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Effects of Uncertainty on Perceived and Physiological Stress and Psychological Outcomes in Stroke-Survivor Caregivers

Abstract

Caregiver status is a known risk factor for morbidity and mortality. In the time period immediately after a stroke, high levels of uncertainty about the family member's recovery and the sudden assumption of a new caregiver role may be acutely stressful. Little is known, however, about caregivers' experiences in the very early period of caregiving or how caregiver stress may contribute subsequently to health. The purpose of this study was to examine the effect of uncertainty on caregiver perceived and physiological stress and psychological outcomes (burden, health-related quality of life [HRQOL] and depressive symptoms) within 2 weeks poststroke (baseline) and at 6 weeks poststroke. In addition, the mediator effect of stress on the relationship between uncertainty and psychological outcomes was explored. A prospective, longitudinal observational study was conducted using a convenience sample of 63 caregivers and their stroke-survivor relatives recruited from acute-care settings in two academic health-science centers. Multivariate stepwise regression was used to achieve the overall aim of this study. Additionally, multivariate regression was used to explore the mediator effect of stress on the relationship between uncertainty and psychological outcomes. Level of uncertainty at baseline was higher than reported in several other caregiver populations and it remained so at 6 weeks poststroke. Greater level of uncertainty was associated with higher perceived stress at baseline ($p < 0.001$) and at 6 weeks poststroke ($p < 0.001$). Uncertainty, however, was not a significant predictor of physiological stress at either time point. Overall, greater uncertainty was associated with greater burden ($p < 0.001$ at baseline and $p = 0.031$ at 6 weeks poststroke), poorer HRQOL ($p < 0.001$ at baseline and $p = 0.023$ only in univariate analysis at 6 weeks poststroke) and greater depressive symptoms ($p = 0.002$ at both observations). By 6 weeks poststroke, perceived stress fully mediated the relationship between uncertainty and depressive symptoms. Healthcare providers in neuroscience must become sensitized to caregiver uncertainty in the early period of caregiving. Using uncertainty as a predictor may help identify caregivers at risk for stress, burden, poor HRQOL or depressive symptoms, that is, those in need of additional support. Further research exploring uncertainty and the development and testing of target interventions for it may reduce the early uncertainty and stress of caregivers of stroke survivors and prevent negative longer term health outcomes.

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EFFECTS OF UNCERTAINTY ON PERCEIVED AND PHYSIOLOGICAL STRESS
AND PSYCHOLOGICAL OUTCOMES IN STROKE-SURVIVOR CAREGIVERS

Eeeseung Byun

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EFFECTS OF UNCERTAINTY ON PERCEIVED AND PHYSIOLOGICAL STRESS
AND PSYCHOLOGICAL OUTCOMES IN STROKE-SURVIVOR CAREGIVERS

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Eeeseung Byun

DEDICATION

To my husband, Marc Swingler, my parents, Changwon Byun and Yangsun Lee, my sister, Meeseung Byun and my niece, Eunsu Song, for their unwavering love, support and encouragement.

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ABSTRACT

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Eeeseung Byun

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so at 6 weeks poststroke. Greater level of uncertainty was associated with higher perceived stress at baseline ($p < 0.001$) and at 6 weeks poststroke ($p < 0.001$). Uncertainty, however, was not a significant predictor of physiological stress at either time point. Overall, greater uncertainty was associated with greater burden ($p < 0.001$ at baseline and $p = 0.031$ at 6 weeks poststroke), poorer HRQOL ($p < 0.001$ at baseline and $p = 0.023$ only in univariate analysis at 6 weeks poststroke) and greater depressive symptoms ($p = 0.002$ at both observations). By 6 weeks poststroke, perceived stress fully mediated the relationship between uncertainty and depressive symptoms. Healthcare providers in neuroscience must become sensitized to caregiver uncertainty in the early period of caregiving. Using uncertainty as a predictor may help identify caregivers at risk for stress, burden, poor HRQOL or depressive symptoms, that is, those in need of additional support. Further research exploring uncertainty and the development and testing of target interventions for it may reduce the early uncertainty and stress of caregivers of stroke survivors and prevent negative longer term health outcomes.

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CHAPTER 1: INTRODUCTION

In the United States, approximately 66 million people serve as informal caregivers of family members or friends who are older, chronically ill or disabled (National Alliance for Caregiving and AARP, 2009). Caregiver status is a known risk factor for morbidity and mortality (Haley, Roth, Howard, & Safford, 2010; Schulz & Beach, 1999). Further, immune-system suppression in caregivers is quite common (Bauer et al., 2000) and a meta-analysis reports that stress hormones such as cortisol are elevated in caregivers (Vitaliano, Zhang, & Scanlan, 2003). Although the literature on the long-term effects of caregiving is well developed, little is known about either the immediate period (within the first 2 weeks) when a family or friend initially assumes the caregiver role, or the long-term consequences for caregivers of their experiences during this period. To better understand what occurs during this early period, which may impact caregiver outcomes, I studied stroke-survivor caregivers. This population exemplifies those who encounter the uncertainties and other stressors associated with a family member's sudden, serious health event (Brereton & Nolan, 2002; Burman, 2001; Forsberg-Warleby, Moller, & Blomstrand, 2001; Hunt & Smith, 2004; O'Connell, Baker, & Prosser, 2003) and subsequent caregiver-role assumption. Caregiving in this population is associated with stressors related to both physical and psychological health as well as related morbidities and illness-related symptoms, such as depression (Anderson, Linto, & Stewart-Wynne, 1995; Bauer et al., 2000; Berg, Palomaki, Lonnqvist, Lehtihalmes, & Kaste, 2005; Blake, Lincoln, & Clarke, 2003; Burman, 2001; Forsberg-Warleby, Moller, & Blomstrand, 2002; McCullagh, Brigstocke, Donaldson, & Kalra, 2005; Pierce, Steiner, Hicks, & Holzaepfel, 2006; White, Mayo, Hanley, & Wood-Dauphinee, 2003), hypertension and

angina (White et al., 2003).

Background

Stroke is a common global phenomenon, with more than 15 million stroke cases annually worldwide (Mackay & Mensah, 2004). Stroke caregiving is also an important public health problem in the United States where approximately 795,000 new or recurring strokes occur each year. Of these, a large proportion—65%—occurs among adults aged 65 and older (Lloyd-Jones et al., 2009). More than 7 million stroke survivors live with poststroke effects in the United States (National Stroke Association, 2013), and 40% have permanent moderate-to-severe impairments (National Stroke Association, 2013). Because of these impairments and associated functional deficits (Forsberg-Warleby et al., 2001, 2002; Visser-Meily et al., 2009), stroke survivors often require assistance from caregivers in performing activities of daily living. Because stroke is usually a sudden event, family members must abruptly assume the role of informal caregiver without an opportunity to adjust. In contrast, family members of persons with a chronic illness can more gradually adapt to the caregiver role. These differences in caregiver populations warrant further investigation.

In the United States, the length of stay in the hospital after stroke averages 5.7 days; within 30 days, all stroke survivors will have been discharged to home (31%), home with home-health services (15%), rehabilitation hospitals (20%) and/or skilled nursing facilities or other long-term care (34%; Kind, Smith, Frytak, & Finch, 2007). Given that caregivers need to assume their new role as informal caregivers in a relatively short period of time, they may experience uncertainty, stress and early signs of burden associated with these new caregiving experiences. A beginning literature review

suggested that burden may be present as early as 10 days to 30 days poststroke (Bugge, Alexander, & Hagen, 1999; Forsberg-Warleby et al., 2001, 2002). Not surprisingly, caregivers report physical and physiological health problems when measured months to years after their relative's stroke event (Anderson et al., 1995; Berg, Palomaki, Lehtihalmes, Lonnqvist, & Kaste, 2003; Berg et al., 2005; White, Lauzon, Yaffe, & Wood-Dauphinee, 2004).

Informal caregivers contribute “activities and experiences that provide help and assistance to relatives or friends who are unable to provide for themselves” (Pearlin, Mullan, Semple, & Skaff, 1990, p. 583). The general literature on caregiving demonstrates several stress-related outcomes including higher mortality rates in those with greater emotional strain (Schulz & Beach, 1999), increased risk for stroke in spousal caregivers reporting higher strain (Haley et al., 2010) and increased coronary heart disease in female spousal caregivers (S. Lee, Colditz, Berkman, & Kawachi, 2003).

Perceived stress (self-reported) is typically reflected in physiological stress, including elevated neuroendocrine mediators such as cortisol and norepinephrine (Morgan et al., 2002). Acute stress is associated with a disruption in circadian rhythms (Fève-Montange et al., 1981) and, after exposure to acute stress, elevated levels of plasma and salivary cortisol (Morgan et al., 2002). In a laboratory study of caregivers whose spouses suffered from dementia, Cacioppo et al. (2000) found that when caregivers were exposed to a stressor, they had higher blood pressures and heart rates than noncaregivers. These results signify higher sympathetic activation (Cacioppo et al., 2000), which is indicative of acute stress response. It is not known, however, whether stress hormones are elevated in caregivers experiencing acute stress in a natural or

clinical environment (vs. the laboratory) or in those caring for persons with disorders other than dementia, a question explored in the present study.

Among psychological outcomes for stroke-survivor caregivers, prevalence of depression is known to be high (23% to 33%; Berg et al., 2005; Blake et al., 2003) and longer term outcomes include caregiver burden (Blake et al., 2003; Bugge et al., 1999; Forsberg-Warleby et al., 2001; Tooth, McKenna, Barnett, Prescott, & Murphy, 2005) and decreased health-related quality of life (HRQOL; White et al., 2004).

A study of caregivers' responses in the early poststroke period is critical to understanding the role of uncertainty and stress as potentially modifiable factors affecting caregiver health outcomes. There is currently little information that addresses the relationship between caregiver uncertainty and psychological outcomes. This study adds to the body of knowledge about the early period of caregiving by including, at two distinct time points, measures of uncertainty as well as perceived and physiological stress and caregiver psychological outcomes.

Purpose

The high levels of uncertainty about both the family member's recovery following a stroke and the sudden assumption of a new caregiver role may be acutely stressful, and yet little is known about the caregivers' experience in the first 2 to 6 weeks of caregiving or how it may contribute subsequently to caregivers' health. Thus, the overall purpose of this study was to examine the effect of uncertainty on caregiver perceived and physiological stress and psychological outcomes (burden, HRQOL and depressive symptoms) within the first 6 weeks of caregiving following a sudden, serious health event in a family member: stroke.

Aims and Hypotheses

I implemented a prospective, longitudinal observational study design during the time period immediately poststroke (within 2 weeks, T1) and 4 weeks later (when stroke survivors were at home, in rehabilitation hospitals or in nursing facilities, T2) to study the following aims:

Aim 1: Determine at each time point if uncertainty (regarding stroke survivors' health outcomes and new caregiver role) predicts levels of caregivers' perceived stress.

H1: At each time point, greater uncertainty scores will be positively associated with higher levels of perceived stress.

Aim 2: Determine at each time point if uncertainty predicts levels of caregivers' physiological stress (salivary cortisol).

H2: At each time point, greater uncertainty scores will be positively associated with elevated levels of salivary cortisol.

Aim 3: Examine at each time point the relationship of uncertainty to psychological outcomes (burden, HRQOL and depressive symptoms).

At each time point, greater uncertainty scores will be positively associated with

H3: greater burden,

H4: poorer HRQOL and

H5: greater depressive symptoms.

Aim 4: Explore at each time point the mediator effect of stress (perceived stress and physiological stress) on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms).

At each time point, perceived stress and salivary cortisol will mediate the relationship between uncertainty and

H6: burden,

H7: HRQOL and

H8: depressive symptoms.

Significance of the Study

The uncertainty associated with the early caregiving experience (within the first 6 weeks of the sentinel event) may predict the caregiver's experience and its consequences over time. If uncertainty during this period is found to contribute significantly to stress, it may be possible to develop interventions to reduce uncertainty and thereby contribute to healthier outcomes for caregivers over time. For example, persons with higher levels of baseline uncertainty had higher levels of anxiety and depression and lower levels of perceived control and HRQOL 1 year after angiography compared to those with lower levels of baseline uncertainty (Eastwood, Doering, Roper, & Hays, 2008). Thus, the study results could inform early interventions that may have long-term impact. Further, the study contributes important information regarding perceived and physiological stress during the early caregiving experience and its association with uncertainty and with psychological outcomes of caregiving.

In addition, it is not known whether stress hormones are elevated in caregivers of stroke survivors or, indeed, among any caregivers experiencing new, acute stress. By including direct measures of salivary cortisol as well as measures of caregiver psychological, behavioral and environmental factors that influence hypothalamic-pituitary-adrenal reactivity (HPA) in the brain, any change that occurs in the early period

of caregiving can be further illuminated (Pearlin et al., 1990) and, perhaps, suggest areas for further intervention. For example, a stress-management program targeting areas related to stress revealed in this study may reduce caregiver perceived stress and elevated cortisol levels and prevent stress-related illnesses.

Understanding the impact of caregiver uncertainty on perceived stress, physiological stress and psychological outcomes in the early weeks of caregiving is essential in designing a future intervention study aimed at preventing related morbidities in caregivers. Further, timely intervention resolving uncertainty and reducing caregiver stress may help family members better cope in their role as informal caregivers and result in better health outcomes for themselves and the stroke survivor.

Given the high prevalence of stroke, efforts to shore up the informal-caregiving system, which may reduce healthcare costs by protecting the health of family caregivers, are vital to public health. These findings also may be salient in a variety of other caregiving situations when care recipients experience a sudden or serious health event, such as brain injury or myocardial infarction.

CHAPTER 2: REVIEW OF LITERATURE

This chapter comprises a synthesis and evaluation of the existing literature on family caregivers of stroke survivors and suggests fruitful areas for confirmation or further exploration. The chapter is organized into four sections. Section one is the conceptual framework for this study. Section two is a discussion of each of the main variables in the study described from the perspective of existing literature: (a) uncertainty and its relationship to perceived and physiological stress and psychological outcomes including caregiver burden, health-related quality of life (HRQOL) and depression/depressive symptoms; (b) stress including perceived and physiological stress; (c) psychological outcomes including caregiver burden and HRQOL and depression/depressive symptoms; and (d) relevant caregiver and stroke-survivor characteristics. Section three provides a summary of known factors affecting caregiver outcomes. Finally, a summary of gaps in the literature and the current study solutions are presented.

