ORIGINAL ARTICLE

Impairment in Health-Related Quality of Life among Community-Dwelling Stroke Survivors

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ABSTRACT: ***Introduction:*** Health utility instruments are increasingly being used to measure impairment in health-related quality of life (HRQoL) after stroke. Population-based studies of HRQoL after stroke and assessment of differences by age and functional domain are needed. ***Methods:*** We used the Canadian Community Health Survey linked with administrative databases to determine HRQoL using the Health Utilities Index Mark 3 (HUI3) among those with prior hospitalization or emergency department visit for stroke and compared to controls without stroke. We used multivariable linear regression to determine the difference in HUI3 between those with stroke and controls for the global index and individual attributes, with assessment for modification by age (<60, 60–74, and 75+ years) and sex, and we combined estimates across survey years using random effects meta-analysis. ***Results:*** Our cohort contained 1240 stroke survivors and 123,765 controls and was weighted to be representative of the Canadian household population. Mean health utility was 0.63 (95% confidence interval [CI] 0.58, 0.68) for those with stroke and 0.83 (95% CI 0.82, 0.84) for controls. There was significant modification by age, but not sex, with the greatest adjusted reduction in HUI3 among stroke respondents aged 60–74 years. Individual HUI3 attributes with the largest reductions in utility among stroke survivors compared to controls were mobility, cognition, emotion, and pain. ***Conclusions:*** In this population-based study, the reduction in HUI3 among stroke survivors compared to controls was greatest among respondents aged 60–74, and in attributes of mobility, cognition, emotion, and pain. These results highlight the persistent impairment of HRQoL in the chronic phase of stroke and potential targets for community support.

RÉSUMÉ : Détérioration de la qualité de vie liée à la santé chez les personnes qui ont survécu à un accident vasculaire cérébral et qui vivent dans la collectivité. ***Introduction*** **:** On utilise de plus en plus des instruments de mesure de l'utilité afin d'évaluer la détérioration de la qualité de vie liée à la santé (QVLS) à la suite d'un accident vasculaire cérébral (AVC). Il existe peu d'études en population sur la QVLS après un AVC et peu de données sur l'évaluation des différences par tranche d'âge et par domaine fonctionnel. ***Méthode*** **:** L'équipe de recherche a utilisé le formulaire d'Enquête sur la santé dans les collectivités canadiennes lié à des bases de données administratives afin de déterminer la QVLS à l'aide du système de classification Health Utilities Index Mark 3 (HUI3) chez les personnes ayant déjà été hospitalisées ou traitées au service des urgences pour un AVC, puis a comparé les résultats avec ceux de témoins n'ayant pas subi d'AVC. Les différences sur l'HUI3 entre les malades ayant subi un AVC et les témoins ont été établies à l'aide d'une régression linéaire plurifactorielle en ce qui concerne le score total et les attributs individuels, puis affinées par une évaluation des modifications selon l'âge (< 60 ans; 60-74 ans; et 75+ ans) et le sexe; a suivi une mise en commun des estimations pour toutes les années d'enquête à l'aide d'une méta-analyse à effets aléatoires. ***Résultats*** **:** La cohorte comptait 1240 survivants d'un AVC et 123 765 témoins, et a été pondérée de manière à être représentative de la population vivant en ménage au Canada. La valeur moyenne de l'utilité était de 0,63 (IC à 95 % : 0,58-0,68) parmi les survivants d'un AVC et de 0,83 (0,82-0,84) parmi les témoins. Par ailleurs, une différence significative liée à l'âge, mais non au sexe, a été observée chez les survivants d'un AVC âgés de 60 à 74 ans, différence qui a entraîné la baisse la plus importante du score rajusté sur l'HUI3. Enfin, les attributs individuels évalués sur l'HUI3, ayant subi les diminutions les plus notables de la valeur d'utilité parmi les survivants d'un AVC comparativement aux témoins étaient la mobilité, la fonction cognitive, l'état émotionnel et la douleur. ***Conclusions*** **:** D'après cette étude en population, la diminution la plus forte du score sur l'HUI3 parmi les survivants d'un AVC par rapport aux témoins a été enregistrée dans la tranche d'âge de 60 à 74 ans, et les attributs les plus touchés étaient la mobilité, la fonction cognitive, l'état émotionnel et la douleur. Ces résultats font ressortir la détérioration constante de la QVLS durant la phase chronique de l'AVC et les cibles potentielles de soutien communautaire.

