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Impact of Strokes: The Burden of Care, Post-CVA Fatigue & Caregiver Role Strain

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Impact of Strokes: The Burden of Care, Post-CVA Fatigue & Caregiver Role Strain

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Abstract

Strokes and cerebral vascular accidents (CVAs) and related disease events are an unfortunate circumstance that inflicts individuals around the world and impacts people every day as individuals and their caregivers. The consequences of these strokes or CVA events are life-changing for all those involved. As a result of long-term disability related to strokes, the caregiver may undergo many emotional, psychological, and physical factors that impact their daily lives. There is a relatively short period of time to react to the necessary change and as a result there may be differences in coping associated with these unexpected health circumstances. Many stroke victims experience motor, cognitive, emotional, and psycho-social deficits and their caregivers may not be prepared for these abrupt life altering effects. The impact for caregivers, factors impacting strokes, and solutions for care will be addressed in the paper. Evidence suggests that post fatigue stroke (PFS) may be triggered by a dysfunction of the stress system. Family caregivers with a low level of social engagement may be more likely to perceived stress, and increased risk for caregiver role strain.

Keywords

Stroke, Cerebral Vascular Accidents (CVA), Caregiver Role Strain, Chronic Fatigue Syndrome (CFS), Post-Stroke Fatigue (PSF)

1. Introduction

Stroke occurs when there is an interruption in the blood supply to the vessels of the brain, caused by the rupture, blockage, or occlusion of the blood vessels, resulting in localized tissue injury and tissue death [1]. Globally there are 101 million people who are living with the effects of a stroke annually and there are over 12.2 million new strokes each year. Globally, one in four people over age 25 will

have a stroke in their lifetime [2]. Strokes are disorders that predominantly affect older individuals. Studies have been done to evaluate the effects of long-term care for stroke victims and their caregivers for quality-of-life pre and post intervention during various time periods during rehabilitation and recovery following a stroke. Fatigue is a common and distressing problem after stroke, but no intervention has been recommended to treat or prevent it in people with stroke [3]. Thus, it is important to find out if any intervention could reduce the presence or severity, or both, of fatigue in people with stroke. PSF has a relationship to function and has been attributed to functional limitations related to fatigue and the necessary social support due to reduced physicality [4]. PSF has an important tell-tale for predictable social isolation and may also be a predictor for increased fall risk [4]. Pollack *et al.*, [5], identified priorities in a survey conducted for treatment uncertainties which identified 548 questions as a result of their query of 15 stroke groups/clubs (183/548), 22 individual stroke survivors (77/548), four individual carers (21/548), four health professional groups/meetings (37/548), 61 individual health professionals (198/548), and three guidelines/research recommendations (32/548) were listed as priorities. The study revealed a greater focus should be on specific stroke-related impairments, including cognition, aphasia, vision, upper limb, mobility, and fatigue, which would all be classified as “body functions” that had the most challenging effects for caregivers and patients alike [5].

Chronic fatigue syndrome (CFS) is a disabling set of symptoms that present as a collection of conditions that produce long-term effects that are understood internationally as a syndrome including sleep disturbances, diffuse musculoskeletal pain, disabling fatigue, and difficulty concentrating as the core symptoms [6]. Several other symptoms may be included in the disruption for CFS and add to the debilitating nature of physical illness, which may weigh heavily on one’s mental health, self-esteem, and behaviors [7]. Given there is no objective test for the CFS condition, it remains a diagnosis of exclusion [7]. In a proposed model for CFS developed by Jameson [6], it was identified that various theories for viruses leading to findings that deconditioning, exercise avoidance and cognitive behavioral factors do not satisfactorily explain the etiology of CFS as there is not a single virus to depict this circumstance or condition [6]. CFS is frequently co-morbid with fibromyalgia, multiple chemical sensitivity, irritable bowel syndrome and temporomandibular joint disorder [6].

Role perspective suggests daughters are more inclined to care for their elderly parents along with spouses. In a study conducted with 23 of 41 daughters, it was identified that the daughters experienced more role overload due to juggling multiple responsibilities and other role demands [8]. Role overload often limits a daughters’ ability to engage with their families, which contributes to marital conflicts and disruption with their children. In response to role overload, daughters tended to prioritize familial responsibilities by restricting their participation in leisure activities and employment responsibilities, resulting in reduced partici-

pation of other leisure or social activities [8].