Conceptual Framework

Mishel's uncertainty-in-illness model (Mishel, 1988) and Schulz's caregiver-coping model (Schulz, Tompkins, & Rau, 1988) informed the conceptual framework proposed to explore how uncertainty may influence caregiver perceived stress, physiological stress and longer term psychological outcomes including burden, HRQOL and depressive symptoms. Mishel's model explains that uncertainty occurs when decision makers cannot define meaning for illness-related events, predict what will happen next or predict the consequences from the event (Mishel, 1981). Uncertainty is a neutral concept that can be perceived either as danger or opportunity (Mishel, 1981, 1988). When

perceived as danger, people cope by trying to adapt to the situation and thereby resolve uncertainty (Mishel, 1997a).

In addition to Mishel's uncertainty-in-illness model (Mishel, 1988), Schulz' caregiver-coping model, used with caregivers for stroke survivors (Schulz et al., 1988), suggested the majority of variables used in this study. Schulz' caregiver-coping model identifies patient characteristics (e.g., functional status including independence in activities of daily living, patient affective state, manifestations of disability and prognosis) and caregiver characteristics (e.g., health, income, social support, satisfaction with social contacts and coping strategies) affecting both caregiver perceived stress and caregiver outcomes (psychological well-being, life satisfaction, depression and physical well-being) as responses to that stress.

The resulting proposed conceptual framework (see Figure 1) specifies the relationships among the main variables of interest: uncertainty, caregiver stress (perceived and physiological stress) and psychological outcomes (burden, HRQOL and depressive symptoms). Uncertainty is directly associated with caregiver stress (perceived and physiological [salivary cortisol]). In addition, uncertainty is believed to directly affect psychological outcomes and also to have an indirect impact on these outcomes through their effects on caregiver stress, adjusting for covariates. Caregiver stress (perceived and physiological [salivary cortisol]) is also directly associated with psychological outcomes (burden, HRQOL and depressive symptoms), adjusting for covariates. Known covariates affecting stroke-survivor caregiver outcomes include caregiver characteristics (comorbidity, coping capacity, social support and sociodemographics) and stroke-survivor characteristics (severity of stroke, functional

status, comorbidity and sociodemographics).

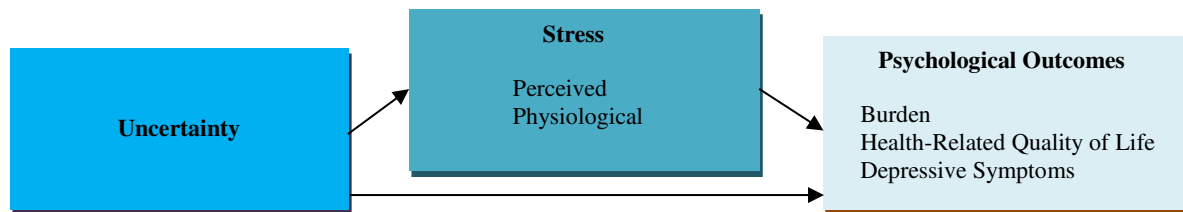


Figure 1. Conceptual framework.

Note. Derived from Mishel’s Uncertainty-in-Illness Model (Mishel, 1988) and Schulz’s Caregiver-Coping Model (Schulz et al., 1988).

Uncertainty

According to the uncertainty-in-illness model, uncertainty is defined as the “inability to determine the meaning of illness-related events” (Mishel, 1988, p. 225) and includes four dimensions: (a) ambiguity about the illness state; (b) complexity regarding available information, treatment, the healthcare system and relationship with healthcare providers; (c) lack of information about the diagnosis, seriousness of the illness, treatment and symptoms; and (d) unpredictability of the illness course and prognosis (Mishel, 1988). When people perceive uncertainty as danger, they try to cope with the situation and resolve uncertainty, for example, by seeking knowledge or information or adopting health-promoting behavior (Mishel, 1997a). Caregivers of stroke survivors are not certain what to expect either in the disease trajectory or how fully the stroke survivor will recover (Brereton & Nolan, 2002; Forsberg-Warleby et al., 2001; Hunt & Smith, 2004; O’Connell et al., 2003). Uncertainty arises when the decision maker cannot anticipate outcomes because of lack of resources or information (Mishel, 1997a). Caregivers’ uncertainty about stroke survivors’ outcomes from lack of information or

knowledge may be heightened because of the very real difficulty in the early poststroke period to predict just how much physical or cognitive impairment will remain (Forsberg-Warleby et al., 2001; O'Connell et al., 2003). In contrast, by 1 year poststroke, recovery is relatively stable (Anderson et al., 1995). Because stroke has a sudden onset, family members need to adjust to a new relationship with stroke survivors and take on new responsibilities as informal caregivers, potentially without adequate support or knowledge (Coombs, 2007). Thus, in this study, uncertainty is defined as caregivers' inability to determine the meaning of stroke survivors' health outcomes and the new caregiver role.

The concept of uncertainty in adults with chronic disease or cancer is well established and parents' uncertainty about the prognosis of children with cancer has also been documented in the current literature. Few researchers, however, have systematically studied uncertainty in caregivers for persons with acute or chronic disorders. Northouse, Laten, and Reddy (1995) reported that caregivers of persons with breast cancer had greater uncertainty about the patients' illness than did the patients themselves and also had difficulty adjusting to their new role. In another study, uncertainty in caregivers for persons with breast cancer was correlated with caregiver emotional distress and caregiver role adjustment (Northouse, Dorris, & Charron-Moore, 1995). Mitchell and Courtney (2004) reported that uncertainty in family caregivers around transfer from intensive care was significantly related to anxiety. As previously noted, persons with higher uncertainty at baseline had poorer health outcomes (e.g., higher levels of anxiety and depression and lower levels of perceived control and HRQOL) 1 year after angiography than those with lower uncertainty at baseline (Eastwood et al., 2008). Regardless, caregivers' uncertainty

in the early weeks of caregiving, not only for stroke survivors, but also for patients with other disorders, has not been well explicated.

Uncertainty and stress.

Uncertainty and perceived stress. The impact of uncertainty on caregiver perceived stress has not yet been made clear. One study reported that a mother's uncertainty about her infant's HIV serostatus was related to the mother's perceived stress (Shannon & Lee, 2008). Uncertainty in illness was also correlated with posttraumatic stress symptoms in young-adult childhood cancer survivors (Santacrose & Lee, 2006). This study did not control for other covariates that may affect posttraumatic-stress symptoms; the results, however, indicate that uncertainty may be a potential factor that influences perceived stress in caregivers and is, thus, a target for intervention. Further, the results of this study regarding posttraumatic-stress symptoms as mediators between uncertainty and health-promotion behavior support one of the proposed hypotheses in this study, i.e., that perceived stress will mediate the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms).

Uncertainty and physiological stress. The relationship between uncertainty and physiological stress has not been investigated in the current literature. Mishel (1990) noted that chronically ill persons who are uncertain can develop symptoms related to pathological response to stressors. Caregivers for stroke survivors may have struggled with new responsibilities in their role as informal caregivers in the early poststroke period. Uncertainty regarding stroke survivors' outcomes as well as the new caregiver role is likely to be stressful. Understanding the relationship between uncertainty and physiological stress will expand knowledge in the current literature and contribute to

development of a biobehavioral model to guide a future intervention study.

Uncertainty and psychological outcomes.

Uncertainty and burden. The impact of uncertainty on caregiver burden has not been documented in the current literature. In a related study, 30% of 44 caregivers for patients with Parkinson's disease reported psychological distress, and uncertainty was a significant determinant for it (Sanders-Dewey, Mullins, & Chaney, 2001). In the existing literature, caregivers for stroke survivors conveyed caregiver burden beginning at least 1 month poststroke (Bugge et al., 1999). Whether early uncertainty influences later caregiver burden is not clear, and a study in the early weeks of caregiving is, thus, required to reveal this relationship. If found, relieving some of this early uncertainty may be important to decreasing later caregiver morbidity and mortality associated with burden.

Uncertainty and health-related quality of life. The relationship between uncertainty and HRQOL in caregivers for persons with recurrent breast cancer was studied by Northouse et al. (2002). Compared with estimated norms, caregivers for persons with breast cancer had lower (poorer) mean scores (mean 48.4, $p = 0.03$) in mental health dimensions of HRQOL, as measured by the Medical Outcomes Study SF-36. Mean scores in physical health dimensions of HRQOL, however, were similar to norm values. In their study, caregiver uncertainty was associated with mental health dimensions of HRQOL, adjusting for caregiver characteristics (age, education, self-efficacy, current concerns, family hardiness, social support and symptoms) as well as patient characteristics (symptom distress, stage of disease and length of the disease-free interval between stage of disease and recurrence). Eastwood et al. (2008) found worse HRQOL 1 year later in coronary angiography patients with high baseline uncertainty.

The influence of uncertainty on HRQOL in caregivers of stroke survivors, however, has not been documented in the current literature.

Uncertainty and depression or depressive symptoms. Depression or depressive symptoms are common in caregivers of stroke survivors, but, there is little research linking caregiver uncertainty and depression. Sanders-Dewey et al. (2001) reported that uncertainty in caregivers for individuals with Parkinson's disease was correlated with their depression, but no further predictive analysis was reported. Caregiver uncertainty about a family member's transfer from intensive care was significantly associated with anxiety (Mitchell & Courtney, 2004). Patients with higher levels of uncertainty than those with lower levels of uncertainty had more anxiety and depression at 1 year after coronary angiography (Eastwood et al., 2008). Further study is required to identify the impact of uncertainty on caregiver depression while controlling for known risk factors for depression in caregivers of stroke survivors, including the survivors' stroke severity and older age (Berg et al., 2005) and caregivers' social support (Grant et al., 2006).

Stress

Perceived stress. Caregivers' perceived stress includes "domestic upset, negative feelings toward the patient and personal distress in relation to the patient" (Draper et al., 2007, p. 124). Caregivers experience higher perceived stress than do noncaregivers (Bauer et al., 2000) due to exposure to complex stressors (Pearlin et al., 1990). The literature on caregiving reported (Pearlin et al., 1990) that caregiving stressors can be broadly divided into two categories: primary (i.e., patient characteristics and caregivers' perspectives on these characteristics including cognitive status, behavioral symptoms and activities of daily living) and secondary (i.e., family conflict, job-caregiving conflict,

economic problems and constriction of social life).

Stress from caregiving has been associated with effects on health and risk factors for mortality. Caregivers with greater emotional strain have 63% higher mortality rates than do noncaregivers (Schulz & Beach, 1999). Spousal caregivers with higher strain have increased risk for stroke (Haley et al., 2010) and female spousal caregivers are at higher risk for coronary heart disease (S. Lee et al., 2003). In caregivers of stroke survivors, significant stress was reported within the first year poststroke and one of its significant predictors was the functional status of the stroke survivor. Related caregiver factors include caregiver gender, age, caregiver health, time since providing care for stroke survivors, coping strategy/capacity, social support and preparedness for caregiving (Ostwald, Bernal, Cron, & Godwin, 2009). With stroke's sudden onset, the early poststroke period may especially be acutely stressful for caregivers, but acute stress in caregivers during the early poststroke period has not yet been described.

After stroke, caregivers need to address and become accustomed to patients' functional deficits (Visser-Meily et al., 2009). In the acute stage of stroke, providers cannot anticipate exactly how much physical or cognitive impairment will remain (O'Connell et al., 2003), and the process of recovery from stroke is gradual. In the literature on family caregivers of stroke survivors, the concept of stress has been integrated with the explanation of caregiver burden. Little has been reported on perceived stress in the early weeks of caregiving.

Physiological stress. Perceived stress is correlated with physiologic response, including elevated neuroendocrine mediators such as norepinephrine or cortisol (Morgan et al., 2002). As an allostatic response, that is, the ability to achieve stability during

change (McEwen, 1998), stress stimulates the sympathetic nervous system as well as activates the hypothalamic-pituitary-adrenal (HPA) axis. Sympathetic nervous-system stimulation results in norepinephrine (catecholamine neurotransmitter) release from sympathetic nerves into target tissues and epinephrine release from adrenal medulla into circulation. The activation of the HPA axis causes the adrenal cortex to release glucocorticoids, principally cortisol in humans. Salivary cortisol has often been measured to assess stress in caregivers, especially those caring for dementia patients; these caregivers have an increase in cortisol levels (Bauer et al., 2000; Da Roza Davis & Cowen, 2001; de Vugt et al., 2005; Vedhara et al., 1999). Receptor-mediated actions of cortisol cause immunosuppressive and anti-inflammatory effects on target immune tissues and cells (Elenkov, Webster, Torpy, & Chrousos, 1999), and the immune system is known to be suppressed in caregivers of dementia patients (Vitaliano et al., 2003). One study reported diurnal salivary-cortisol patterns in caregivers of stroke survivors; levels of salivary cortisol were lower across the day in caregivers with greater depressive symptoms than in those with less (Saban, Mathews, Bryant, O'Brien, & Janusek, 2012). This study found that younger age was associated with lower levels of cortisol on waking and 30 minutes postwaking.

In the case of acute stress, a significant association with disrupted circadian rhythms, defined as a 24-hour cycle of physiological, biochemical and behavioral processes, was reported (Fève-Montange et al., 1981). After exposure to acute stress, levels of plasma and salivary cortisol and their ratios were significantly increased (Morgan et al., 2002) and acute stress also had long-term health implications (McEwen, 1998). The activation of the sympathetic nervous system releases catecholamines

resulting in a broad physiologic response (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997): increased blood pressure, heart rate, breathing rate and blood-glucose level and intensifies muscle tension (Preville, Zarit, Susman, Boulenger, & Lehoux, 2008). To date, physiologic response from acute stress in caregivers has been measured only in experimental settings. When caregivers of demented spouses were asked to provide care for their spouses in the laboratory, they had higher blood pressure and heart rate than did noncaregivers, indicating they were experiencing acute stress and higher sympathetic activation (Cacioppo et al., 2000).