Keywords: Stroke, Epidemiology, Quality of life

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Background

Stroke is the second most common cause of death[1] and a leading cause of disability worldwide. It is estimated that the prevalence of disability due to stroke will increase by 24% between now and 2030.[2] Patient-reported physical and social well-being have been recognized as important outcomes after stroke.[3,4] There has been increasing interest in the use of health utility scores to capture health-related quality of life (HRQoL) in stroke survivors[5,6] as utility scales provide an assessment of HRQoL that reflects the preference valuation of health states by community members. Prior studies have shown reduced HRQoL in patients with stroke using measures such as the EuroQol-5 Dimension (EQ-5D)[4,7–11] and Health Utilities Index Mark 3 (HUI3),[12–14] and more recently major clinical trials in stroke have incorporated HRQoL assessments.[15,16]

The EQ-5D and HUI3 both correlate strongly with the Barthel index and Rankin scale,[14] although contain additional important domains such as mood and cognition. Prior studies have assessed the HUI3 in stroke,[13,14,17,18] although many are outdated, relied on self-report of stroke, and did not assess differences by age. There is also a lack of population-based studies on HRQoL after stroke comparing to controls without stroke.

An updated understanding of post-stroke dysfunction and HRQoL is needed to design and implement programs to better address the needs of stroke survivors. To overcome the limitations of prior survey research that relied on patient-reported stroke history, we linked the Canadian Community Health Survey (CCHS) to population-based universal healthcare administrative databases to ascertain physician-diagnosed stroke cases, and then compared HRQoL to those without a stroke linkage. We assessed differences by age, sex, and health attribute. We hypothesized that younger individuals with stroke would suffer greater losses in HRQoL compared to older individuals, and that impairments would be most pronounced in domains of mobility, cognition, and emotional health.

Methods

Study Sample: Canadian Community Health Survey

The CCHS is an annual cross-sectional survey, representing 97% of the Canadian population aged 12 years and older. The survey randomly samples households nationwide and selects one respondent from each household. The CCHS collects information about health status, health determinants, and health care utilization of the household population. We used CCHS years 2009, 2010, 2013, 2014, and 2015 as the HUI3 was a mandatory component of the questionnaire in these years. Interviews are conducted using computer-assisted personal and telephone interview software.[19] Before releasing the CCHS for use, data are assessed for quality and compared to previous cycles to avoid errors. Approximately 3% of the Canadian population is excluded from the survey target population, which includes those living on Indigenous reserves, those living in foster care, full time members of the Canadian Armed Forced, the institutionalized population and the remote Région du Nunavik and Région des Terres-Cries-de-la-Baie-James. Data were collected by Statistics Canada using a multistage sample allocation strategy to support estimation at the health region and provincial level.[19]

While the CCHS contains an item on the questionnaire regarding a history of stroke diagnosis, self-report of stroke is subject to recall bias and there is a large discordance between individual self-report and medical diagnosis of stroke derived from administrative data.[20,21] The CCHS has recently been linked to administrative databases of hospital discharge and emergency department visits,[22] allowing more accurate determination of stroke cases.

CCHS Sharelink

CCHS Sharelink is a CCHS sub-sample with about 85% of total respondents, who agreed to have their responses linked to administrative records. Statistics Canada created sample weights for CCHS Sharelink to retain population representativeness. CCHS Sharelink resembles CCHS in sociodemographic characteristics.[22] Linkages were performed by Statistics Canada and included the Canadian Institutes of Health Discharge Abstract Database (CIHI-DAD) for hospitalizations and the National Ambulatory Care Reporting System (NACRS) for emergency department visits. The DAD is an administrative database which collects demographic, diagnostic, and treatment information from all admitted patients in Canada, excluding the province of Quebec. NACRS collects similar information for visits to the emergency department. CIHI-DAD was linked back to 1999–2000 and NACRS to 2002–2003.