2. Background

The World Stroke Organizations (WSO) identified modifiable factors that contribute to stroke and listed the following metabolic risks (high systolic blood pressure (SBP), high body-mass index (BMI), high fasting plasma glucose (FPG), high total cholesterol, and low renal function or reduced renal perfusion (low glomerular filtration rate) account for 71.0% of the stroke burden and behavioral factors including smoking, poor diet, and low physical activity account for 47.0% of the stroke burden [2]. All contributing factors identified as leading to stroke include: dietary risk factors, such as dietary risks for a diet high in sodium, high forms of red meat, a diet low in fruits, vegetables, or whole grains (30.0%), high body mass (BMI) index qualifies for those above a BMI of 25% (23.6%), smoking (17.1%), high fasting glucose (20.1%), alcohol use (5.8%), high LDL cholesterol (9.6%), impaired kidney function (8.2%), and low physical activity (1.8%) WSO, 2023). While atrial fibrillation and flutter (AF) are well-established as risk factors for ischemic stroke, however they are not currently included in the global burden of disease for the calculated stroke burden estimate per WSO data collection [9].

During the first-year post-stroke, in a study of 83 stroke victims under the age of 75 years who were recovering from their first stroke being cared for by their female spouses caring for male survivors reported lower life satisfaction [10] and were more often depressed, generally. Berg *et al.*, [11] conducted a study of 98 caregivers of new onset stroke survivors during their first 18 months of recovery and found 30% to 33% of all caregivers were depressed during the 18-month follow-up. In addition, in a study conducted with 1002 spouses or companion caregivers who were faced with physical, psychosocial, and emotional problems were more exposed to burnout, particularly if they are women and if they are older [12]. Stroke survivors experience physical impairments require family caregiver support in their selfcare (help with showering, dressing, taking transport, preparing food, managing the shopping) and with mobility (walking, managing stairs, bending down while unsteady on their feet, standing for any length of time). As a consequence of strokes, family members may perceive themselves to be in a constant low life satisfaction state as observed by Baumann & Bucki [13] within their study findings that those family caregivers with low life satisfaction were more likely to perceive themselves as in a permanent state of fatigue and to feel that caregiving was taking all their physical strength. This constant fatigue may be attributable to the constant disruptions in their routine activities related to their caregiving role that make finding time for relaxation and social life difficult. Daughters identified as caregivers were creative to come up with work options such as “Telecommuting” as a form of flexible work arrangement could allow caregivers to maintain employment while simultaneously attending to their parent’s changing care needs [8]. Expanded leave options may optimize job per-

formance and contribute to securing daughters' jobs in times of prolonged absence, thereby reducing the need to permanently disengage from an employment opportunity [8]. Because there is a need for more interventions in web-based formats that focus on caregiver psycho-education and skills building research has focused on this formatting intervention [14].

3. Research

A pilot study was devised by Jordan *et al.* [14] to determine the feasibility, acceptability, and value of an active, 4-week telephone and web-based intervention for stroke caregivers. The study consisted of one group, who underwent pretest and posttest designs using a mixed-methods approach for online web-based training to evaluate problem-solving abilities and health-related quality of life topics. Seventy-eight percent of caregivers rated the intervention sessions with the nurses as very helpful or extremely helpful, and 76% reported using the problem-solving strategies a moderate amount to extremely often. Interviews suggest that the intervention was valuable and led to new strategies to relieve stress and prioritize health. Topics included in the training and discussion included education for stroke care, factsheets about strokes, after strokes, personality changes associated with strokes, rapport building strategies, communication techniques, fall prevention, and managing medicines to name a few of the covered topics. The identified interviews did show a promise for other web-based instruction as the individuals experienced a feasible intervention with valuable instruction that led to new strategies to relieve stress and to prioritize their health needs, however, the study showed no change in the problem-solving or health-related quality of life itself showed no change [14].