In contrast to dementia, which is a chronic progressive disorder, stroke has a sudden onset and, thus, in the early poststroke period stroke-survivor caregivers are likely to experience acute stress. One study reported that levels of salivary cortisol were decreased across the day in caregivers with greater depressive symptoms compared with those with fewer depressive symptoms (Saban et al., 2012). It is not well known whether stress hormones are elevated, decreased or affected at all in caregivers of stroke survivors when they first confront their new role as a caregiver in a natural environment. Caregivers may also experience stress due to their own personal problems in addition or unrelated to their family members' sudden onset of stroke or their new caregiving situation. Thus, in this study I attempted to capture these other precipitants by asking caregivers about their other potentially stressful life events in the past 3 months (e.g., death, moving, retirement and marriage).

Salivary cortisol. Salivary cortisol has often been used as a biomarker of psychological stress. The salivary-cortisol level is reliable in assessing the variation in endocrine activity and response to acute stress (Fève-Montange et al., 1981). One

advantage of salivary cortisol is that one can measure the free unbound fraction of cortisol because it is the last output of the HPA axis that remains high in acute stress with its disruption of circadian rhythms (Feve-Montange et al., 1981; Hellhammer, Wust, & Kudielka, 2009). In addition, salivary cortisol acts independently of competition with other steroid hormones to bind cortisol globulin (Woods et al., 2008). Salivary cortisol is correlated with serum cortisol (Kirschbaum & Hellhammer, 1994; Shimada, Takahashi, Ohkawa, Segawa, & Higurashi, 1995) and contains up to 10% of serum cortisol (Woods et al., 2008). Assessing salivary-cortisol levels in caregivers of stroke survivors can contribute to a better understanding of caregiver stress.

Psychological Outcomes

Burden. Caregiver burden for stroke survivors refers to family members' feelings of being overwhelmed and strained in assisting their care recipients (Elmstahl, Malmberg, & Annerstedt, 1996). The general concept of caregiver burden itself is dynamic. Zarit, Todd, and Zarit (1986) defined caregiver burden as "the extent to which caregivers perceived their emotional or physical health, social life and financial status as suffering as a result of caring for their relative" (p. 261). Although in the current literature the term "demand" has been recently used to describe caregiver burden, the majority of the literature on caregiving in stroke survivors continues to use the term "burden." Thus, "caregiver burden" was used in this study.

Objective burden is defined as "caregiving situations" such as "the caregiving tasks that are performed, like assistance with self-care, mobility, instrumental activities and financial management and the time spent on each task" (van Exel, Koopmanschap, van den Berg, Brouwer, & van den Bos, 2005, p. 12). One third of caregivers for stroke

survivors reported they were burdened by household responsibilities and caregiving (Thommessen, Wyller, Bautz-Holter, & Laake, 2001).

Subjective burden is defined as “the psychological, social or emotional impact caregivers experience from the objective burden of caregiving” (van Exel et al., 2005, p. 12) or “the distress experienced” (Thommessen et al., 2002, p. 79). Few studies distinguish between objective burden and subjective burden, rather reporting on burden in general.

As demonstrated in existing literature, caregivers reported a sense of burden from at least 1 month to 1 year poststroke (Blake et al., 2003; Bugge et al., 1999; Forsberg-Warleby et al., 2001; Tooth et al., 2005). Of spousal caregivers of stroke patients, 34% reported burden at 3 months poststroke and 40% had burden at 6 months poststroke (Blake et al., 2003). Significant burden was reported in the first 12 months poststroke (Tooth et al., 2005). Some studies reported that burden of caregivers decreased over time, that is, baseline to 6 months (McCullagh et al., 2005; Vincent, Desrosiers, Landreville, Demers, & BRAD group, 2009), whereas others revealed that caregiver burden continued from 2 months to 6 months (Ilse, Feys, de Wit, Putman, & de Weerd, 2008) or from 1 month to 6 months (Blake et al., 2003; Bugge et al., 1999).

Several caregiver sociodemographic factors are known predictors for burden: relationship to stroke survivors (Van Puymbroeck & Rittman, 2005), gender (Bugge et al., 1999), age (Periard & Ames, 1993; Schulz et al., 1988; van Exel et al., 2005), time spent helping the survivors (Bugge et al., 1999) and coping capacity (Cameron & Gignac, 2008; Forsberg-Warleby et al., 2001; Van Puymbroeck & Rittman, 2005; Visser-Meily et al., 2009). Stroke-survivor characteristics affecting burden include functional status (Ilse

et al., 2008), cognitive impairment (Thommessen et al., 2001) and communication loss/aphasia (Vincent et al., 2009). HRQOL of caregivers at 6 months poststroke is also strongly related to caregiver burden (van Exel et al., 2005). The effect of uncertainty on caregiver burden, however, has not yet been studied.

Health-related quality of life. Quality of life is a broad concept that includes HRQOL. Quality of life can reference personal well-being or satisfaction with life. HRQOL focuses aspects on perceived health or illness. General caregiving literature reports that quality of life of caregivers is lower than that of noncaregivers (Roth, Perkins, Wadley, Temple, & Haley, 2009). Caregivers of stroke survivors also experienced decreased HRQOL from 1 month to several months poststroke (White et al., 2004). Increased caregiver burden was associated with decreased caregiver HRQOL (Larson et al., 2005; van Exel et al., 2005; Van Puymbroeck & Rittman, 2005), especially in the area of mental health (Morimoto et al., 2003). Caregiver HRQOL was predicted by caregiver age and gender (McCullagh et al., 2005). New caregivers of stroke survivors must confront issues of independence and managing comorbid conditions in stroke survivors, balance roles (e.g., caregiver, spouse and employee) and participate in physical therapy (Pierce et al., 2006). They must also deal with a number of factors affecting themselves and stroke survivors: emotions such as depression or anger, living with physical limitations and sleep problems (Pierce et al., 2006). These factors may affect their HRQOL. Uncertainty was associated with the mental health dimensions of HRQOL in caregivers for persons with recurrent breast cancer (Northouse et al., 2002). Whether uncertainty affects HRQOL in caregivers of stroke survivors, however, has not been studied.

Depression/depressive symptoms. Prevalence of depression is high among caregivers of stroke survivors; as many as 23% to 33% of caregivers experience depression during the 18-month follow-up period poststroke (Berg et al., 2005; Blake et al., 2003). Bakas, Kroenke, Plue, Perkins, and Williams (2006) reported that 18% of caregivers for stroke survivors had moderate depressive symptoms. In their study, an additional 18% of caregivers who were taking antidepressant medications showed no depressive symptoms, suggesting that approximately 36% of caregivers of stroke survivors may have symptoms of depression (Bakas, Kroenke, et al., 2006). Predictors for depression in caregivers include severity of stroke and older age of stroke survivors (Berg et al., 2005), caregiver social support (Grant et al., 2006), race, gender, hours spent providing care per day (Van Puymbroeck, Hinojosa, & Rittman, 2008) and younger age (Saban et al., 2012). Positive aspects of caregiving that protect against depression in caregivers of stroke survivors were also reported: a high sense of coherence at 1 month poststroke was associated with less depressive symptoms at 12 months poststroke (Van Puymbroeck et al., 2008). A longitudinal study reported moderate caregiver depression in 2% of participants at baseline, 6% at 6 months poststroke and 9% at 18 months poststroke (Berg et al., 2005). Whether caregiver uncertainty influences depression, after adjusting for other known factors, has not been studied.

Relevant Caregiver and Stroke-Survivor Characteristics

Caregiver characteristics.

Comorbidity and health status. Comorbidity is defined as the presence of coexisting diseases or conditions with reference to an initial diagnosis or the index condition that is the subject of study (Webster's Online Dictionary, 2011). Caregivers of

stroke survivors have comorbidities (Hodgson, Wood, & Langton-Hewer, 1996) and confront new physical-health issues, comorbid issues and high numbers of illness-related symptoms including depression (Anderson et al., 1995; Bauer et al., 2000; Berg et al., 2005; Blake et al., 2003; Burman, 2001; Cameron & Gignac, 2008; Forsberg-Warleby et al., 2002; McCullagh et al., 2005; Pierce et al., 2006; White et al., 2003). Of caregivers of stroke survivors, 54% already had preexisting medical conditions, including arthritis, vertigo or back problems that can influence their caregiving for stroke survivors over time (Hodgson et al., 1996). Caregivers studied during the first and second year poststroke reported a range of disorders including hypertension, arthritis, cataracts, bronchitis, angina, history of myocardial infarction, diabetes, asthma and ulcer disease (White et al., 2003). Reported psychological symptoms included depression, fear, frustration, resentment, impatience, guilt (Anderson et al., 1995), anxiety (Anderson et al., 1995; McCullagh et al., 2005), worry, concern (Cameron & Gignac, 2008), anger (Pierce et al., 2006) and fear about the recurrence of stroke or other medical complications in their family members (Forsberg-Warleby et al., 2002).

In addition to comorbidities, caregivers' own perceived health status also affects their experience of burden (Bugge et al., 1999) and HRQOL (Morimoto et al., 2003). Comorbidity of caregivers is believed to influence the relationship between uncertainty, perceived stress and caregiver outcomes. Thus, in this study, the effect of comorbidity on outcomes was controlled.

Coping capacity. Coping is defined as “one’s ability to respond to stressors by the appropriate use of adaptive coping resources” (Chumbler, Rittman, Van Puymbroeck, Vogel, & Qin, 2004, p. 944). When individuals confront stressful life events, they use

strategies to cope and adapt to the situation to decrease harmful effects that may arise from stress or to reduce emotional distress as a response to the event (Visser-Meily et al., 2009). Coping capacity has been highly associated with burden (Cameron & Gignac, 2008; Forsberg-Warleby et al., 2001; Van Puymbroeck & Rittman, 2005; Visser-Meily et al., 2009), quality of life (Visser-Meily et al., 2009) and depression (Visser-Meily et al., 2009) in caregivers of stroke survivors. Thus, the effects of coping capacity on caregiver perceived and physiological stress and psychological outcomes (burden, HRQOL and depressive symptoms) in the early poststroke period were examined.

Social support. Social support is defined as caregivers' perceptions about the availability of relationships that provide help or support them and prevent negative outcomes from the stressful event (Sherbourne & Stewart, 1991). Less perceived availability of social support predicted depression in caregivers of stroke survivors (Grant, Bartolucci, Elliot, & Giger, 2000), whereas caregivers of stroke survivors who reported more perceived social support had less depression (Grant et al., 2006). Caregivers who reported greater satisfaction with social support had less caregiver strain (van den Heuvel, de Witte, Schure, Sanderman, & Meyboom-de Jong, 2001). Furthermore, social support was a significant determinant of better well-being and general health in caregivers (Grant et al., 2006).

Sociodemographics. Caregivers' burden has been shown to be associated with their sociodemographic characteristics. The relationship to patients with stroke was a predictor of caregiver burden: spousal caregivers at 1 month poststroke report higher levels of burden than nonspousal caregivers (Van Puymbroeck & Rittman, 2005). Gender also appeared to be important: the majority of caregivers are women, and female

caregivers experience greater caregiver burden than do male caregivers (Bugge et al., 1999). Caregivers of stroke survivors spend significant time assisting patients with daily activities (Tooth et al., 2005): approximately 4.6 hours per day at 6 months poststroke and approximately 3.6 hours per day at 12 months poststroke (Tooth et al., 2005). The time spent helping stroke survivors was associated with caregiver strain at 1, 3 and 6 months poststroke (Bugge et al., 1999). Age was also one of the predictors of caregiver burden at 6 (van Exel et al., 2005), 7 or 9 months after stroke (Schulz et al., 1988). In contrast, in at least one study, the caregiver-burden score decreased as the age of participants increased (Periard & Ames, 1993). Predictors of caregiver quality of life at 3 months and 1 year poststroke have also been shown to include age and gender (McCullagh et al., 2005). Women caregivers had lower psychological well-being, which in turn, was related to lower quality of life (Larson et al., 2008).

Stroke-survivor characteristics.

Severity of stroke. Severity of stroke or resulting level of impairment also affects caregiver outcomes. In a study of 212 caregivers for stroke survivors, severity of stroke was found to be related to caregiver strain (van den Heuvel et al., 2001). Moderate impairment from stroke, together with a number of other factors, explained 56% of the variance in caregiver HRQOL (Berg et al., 2005; White et al., 2003). Berg et al. (2005) found that caregiver depression was predicted by severity of stroke in stroke survivors, whereas no such relationship was found in another study (Davis et al., 2009). Additional work to explore the association between severity of stroke and caregiver outcomes, including depressive symptoms, is required; these associations are clarified in the present study.

Functional status. In this study, functional status is defined as a stroke survivor's motor and cognitive ability to perform activities of daily living. Stroke occurs when blood flow in the brain is interrupted by obstruction or hemorrhage of blood vessels (Nestler, Hyman, & Malenka, 2009). The specific lesions caused by stroke may predict the resulting types of neurological impairments. Broadly, physical performance, including motor or sensory performance, is affected by impairment of the sensorimotor cortex (Kunesch, Binkofski, Steinmetz, & Freund, 1995). Both location and size of damage as a result of stroke are related to resultant motor function (Chen, Tang, Chen, Chung, & Wong, 2000). Because of these neurological impairments and related impaired functional status, stroke survivors often require assistance from caregivers to perform activities of daily living (Forsberg-Warleby et al., 2002; Visser-Meily et al., 2009). Some investigators have reported that stroke survivors' functional status predicts caregiver stress (Ostwald et al., 2009), burden (Ilse et al., 2008) and time spent providing care (Tooth et al., 2005), whereas others reported no such association with caregiver burden (Morimoto et al., 2003), emotional illness (Anderson et al., 1995) or quality of life (White et al., 2003).

