [11], yet there was no study have been conducted. The pathway linking disability and poor HRQOL remained unexamined. Specifically in east Africa, no previous study has been conducted using causal mediation framework to assess the relationship between disability-depression-HRQOL among stroke survivors. Understanding these pathways is essential for developing targeted interventions to improve outcomes or HRQOL of stroke survivors in this population. Therefore, the aim of this study was to apply causal mediation analysis to quantify the extent to which depression mediates the relationship between disability and HRQOL of stroke survivors in Addis Ababa, Ethiopia.

2. Method and materials

2.1 Study design and setting

A health facility-based, a cross-sectional study was conducted among stroke survivors at Zewditu Memorial Hospital (ZMH) and Yekatit 12 Medical College Hospital (Y12MCH) in Addis Ababa, Ethiopia. These two hospitals were randomly selected from six government hospitals in Addis Ababa providing specialized stroke care to ensure feasibility and representativeness within the study timeline.

2.2 Study population

2.2.1 inclusion and exclusion criteria

Stroke survivors aged 18 and above with documented follow-up data for at least three months at these two hospitals were included. Stroke survivors with pre-stroke traumatic brain injury, pre-disability, spinal cord injury and missing data were excluded from the study.

2.3 Sample size and sampling procedure

2.3.1 Sample size

The data for this analysis were drawn from a parent cohort study designed to predict stroke recurrence, with a target enrollment of 375 participants based on the events-per-variable principle. The final analytical sample after excluding 32 cases with missing data comprised 364 participants. A post-hoc Monte Carlo power analysis (10,000 simulations) confirmed that N = 364 provides 82% power to detect the indirect effect through depression at $\alpha = 0.05$, based on standardized path coefficients from prior post-stroke literature. The sample is therefore adequate for the primary mediation analysis, though precision around the indirect effect may be limited.

2.3.2 Sampling procedure

A systematic sampling approach was used to select participants from the daily roster of stroke survivors presenting for follow-up care. The first participant each day was randomly selected, and subsequent participants were selected at a fixed interval ($k = 2$). Enrollment continued until the target sample size was reached. The final analytical sample comprised 364 participants with complete data on all key variables. (Fig. 1 should be placed after sampling procedure paragraph)

2.4 variables and measurements

2.4.1 Outcome variable – Health-related quality of life

HRQOL of stroke survivors for this study was assessed using stroke-specific quality of life (SSQOL). A validated patient-centered 49 items tool to asses HRQOL of stroke survivors across 12 domains: mobility, energy, upper extremity function, work/ productivity, mood, self-care, social roles, family roles, vision, language, thinking, personality [12]. The Amharic version of SSQOL-AM is also a valid and reliable outcome measurement for Amharic-speaking post-stroke patients. With an excellent test-retest reliability

(ICC = 0.98) and internal consistency (Cronbach's alpha = 0.96). The cut-off point to distinguish between good HRQOL and poor HRQOL was below 123 score [13].

2.4.2 Exposure variable - disability

Disability was assessed using modified Rankin scale (mRS), a valid and reliable global outcome rating scale to assess the functional independence. A single item with 5 grading scores 0-no disability, 1-no significant disability despite the symptoms, 2-slightly disability, 3-moderately disability, 4-moderately severe disability, and 5-sever disability bedridden [14].

2.4.3 Mediator variable – depression

Depression was assessed using Patient Health Questionnaire (PHQ-9), a validated tool to asses a major depressive disorder with a total score ranging 0–27. Having minimal depression status ranging (0–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), and severe depression (20–27).

2.4.4 Covariates

Covariates in this study were age, sex, marital status, educational level, stroke type, stroke severity, duration of stroke, hypertension, diabetes, cardiac disease, body mass index, and physical activity.

2.5 Data processing

Open data kit (ODK) was used for data collection. The collected data coded and checked for its clarity, consistency and completeness up to the end of each data collection period. The data analysis was conducted using R version 4.5.3.

2.6 Statistical analysis

2.6.1 Descriptive analysis

To present the descriptive statistics mean and SD was used for continuous variables. Frequency and percentage was used to summarize categorical variables. The outcome of each survivor dichotomized into poor HRQOL and good HRQOL.

2.6.2 Ordinal logistic regression

Ordinal logistic regression was used to assess the association between covariates and disability. The assumption of proportional odds was assessed graphically, and explanatory variables with p-value < 0.2 in the bivariate analysis was used as a candidate variable in the multivariable analysis. Results are presented in adjusted odds ratio (AOR) with 95% confidence interval (CI).

2.6.3 Causal mediation analysis

Causal mediation analysis [10]was used to understand how disability affects HRQOL of stroke survivors in this study into

1. Average direct effect (ADE): to assess how disability affects HRQOL of a patient without considering or involving depression.
2. Average causal mediation effect (ACME): to assess how much disability affects HRQOL of patient by first causing depression and then lowering HRQOL.
3. Total effect which is the sum of both average direct effect and average causal mediation effect.
4. Proportion mediated: the percentage of total effect that goes through the depression pathway.

2.6.4 Sensitivity analysis

Sensitivity analysis was used to assess the robustness of the mediation results to hidden factors that influence both depression and HRQOL of stroke survivors, and also computed correlation between error terms of mediator and the outcome model to quantify how strong unmeasured confounder that need to be explain in the indirect effect.