Denno *et al.* [15] identified in a study conducted with 153 caregivers 18 years or older who cared for stroke survivors during a two-year period, that there was an increase in caregiver burden was associated with significantly poorer mental health of informal caregivers of stroke survivors with spasticity. The study revealed anxiety and depression as physician identified medical conditions that were self-reported by the caregiver and depression severity was measured by the Patient Health Questionnaire-9 (PHQ-9). The caregiver burden was measured by the Oberst Caregiving Burden Scale (OCBS) and the Bakas Caregiving Outcomes Scale (BCOS). Logistic regression analyses were conducted with anxiety, depression, and the PHQ-9 depression severity categories as a result of each caregiver burden scale. The caregivers were predominantly white women, who participated in the informal online study of caregivers of stroke survivors with spasticity. The research recognized the Oberst Caregiving Burden Scale (OCBS) tool, the 15-item questionnaire that demonstrated rates for 15 different types of caregiving tasks for stroke survivors based on perceived time (OCBS-Time) and difficulty (OCBS-Difficulty) of the task and the results showed the odds of anxiety was 2.57 times as great ($P < 0.001$) and for depression the results were 1.88 times as great ($PZ.007$) for those caregivers caring for stroke survivors with spas-

ticity, [15].

In a study by Michael, *et al.*, [8] conducted with 53 men and women of ages between 48 - 84 years who were experiencing hemiparetic gait deficit related to their stroke with noted asymmetry of their gait, reduced stance time or increases swing time of the affected limb, were evaluated on a 10-minute timed walk test after six months of traditional post-stroke rehabilitation therapy and it was determined that they these individuals remained at mild to moderate risk for fall.

Fens, *et al.* [16] conducted several homecare visits during a period of 18 months to instruct patients and caregivers for stroke care through a stroke care coordinator service and reviewed process related factors have to evaluate the effectiveness of interventions. In that study period, various topics and activities were introduced that required instruction and training. Some of these topics included activities of daily living (ADLs) (bathing, toileting, dressing, eating), various social activities such as communication tools, instructions for cognition, psycho-emotional status, fatigue, and topics related to caregiver strain and other medical conditions/ consumption, and financial concerns were items instructed and discussed with patients and caregivers during the training period. The results demonstrated effective interventions for improving the levels of social activities, caregiver awareness of support services and resources [16] [17].

A systematic review to evaluate caregiving outcomes after a stroke with synthesized results were identified by Gaugler [18] and found that duration of care did not emerge as a significant predictor of stroke caregiving outcomes in most cross-sectional quantitative studies. Terms such as identified caregiver stress, depression, and subjective health measures did not tend to demonstrate significant change in the 117 longitudinal quantitative studies reviewed from the original 1188 studies selected. In a study conducted by through telephone interviews of informal caregivers by Navaie-Waliser, *et al.*, [12] generated by a nationally representative cross-section of 4874 households' eligible candidates for study inclusion was restricted to persons aged 18 years or older who were directly providing unpaid care or arranging for paid care to a relative or friend at any time during the 12 months preceding the study. The study was conducted with 1002 the vulnerable caregivers who were identified with poor health or a serious health condition and they were compared with nonvulnerable caregivers revealed 36% of vulnerable caregivers were more likely to have difficulty providing care or providing higher-intensity care. Those vulnerable caregivers who were also aged 65 years or older, married, and having less than 12 years of education reported that their physical health had suffered since becoming a caregiver.

PSF interventions were investigated as a systematic review by Wu *et al.* [3], to investigate if interventions were available to reduce the post-stroke fatigue. They researched international databases for 12,490 citations and obtained 58 studies and 12 clinical trials for their research into the interventions to offset post-stroke fatigue. Many of the studies were small and revealed limited evidence to suggest any interventions were successful for effective treatment of PSF during the 2008-

2014 time period. Ultimately, the conclusion determined some interventions appeared hopeful and should be investigated as randomized control trails utilizing a larger, more robust sample size [3]. In the study conducted by Michaels, *et al.* [4], their research identified self-reported and self-rated fatigue that was more severe was indicative of the reduction in physical function, exercise behavior and self-motivation resulting in the lowest levels of self-confidence for performing ADLs. Falls efficacy was predictive of fatigue or PFS and fatigue severity was not predictive of ambulatory activity, but the Berg Balance Scale scoring did emerge as the main determinant of ambulatory activity in the study conducted by Michael *et al.* [4]. The PSF individuals reported significantly lower social support networks as compared to those who did not report fatigue with their physical limitations, which is more telling for participation of therapy and overall negative outcomes and perception of about disability contributing to social isolation [4].