The prevalence of cognitive impairment after stroke ranges from 30% to 40% (del Ser et al., 2005; Nestler et al., 2009; Patel, Coshall, Rudd, & Wolfe, 2002; Tatemichi et al., 1994). When patients' stroke is located in the cerebellar region, more than 80% of survivors have cognitive deficits (Kalashnikova, Zueva, Pugacheva, Korsakova, & Zueva, 2005). Stroke in the prefrontal cortex mainly affects cognitive function, emotion, decision making or behavior, but is not involved in motor, sensory or language function (Nestler et al., 2009). Poststroke cognitive impairment was associated with low functional status in

stroke survivors (Patel et al., 2002; Tatemichi et al., 1994) and, for their caregivers, with low quality of life (White et al., 2003) and higher burden (Thommessen et al., 2001).

Communication. Of stroke survivors, 21 to 38% experience aphasia (loss of communicative ability), including impaired language understanding or expression (Berthier, 2005). Aphasia was associated with caregiver burden (Vincent et al., 2009) and decreased quality of life (White et al., 2003). Caregivers for stroke survivors with aphasia rated communication as the most upsetting factor to them (Bakas, Kroenke, et al., 2006). They also reported having more difficulty with caregiving tasks than did caregivers for stroke survivors without aphasia (Bakas, Kroenke, et al., 2006). Although communication is essential to overall functional status, it is not necessarily included as a specific item in functional-status assessment. Thus, I addressed communication separately in this study.

Comorbidity. Comorbidity is defined as the presence of coexisting diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study (Webster's Online Dictionary, 2011). Stroke survivors themselves often have comorbid diseases, as the major risk factors of stroke include hypertension, dyslipidemia, cigarette smoking, diabetes mellitus, carotid stenosis, arterial fibrillation and valvular heart disease (Hankey, 2006). Additionally, 95% of ischemic stroke survivors have medical complications (Johnston et al., 1998). Although few studies have reported any association between stroke-survivor comorbidity and caregiver outcomes, one recent investigation found that stroke survivors' chronic medical conditions (as measured by the Charlson Index, a tool that does not include depression screening measures) were not significant factors influencing caregiver depression; however, stroke-survivor depression was highly associated with caregiver depression (Davis et al., 2009).

Sociodemographics. Caregivers experience more strain when stroke survivors are older (Berg et al., 2005). The present study focused exclusively on caregivers of stroke survivors aged 65 or older in an effort to reveal the impact of age (e.g., the oldest old, such as those 85 years of age or older) on caregiver outcomes. Other stroke-survivor sociodemographics have not been found to be significant factors affecting caregiver outcomes. This study further clarifies the relationship between stroke-survivor sociodemographics and caregiver outcomes.

Summary of Known Factors Affecting Caregiver Outcomes

Table 1 summarizes known factors affecting caregiver stress, burden, HRQOL and depression or depressive symptoms in caregivers of stroke survivors. (To my knowledge, with the exception of one study by Saban et al. (2012), direct measurement of physiological stress in caregivers of stroke survivors has not been studied.) What is not well known, however, is whether these same characteristics affect caregiver stress in the early poststroke period, nor is the role of uncertainty in caregiver perceived or physiological stress and these same psychological outcomes known.

Table 1

Summary of Known Factors Influencing Caregiver Stress and Psychological Outcomes (Burden, Health-Related Quality of Life and Depressive Symptoms) in Caregivers of Stroke Survivors

Outcomes	Factors influencing Outcomes
Stress	
Perceived	Caregiver gender, age, caregiver health, time since providing care for stroke survivors, coping strategy/capacity, social support, preparedness for caregiving and number of close friends and relatives; stroke-survivor function (Ostwald et al., 2009)
Physiological	Caregiver younger age (Saban et al., 2012)
Psychological Outcomes	
Burden	Caregiver relationship to the stroke survivor (Van Puymbroeck & Rittman, 2005), age (Periard & Ames, 1993; Schulz et al., 1988; van Exel et al., 2005), gender, time spent helping the stroke survivor, health status (Bugge et al., 1999) and coping capacity (Cameron & Gignac, 2008; Forsberg-Warleby et al., 2001; Van Puymbroeck & Rittman, 2005; Visser-Meily et al., 2009); stroke-survivor functional status (Ilse et al., 2008), cognitive impairment (Thommessen et al., 2001) and communication loss/aphasia (Vincent et al., 2009)
Health-Related Quality of Life	Caregiver age, gender (McCullagh et al., 2005), health status (Morimoto et al., 2003) and coping capacity (Visser-Meily et al., 2009)
Depression/Depressive Symptoms	Caregiver social support (Grant et al., 2006), race, gender, hours spent providing care per day (Van Puymbroeck et al., 2008) and younger age (Saban et al., 2012); severity of stroke and older age of stroke survivors (Berg et al., 2005)

Gaps in the Literature and Current Study Solutions

Although the literature on the long-term effects of caregiving is well developed, little is known about the immediate, early period after an acute event that precipitates assumption of the caregiver role by a family member or friend. Thus, this study incorporated prospective and longitudinal aspects to explore whether the level of uncertainty about stroke survivor's health outcomes as well as uncertainty about assuming a new role predict caregiver perceived stress, physiological stress and psychological outcomes (burden, HRQOL and depressive symptoms) in the early poststroke period.

The literature review confirmed that the effect of uncertainty on perceived stress has not been clearly differentiated. Researchers have studied mothers' uncertainty about infant HIV serostatus (Shannon & Lee, 2008) and uncertainty in young-adult childhood-cancer survivors (Y. L. Lee, 2006; Santacroce & Lee, 2006), and revealed the correlation between uncertainty and stress. These investigators failed, however, to control for other factors that may influence perceived stress. Further, to my knowledge, the relationship between uncertainty and perceived stress in caregivers of stroke survivors has not been documented. Thus, a study of caregivers' responses in the early poststroke period is critical to understanding the role of uncertainty and stress as potential factors affecting caregiver outcomes.

No studies regarding the influence of uncertainty on caregivers' physiological stress have been found in the current literature. In studies of caregivers of stroke survivors, the concept of stress has more often been integrated with the operational definitions of caregiver burden or HRQOL, rather than treated as a separate concept, or

measured solely as perceived stress. Only one study was found that included direct measurement of physiological stress in caregivers of stroke survivors. The present study contributes to filling important gaps in the current literature.

This study is innovative not only in measuring immediate physiological stress, but also by assessing the association of uncertainty with psychological outcomes (burden, HRQOL and depressive symptoms) 1 month after the first interview (around 6 weeks poststroke). There is limited information that addresses the relationship between uncertainty and caregiver psychological outcomes. Examining the mediating effect of caregiver stress (perceived and physiological [salivary cortisol]) on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms) at each of these two time points is essential to begin to fill in these gaps.

The robust biological and behavioral data collected are critical to prevention of untoward sequelae, resulting in better long-term health outcomes for caregivers. The findings may inform the development of a biobehavioral theoretical model that can serve as a foundation for future intervention studies. These intervention studies may result in supporting care-related decisions, preventing disease and promoting long-term health in caregivers.

CHAPTER 3: RESEARCH DESIGN AND METHODS

Research Design and Study Overview

A prospective, longitudinal observational study was conducted using a convenience sample of caregivers and their stroke-survivor relatives recruited from acute-care settings in two Philadelphia academic health-science centers. Caregivers were enrolled and entered in the study within the first 2 weeks following their relatives' stroke (T1) and revisited 4 weeks later (T2; ~ 6 weeks post stroke). This design enabled me to gain comprehensive information about the influence of uncertainty at two separate time periods during the early poststroke period. The study involved quantitative measures of caregiver and stroke-survivor characteristics and outcomes to allow the testing of hypotheses about relationships among the variables of interest (Burns & Grove, 1997). Participant enrollment and data collection for the entire study were completed over an 8-month period; each participant was actively involved for approximately 4 weeks. Overall data analysis of study aims was conducted at the University of Pennsylvania School of Nursing. Salivary-cortisol assays were analyzed at the University of Pennsylvania Pearlman School of Medicine Clinical and Translational Research Center. The specific aims for the study were:

Aim 1: Determine at each time point if uncertainty (regarding stroke survivors' health outcomes and new caregiver role) predicts levels of caregivers' perceived stress.

Aim 2: Determine at each time point if uncertainty predicts levels of caregivers' physiological stress (salivary cortisol).

Aim 3: Examine at each time point the relationship of uncertainty to psychological outcomes (burden, health-related quality of life [HRQOL] and depressive symptoms).

Aim 4: Explore at each time point the mediator effect of stress (perceived stress and physiological stress) on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms).

Sample and Settings

The convenience sample of caregivers, the primary participants for this study, and their stroke survivors were recruited from the large neurology and neurosurgery services at the Hospital of the University of Pennsylvania and the Thomas Jefferson University Hospital/Jefferson Hospital for Neurosciences in Philadelphia, PA. Caregivers' relatives with stroke were also enrolled in order to collect relevant medical information from their medical records.

To be included in the study, caregivers had to (a) self-identify as a family member, (b) self-identify as the expected primary caregiver for an older adult (age 65 or older) who was diagnosed within the past 2 weeks with new or recurrent ischemic or hemorrhagic stroke, (c) communicate in English, (d) demonstrate capacity for informed consent (see the consent capacity guide in Appendix N) and (e) be 21 years old or older.

Given the higher incidence of stroke in older adults, this study enrolled only caregivers whose relatives were age 65 or older. In addition, all stroke survivors (a) had a family caregiver participating in the study, (b) had been diagnosed with new or recurrent stroke, (c) were within the first 2 weeks of stroke onset and (d) agreed (either self or surrogate) to a medical-chart review.

Power Analysis

Because this study spans only 1 month per participant, I did not expect significant attrition. Originally, I proposed to enroll a total of 115 subjects to account for an attrition rate of 15% for a sample size of 100. In 2009, the Hospital of the University of Pennsylvania admitted approximately 1,000 adults over age 65 with stroke (ICD9 code range 430–438); thus, I expected little difficulty in enrolling 115 subjects. Power estimation was based on a sample size of 100 with the assumed ability to accrue 115 caregivers and satisfy Aim 1, regressing caregiver perceived stress on uncertainty using multiple regression. Ostwald et al. (2009) published that predictors for caregiver perceived stress (perceived stress scale) were caregiver gender, caregiver age, caregiver health, time since providing care for stroke survivors, stroke-survivor function, coping strategy, social support, preparedness for caregiving and number of close friends and relatives. I ran a power analysis based on findings from a published study of uncertainty and distress in family caregivers for persons with Parkinson's disease (Sanders-Dewey et al., 2001) and a series of values corresponding to variance in perceived stress in stroke-survivor caregivers, explained by nine covariates (caregiver gender, caregiver age, caregiver health, time since providing care for stroke survivors, stroke-survivor function, coping strategy, social support, preparedness for caregiving and number of close friends and relatives). Using an *F*-test with 0.05 significance level, a sample size of 100 would achieve 98% power to detect an *R*-squared of 0.11 attributed to one independent variable, namely uncertainty, accounting for 20% of variance explained by the nine control variables in caregiver perceived stress.

I enrolled a total of 63 participants at T1, however, and 40 of these remained and completed the study at T2. Thus, I recalculated power, based on sample size 40 and revealed *R*-Squared of uncertainty as well as covariates for Aim 1 at T2, regressing caregiver perceived stress on uncertainty using multiple regression. Using an *F*-test with a significance level of 0.05, the achieved sample of 40 participants had 99.6% power to detect an *R*-squared of 0.26 attributed to one independent variable, namely uncertainty. The variables tested were adjusted for an additional two independent variables associated with perceived stress at T2 (social support and stroke-survivor income), with an *R*-squared of 0.28.

Study Variables and Instruments

A paper and pencil survey was constructed that included instruments and items (see Appendices A–M) to measure each of the study variables. These are summarized in Tables 2 and 3. Additionally, participants self-collected and submitted samples of caregiver saliva at each time point. A chart abstraction form was used to obtain medical-record information about each stroke patient. The study variables and their measures are described here.

Uncertainty. The 31-item Perception of Uncertainty in Illness Scale for Family Members (Mishel, 1997b; see Appendix B) was used to measure caregivers' degree of uncertainty (inability to determine the meaning of illness-related events) regarding stroke survivors' health outcomes and the new caregiver role. Each of 31 items was scored on a scale of 1 (*strongly disagree*) to 5 (*strongly agree*). Total sum scores range from 31 to 155; high scores indicate greater uncertainty. In the present study, total sum score measured on a continuum was used for statistical analysis. Construct validity of the

Parent Perception of Uncertainty Scale (the original scale used to measure parents' perceptions of uncertainty by using the word *child* instead of *him/her*) is supported by correlation between factors and total scale ($r = 0.50\text{--}0.89$) as well as correlation between total score and the judged seriousness of their child's illness ($r = 0.16, p < 0.004$; Mishel, 1983). Internal consistency for the total scale is from 0.81 to 0.92 (Cronbach's alpha) for family caregivers (Mishel, 1997b). In the present study, Cronbach's alpha for the 31 items was 0.92 at T1 and 0.95 at T2.

Stress.

Perceived stress. The Perceived Stress Scale (PSS) includes 14 items designed to assess symptoms of stress and global measures of the degree of stress experienced in the last month including today (see Appendix C). In the present study, the time parameter was modified to ask about stress experienced in the past day (24 hours). This modification was made because the period of "the last month" would actually precede the occurrence of the serious health event in the family member: stroke; the value of interest is the stress that participants have experienced since the event. The same language was used for the T2 interview (4 weeks later), as the more recent experience of stress was viewed as most relevant to the study outcomes and also most comparable to the T1 measure. Items are related to how unpredictable, uncontrollable and overloaded respondents find their lives. Each item is scored from 0 (*never*) to 4 (*very often*) with total sum scores ranging from 0 to 56; higher scores indicate higher perceived stress. Total sum score measured on a continuum was used for statistical analysis in this study. One advantage of this instrument is that it has a normative value per age group (B. Cohen & Williamson, 1988) and the scale has been validated and correlated with depressive

($r = 0.65 - 0.76, p < 0.001$) and physical symptomatology ($r = 0.52 - 0.65, p < 0.001$) and social anxiety ($r = 0.37 - 0.46, p < 0.001$) in college students (S. Cohen, Kamarck, & Mermelstein, 1983). Cronbach's alpha of the PSS ranges from 0.84 to 0.86 (S. Cohen et al., 1983), and 0.91 in older African American and European American females (McCallum, Sorocco, & Fritsch, 2006), which represents the majority of participants in this study. Cronbach's alpha for the PSS in the present study was 0.86 at T1 and 0.88 at T2, indicating good internal consistency at each time point.