2.6.5 Subgroup analysis

Pre-specified subgroup analyses were conducted to explore whether the proportion mediated differed by sex (male vs. female), stroke type (ischemic vs. haemorrhagic), hypertension status, and diabetes status. Results are presented as a forest plot

2.7 Ethical consideration

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the ethics committee of the School of Public Health, College of Health Science, Addis Ababa University, and verbal informed consent to participate in this study was obtained from each study participant, which was approved by the ethics committee of the School of Public Health, College of Health Science, and Addis Ababa University.

3. Results

3.1 descriptive statistics

A total of 364 stroke survivors were participated in this study. The mean age of participants was 53.2 years (SD = 9.15), gender was evenly distributed in this study 50.3 of participants were male, married participants were 206 (60%), and 23 (10.9%) doesn't attend any formal education. Ischemic stroke was the most common type in this study 266 (73%), with mean duration of stroke was mean of 3.1 years (SD = 1.55). About 46% (166) stroke survivors had moderately severe stroke. From a total 364 stroke survivors 221 (61%) had poor HRQOL, and moderate disability present in 222 (61%), moderately severe post-stroke depression (PHQ-9) was observed among 122 (55.2%) of participants. Aphasia was presented in 247 (68%), hypertension in 280 (77%), diabetes in 221(61%), and cardiac disease in 145 (40%) of stroke survivors in this study.

To compare each characteristics by HRQOL status, those participants with poor HRQOL had significantly older age (60.8+-8.8 vs. 45.6+-9.5 years; t = -15.2, d.f = 362, p-value < 0.001), more of female participants (57% vs. 43%; χ^2 = 11.95, p-value < 0.001), married (45.5%; χ^2 = 78.6, p-value < 0.001), and no formal educational status (9.5%; χ^2 = 140, p-value < 0.001). stroke survivors with poor HRQOL had high prevalence of aphasia (93.7% vs. 6.3%; χ^2 = 171.8, p-value < 0.001), hypertension (98.2% vs. 1.8%; χ^2 = 143.3, p-value < 0.001), diabetes (88.2% vs 11.8%; χ^2 = 178.6, p-value < 0.001), cardiac disease (60.6% vs. 39.4%; χ^2 = 101.5, p-value < 0.001), moderate disability (86.4% vs. 0.5%; χ^2 = 308.9, p-value < 0.001), and all participants with significant depression reported poor HRQOL. (Table.1 should be placed after descriptive statistics paragraph)

Table 1
Socio-demographic and clinical characteristics of stroke survivors at ZMH and Y12MCH by HRQOL, Addis Ababa, Ethiopia.

Variables	Good_HRQOL	Poor_HRQOL	Test Statistic	P.value
Sample size, n	143	221		
Age, years, mean (SD)	45.6 (9.5)	60.8 (8.8)	t = -15.31	< 0.001
Gender, n (%)			χ^2 = 11.95	< 0.001
Male	88 (61.5%)	95 (43%)		
Female	55 (38.5%)	126 (57%)		< 0.001
Marital status, n (%)			χ^2 = 78.6	< 0.001
Single	22 (15.4%)	4 (1.8%)		
Married	106 (74.1%)	100 (45.2%)		
Divorced	6 (4.2%)	35 (15.8%)		
Widowed	9 (6.3%)	82 (37.1%)		< 0.001
Educational status, n (%)			χ^2 = 140.63	< 0.001
No formal education	2 (1.4%)	21 (9.5%)		
Primary	18 (12.6%)	37 (16.7%)		
Secondary	24 (16.8%)	23 (10.4%)		
Tertiary	19 (13.3%)	13 (5.9%)		
Stroke type, n (%)			χ^2 = 22.26	< 0.001
Ischemic	124 (86.7%)	142 (64.3%)		
Haemorrhagic	19 (13.3%)	79 (35.7%)		
Stroke severity, n (%)			χ^2 = 216.06	< 0.001
No/minor symptoms	5 (3.5%)	0 (0%)		
Moderate stroke	127 (88.8%)	31 (14%)		
Moderate-severe	10 (7%);	156 (70.6%)		
Severe	1 (0.7%)	34 (15.4%)		
Stroke duration, years	2.3 (1.7)	3.9 (1.4)	t = -9.79	< 0.001
Aphasia, n (%)			χ^2 = 171.79	< 0.001
No	103 (72%)	14 (6.3%)		

Variables	Good_HRQOL	Poor_HRQOL	Test Statistic	P.value
Yes	40 (28%)	207 (93.7%)		
Hypertension, n (%)			$\chi^2 = 143.33$	< 0.001
No	80 (55.9%)	4 (1.8%)		
Yes	63 (44.1%)	217 (98.2%)		
Diabetes, n (%)			$\chi^2 = 178.63$	< 0.001
No	117 (81.8%)	26 (11.8%)		
Yes	26 (18.2%)	195 (88.2%)		
Cardiac disease, n (%)			$\chi^2 = 101.53$	< 0.001
No	132 (92.3%)	87 (39.4%)		
Yes	11 (7.7%)	134 (60.6%)		
Disability (mRS), n (%)			$\chi^2 = 308.96$	< 0.001
No/ Minor disability	112 (78.3%)	1 (0.5%)		
Moderate disability	31 (21.7%)	191 (86.4%)		
Moderately severe disability	0(0%)	29 (13.1%)		
Depression (PHQ-9), n (%)			$\chi^2 = 355.76$	< 0.001
Minimal	89 (62.2%)	0 (0%)		
Mild	53 (37.1%)	1 (0.5%)		
Moderate	1 (0.7%)	65 (29.4%)		
Moderately severe	0 (0%)	122 (55.2%)		
Severe	0(0%)	31(14.9%)		

3.2 Ordinal logistic regression to assess factors associated with higher disability

Ordinal logistic regression was used to assess factors associated with higher disability. Variables for the final model was selected using stepwise AIC method, the variables selected to be included in the final model were depression (ordinal), age, gender, aphasia, hypertension, cardiac disease, and physical activity.