A consensus group identified the top 10 research priorities cited by Pollack *et al.* [5] relating to life after stroke have been identified using a rigorous and person-centered approach. These should be used to inform the prioritization and funding of future research relating to life after stroke. The consensus group members were identified as follows: Twenty-eight people (16 stroke survivors/caregivers and 12 health professionals) attended a final consensus meeting on 16 November 2011. Health professionals included stroke physician (1), nurse (1), physiotherapist (2), occupational therapist (2), speech and language therapist (2), orthotist (1), orthoptist (1), neuropsychologist (1), and social worker (1). Pollock *et al.* [5], described six of the top 10 research priorities as focused on specific stroke-related impairments, including cognition, aphasia, vision, upper limb, mobility, and fatigue, which would be classified as “body functions” within the International Classification of Function, Disability and Health (ICF) framework. This consensus group determined “Living with a stroke” topics constituted three of the top ten themes while the remaining top topics were associated with secondary consequences of stroke and classified as activities and participation. The top ten questions to explore [5] are listed as follows:

- What are the best ways to improve understanding (cognition) after stroke?
- What are the best ways of helping people come to terms with the long-term consequences of stroke?
- What are the best ways to help people recover from aphasia?
- What are the best treatments for arm recovery and function?
- What are the best ways to treat visual problems after stroke?
- What are the best ways to manage and/or prevent fatigue?
- What are the best treatments to improve balance, gait, and mobility?
- How can stroke survivors and families be helped to cope with speech problems?
- What is the best way to improve confidence after a stroke?
- Are exercise and fitness programs beneficial at improving function and qual-

ity of life and avoiding subsequent stroke?

4. Health-Related Quality of Life Measures

Wai-Kwong Tang, *et al.* [19] discuss the health-related quality of life (HRQOL) scoring that is gaining acceptance as an important measure of outcome in stroke research. In clinical practice, apathy is commonly defined as a lack of, or diminished response for emotion, interest, concern, and motivation, manifesting as poor engagement with significant others and in social activities, and a loss of pleasure in usual interests. Apathy has a negative influence on recovery after stroke, particularly in terms of daily functioning and cognition. Apathy Evaluation Scale, clinician version (AES-C) and the self-reported Barthel Index (BI), a frequently used measure in stroke rehabilitation, assessed the extent of patients' disability in carrying out daily functions. In the study by Wai-Kwong Tang, *et al.* [19], stroke survivors with and without apathy differed in terms of gender (sex, women), lower education level, diabetes mellitus, neurologic deficits, and cognitive and physical impairments; depressive symptoms were associated with apathy after stroke. The mental health aspect of HRQOL demonstrated a significant association for apathy in stroke survivors. There is evidence that the prevalence of apathy drops over time: the rate of apathy was 21.7% at baseline and was 17.9% at 15 months after stroke. These authors also suggested that almost 21.7% of patients with apathy after stroke recovered from apathy, but 18.1% of patients who were nonapathetic developed apathy by the 15-month follow-up [19].

5. Caregiver Burden

Wai-Kwong Tang, *et al.* [20], studied the predictive factors of family caregivers' burden in Chinese stroke patients in Hong Kong. Caregivers' burden was assessed with the Caregiving Burden Scale (CBS) in a study of 1232 stroke individuals. The results in the univariate analysis, the CBS score had significant correlations with certain characteristics of caregivers (sex, GDS, HADS, depressive symptoms, fatigue, and MLES) and those of patients' (sex, age, education, GDS). Regression analysis revealed that caregivers' GDS and patients' education were the independent correlates of the CBS. The study conclusions determined the severity of depressive symptoms in Chinese stroke caregivers and patients' education are independent factors associated with the caregivers' burden.

Role strain may be amplified in family systems living in rural areas due to limited access to resources. It is important for medical professionals such as couples therapy, marriage counselors, and family therapists to understand what facets of stroke disability are linked with caregiver strain as well as to explore and understand various interventions that may ease caregiver burden [21]. Factors evaluated for caregiver role strain included time dependency, development, physical health, emotional health, and social relationships [22]. In a study conducted by Peng *et al.*, [21] there were 177 pairs of stroke survivors and their caregivers/family members who were studied for caregiver role strain. The catego-

ries with the highest impacts for caregiver burden were caregiver physical health (84%), social relationships (89%), caregiver development (91%), caregiver emotional health (7%) and time dependency (78%) followed by patient physical functioning (33%) having an impact on the caregiver [21].