Case Definition

We first excluded respondents from Quebec, as Quebec does not contribute data to CIHI-DAD. We also excluded respondents under 40, due to very few stroke cases in that age group. All cases of first stroke were identified in CIHI-DAD and NACRS from 1999 to 2015 using International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD-10-CA) codes (ischemic stroke: I63.x, I64.x, H34.1; intracerebral hemorrhage [ICH]: I61.x). ICD-9 codes [ischemic stroke: 434.01, 434.11, 434.91, 436; ICH: 431] were used to obtain cases prior to 2003. These case definitions used have high validity in Canada.[23,24] Individuals who had a prior episode of stroke captured in the administrative databases and who participated in the CCHS in the selected years were included in the stroke cohort. Control subjects without prior identification of stroke comprised the remainder of individuals in the CCHS in the selected years.

Covariates

Covariates were obtained from the CCHS, including age, sex, year of survey, province of respondent, rural residence, ethnicity, education level, total household income quartile, marital status, and self-reported body mass index (BMI), smoking status, hypertension, diabetes, heart disease, chronic obstructive pulmonary disease (COPD), arthritis, and asthma. Age was categorized as <60, 60–74, and 75+. Categorization of the remainder of variables can be seen in Table 1. Due to known biases in self-report of BMI, we employed a correction suggested by Statistics Canada.[25] Chi-square test was used to assess differences in proportions between those with and without stroke. All numerical estimates were rounded as per Statistics Canada confidentiality policies.

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Table 1: Weighted percentages and means of sample characteristics by stroke status

Variable	No stroke ($n = 123,765$)	Stroke ($n = 1240$)	p-value
Age, mean	59.6	70.4	<0.001
Age categories (%)			<0.001
Age < 60	59.2	16.3	
Age 60–74	29.2	45.7	
Age 75+	11.6	39.2	
Females	51.5	40.3	<0.001
Education			<0.001
Less than secondary school	14.7	31.6	
Secondary school graduation	19.8	19.6	
Any post-secondary	64.3	46.8	
Lowest income quartile	22.4	28.3	<0.001
Ethnicity			<0.001
Caucasian	69.2	78.4	
Asian	7.5	6.5	
First Nations	2.9	2.2	
Marital status			<0.001
Married/common law	72.7	65.3	
Single	8.3	6.5	
Widowed/separated/divorced	18.9	28.3	
Rural residence	19.5	18.5	0.01
Smoking			0.17
Daily/occasionally	17.6	19.6	
Occasionally	3.2	2.2	
Not at all	82.4	79.5	
Cancer	7.8	9.8	<0.001
Hypertension	30.0	63.2	<0.001
Diabetes	10.5	28.3	<0.001
Heart disease	7.5	32.7	<0.001
COPD	4.6	9.8	<0.001
Arthritis	28.6	47.9	<0.001
Asthma	7.4	7.6	0.7
Proxy interview	2.5	13.0	<0.001
HUI3 index score, mean (95% CI)			
Overall cohort	0.83 (0.82, 0.84)	0.63 (0.58, 0.68)	<0.001
Age < 60	0.85 (0.84, 0.86)	0.64 (0.50, 0.78)	<0.001
Age 60–74	0.83 (0.82, 0.84)	0.65 (0.55, 0.75)	<0.001
Age 75+	0.75 (0.73, 0.77)	0.60 (0.49, 0.71)	<0.001
Male	0.84 (0.83, 0.85)	0.65 (0.58, 0.72)	<0.001
Female	0.82 (0.81, 0.83)	0.60 (0.52, 0.68)	<0.001

CI = confidence interval; COPD = chronic obstructive pulmonary disease; HUI3 = Health Utilities Index Mark 3.
Proportions are obtained by following Statistics Canada procedures on weighting and rounding and categories may not always sum to 100.