Depression, gender, hypertension, cardiac disease, and physical activity were significant variables. A stroke survivor increasing 1 unity in depression severity status from minimal to severe was associated with a 5.66 times higher odds of more severe disability (95% C.I; 3.74–8.57, p.value < 0.001) showing a

significant association between disability and depression. Female gender was associated with 1.96 times higher odds of more severe disability (95% C.I; 1.07–3.59, p.value = 0.029) than that of male stroke survivors. Hypertensive stroke survivors had 4.38 times higher odds of more severe disability (95% C.I; 1.87–10.27, p.value = 0.001) than non-hypertensive survivors, participants with any cardiac disease history had also 1.64 times higher odds of more severe disability (95% C.I; 1–2.67, p.value = 0.048) than that of survivors without any cardiac disease history, finally stroke survivor who exercise more than 2 hrs/ week had 0.78 times lower odds of more severe disability (95% C.I; 0.64–0.94, p.value = 0.009) than survivors who doesn't exercise weekly for at least 2 hours. (Table.2 should be placed after ordinal logistics regression paragraph)

Table 2
Ordinal logistic regression of factors associated with higher disability among stroke survivors at ZMH and Y12MCH, Addis Ababa, Ethiopia.

Variable	Categories	OR	Lower C.I	Upper C.I	P.value
Depression ordinal		5.66	3.74	8.57	< 0.001
Age		1.02	0.99	1.06	0.143
Gender	Female VS. Male	1.96	1.07	3.59	0.029
Aphasia	Yes vs. no	1.97	0.90	4.29	0.089
Hypertension	Yes vs. no	4.38	1.87	10.27	< 0.001
Cardiac disease	Yes vs. no	1.64	1.00	2.67	0.048
Physical activity	Yes vs.no	0.78	0.64	0.94	0.009

3.3 Causal mediation analysis

Figure2. above showed that the conceptual mediation model with the estimated effects the pathway from disability to HRQOL, the natural direct effect which is the effect depression doesn't mediated between disability and HRQOL (OR = 1.09), and the indirect effect that is depression mediated between these two disability and HRQOL (OR = 1.15). Depression mediated 39.1%, (95% C.I; 10.4–90.9%) of the total effect.

The average direct effect (ADE) of disability on HRQOL without depression mediating was 0.087 (95% C.I; 0.019–0.214, p.value = 0.004). The average causal mediation effect (ACME) the effect of disability on HRQOL through depression mediating was 0.136 (95% C.I; 0.017–0.183, p.value = 0.004). The total effect of disability on HRQOL was 0.223 (95% C.I; 0.017–0.429, p.value = 0.004). The proportion of effect that have been mediated by depression was 39% (95% C.I; 10.4–90.9, p.value = 0.004) (Table 3).

Table 3
Causal mediation analysis: Depression as a mediator between disability and HRQOL among stroke survivors at ZMH and Y12MCH.

Effect	Estimate	Lower	Upper	P.value
Total Effect	0.223	0.017	0.429	0.004
Average Direct Effect (ADE)	0.087	0.019	0.214	0.004
Average Causal Mediation Effect (ACME)	0.136	0.017	0.183	0.004
Proportion Mediated	39.100	10.412	90.908	0.004

Figure3. Represents that mediation effect of depression through disability and HRQOL, showing ADE represents direct effect of disability on HRQOL that was not mediated through depression was 0.087. The ACME represents the indirect effect of disability on HRQOL that was mediated through depression was 0.136 showing depression was dominant pathway of depression. The total effect (the sum of direct and indirect effect) was 0.223.

3.4 Sensitivity analysis

To assess the robustness of the mediation results to potential unmeasured confounding variables sensitivity analysis was done. Explanatory variables in the model explained 77.3% of variation in depression, and 95.6% of variation in HHRQOL which indicates an excellent model fit. And unmeasured confounder needs a very strong correlation (ρ = 0.86) to nullify the indirect effect depression on the relationship between disability and HRQOL. (Table.4 should be placed after sensitivity analysis paragraph)

Table 4
Sensitivity Analysis: Robustness of the Mediation Effect to Unmeasured Confounding

Effect	R2_M	R2_Y	Rho_Required	Conclusion
Indirect Effect (ACME)	0.773	0.956	0.86	Robust
Direct Effect (ADE)	0.773	0.956	0.86	Robust

The Fig. 4 below shows that the sensitivity analysis for unmeasured confounding variables. The ACME shows positive across all values (-0.6 to 0.6) showing that unmeasured confounding that could eliminate the mediation effect should have to be very strong.