Family caregivers can make a significant impact on the recovery of their loved one who has experienced a stroke. The functional deficits of the victim alone are not the only issue when dealing with an individual's post CVA. Fens, *et al.* [16] [17] conducted studies of 77 stroke patients, 59 caregivers and 4 stroke care counselors (SCC) participated in a study to evaluate follow-up care after stroke, but there is no consensus about the way to organize follow-up care for stroke patients and caregivers. The intervention showed favorable effects on the level of social activities, specifically. The intervention consisted of home visits during an 18-month period post-stroke hospital discharge. The home visits were conducted by the SCC using a structured assessment tool. The objective of this study was to examine process-related factors that could have influenced the effectiveness of the intervention. Stroke patients and caregivers were very satisfied with the intervention. A caregiver's motivation and empathy are a bigger part of the recovery process. Jin, *et al.* [23] discussed the poststroke care status and highlighted the impact of caregiver mood states, caregiver fatigue, and caregiver empathy in their study which demonstrated caregiver fatigue was the only mood state significantly associated with empathetic responses towards the poststroke victims. Mood states may be transient and fluctuating. It is important for caregivers to understand their emotional status, factors progressing or impacting worsening fatigue, and the effects of physical limitations for the caregiver role of a stroke survivor to minimize caregiver role strain. Higher caregiver fatigue was associated with lower empathetic scores [23].

6. Caregiver Knowledge

Ang, *et al.* [24] identified knowledge gaps through their literature review of Caregivers' ability to cope with these stroke survivor challenges that indirectly affect the recovery of the stroke survivors. The aim of their literature review (for the years 2002 to 2012) was to synthesize and summarize the existing knowledge about how family caregivers cope while caring for people with stroke, and the coping strategies they adopt. The six major themes of coping strategies identified in their literature review search are: 1) letting nature takes its course; 2) learning the ropes of caregiving; 3) making changes to integrate caregiving; 4) expressing thoughts and emotions; 5) using psycho-socio-spiritual strategies; and 6) depending on social support.

In the studies conducted by Fens, *et al.* [16] [17] to evaluate follow-up care after stroke, it was revealed that the main problems experienced by the stroke patients and caregivers were being identified for their physical needs in the care of the patient. The biggest risk factor for caregivers was identified as physical fatigue and that issue was the most important problem throughout the 18-month

follow-up period. Risk factors for caregiver burn-out were studied by van de Heuvel, *et al.* [25] and identified those risk factors for burn-out amongst caregivers of stroke patients living at home. During a study conducted with 63 stroke patients during 2000, van de Berg, *et al.* [26] noted that those with the highest levels of strain are at higher risk for caregiver burn-out. Factors for increased risk of caregiver strain include physical health of the caregiver, mental well-being, coping strategies, resources available, and caregiver vitality. The conclusion identified women, younger caregiver's, caregivers in poor physical health, and those who had patients with severe changes because of their stroke effects were at highest risk for burn-out. A review of the caregiver characteristics, resources, available and additional coping strategies were considered for the influence for a caregivers coping abilities, their mental well-being and vitality as influences for predictability of burn-out in caring for those who had severe emotional, cognitive changes, and behavioral as well as physical consequences for their stroke had significant negative impact on the caregiver, particularly for women and younger caregivers who may not have the physical stamina, other obligations (work), or a lack of resources available to perform the required care [25]. The importance of active coping strategies to off-set risks for burn-out was discussed in the research.

7. What Can Be Done?

Reducing the overall stroke risk will also minimize the risk for caregiver's need. Factors influencing caregiver fatigue and increased caregiver burnout are associated with the things not within the caregiver's immediate control, such as post-stroke fatigue and the limitations this present physically for the caregiver, reduced cognition post stroke can be very labile and fluctuant depending on the demands and thus the situation may change for day to day or within the day, depending on how much is required of the post-CVA patient. Communication becomes challenging when the brain is disrupted so recognizing various forms of communication may also be unfamiliar to a caregiver. The physical demands required for taking care of the post-stroke patient will also be worn on the caregiver as the ADLs and IADLs needs built during the care delivery. It would be important to offer community services for family caregiver support to assist with the direct care needs for post-stroke survivor to assist with showering, dressing, food preparation, shopping, pr transportation services, having hired or volunteer support to assist with mobility needs, such as walking, managing stairs, bending down while unsteady on their feet, standing for any length of time to prevent injuries for both the post-CVA victim or the caregiver who may not be physically able or aware of their own self-care safety risks.