Health Utilities Index Mark 3

The HUI3 is a generic, preference-based measure of health status, which includes the attributes of vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain, with five or six levels for each attribute (Supplemental Table 1) and incorporates utility weights based on standard gamble studies in a

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general population sample. The HUI3 has been validated for use in the Canadian stroke population.[17] The summary index ranges from −0.36 (state worse than dead) through 0 (similar to dead) to 1 (perfect health)[26] and is obtained by multiplying each individual attribute rank by its multi-attribute weight, and then using the following equation: HUI3 score = 1.371*(Vision*Hearing*-Speech*Dexterity*Mobility*Emotion*Cognition*Pain) − 0.371. The single attribute weights were used when analyzing individual attributes.[27]

Analysis

HUI3 index score means with 95% confidence intervals (CIs) were stratified by age and sex and *t*-tests were used to evaluate the difference between those with and without stroke. Chi-squared tests were used to compare proportions across categories of global impairment[28] [none (1), mild (0.89–0.99), moderate (0.7–0.88), severe (>0–0.69), or equal to or worse than dead (0 or below)]. We used multivariable linear regression to determine the association between history of stroke and mean difference in HUI3 score using the multi-attribute weights, separately for each CCHS survey year. Because the CCHS uses a multi-stage sampling procedure and several sampling frames, a replicate bootstrap weighting procedure is recommended to deal with design effects. A set of 500–1000 bootstrap weights provided by Statistics Canada were used to account for clustering and variation in selection probabilities. These bootstrap weights also include adjustments for non-response to help minimize selection bias. We used bootstrap weights for the linear regression in each survey year separately, and then combined the coefficients at the survey level using random effects meta-analysis.

To assess for the presence of modification by age or sex, we first ran a simple model with mean HUI3 as the outcome, stroke as the exposure, and age and sex included as interaction terms, using the Wald test to assess for a significant interaction ($p < 0.05$). Age was categorized as <60, 60–74, and 75 and older, with <60 serving as the reference group. As this model demonstrated modification by age, we then fit individual age-specific models, with the simple model adjusted for only sex. The full model included sex and the remainder of the covariates. All covariates demonstrated evidence of confounding in at least one age- and year-specific model defined as a change in the stroke-HUI3 regression coefficient by >10%. As NACRS cases were predominantly from provinces Ontario, Alberta, and British Columbia, we conducted a sensitivity analysis excluding stroke cases identified by NACRS only. We also did a sensitivity analysis excluding those with self-reported stroke from the control group.

For each of the individual attributes, we determined the proportions of respondents with and without stroke who had level 1, level 2, or level 3+ (see Supplemental Table 1 for description of all levels). We then determined the association between stroke and HUI3 for the eight individual attributes in the same fashion as the global analysis, using the single attribute weights.

Multiple Imputation

The HUI3 score was missing in 4.3% of controls and 8.5% of stroke respondents. The vast majority of cases were due to non-answer of one attribute on the HUI3. We conducted a multiple imputation analysis with ordinal regression to replace the missing HUI3 attribute values, using all covariates and the remaining seven attributes as predictors in the model. Visual inspection of the replaced values was done to ensure face validity. The linear regressions were then repeated with the imputed values.

Analyses were done in the Prairie Regional Data Centre at the University of Calgary using Stata 16.0 (College Station, TX). Threshold of significance for *p*-values was <0.05. Under Tri-Council guidelines, this analysis did not require approval by a research ethics board.

Results

There were 1240 people with prior stroke (91% with ischemic stroke and 9% with ICH), and 123,765 controls. Eleven percent of stroke records were identified from emergency room records only and the remainder from hospital admissions. Proxy interviews were conducted in 2.5% of controls and 13.0% of stroke respondents. The median time between stroke diagnosis and CCHS interview was 4.3 years (IQR 1.8–7.2). The I^2 values in the meta-analyses ranged from 0% to 59.7%.

Compared to those without a history of stroke, those with stroke had older age, were more likely to be male, had a lower education, lower income and had a higher proportion of vascular risk factors. All baseline characteristics are shown in Table 1. Mean unadjusted HUI3 was lower for those with stroke, for females, and individuals at older age (Table 1). Compared to controls, there was a much lower proportion of stroke respondents with no or minimal impairment in health utility and a greater proportion with severe impairment (shown in Figure 1).