3.5 Sub-group analysis

A forest plot was used to examine if the mediation effect varied across sub-groups. The mediation effect was stronger among female survivors than male, hypertensive survivors than non-hypertensive, haemorrhagic survivors than ischemic survivors, and stroke survivors who are diabetic than non-

diabetic. However, the confidence interval for all sub-groups overlapped indicating no statistical significant effect modification. (Fig. 5 should be placed after sub-group analysis paragraph)

4. Discussion

This study was conducted to quantify to which extent does depression mediates the relationship between disability and HRQOL among stroke survivors who had a follow-up at ZMH and Y12MCH in Addis Ababa, Ethiopia. Approximately 61% of study survivors had reported poor HRQOL. Depression, female gender, hypertension, cardiac disease and physical inactivity were significant variables in predicting poor HRQOL. Survivors with poor HRQOL, 99% had reported moderate to severe disability. Depressive symptoms were present in all study participants with poor HRQOL. And depression mediates nearly two-fifths of the relationship between disability and HRQOL. The effect of disability on HRQOL which was average direct effect (ADE = 0.087, 95% CI; 0.019–0.214) and the effect of disability on HRQOL through depression mediating average causal mediation effect (ACME = 0.136, 95% CI; 0.017–0.183).

The prevalence of poor HRQOL in this study was approximately 61%. Consistent with our study a cross-sectional study conducted in India using world health organization quality of life brief version (WHOQOL-BREF) reported that 60.4% of stroke survivors in this study had poor HRQOL[15]. This might be due to both countries Ethiopia and India are LMIC where health services, physiotherapy, and psychological support are limited and not easily accessible. In contrast a study conducted in Australia using assessment of quality of life (AQOL) reported that 25% of stroke survivors had poor HRQOL[16]. Showing that stroke is a universal burden which deteriorates HRQOL of survivors. But the burden is dis-proportionately affecting LMIC. In-high income countries the burden is relatively less, where health services, rehabilitation, mood, and pain are modifiable determinants of HRQOL. While in LMIC even basic physiotherapy and psychological support is not easily accessible.

Depression was the most common significant variable, depression and disability had a bi-directional relationship[17] disability was one of the most powerful predictors for post stroke depression, while depression significantly affect functional recovery. Consistent with our study a study conducted in Ghana and Nigeria[18], Uganda[19], and Ethiopia[20] reported that stroke survivors had depression about half of survivors had depression and disability, while depression also prolongs functional recovery and this significantly worsen HRQOL of stroke survivors.

Female stroke survivors experience more worsen disability than male survivors. Similarly a spooled analysis of 19 studies in Australia[21] and the INTERSTROKE study[22] reported that female stroke survivors had higher risk of disability and worsen HRQOL than male survivors. Particularly in LMIC females had higher burden related to healthcare services, financial independency, and social support. From total participants about 77% of survivors were hypertensive, hypertension was a significant predictors associated with higher disability. Consistent with this study the INTERSTROKE[22] study reported hypertension was a significant modifiable risk factor for stroke, and higher risk of post stroke disability

through larger infract volumes, greater neurological deficit, and cerebral small vessel disease. Cardiac disease was presented among 40% of survivors, which was associated with higher disability similarly the INTERSTROKE study reported that cardiac diseases were associated with worsen the stroke outcome. Cardio embolic strokes will produce larger infracts a severe neurological deficit, while cardiac limitations reduce exercise tolerance during rehabilitation creating a vicious cycle. Physical activity was a protective predictor in this study; stroke survivors who were active participants are less likely to experience a significant disability. In line with this study a systematic review [23] reported that exercise improves functional recovery, and enhanced cardiovascular fitness and improvement.

The main aim of this study was to assess to which extent depression mediates the relationship between disability and poor HRQOL, depression mediates 39% of total effect of disability on poor HRQOL. Showing psychological pathway linked to physical impairment and that worsen HRQOL of stroke survivors. Shows depression partially mediates the impact of disability on the HRQOL among patients with multiple sclerosis[24]. Another study reported that disability doesn't only affects HRQOL of stroke survivors, it affects the psychological disorder and it indirectly deteriorates or diminish HRQOL[25]. Depression mediates 39.1% of relationship between disability and HRQOL, showing that psychological pathway linked physical impairment that significantly deteriorates HRQOL of stroke survivors. This study used counterfactual framework to decompose the total effect (0.223 p-value = 0.004) into ADE (0.087 p-value = 0.004), and ACME (0.136 p-value = 0.004). ACME reported about 40% of disability effect on HRQOL was through psychological pathway. Similarly a study conducted in South Korea using sequential equation modeling, reported that 40.2% of relationship between disability and HRQOL was mediated by depression. Showing that the mediation of depression between disability and HRQOL had a universal consistency[26]. Also a study conducted among diabetic patients[27] and patients with multiple sclerosis[28] reported that depression mediates more than one-third of relationship between disability and HRQOL of a person. Showing that regardless of the disease type depression significantly mediates the relationship between disability and HRQOL.

5. Conclusion and recommendation

Conclusion

This study was conducted among 364 stroke survivors who were attending at Zewditu memorial hospital and Yekatit 12 medical college hospital, Addis Ababa, Ethiopia. In this study depression mediates 39.1% of the relationship between disability and HRQOL of stroke survivors. The total effect of disability on HRQOL of stroke survivors was 0.223. The average direct effect (ADE) was 0.087; the indirect effect which is average causal mediation effect (ACME) was 0.136 with p-value of 0.004. The significant variables for higher disability were depression, gender, hypertension, cardiac disease, and physical activity. The sensitivity analysis showed that unmeasured confounder needs a very strong correlation (ρ = 0.86) to nullify the indirect effect depression on the relationship between disability and HRQOL. The overall subgroup analysis reported that there was no statistically significant difference in the subgroups.