We recognize that stroke support organizations need to be in locations accessible to the population, but the importance of these may not be recognized. Governments, and system leaders, need to arrange for public health announcements and available through public health facilities for those at greatest risk with

limited resources and funding. Public health organizations need to increase efforts for raising awareness, educating individuals and populations of their risk factors, implement more effective and widely available stroke risk prevention strategies (for example, the free Stroke Riskometer app supported by the WSO and already translated into 19 languages and available [9]). Health-care providers need to stay abreast the guidelines for prevention, raise awareness for disease risks, and be more diligent in the management of the various disease processes that impact the risk factors for strokes. Post-CVA healthcare services should be widely available for the ongoing post-CVA needs and caregiver education/training. The general population needs to become more aware of their behaviors, habits, and life choices that increase their own risk factors but also need to modify their diet and exercise, reduce their alcohol intake, and become more aware of symptoms that lead to strokes. Reducing the overall stroke risk will also minimize the risk for caregiver's need.

8. Discussion

Expanding the discussion for risk factors associated with strokes opens up the conversation of behaviors and lifestyle choices that increase the risk of stroke by 87%. Choosing to exercise, encouraging a healthy diet, staying at a healthy BMI, preventing smoking, avoiding over-consumption of alcohol, and minimizing disease processes that put people at risk are areas to focus upon. Reducing the overall stroke risk will also minimize the risk for caregiver's need. Factors influencing caregiver fatigue and increased caregiver burnout are associated with the things not within the caregiver's immediate control, such as post-stroke fatigue and the limitations this present physically for the caregiver, reduced cognition post stroke can be very labile and fluctuant depending on the demands and thus the situation may change for day to day or within the day, depending on how much is required of the post-CVA patient. Communication becomes challenging when the brain is disrupted so recognizing various forms of communication may also be unfamiliar to a caregiver. The physical demands required for taking care of the post-stroke patient will also wear on the caregiver as the ADLs and IADLs needs built during the care delivery.

Many studies have demonstrated predictable stroke caregiver outcomes such as role strain, burn-out, depression and anxiety over time. Analyzing and using the research to determine the risk factors and solutions for risk are important aspects for caregiver selection and training. Stroke support groups and other resources are typically available in larger communities or in locations where there are hospitals providing care for stroke patients. Solutions to the problem include support groups, utilizing resources, training and education as well as sharing the burden of care of the stroke patient through resources for caregiver support services—that may offer a necessary link for preservation of the caregiver; may prevent caregiver fatigue; reduce caregiver stress; and permit more supportive services to assist in care delivery to reduce the physicality of being a caregiver. Pub-

lic education for risk factors associated to nutrition, diet, a healthy BMI, exercise, tobacco use, alcohol consumption, and modifiable diseases that put people at higher risk for stroke need to be made aware in the educational system when children are young. Families need to be familiar with the factors related to stroke, and the symptoms recognized as those of an impending stroke. Everyone needs to have access to healthcare services and public health funding needs to be utilized for conditions that impact high numbers of people, such as strokes. Additional services for education and training may also relieve the caregiver of untoward physical demands through ergonomics and exercise, which may also demonstrate understanding prior to experiencing struggles for adapting as a caregiver through the various educational courses to train the caregiver for transitions in care [18].

Much research reports it is essential for caregivers to take time to prioritize their own personal and mental care needs. Many services do exist for those who wish to have supportive services such as community resources like respite care, adult day care, home health services, meal programs, and homemaker assistance help for both the stroke survivor and the caregiver. National stroke organizations may be the first step in offering resources or services in your area.

Exploration Questions

- At what cost does a family and their caregivers experience the effects of a stroke?
- Are there enough follow-up care programs to support communities and to offer appropriate resources for caregivers' utilization?
- What physical activities might a caregiver need to undergo in preparation or physical readiness to prepare for the post stroke family member?
- Are there insurance plans or other programs available for purchase in caring for a stroke victim?
- What types of resources are necessary to offset the burden of post stroke fatigue?

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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