In the linear regression, there was evidence of significant modification by age ($p = 0.033$ for age 60–74). There was no significant modification by sex ($p = 0.34$). In the stratified age-specific simple models, mean HUI3 difference between those with stroke and without stroke was greatest in those aged 60–74 years (−0.22, 95% CI −0.27 to −0.17), compared to those < 60 years (−0.17, 95% CI −0.24 to −0.10) and 75+ years (−0.13, 95% CI −0.19 to −0.07; Figure 2A). The age-specific pattern was similar in the fully adjusted model (Figure 2B), when excluding cases only identified in the emergency department, when excluding self-reported stroke from the control group, and when imputing missing HUI3 values (Supplemental Figure 1).

Respondents with stroke had greater proportion of moderate to severe impairment in all HUI3 attributes compared to controls, especially mobility (level 3 or above 34%), cognition (46%), and pain (35%; Figure 3). There was no significant interaction by age or sex for any of the individual HUI3 attribute utilities. In the simple model, stroke was significantly associated with reductions in all attributes except hearing, with the greatest reductions occurring in attributes emotion, cognition, pain, and mobility (Figure 4A). In the fully adjusted model, dexterity, emotion, cognition, and mobility remained significantly impaired in those with stroke versus controls, with most impairment in cognition and mobility (shown in Figure 4B). Results were similar after imputation of missing HUI3 attribute scores (Supplemental Figure 2).

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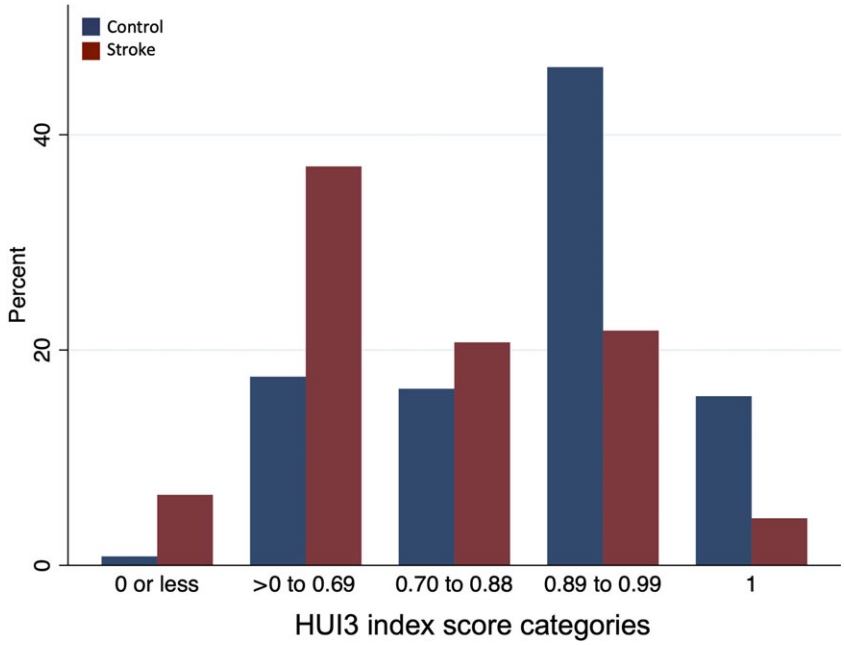

Figure 1: *Weighted percentages in each Health Utilities Index Mark 3 (HUI3) index score category by stroke status.*