Physiological stress. Salivary-cortisol level is a reliable way to assess the variation in endocrine activity and response to acute stress (Fève-Montange et al., 1981). Salivary cortisol is highly correlated with serum cortisol: correlation coefficients range from 0.71 in patients with alpha-cholinergic medication to 0.96 in healthy older adults (Kirschbaum & Hellhammer, 1994). Sample collection was noninvasive, which can reduce the stress-inducing effects on cortisol levels by venipuncture (Stone et al., 2001) or burdensome 24-hour urine-specimen collection.

Cortisol levels follow a circadian rhythm (Preville et al., 2008); levels normally reach their peak in the early morning, and the concentration is lower at night (Chernow et al., 1987). Woods et al. (2008) reported that cortisol levels measured in the morning (09:00) and afternoon (16:00) in some samples did not coincide with a normal circadian rhythm pattern, whereas peak levels on waking and lower levels in the evening were generally consistent across samples. Cortisol dysregulation is more likely to be detected in the evening (Woods et al., 2008). Thus, it is also important to observe for higher cortisol levels in the evening by comparing the findings with normal levels in the evening. To capture diurnal variations in cortisol concentration in this study, caregivers collected

saliva using Salimetrics oral swabs on waking and again at 2100 h (see Appendix D; McCallum et al., 2006).

The Salimetrics salivary-cortisol kit is immunoassay designed and validated for detecting salivary-cortisol levels from .003 to 3.0 µg/dL using 25 µL of saliva per sample (Woods et al., 2008). The Salimetrics Kits' sensitivity is < 0.003 µg/dL (Salimetrics, 2011). Salivary cortisol using a Salimetrics enzyme immunoassay kit is highly correlated with serum ($r = 0.91$, $p < 0.0001$; Salimetrics, 2011). An inter-assay coefficient of variation is 6.41% across 12 runs and an intra-assay coefficient of variation is 3.65% (Woods et al., 2008). In the present study, an inter-assay coefficient of variation was 6.56% and intra-assay coefficient of variation was 4.61%. The minimum detectable limit was 0.010 µg/dL.

Psychological outcomes.

Burden. The Zarit Burden Interview scale includes 22 items related to “problems including caregivers’ health, psychological well-being, finances, social life and the relationship between the caregiver and the impaired person” (Zarit, Reever, & Bach-Peterson, 1980, p. 651; see Appendix E). The original Zarit Burden Interview had 25 items (Zarit et al., 1980), but the revised version with 22 questions is more widely used (Whitlatch, Zarit, & von Eye, 1991). Each item is scored from 0 (*never*) to 4 (*nearly always*). Total scores range from 0 to 88 (severe burden 61–88; moderate to severe burden 41–60; mild to moderate burden 21–40 and little or no burden 0–21; Zarit & Zarit, 1987). The sum score for two subscales—personal strain (six items) and role strain (12 items)—together with four items not included in any factor are commonly used as an overall measure of burden (Whitlatch et al., 1991). Thus, the total score measured on a

continuum was used for statistical analysis. Construct validity for the Zarit Burden Interview score is high (Seng et al., 2010); the Zarit Burden Interview score is highly correlated with the Burden Assessment Scale score ($r = 0.73, p < 0.0001$), General Health Questionnaire score ($r = 0.62, p < 0.0001$), Dementia Management-Strategies Scale score ($r = 0.53, p < 0.0001$) and Revised Memory and Behavior Problems Checklist score ($r = 0.53, p < 0.0001$). Cronbach's alpha ranges from 0.87 to 0.93 for caregivers of stroke survivors (Visser-Meily, Post, Riphagen, & Lindeman, 2004) and 0.89 for older caregivers of stroke survivors (Hartke & King, 2002). The test-retest reliability (Kappa) carries a value of 0.71 (Vitaliano, Young, & Russo, 1991). In the present study, Cronbach's alpha ranged from 0.92 at T1 to 0.94 at T2.

Health-related quality of life. The EQ5D of the EuroQol is a generic HRQOL measure that consists of five descriptive items (see Appendix F). Each question of the EQ5D investigates one of five concepts: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with scoring from 1 (*no problems or symptoms*) to 3 (*serious problems or symptoms*). Total score measured on a continuum was used for statistical analysis. The EuroQol has been demonstrated to be a valid and reliable measure of HRQOL in various populations (Dorman, Slattery, Farrell, Dennis, & Sandercock, 1998; Fransen & Edmonds, 1999; Hurst, Kind, Ruta, Hunter, & Stubbings, 1997; Schweikert, Hahmann, & Leidl, 2006). The validity correlation coefficients with the 36-item short-form health-survey subscales and EQ5D index score range from 0.57 to 0.74 in patients with acute coronary syndromes (Schweikert et al., 2006). The intraclass correlation coefficient is 0.70 (Fransen & Edmonds, 1999). Cronbach's alpha in an evaluation of HRQOL in patients with cancer was 0.68 (Pickard, Neary, & Cella, 2007).

In the present study, Cronbach's alpha was 0.48 at T1 and 0.59 at T2, which was minimally acceptable.

Depressive symptoms. The Patient Health Questionnaire (PHQ-9) is a 9-item scale used as a diagnostic screening measure for major and minor depression (see Appendix G). The items in the PHQ-9 correspond with the full range of symptoms listed in the *Diagnostic and Statistical Manual of Mental Disorders* major depressive-disorder category (Kroenke & Spitzer, 2002). This scale assesses the frequency of symptoms such as disinterest, low mood, sleep disruption or tiredness over the last 2 weeks, and each item is scored from 0 (*Not at all*) to 3 (*Nearly every day*). Total score ranges between 0 and 24 and severity of depression can be described as none (score 1 to 4), mild (5 to 9), moderate (10 to 14), moderately severe (15 to 19) and severe (20 to 27; Kroenke & Spitzer, 2002). Total sum score measured on a continuum was used for statistical analysis. This scale has demonstrated excellent internal consistency reliability ($\alpha = 0.86$ to 0.89), test-retest reliability ($r = 0.84$) and construct validity (correlation coefficients range from 0.33 to 0.73 between depression severity scores and worsening function with the subscale of the 20-item Short-Form General Health Survey; Kroenke, Spitzer, & Williams, 2001). Internal consistency reliability for caregivers of stroke survivors ranges from 0.80 to 0.86 (Bakas, Champion, Perkins, Farran, & Williams, 2006; Bakas, Kroenke, et al., 2006). In the present study, reliability was demonstrated by Cronbach's alpha of 0.84 at T1 and 0.86 at T2.

Caregiver characteristics: Covariates.

Comorbidity. A modified version of the Cumulative Illness Rating Scale (CIRS; Miller et al., 1992) was used to measure comorbidity, that is, the presence of coexisting

diseases in caregivers (see Appendix H). The CIRS total scores (Miller et al., 1992) range from 0 (*no impairment*) to 56 (*maximal impairment*) across 14 systems. Scoring of each system followed the guidelines proposed by Hudon, Fortin, and Vanasse (2005). The total sum score measured on a continuum was used for statistical analysis. The CIRS is valid and reliable in measuring multimorbidity, a condition with more than one chronic disease, in a family practice (Hudon et al., 2005). There is correlation ($r = 0.58, p < 0.02$) between the CIRS scores and the Older American Activities of Daily Living Scale scores (Miller et al., 1992). The intraclass correlation coefficients to evaluate multimorbidity by interviewing patients in a family practice ranges from 0.70 to 0.89 (Hudon et al., 2005). In the present study, Cronbach's alpha was not calculated because items (i.e., heart vs. lower gastrointestinal) are not necessarily closely related to others in the group.

Health status. A single index on the EuroQol, a visual-analog scale (VAS), was used to measure health status (see Appendix F). The VAS evaluates current perceived health status on a scale of 0 to 100, with 100 indicating the best imaginable health status. In the present study, the self-rated score measured on a continuum was used for statistical analysis. The validity correlation coefficients with the 36-item Short form Health Survey subscales and the VAS score range from 0.21 to 0.72 in patients with acute coronary syndromes (Schweikert et al., 2006). See the previous HRQOL section for validity and reliability of the overall EuroQol.

Coping capacity. A 13-item short-form version of the Sense of Coherence (SOC) tool (Antonovsky, 1987) was used to measure how well caregivers coped with stress associated with caregiving (see Appendix I). The SOC refers to "one's ability to respond to stressors by the appropriate use of adaptive coping resources" (Chumbler et al., 2004,

p. 944). Each item is scored from 1 (*never*) to 7 (*very often*), with total scores ranging from 13 to 91 where higher scores indicate greater coping. Total score measured on a continuum was used for statistical analysis. Construct-validity correlations between the SOC scale and the Self-Esteem Scale, the Mastery Scale (used to measure perception of control) and the Life Orientation Test (used to measure dispositional optimism) are 0.61, 0.54 and 0.53, respectively (Pallant & Lae, 2002). Internal consistency is 0.86 (Cronbach's alpha) for caregivers of stroke survivors (Chumbler et al., 2004). In the present study, Cronbach's alpha was 0.81 at T1 and 0.83 at T2.

Social support. Social support was measured using the Multidimensional Scale of Perceived Social Support (MSPSS; Zimet, Dahlem, Zimet, & Farley, 1988; see Appendix J). The MSPSS is a 12-item scale that assesses perceptions about support from family, friends and a significant other. Responses range from 1 (*very strongly disagree*) to 7 (*very strongly agree*) and higher scores indicate better levels of perceived social support. Total score measured on a continuum was used for statistical analysis. This scale shows excellent internal consistency ($\alpha = 0.92$), good test-retest reliability ($r = 0.85$) and moderate construct validity ($r = -0.13$ – -0.25 with anxiety and depression subscales of the Hopkins Symptom Checklist; Zimet et al., 1988). Internal consistency for caregivers of persons with traumatic brain injury is excellent ($\alpha = 0.95$; Davis et al., 2009). In the present study, Cronbach's alpha reliability scores were 0.94 at both T1 and T2.

Sociodemographics. Sociodemographics were assessed using a standard set of investigator-developed items (see Appendix A). The items included age, gender, race/ethnicity, native language, relationship to the stroke survivor (e.g., spouse or child), perceived quality of relationship with the stroke survivor (on a scale of 1 = *excellent* to

4 = *poor*), duration of caregiving role for the stroke survivor (prior to as well as since stroke), hours spent caring each day (prior to and since stroke), length of time since the stroke survivor was diagnosed with stroke, perceived level of preparedness for caregiving (on a scale of 1 = *well prepared* to 4 = *not at all prepared*), insurance type including Medicare/Medicaid, number of close friends and relatives, distance between site of care (e.g., hospital) and caregiver's home, education, employment status, income and other life events (e.g., death, moving, retirement or marriage) in the past 3 months (at T1). At T2, selected items including perceived quality of relationship with the stroke survivor, duration of caregiving role for the stroke survivor since stroke, hours spent caring each day since stroke, length of time since the stroke survivor was diagnosed with stroke, perceived level of preparedness for caregiving, distance between site of care and home and other life events since the first interview were assessed.

Stroke-survivor characteristics: Covariates.

Severity and description of stroke. Severity of stroke was operationalized by the National Institute of Health (NIH) Stroke Scale, a standard neurological examination tool that measures consciousness, language, neglect, visual-field loss, extraocular movements, motor strength, ataxia, dysarthria and sensory loss (see Appendix L). This scale has 13 items and total scores range from 0 (*not impaired*) to 42 (*fully impaired*). Total score measured on a continuum was used for statistical analysis. This tool has been shown to be reliable overall (Cronbach's alpha > 0.5) and highly validated (Brott et al., 1989; Goldstein, Bertels, & Davis, 1989; Lyden et al., 1994). The validity correlations between NIH Stroke Scale scores and stroke-lesion size and patient outcome are 0.68 and 0.79, respectively (Brott et al., 1989). The stroke survivor's medical chart was reviewed to

assess severity of stroke; the intraclass correlation coefficient was 0.82 in assessing neurological impairment by medical-chart review (Kasner et al., 1999). In the present study, Cronbach's alpha was 0.88. In addition, a chart-abstraction form was used to describe the type of stroke, area of the stroke, communication disability (yes/no) and time poststroke in days.

Functional status. Caregiver perception of the survivor's ability to perform activities of daily living was measured using the Barthel Index (Mahoney & Barthel, 1965; see Appendix M). The Barthel Index has 10 items that assess activities of daily living: self-care, continence of bowel and bladder and mobility. Each is scored from 0 to 15. Total scores range from 0 to 100 where higher scores indicate independence from any help. Total sum score measured on a continuum was used for statistical analysis. The Barthel Index has well-established validity and reliability in measuring the functional status of stroke patients (Wade & Hower, 1987; White et al., 2003). The validity correlations between the Barthel Index and the Motricity Index arm, leg, and total scores range from 0.73 to 0.77 on stroke patients (Wade & Hower, 1987). Cronbach's alpha with patients with stroke is 0.93 (White et al., 2003). Internal consistency in patients with stroke ranges from 0.87 to 0.92 (Shah, Vanclay, & Cooper, 1989). The intraclass correlation for caregiver proxy measure is excellent: 0.71 (Saban et al., 2012). In the present study, Cronbach's alpha was 0.94 at both T1 and T2.