Recommendations

Depression mediates two-fifth of the relationship between disability and HRQOL. Incorporating depression screening with the follow-up and treating depression can significantly improves HRQOL of stroke survivors. For the future to conduct randomized controlled trial longitudinal and qualitative studies.

Strengths and limitations

To our knowledge this study was the first to apply causal mediation analysis among African stroke survivors. We had used counterfactual framework, to divide the total effect into direct and indirect effect showing methodological advancement over traditional methods. The sensitivity analysis = 0.86 shows strong evidence for the robustness of dedicated pathway to unmeasured confounding. And we used stroke specific quality of life (SSQOL-49) to measure quality of life of stroke survivors. And finally high model fit indicating our model fit the data well.

This study used a cross-sectional study design, can't distinguish the relationship between depression and disability us bi-directional or reverse pathway can't be distinguished. The number of samples included in the study was smaller, and the number of mediator in this study was only depression.

Abbreviations

ACME
Average causal mediation effect
ADE
Average direct effect
AIC
Akaike information criteria
BMI
Body mass index
CI
Confidence interval
HRQOL
Health-related quality of life
LMIC
Low-and middle-income countries
MRs
Modified Rankin scale
OR
Odds ratio
PM

Proportion mediated

SD

Standard deviation

WHO

World health organization

WHOQOL-BREF

World health organization quality of life brief version

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the ethics committee of the School of Public Health, College of Health Science, Addis Ababa University, and verbal informed consent to participate in this study was obtained from each study participant, which was approved by the ethics committee of the School of Public Health, College of Health Science, and Addis Ababa University.

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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Author Contribution

Eden Fiseha was involved in the study conceptualization, designing, analyzing, and interpreting the data, drafting, and final writing of this manuscript. Girma Taye (last author) and Lidya Genene provided the necessary guidance, reviewing and revising the subsequent draft of this manuscript. And Chalachew Gashu and Melat Amberbr provided necessary comments and helped in manuscript writing. All authors read and approved the final manuscript.

Data Availability

The datasets used and/or analyzed during the current study are available from the correspondingauthor on reasonable request.