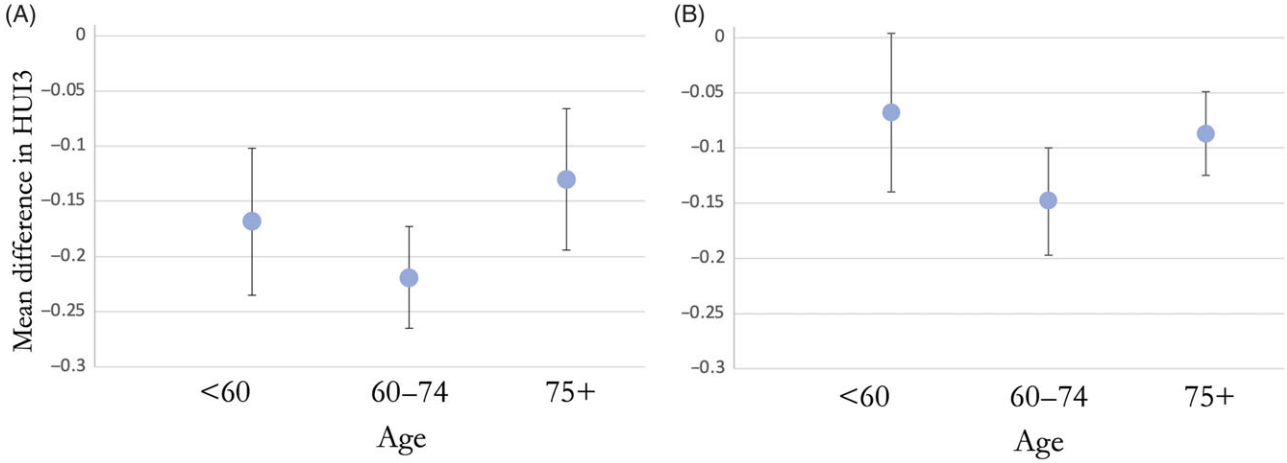

Figure 2: *Adjusted mean difference in HUI3 index score for stroke respondents compared to controls, stratified by age group for simple (A) and full models (B).*

Discussion

In our study of nationally representative cross-sectional surveys linked with administrative data, history of stroke was associated with a lower HRQOL as measured by the HUI3. We found modification by age, whereby those between 60 and 74 years experienced a greater adjusted reduction in HUI3 with stroke compared to those < 60 or 75+. Individuals with stroke had the greatest impairment in attributes of emotion, cognition, pain, and mobility.

Our study utilized administrative data for our case definition of stroke due to greater reliability than self-reported stroke.[21] In a prior study, health utility scores were higher for cases identified by health administrative data, suggesting that milder cases are detected. Prevalence of stroke in health administrative data was also lower as compared to self-report, implying the potential for misclassification bias in survey data.[21] Furthermore, the CCHS questionnaire asks whether the individual experiences the "effects of stroke," which may result in misclassification from individuals with mild or resolved deficits, or misattribution of certain symptoms to other conditions or older age.

In this study, health utility scores for those with stroke based on hospital records were similar to prior published utility values for those with self-reported "effects of stroke" in Canada,[13,29,30] although these studies did not directly model the difference with control subjects. We found a significant reduction in HUI3 in stroke respondents compared to controls after adjustment for demographic, social, and co-morbid factors. The reason for the