Comorbidity. The modified version of the CIRS (Miller et al., 1992, see Comorbidity section in Caregiver Characteristics: Covariates) was used to evaluate the stroke survivor's comorbidity (the presence of coexisting or additional diseases) with reference to an initial diagnosis or with reference to the index condition, that is, stroke,

which is the subject of study (see Appendix H). Data were obtained by medical chart review. The scores of the CIRS (Miller et al., 1992), relative to its 14 systems, range from 0 (*no impairment*) to 56 (*maximal impairment*). This scale has been shown to be valid and reliable in evaluating comorbidity among geriatric populations (Hudon et al., 2005) and in institutionalized older adults (Parmelee, Thuras, Katz, & Lawton, 1995). There is a correlation ($r = 0.58, p < 0.02$) between the CIRS scores and the Older American Activities of Daily Living Scale scores (Miller et al., 1992). The intraclass correlation coefficients range from 0.66 to 0.87 and interrater reliability ranges from 0.80 to 0.89 in assessing comorbidity by medical-chart review in a family practice (Hudon et al., 2005). Total score measured on a continuum was used for statistical analysis. In the present study, Cronbach's alpha for the CIRS was not calculated because items (i.e., heart vs. lower gastrointestinal) are not necessarily closely related to others in the group.

Sociodemographics. Sociodemographic data were collected in the caregiver interview using a standard investigator-developed form (see Appendix K). At T1, caregivers provided stroke-survivor data: age, gender, race/ethnicity, education, employment status, income, insurance including Medicare/Medicaid and time in days since admission to the hospital. At T2, I obtained location (e.g., rehabilitation hospital, nursing facility or home) to which a stroke survivor was initially transferred after hospital discharge, site of current placement and time since admission to any facility or discharge to home. In addition, I assessed duration of rehabilitation including inpatient or outpatient, if relevant.

Table 2

Summary of Main Variables and Measures

Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Uncertainty	Inability to determine the meaning of illness-related events (i.e., stroke survivors' health outcomes and the new caregiver role)	Perception of Uncertainty in Illness Scale/ 31 items (Mishel, 1997b)	Total Score (31 to 155)/ Continuous	Correlation coefficient: 0.50–0.89 between factors and total scale/ 0.16 between total score and the judged seriousness of their child's illness in the Parent Perception of Uncertainty Scale (Mishel, 1983) Cronbach's alpha: 0.81–0.92 for family caregivers (Mishel, 1997b); Cronbach's alpha in the present study: 0.92 to 0.95	Caregiver Interview T1, T2
Perceived Stress	Domestic upset, negative feelings toward the patient and personal distress in relation to the patient	Perceived Stress Scale/ 14 items (S. Cohen et al., 1983)	Total Score (0 to 56)/ Continuous	Correlation coefficient: 0.65–0.76 with depressive and 0.52–0.65 with physical symptomatology and 0.37–0.46 with social anxiety in college students (S. Cohen et al., 1983) Cronbach's alpha: 0.84–0.86 (S. Cohen et al., 1983) and 0.91 in older African American and European American females (McCallum et al., 2006); Cronbach's alpha in the present study: 0.86–0.88	Caregiver Interview T1, T2

Table continues

Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Physiological Stress	Variation in endocrine activity and response to stressor	Salivary Cortisol level; collection at awaking to capture peak levels and at 2100h to capture lower levels using Salimetrics oral swabs (McCallum et al., 2006)	Cortisol in units: $\mu\text{g}/\text{dL}$ / Continuous	<p>Salivary cortisol reflects the variation in endocrine activity and response to acute stress (Feve-Montange et al., 1981) and is a reliable and valid reflection of cortisol in blood (Woods et al., 2008).</p> <p>Collecting salivary cortisol at awaking and in the evening can capture the circadian rhythm (Woods et al., 2008).</p> <p>Correlation between salivary cortisol using a Salimetrics Kit and serum cortisol: 0.91 (Salimetrics, 2011) Salimetrics Kits' Sensitivity: $< 0.003 \mu\text{g}/\text{dL}$; Inter-assay coefficient of variation (CV) across 12 runs: 6.41% (Woods et al., 2008) Intra-assay CV: 3.65% (Woods et al., 2008)</p> <p>Inter-assay CV in the present study: 6.56% Intra-assay CV in the present study: 4.61% Minimum detectable limit in the present study : 0.010 $\mu\text{g}/\text{dL}$</p>	Caregiver Self Collection T1, T2

Table continues

Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Burden	Caregivers' feelings of being overwhelmed and strained in assisting their care recipients	Zarit Burden Interview/ 22 items (Zarit & Zarit, 1987)	Total Score (0 to 88)/ Continuous	Correlation coefficient: 0.73 with the Burden Assessment Scale score, 0.62 with the General Health Questionnaire score, 0.53 with the Dementia Management Strategies Scale score and 0.53 with the Revised Memory and Behavior Problems Checklist score (Seng et al., 2010) Cronbach's alpha: 0.87–0.93 for caregivers of stroke survivors (Visser-Meily et al., 2004); 0.89 for older caregivers of stroke survivors (Hartke & King, 2002); Test–retest reliability (Kappa): 0.71 (Vitaliano et al., 1991); Cronbach's alpha in the present study: 0.92–0.94	Caregiver Interview T1, T2
Health-Related Quality of Life	Personal well-being or satisfaction focusing on aspects of health or illness	EuroQol: EQ5D/ 5 items (EuroQol Group)	Total Score (5 to 15)/ Continuous	Valid and reliable to measure health-related quality of life in various populations (Dorman et al., 1998; Fransen & Edmonds, 1999; Hurst et al., 1997; Schweikert et al., 2006) Correlation coefficient: 0.57–0.74 with the 36-item short-form health-survey subscales in patients with acute coronary syndromes (Schweikert et al., 2006) Intraclass correlation coefficient: 0.70 (Fransen & Edmonds, 1999); Cronbach's alpha in the present study: 0.48–0.59	Caregiver Interview T1, T2

Table continues

Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Depressive Symptoms	Symptoms listed in the <i>Diagnostic and Statistical Manual of Mental Disorders</i> major depressive-disorder category such as disinterest, low mood, sleep disruption or tiredness	Patient Health Questionnaire/ 9 items (Kroenke & Spitzer, 2002)	Total score (0 to 27) Continuous	Correlation coefficient: 0.33–0.73 with depression severity scores and worsening function with the subscale of the 20-item Short-Form General Health Survey (Kroenke et al., 2001) Excellent internal consistency reliability ($\alpha = 0.86–0.89$), test-retest reliability ($r = 0.84$) and validity (Kroenke et al., 2001); Internal consistency reliability for caregivers of stroke survivors: 0.80–0.86 (Bakas, Champion, et al., 2006; Bakas, Kroenke, et al., 2006); Cronbach’s alpha in the present study: 0.84–0.86	Caregiver Interview T1, T2

Table 3

Summary of Covariates and Measures

Caregiver covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Comorbidity	Presence of coexisting diseases	Cumulative Illness Rating Scale/ 14 systems (Miller et al., 1992)	Total Score (0–56)/ Continuous	Correlation coefficient: 0.58 with the Older American Activities of Daily Living Scale scores (Miller et al., 1992) Intraclass correlation: 0.70–0.89 (Hudon et al., 2005)	Caregiver Interview T1, T2
Health status	Self-perceived level of overall wellness in the individual	EuroQol: VAS/ 1 item visual analogue scale (EuroQol Group)	Self-rated Score VAS (0–100)/ Continuous	Correlation coefficient: 0.21–0.72 with the 36-item Short-Form Health-Survey subscales in patients with acute coronary syndromes (Schweikert et al., 2006). Intraclass correlation coefficient: 0.70 (Fransen & Edmonds, 1999)	Caregiver Interview T1, T2
Coping capacity	One's ability to respond to stressors by the appropriate use of adaptive resources	Sense of Coherence/ 13 items (Chumbler et al., 2004)	Total score (13–91)/ Continuous	Correlation coefficient: 0.61 with the Self-Esteem Scale, 0.54 with the Mastery Scale (used to measure perception of control), 0.53 with the Life Orientation Test (used to measure dispositional optimism; Pallant & Lae, 2002) Internal consistency; alpha = 0.9 (Chumbler et al., 2004); Cronbach's alpha in the present study: 0.81–0.83	Caregiver Interview T1, T2

Table continues

Caregiver covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Social support	Perceptions about the availability of relationships that provide help and prevent negative outcomes from the stressful event	Multidimensional Scale of Perceived Social Support/ 12 items (Zimet et al., 1988)	Total score (7–84)/ Continuous	Correlation coefficient: -0.13 – -0.25 with the anxiety and depression subscales of the Hopkins Symptom Checklist (Zimet et al., 1988) Excellent high internal consistency ($\alpha = 0.92$) and good test–retest reliability ($r = 0.85$), correlated with the full version (Zimet et al., 1988); Internal consistency for caregivers of persons with traumatic brain injury: $\alpha = 0.95$ (Davis et al., 2009); Cronbach’s alpha in the present study: 0.94–0.94	Caregiver Interview T1, T2
Sociodemographics	At T1, age, duration of caregiving in days (prior to and since stroke), hours spent caring each day (prior to and since stroke), days since stroke, number of close friends and relatives, distance between site of care and home in miles, perceived quality of relationship with the stroke survivor, perceived level of preparedness for caregiving, other life events in the past 3 months, gender, race/ethnicity, native language, relationship to the stroke survivor, health insurance, education, employment status and income	Investigator Developed Form	Continuous Ordinal Dichotomous or Categorical	N/A	Caregiver Interview T1, T2

Table continues

Caregiver covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
	At T2, hours spent caring each day since stroke, duration of caregiving role for the stroke survivor since stroke in days, days since stroke, distance between site of care and home in miles, perceived quality of relationship with the stroke survivor, perceived level of preparedness for caregiving and other life events occurring since the 1st interview				
Stroke-survivor covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Severity of stroke	Measures of consciousness, language, neglect, visual-field loss, extra-ocular movements, motor strength, ataxia, dysarthria and sensory loss	National Institutes of Health Stroke Scale/ 13 items (Know Stroke, 2010)	Total score (0–42)/ Continuous	Correlation coefficient: 0.68 with stroke-lesion size and 0.79 with patient outcome (Brott et al., 1989)	Chart Review T1
				The intraclass correlation coefficient: 0.82 by medical-chart review (Kasner et al., 1999); Cronbach's alpha in the present study: 0.88	
Description of stroke	Measures of communication disability (yes/no), type of stroke, area of stroke and time poststroke	Investigator-developed form	Dichotomous or Categorical	N/A	Chart Review T1

Table continues

Stroke-survivor covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Functional status	Ability to perform activities of daily living	Barthel Index/ 10 items (Mahoney & Barthel, 1965)	Total score (0 to 15)/ Continuous	Correlation coefficient: 0.73–0.77 with the Motricity Index arm, leg and total scores range from on stroke patients (Wade & Hewer, 1987). Cronbach's alpha: 0.93 (White et al., 2003); Internal consistency: 0.87–0.92 (Shah et al., 1989) in stroke patients); Intraclass correlation for caregiver proxy measure: 0.71 (Saban et al., 2012); Cronbach's alpha in the present study: 0.94–0.94	Caregiver Interview T1, T2
Comorbidity	Presence of coexisting diseases	Cumulative illness rating scale/ 14 systems (Miller et al., 1992)	Total Score (0 to 56)/ Continuous	Correlation coefficient: 0.58 with the Older American Activities of Daily Living Scale scores (Miller et al., 1992) Intraclass correlation coefficients; 0.66–0.87; Interrater reliability; 0.80–0.89 in assessing comorbidity by medical-chart review	Chart review T1

Table continues

Stroke-survivor covariates					
Research variable	Theoretical definition	Instrument/ items (source)	Total score range/ data type	Validity/reliability	Source for data collection
Sociodemographics	At T1, age, days since admission to the hospital, gender, race/ethnicity, education, employment status, income and health insurance At T2, duration of rehabilitation in days, if relevant, location to which a stroke survivor initially placed after hospital discharge and/or now currently placed and days since admission to any facility or discharge to home	Investigator-developed form	Continuous or Categorical	N/A	Caregiver interview T1, T2

Procedures

Participant recruitment, screening and informed consent. Approval for the proposed study was obtained from the Institutional Review Boards (IRBs) at the University of Pennsylvania and Thomas Jefferson University. A member of the research team, either a research assistant or I (hereafter referred to as “research team member”), trained in the study protocol, visited each unit during weekdays and/or on weekends to identify, screen and enroll eligible participants. The research team member first inspected a daily list from the electronic medical records to identify patients admitted with stroke. Stroke survivors’ paper charts as well as electronic medical records were then reviewed by the research team member to identify eligible potential participants. In addition, nursing leaders on the units helped identify potential caregiver participants. As a recruitment strategy at the Hospital of the University of Pennsylvania, we posted IRB-approved recruitment flyers in the units and added them to patient-education brochures that are routinely distributed to patients and caregivers by nursing staff when patients are admitted to the hospital (see Appendix X). At Thomas Jefferson University, IRB-approved recruitment flyers were distributed to potential participants by a research team member.

Ideally, a research team member tried to make first contact with caregivers for enrollment and T1 data collection while caregivers were visiting on the unit following their introduction by the nursing staff (See Appendix V). Alternatively, the research team member telephoned caregivers to explain the study and arrange a convenient meeting at the hospital or at their homes (See Appendix W). The research team member then talked with caregivers and determined their interest in study participation.

If caregivers met all of the inclusion criteria and expressed an interest in participating, a research team member obtained written informed consent. An effort was made to recruit caregivers within the first week of their relatives' stroke since it was expected that this period would best capture caregivers' acute stress in the natural environment. For caregivers who initially expressed being too overwhelmed to participate in an interview, the research team member sought their permission to approach them again up to 2 weeks poststroke.

Informed consent. A research team member informed potential participants in lay language that participation was voluntary and the purpose of the study, potential risks, and what they would need to do if they chose to participate. The research team member also encouraged potential participants to discuss participation with their family, friends and/or healthcare providers. The research team member judged the decision-making capacity of caregivers to consent, based on the person's ability to "understand, appreciate, compare and choose" (Ulrich & Karlawish, 2006, p. 57). The consent capacity guide used is found in Appendix N.