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Figures

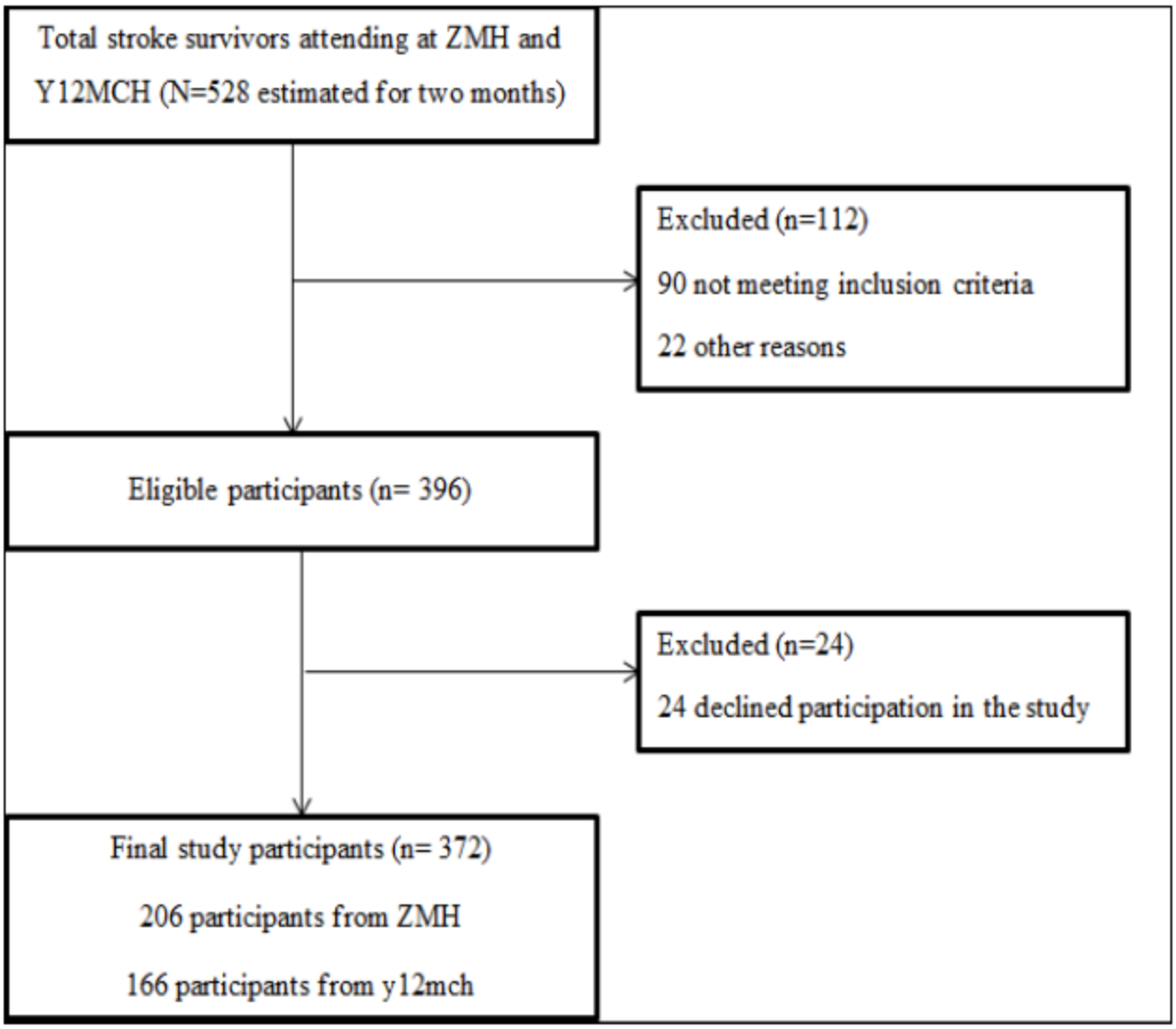


Figure 1

Sampling procedure for the study HRQOL and associated factors among stroke survivors at Zewditu Memorial Hospital and Yekatit 12 Medical College Hospital, Addis Ababa, Ethiopia, 2024.