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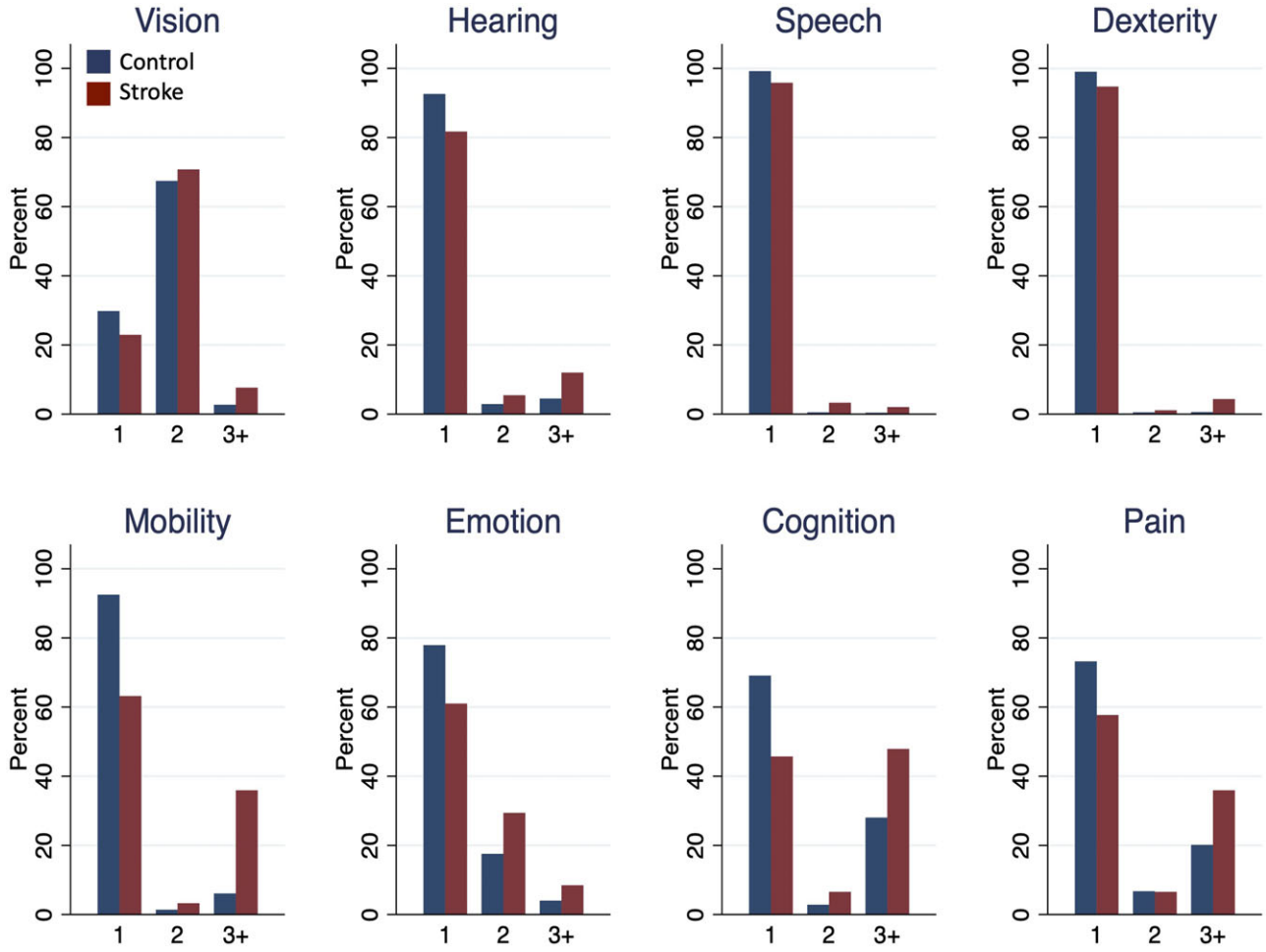

Figure 3: *Weighted percentage of impairment for levels of each HUI3 attribute (higher level is worse impairment), among stroke respondents and controls. See Supplemental Table 1 for description of all levels.*

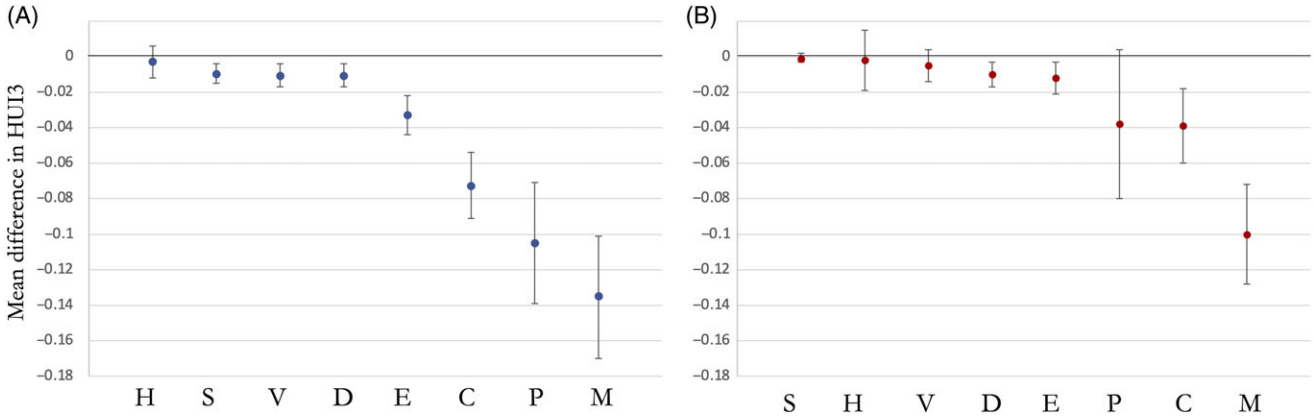

Figure 4: *Adjusted mean difference of individual HUI3 attribute weights for stroke respondents compared to controls, for simple (A) and full model (B), plotted in order of greater HUI3 difference. H indicates hearing; S, speech; V, vision; D, dexterity; E, emotion; C, cognition; P, pain; and M, mobility.*