After recruitment and obtaining informed consent from caregivers, the research team member also obtained from stroke survivors or their surrogates informed consent and Health Insurance Portability and Accountability Act of 1996 (HIPPA) authorization to access the stroke survivor's medical record (see Appendices P, Q, S, T and U). Some stroke survivors who are cognitively impaired may or may not be able to demonstrate capacity for informed consent. For those lacking decision-making capacity, federal regulations require researchers to obtain written informed consent from their legally authorized representatives. For this study, we used the MacArthur Competency

Assessment for Clinical Research (MacCAT-CR; Appelbaum & Grisso, 2000) for situations in which it was not clear whether the stroke survivor did or did not demonstrate capacity for informed consent. The MacCAT-CR is a semistructured interview with open-ended questions and has been used to test capacity for decision making for consent in patients with Alzheimer's disease (Kim, Caine, Currier, Leibovici, & Ryan, 2001; Kim, & Karlawish, 2003; Ulrich & Karlawish, 2006). The original MacCAT-CR tool was developed for a clinical trial and some questions did not fit our study design. Thus, we modified relevant questions and a new cut-off point: 13 was used to determine capacity for informed consent in the group of stroke survivors with unclear capacity (see Appendix O). In cases when it was still unclear whether care recipients (stroke survivors) had the capacity to consent to the study, we used the "dual consent process" (see Appendix R), based on the recommendations of Barron, Duffey, Byrd, Campbell, and Ferrucci (2004, p. 82).

Data collection. Data collection from caregiver participants occurred at two time points: within 2 weeks poststroke (T1) while stroke survivors were still in the hospital and then 4 weeks after the first interview (T2) (hereafter referred to as "6 weeks poststroke"). At each time point, participants completed a quantitative survey instrument and provided salivary specimens. Data from the stroke survivor's medical record were collected only at T1; selected items were repeated with the proxy at T2.

Survey instrument administration. After recruiting participants and obtaining informed consent, a research team member interviewed consenting caregivers in a quiet place at the hospital or in caregivers' homes to provide privacy and protect confidentiality. With a few exceptions at T2, according to protocol, caregiver participants

were interviewed in person at each time point. The interviews required as much as 40–50 minutes (including enrollment procedures) at T1 and as much as 30–40 minutes at T2. The research team member gave caregivers the option to stop the interview or take a break if needed. Quantitative paper and pencil survey instruments were administered by reading questions to participants and recording their answers. The participant was given a large print copy of the instrument to follow along to help overcome potential barriers in reading level or literacy in the study population. Alternatively, participants read and filled out the survey questions first and the research team member reviewed their answers for clarity and completeness. For T2 data collection (4 weeks after the first interview), the research team member contacted the caregiver participant by telephone to arrange to meet at a place convenient to them. For caregiver participants who were not available to meet in person at T2, we provided a copy of the survey instruments in advance, arranged a telephone interview and read questions aloud as necessary to enable participants to answer the survey questions by phone. Alternatively, some participants filled out the survey questions and collected the second saliva sample by themselves and mailed both to us. The research team member subsequently called the participants to review the survey answers for clarity and completeness.

The research team member tried to minimize missing data by providing a quiet room for privacy, if the interview was conducted in a hospital or other healthcare setting. Missing data due to interviewer error was corrected in one of two ways. The research team member carefully reviewed the survey form for completeness before concluding each interview, or we telephoned participants to ask about any missing data and to confirm responses.

Chart review for stroke survivors. After having obtained informed consent and HIPAA authorization from patients or surrogates, a research team member reviewed the medical record of consenting stroke survivors at T1 to obtain information about their stroke severity, description of stroke and comorbidities. These data were subsequently reviewed for completeness and charts revisited to supply any missing data.

Saliva-specimen collection. Caregivers were taught self-collection of saliva in an in-person demonstration at T1. On a day following the interview at T1 and before the interview at T2, caregivers were asked to collect their saliva samples. They were instructed to collect saliva at home at T1 and T2 using the same procedure. Written and diagrammatic instructions along with the collection kits were sent home with the caregiver and instructions were reviewed by telephone prior to the day they were to collect the samples at each time point. To capture diurnal variations in cortisol concentration, caregivers collected saliva on waking and again at 2100 h (McCallum et al., 2006). Caregivers were instructed not to eat food, drink liquid or brush teeth for 30 minutes before collecting saliva and not to smoke for 60 minutes before collecting saliva. Caregivers put the Salimetrics oral swab under their tongue for 1 minute to collect saliva. They then inserted the oral swab into the tube, replaced the cap and filled out and placed the label on the storage tube. Saliva collection and labeling took up to 5 minutes each time. For each data collection (on waking and 2100 h), they placed the tube in a sealed plastic bag and placed the bag in the freezer overnight as instructed. The research team member picked up the samples and transported them in a cooler bag to the School of Nursing Biobehavioral Laboratory for storage. Alternatively (for those few caregivers living at extreme distance), caregivers placed the bags of tubes in a prepaid post office

envelope and mailed it to us. In either case, the sample was delivered, placed in a project-labeled container and stored in a freezer at -80° C for later analysis.

Retention. To avoid losing contact with participants, the research team member requested two telephone numbers (home phone and cellular phone) as well as street and e-mail addresses and an alternative contact for each participant. Every attempt was made to locate and contact the participant for the T2 data collection using this information. For participants who did not respond to our telephone calls, the research team member sent e-mail messages as well as letters via the U.S. Postal Service.

As an additional strategy for retention, thank-you notes with a \$10 gift card per participant were given after data collection was completed at each time point for a total maximum value of \$20. The participant received the gift card in person or by U.S. mail upon completion of the quantitative interview and saliva data collection for each T1 and T2. If they withdrew from the study before T2, they kept the T1 gift card they had already received. If stroke survivors died following T1 data collection, an attempt to retain their caregiver participant for T2 data collection was made.

Data Management

All data were kept anonymous to protect the confidentiality of participants; identification numbers rather than names were assigned sequentially and were used on all paper and electronic materials that referenced participants. Paper forms were locked in a cabinet in a locked data-repository room at the University of Pennsylvania School of Nursing, separate from signed consent forms and lists of participants with code numbers. All data were entered into an electronic file. Double data entry was used and any discrepancy between the two data sets was compared and cleaned. Electronic data and

results of all analyses were stored and managed using a secure research server at the University of Pennsylvania School Nursing.

The salivary-cortisol samples were kept in freezer storage at the Biobehavioral Laboratory at the University of Pennsylvania School of Nursing until data collection was complete, and then transported to the University of Pennsylvania Pearlman School of Medicine Clinical and Translational Research Center where the assays were completed all at one time by the trained laboratory staff. This updated 2,000-square-foot laboratory for biological research provides optimal -80° C freezer space and an established protocol for the assay of salivary cortisol using enzyme-linked immuno sorbent assay.

Statistical Analysis

Overall analysis. All data were analyzed using SPSS 20.0 for Windows and STATA 12. All variables were described using descriptive statistics and bivariate analysis. In addition, for participants with complete data at both time points, a paired *t*-test (for continuous variables) and Fisher's exact test (for categorical variables) were used to explore any changes over time. For the development of multivariable models, multivariate stepwise regression was conducted to evaluate study hypotheses while adjusting for important covariates related to study outcomes for Aims 1, 2 and 3. For Aim 4, univariate or multivariate regression in each Baron and Kenny (1986) step was used in establishing the mediator effect of perceived stress and salivary cortisol on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms). The robust standard error was used to protect against violations in the homoscedasticity assumption in all regression analyses.

Preliminary analysis. Descriptive estimates of all measures were generated: frequencies and percents for categorical variables and estimates of central tendency (means and medians), measures of variability (standard deviations, interquartile ranges and ranges) and derived moments of skewness and kurtosis for continuous variables. An analysis of distributional properties using histograms and Shapiro-Wilk tests were performed to determine if variance stabilizing should be applied. Outliers were accessed via visual inspection of distributions and checked for accuracy.

Comparison of study variables at T1 and T2. A paired *t*-test (for continuous variables) and Fisher's exact test (for categorical variables) were used to examine differences in study variables measured at both time points in participants with complete datasets.

Bivariate analysis.

Correlations. I estimated correlations among caregiver or stroke-survivor characteristics and the main study variables—uncertainty, perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms. I calculated Pearson's correlation coefficient when two variables were normally distributed and Spearman's correlation coefficient when one of the variables was not normally distributed or was ordinal.

Differences in continuous variables by categories of caregiver and stroke-survivor characteristics. Two-sample *t*-tests (for dichotomous variables) and one-way analysis of variance (ANOVA; for categorical variables having more than two levels) were used when comparing with continuous variables. For the positively skewed and not normally distributed variables, Mann-Whitney *U* test (for dichotomous variables) and the Kruskal-Wallis test (for categorical variables on more than two levels) were used to

examine differences in continuous variables between categories of caregiver and stroke-survivor characteristics.

Multivariate analysis. Multivariate stepwise regression and a p -value cut off point of 0.05 were used to determine the effect of uncertainty on perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms (Aims 1, 2 and 3), controlling for covariates. Given the large number of covariates available and the limited sample size, only caregiver and stroke-survivor characteristics that were identified from bivariate analysis on the basis of a p -value less than or equal to 0.05 were entered in the multivariate stepwise regression models to test Aims 1, 2 and 3. Univariate or multivariate regression in each Baron and Kenny step (1986) was used in establishing the mediator effect of perceived stress and salivary cortisol on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms; Aim 4). Covariates, which remained in the final stepwise models for each Aim 1, 2 and 3, were entered in the models to test Aim 4. The robust standard error was used to protect against violations in the homoscedasticity assumption in all analyses. For all analyses, a p -value of less than 0.05 in a two-sided test was considered statistically significant.

Aim 1. Determine at each time point if uncertainty (regarding stroke survivors' health outcomes and new caregiver role) predicts levels of caregivers' perceived stress.

The level of uncertainty measured continuously was modeled as an independent predictor of the dependent variable, perceived stress (total score measured on a continuum). Separate models were estimated for the dependent variable at T1 and at T2. Multivariate stepwise regression and a p -value cut off point of 0.05 were used to individually model the dependent variable as a function of the predictor of interest

(uncertainty) at T1 and at T2, while controlling for potential confounders or precision variables identified from bivariate analysis on the basis of a p -value less or equal to 0.05. To test the linearity assumption, a scatterplot matrix of all independent variables against the dependent measure in a pairwise manner was used. A bivariate correlation matrix of the independent variables combined with the computation of auxiliary R -squared values, tolerance and variance inflation factor were used to check for multicollinearity. Finally, the Huber-White robust sandwich variance estimator was used to protect against violations in the homoscedasticity assumption.

Aim 2. Determine at each time point if uncertainty predicts levels of caregivers' physiological stress (salivary cortisol).

The level of uncertainty measured continuously was modeled as an independent predictor of the dependent variable, salivary cortisol. A multivariate stepwise regression-analysis approach similar to that used for Aim 1 was used for Aim 2. Model assumptions were assessed as described for Aim 1.

Aim 3. Examine at each time point the relationship of uncertainty to psychological outcomes (burden, HRQOL and depressive symptoms).

Separate models were estimated for each dependent variable (burden, HRQOL and depressive symptoms) at T1 and at T2. Multivariate stepwise regression and a p -value cut off point of 0.05 was used to individually model the dependent variable as a function of the predictor of interest (uncertainty) at T1 and at T2, while controlling for potential confounders or precision variables identified from bivariate analysis on the basis of a p -value less or equal to 0.05. Model assumptions were assessed as described for Aim 1.

Aim 4. Explore at each time point the mediator effect of stress (perceived stress and physiological stress) on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms).

To test the hypothesis of stress (perceived or salivary cortisol) as a mediator in the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms) at T1 and at T2, separate models were estimated for each mediator (perceived stress and salivary cortisol) and each dependent variable (burden, HRQOL and depressive symptoms) at T1 and at T2. According to Baron and Kenny (1986) and Judd and Kenny (1981), the following must hold to establish a mediational effect: (a) uncertainty must be significantly associated with each mediator (perceived stress or salivary cortisol); (b) each mediator (perceived stress or salivary cortisol) must reliably predict each psychological outcome (burden, HRQOL or depressive symptoms); and (c) the significant relationship between uncertainty and each psychological outcome should be attenuated when the mediator is added to the model.

First, multiple regression analysis was used to assess the association between uncertainty and each potential mediator (perceived stress or salivary cortisol). Second, multiple regression analysis was used to assess the association between each dependent variable and each potential mediator. Third, uncertainty and the specific covariate were entered into a model estimated for each dependent variable, followed by the addition of the specific mediator. To demonstrate mediation, we observed a change in the relationship between uncertainty and the dependent variable from significant to nonsignificant or attenuated, after adjusting for perceived stress or salivary cortisol. Model assumptions were assessed as described in Aim 1.

Sensitivity analyses.

Comparison of study completers and dropouts. A sensitivity analysis was conducted to compare baseline caregiver and stroke-survivor sociodemographics and stroke-related characteristics between participants who completed the study and those who were excluded in the data analysis at T2.

Repeated-measures analysis for Aims 1, 2 and 3. Separate bivariate linear mixed models with repeated measures of each dependent variable were computed to additionally explore the overall effects of uncertainty or covariates on repeated measures of each dependent variable (perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms). Restricted maximum likelihood was used. Restricted maximum likelihood “chooses as estimates those values that, if true, would maximize the probability of observing what has, in fact, been observed” (Allison, 2002, p. 13). Because restricted maximum likelihood compensates for missing data, all participants who were recruited at T1 were included in the analysis. For participants whose stroke survivor died after T1 data collection, predeath recall of measures of uncertainty, burden or stroke-survivor functional status, as well as current (T2, postdeath) measures for perceived stress, salivary cortisol, HRQOL or depressive symptoms were included as data at T2, because these data are more likely to be similar to real than missing data. For participants who were lost to follow up or withdrew from the study, there were no available data at T2.

First, separate bivariate linear mixed models with repeated measures of each dependent variable (perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms) were computed to assess the overall effects of repeated measures of uncertainty on each dependent variable. The initial model included uncertainty, time and

the interaction between uncertainty and time to determine which factors were significant predictors of each dependent variable. If the interaction variable between uncertainty and time was not significant, this interaction variable was excluded in the final model.