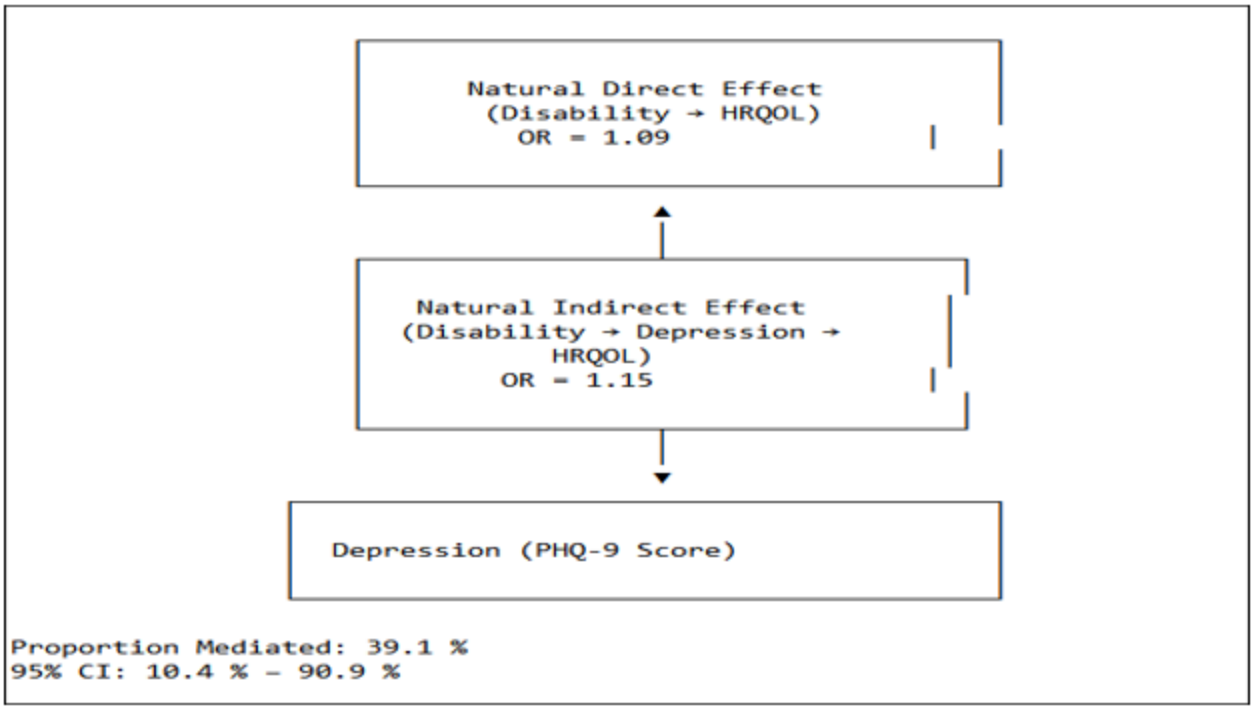


Figure 2

Conceptual Mediation Model: Disability, Depression, and HRQOL

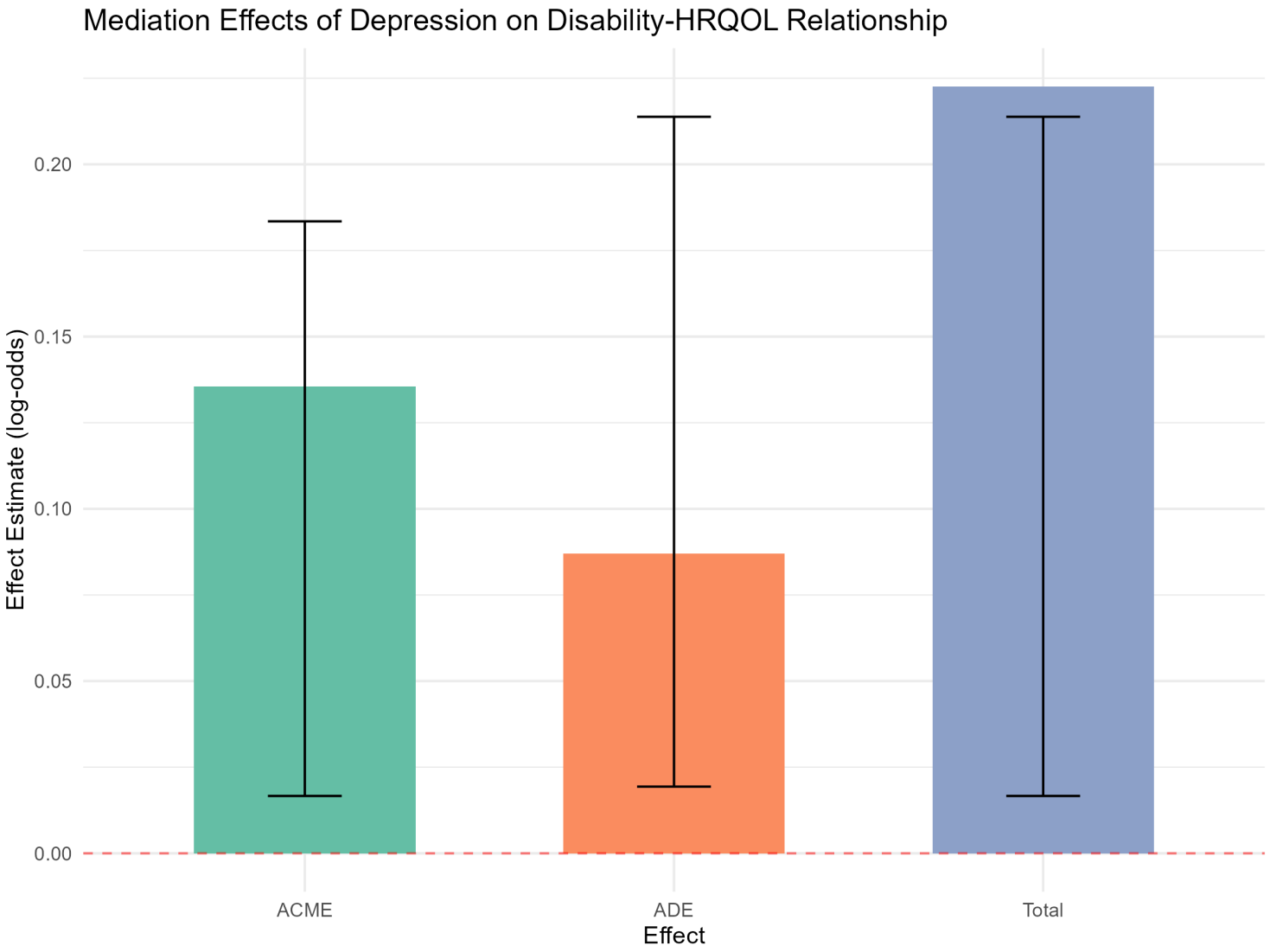


Figure 3

Mediation effect of depression on disability and HRQOL among stroke survivors at ZMH and Y12MCH, Addis Ababa, Ethiopia.