greater reduction in HUI3 score among stroke respondents aged 60–74 is unclear, although may relate to greater capacity for plasticity and recovery in younger individuals, and greater resilience in the elderly.[31] Although floor effects may have played a role in the elderly due to lower baseline HRQoL, the HUI3 does not demonstrate substantial floor effects.[32,33] Survival bias may also result in higher than expected health utility scores in the elderly with stroke. Our results are nevertheless a meaningful and

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practical representation of community-dwelling stroke survivors with implications for resource needs. Stroke among 60–74 may occur when productivity and opportunity cost remain high, yet the adaptive mechanisms are lower, suggesting the potential need for greater post-stroke supports among survivors in the community in this age group.

We found that stroke was associated with the greatest reductions in utility for emotion, cognition, pain, and mobility. Among stroke survivors, 41% have intermediate to high risk of depression,[33,34,32] and symptoms of depression have been found to be predictive of impaired functioning and community re-integration and low quality of life post-stroke.[35] Although best-practice guidelines endorse screening for post-stroke depression,[36–38] under-recognition and under-treatment remains common.[39] The association with pain impairment was attenuated after full adjustment, although over a third of respondents with stroke reported moderate to severe pain. Post-stroke pain is also under-recognized and estimates of post-stroke pain prevalence range from 10% to 30%. Post-stroke pain may be due to central pain or peripheral neuropathic pain and is associated with greater functional dependence, depression, and cognitive decline.[40–42] Finally, respondents with stroke had the greatest proportion of impairment in the cognitive attribute compared to all other attributes, with over half of respondents reporting some degree of impairment. In the Oxford Vascular Study, the incidence of dementia was 34% at 1 year and after severe stroke and 8.2% after minor stroke.[43] Individuals with stroke have faster declines in executive function and global cognition than controls.[44] Our study re-inforces the prominent and persistent impacts of emotional, cognitive, pain, and mobility disturbances on overall HRQoL among community dwellers in the chronic phase of stroke.

Our analysis has numerous strengths, particularly with the quality and reliability of the data and the availability of a large number of baseline variables. The linkages of CCHS with the DAD are of high quality, with few false links.[45] The CCHS provides a large sample size which can be generalized to the Canadian household population. There were some limitations to the study. First, self-reported variables may be associated with response biases, although variables like hypertension and diabetes have shown high reliability in self-report.[21] The wording of questions is modeled after items contained in the US Behavioral Risk Factor Survey and specifies that a self-reported chronic condition must represent a diagnosis from a health professional. Second, individuals with stroke underwent the survey at various times from the stroke, although this is a realistic portrayal of the heterogeneity of stroke survivors living in the community. Third, diagnosis of stroke was reliant on administrative data, although administrative data coding for acute stroke has a high positive predictive value in Canada.[23] Finally, we could not identify individuals hospitalized with stroke prior to 1999, although this provided a 10-year window from the earliest survey year.

We used the HUI3 to demonstrate the overall burden and degree of reduction in global HRQoL and specific attributes among community-dwelling stroke survivors compared to those without stroke. Emotion, cognition, pain, and mobility are particularly impacted among those with stroke. This knowledge could be used for future population-based assessments, measuring effects of interventions in improving HRQoL among stroke survivors, and monitoring of trends over time. Further studies should address whether the HUI3 or other measures of health utility add value to more standard stroke disability measures in routine clinical care or clinical trials.

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Statement of Authorship

RAJ was involved with project conception, analysis, and writing of the manuscript. SP was involved with project conception and critical revision of the manuscript. AL was involved with project conception and critical revision of the manuscript. JW was involved with analysis and critical revision of the manuscript ES was involved with project conception and critical revision of the manuscript.

Supplementary Material

To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2021.119.

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