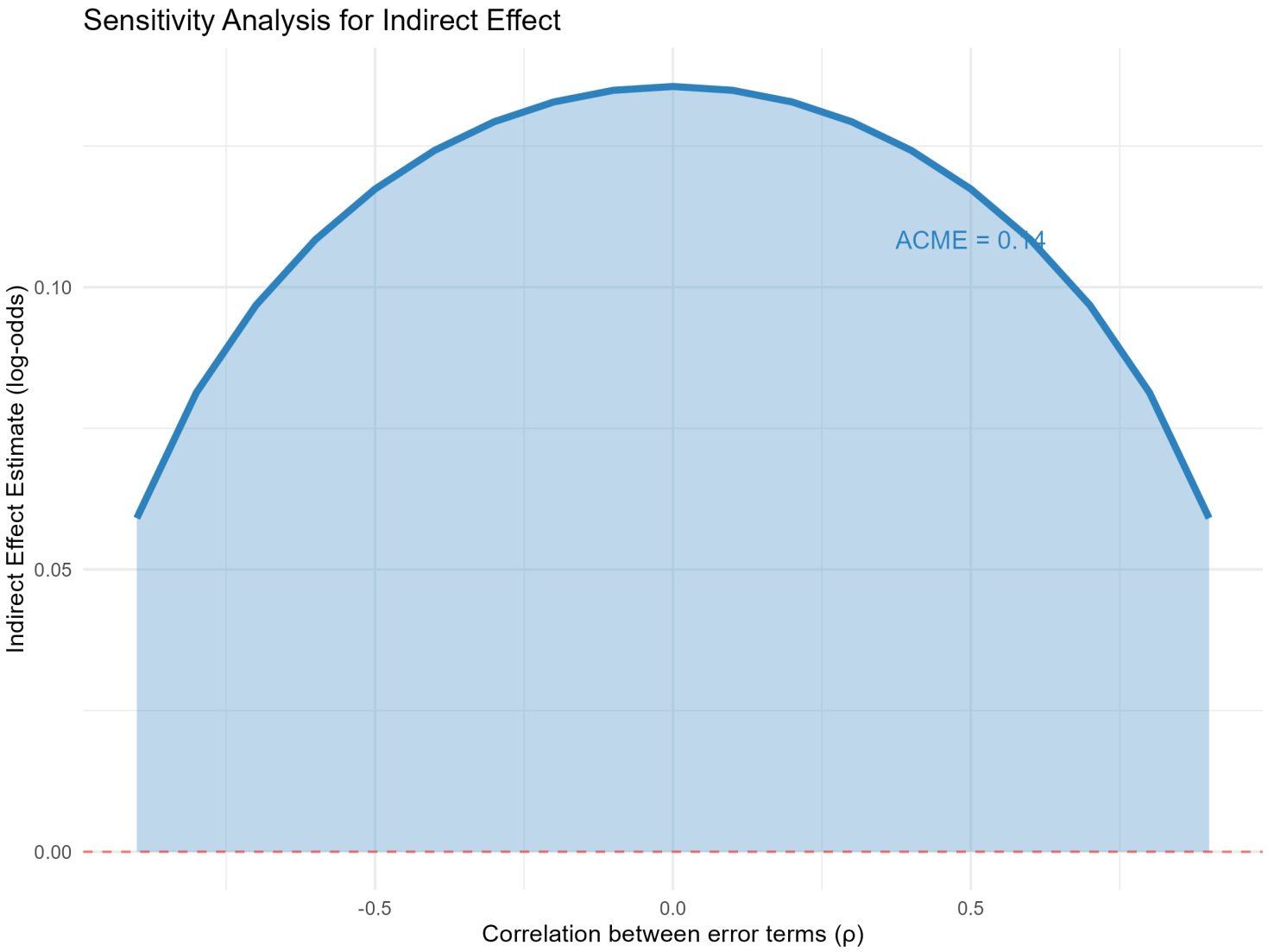


Figure 4

Sensitivity Analysis: Stability of the Indirect Effect to unmeasured mediator-outcome confounding.

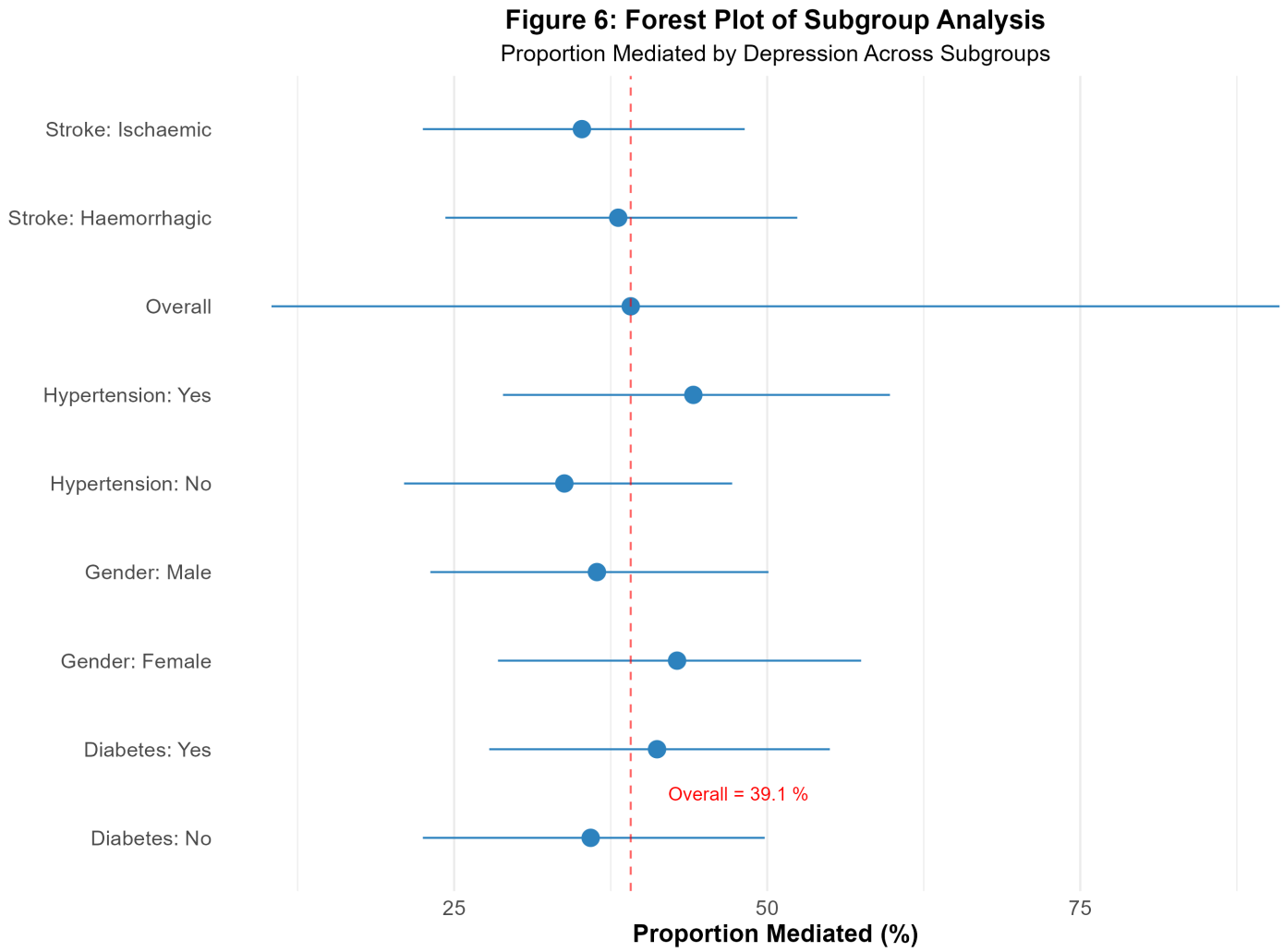


Figure 5

Subgroup Analysis: Proportion Mediated by Depression across Patient Subgroups