Second, separate bivariate linear mixed models with repeated measures of each dependent variable (perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms) were computed to assess the overall effects of each covariate (that remained in the final stepwise regression model) on each dependent variable for Aims 1, 2 and 3. The initial model included each covariate, time and interaction between covariate and time to determine which factors were significant predictors of each dependent variable. If the interaction between covariate and time was not significant, the interaction variable was excluded from the final model.

Third, the effects of time on repeated measures of each dependent variable (perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms) were visually compared to the results from the paired *t*-test that was used to examine any differences in continuous variables measured at both time points for participants with complete datasets.

CHAPTER 4: RESULTS

Introduction

A total of 63 caregivers and stroke survivors agreed to participate in the study. At T1, all 63 caregivers were interviewed using a survey questionnaire; there were no missing data. Fifty seven of these caregivers provided saliva samples on waking and 56 provided saliva samples in the evening. Of the evening samples, however, one lacked sufficient volume of saliva to detect cortisol and another was an extreme outlier when assayed, suggesting contamination; these two samples were excluded from data analysis. Thus, at T1, 57 saliva samples on waking and 54 evening saliva samples were included in the data analysis. Also at T1, the medical records of the 63 stroke survivors were reviewed to obtain information about severity of stroke, description of stroke and comorbidity with no missing data. At T2, 13 stroke survivors had died and their caregivers' data were not included in the analyses of aims at T2; an additional seven caregivers were lost to follow up because we were unable to contact them, despite multiple attempts, and three caregivers withdrew from the study. The participants who withdrew from the study expressed that they could no longer participate due to their caregiving situation and/or personal problems.

Thus, a total of 40 caregivers were included for data analysis at T2. There were no missing survey data for these 40 caregivers; 38 of them provided saliva samples on waking and in the evening, and all of these samples were available for assay. Comparing baseline characteristics of participants who completed the study ($N = 40$) and those who were not included in the data analysis at T2 ($N = 23$), there were no differences in values for caregiver or stroke-survivor characteristics with these exceptions: those who were not

included in data analysis at T2 had more social support at baseline ($p = 0.036$) and they and their stroke survivors were more likely of the non-Hispanic White race ($p = 0.018$ for caregivers, $p = 0.009$ for stroke survivors).

Descriptive Analysis for Sample Characteristics and Main Variables

Caregiver characteristics. The sociodemographic characteristics of the caregivers are reported in Tables 4 and 5. The majority were female (67%) and largely non-Hispanic White (73%) or African American (22%). Caregivers' ages ranged from 30 to 89 years (Mean [M] \pm Standard Deviation [SD]: 56.92 ± 13.81 ; median: 56.00, mode: 41), and 30% were aged 65 years or older. Of caregivers, 60% were adult children and 35% were spouses of stroke survivors. All caregivers had completed at least high school; most had either private, Medicare, or Medicare + supplemental health insurance plans (87%) and worked either full-time (43%) or part-time (11%). Just under half (48%) of caregivers felt comfortable financially and had more than enough funds to make ends meet. They reported an average of 18.37 (± 17.34) close friends and relatives.

Table 5 shows caregiver characteristics measured at both T1 ($N = 63$) and T2 ($N = 40$). In the year prior to the stroke, caregivers had provided help to their family member for an average of 201.75 (± 646.24) days, and time per day spent caring prior to the stroke was 2.90 (± 6.37) hours. At the T1 interview, the duration of caregiving for stroke survivors following the stroke was 4.19 (± 3.37) days and at T2, 36.03 (± 6.96) days. Time spent per day in caregiving since the stroke was 8.59 (± 6.64) hours at T1 and 7.60 (± 6.59) hours at T2. Perceived quality of the relationship with the stroke survivor, on a scale of 1 (*excellent*) to 4 (*poor*), averaged 1.25 (± 0.60) at T1 and 1.5 (± 0.75) at T2. Perceived level of preparedness for caregiving on a scale of 1 (*excellent*) to 4 (*poor*) was

2.21 (1.11) at T1 and 2.25 (\pm 1.01) at T2. At T1, 40% of the caregivers had experienced other significant life events (e.g., a death, moving, retirement or marriage) in the 3 months prior to the stroke in their family member and at T2, 23% reported similar life events that had occurred subsequent to the first interview. Distance between home and site of care was 39.35 miles (\pm 123.28) at T1 when stroke survivors were still hospitalized and 10.95 miles (\pm 20.26) at T2 when stroke survivors were at a rehabilitation hospital, a nursing facility or home.

The average caregiver comorbidity score as measured by the Cumulative Illness Rating Scale (CIRS; higher score reflects greater severity) was 4.90 (\pm 4.20) at T1 ($N = 63$) and 6.20 (\pm 4.69) at T2 ($N = 40$). Caregivers' self-reported health status was also poorer at T2 ($N = 40$) with a mean EQ-Visual-Analog Scale (VAS) score of 74.68 (\pm 15.68) compared to 80.57 (\pm 12.44) at T1 ($N = 63$). The mean coping capacity score as measured by the short-form version of the Sense of Coherence Scale (SOC; higher score reflects better coping) was 65.75 (\pm 11.71) at T1 ($N = 63$) and 67.25 (\pm 15.46) at T2 ($N = 40$). On average, caregivers reported social-support scores of 73.57 (\pm 12.16) at T1 ($N = 63$) and 63.88 (\pm 18.18) at T2 ($N = 40$) on the Multidimensional Scale of Perceived Social Support (MSPSS; higher score represents better social support).

Table 4

Caregiver Sociodemographic Characteristics (N = 63)

Variable	<i>M ± SD or N (%)</i>
Age (years)	56.92 ± 13.81
Gender	
Female	42 (67%)
Male	21 (33%)
Race/Ethnicity	
Non-Hispanic White	46 (73%)
African American	14 (22%)
Asian	1 (< 2%)
Hispanic	1 (< 2%)
Other	1 (< 2%)
Native Language	
English	60 (95%)
Other	3 (5%)
Relationship to the Stroke Survivor	
Spouse	22 (35%)
Child	38 (60%)
Grandchild	1 (2%)
Sibling	2 (3%)
Caregiver Insurance	
Private/Medicare/Medicare + Supplemental Health Insurance Plans	55 (87%)
Medicare + Medicaid/Medicaid/No insurance	8 (13%)
Number of close friends and relatives	18.37 ± 17.34
Education	
Less than High School	0
High School	20 (32%)
Vocational Training	6 (9.5%)
College	23 (36.5%)
Postgraduate	14 (22%)

Table continues

Variable	<i>M</i> ± <i>SD</i> or <i>N</i> (%)
Employment	
Full Time	27 (43%)
Part Tim	7 (11%)
Homemaker	2 (3%)
Unemployed	5 (8%)
Retired	18 (29%)
Leave of Absence	4 (6%)
Income	
Comfortable	30 (48%)
Adequate	26 (41%)
Insufficient	7 (11%)

Note. *M* = mean; *SD* = standard deviation; This information was collected only at T1.

Table 5

Caregiver Characteristics Measured at T1 and T2

Variable	<i>M ± SD or N (%)</i>	
	T1 (<i>N</i> = 63)	T2 (<i>N</i> = 40)
Distance between site of care and home (miles)	39.35 ± 123.28	10.95 ± 20.26
Duration of Caregiving (days)		
Prior to Stroke	201.75 ± 646.24	
Since Stroke	4.19 ± 3.37	36.03 ± 6.96
Days Since Stroke	4.25 ± 3.36	36.45 ± 6.50
Time Spent Caring per Day (hours)		
Prior to Stroke	2.90 ± 6.37	
Since Stroke	8.59 ± 6.64	7.60 ± 6.59
Other significant life events in the past 3 months at T1 or since stroke at T2 (Yes)	25 (40%)	9 (23%)
Perceived Quality of Relationship with the Stroke Survivor [1=Excellent, 4=Poor]	1.25 ± 0.60	1.50 ± 0.75
Perceived Level of Preparedness for Caregiving [1=Excellent, 4=Poor]	2.21 ± 1.11	2.25 ± 1.01
Comorbidity Score	4.90 ± 4.20	6.20 ± 4.69
Health Status	80.57 ± 12.44	74.68 ± 15.68
Coping Capacity	65.75 ± 11.71	67.25 ± 15.46
Social Support	73.57 ± 12.16	63.88 ± 18.18

Note. *M* = mean; *SD* = standard deviation; Higher scores = poorer perceived quality of relationship with the stroke survivor, poorer perceived level of preparedness for caregiving, more comorbidities, better health status, better coping capacity and better social support.

Stroke-survivor characteristics. Table 6 summarizes stroke-survivor sociodemographic characteristics obtained from the caregivers. Just over half of stroke survivors were female (59%) and non-Hispanic White (71%), and most of the remainder were African American (24%). Stroke survivors' ages ranged from 65 to 95 years (75.92 ± 7.82 , median: 75.00, mode: 68), and 86% of them had completed high school or higher education. The majority had either private, Medicare, or Medicare + supplemental health insurance plans (84%). Most (75%) were retired, and their caregivers reported that only 43% of them felt generally financially comfortable or had more than enough funds to make ends meet.

Stroke-related information was obtained from a review of medical records, which was completed, on average, $4.22 (\pm 3.37)$ days poststroke (see Table 7). For the majority of stroke survivors (81%), this was a first stroke, whereas for 19% this was a recurrence (3% of 63 stroke survivors had a history of both stroke and transient ischemic attack) and 11% had a history of transient ischemic attack. The average length of time since admission to the hospital at T1 was $4.49 (\pm 4.75)$ days at time of caregiver interview. The majority had either ischemic (51%) or hemorrhagic stroke (33%). For 43%, the stroke was located in the right hemisphere of the brain and for 44% in the left hemisphere. Of stroke survivors, 43% were unable to communicate verbally. The mean severity of stroke as measured by the National Institutes of Health (NIH) Stroke Scale was $12.98 (\pm 9.92)$; range 0–40, with higher scores reflecting greater severity) and the stroke-survivor comorbidity score, as measured by the CIRS, was $8.37 (\pm 4.37)$; higher scores represent greater severity).

Of the 40 stroke survivors remaining in the study at T2, 60% had been initially discharged from the acute-care hospital to a rehabilitation hospital (vs. 10% to a nursing facility; 22.5% to home and 7.5% to another place or remained in the same hospital). By the time of the T2 interview, only 17 (42.5%) of all stroke survivors were at home (vs. 27.5% at a rehabilitation hospital, 12.5% at a nursing facility and 17.5% at another place). With regard to their rehabilitation experience, 80% had received in-patient rehabilitative therapy (in a rehabilitation hospital or skilled nursing facility) for a mean of 19.34 days (± 9.00) and 38% had received out-patient rehabilitative therapy for a mean of 18.71 days (± 10.80). Stroke-survivor functional status (see Table 7), as measured by the Barthel Index (higher scores reflect better function), was 23.17 (± 28.71) at T1 ($N = 63$) and 43.75 (36.56) at T2 ($N = 40$).

Table 6

Stroke-Survivor Sociodemographic Characteristics (N = 63)

Variable	<i>M</i> ± <i>SD</i> or <i>N</i> (%)
Age (years)	75.92 ± 7.82
Gender	
Female	37 (59%)
Male	26 (41%)
Race/Ethnicity	
Non-Hispanic White	45 (71%)
African American	15 (24%)
Asian	2 (3%)
Hispanic	1 (2%)
Education	
Less than High School	9 (14%)
High School	22 (35%)
Vocational Training	6 (10%)
College	19 (30%)
Postgraduate	7 (11%)
Employment	
Full Time	6 (10%)
Part Time	1 (2%)
Homemaker	7 (11%)
Unemployed	2 (3%)
Retired	47 (75%)
Leave of Absence	0
Income	
Comfortable	27 (43%)
Adequate	27 (43%)
Insufficient	9 (14%)
Insurance	
Private/Medicare/Medicare + Supplemental Health Insurance Plans	53 (84%)
Medicare + Medicaid/Medicaid/No insurance	10 (16%)

Note. *M* = mean; *SD* = standard deviation; This information was collected only at T1.

Table 7

Stroke-Related Characteristics of Stroke Survivors (N = 63)

Variable	<i>M</i> ± <i>SD</i> or <i>N</i> (%)
Days poststroke	4.22 ± 3.37
Days since admission to hospital at time of caregiver interview	4.49 ± 4.75
Type of Stroke	
Ischemic	32 (51%)
Intracerebral Hemorrhage	21 (33%)
Subarachnoid Hemorrhage	10 (16%)
Area of Stroke	
Right	27 (43%)
Left	28 (44%)
Right and Left or Other	8 (13%)
Communication Disability	
Yes	27 (42.9%)
No	30 (47.6%)
Unclassified	6 (9.5%)
Severity of Stroke	12.98 ± 9.92
Comorbidity Score	8.37 ± 4.37
Functional Status	23.17 ± 28.71 at T1 43.75 ± 36.56 at T2 (<i>N</i> = 40)

Note. *M* = mean; *SD* = standard deviation; With the exception of functional status, this information was collected only at T1; Higher scores = greater severity of stroke, more comorbidities and better functional status.

Main study variables. Table 8 summarizes levels of caregiver uncertainty, perceived stress, salivary cortisol on waking and in the evening, burden, health-related quality of life (HRQOL) and depressive symptoms at T1 (*N* = 63) and T2 (*N* = 40). Average uncertainty score on the Mishel Uncertainty in Illness Scale for Family Members (higher scores reflect greater uncertainty) was 84.13 (± 19.93) at T1 and 85.23 (± 23.94) at T2. Their average score on the Perceived Stress Scale (PSS; higher scores reflect higher perceived stress) was 24.21 (± 9.55) at T1 and 24.47 (± 10.74) at T2.

The mean salivary-cortisol level on waking was 0.41 (\pm 0.37) μ g/dL at T1 and 0.33 (\pm 0.21) μ g/dL at T2 and the mean salivary-cortisol level in the evening was 0.13 (\pm 0.11) μ g/dL at T1 and 0.12 (\pm 0.10) μ g/dL at T2 (see Figures 2 & 3). The average time of day participants collected waking saliva was 7.51 (\pm 1.23) hours at T1 and 7.78 (\pm 1.56) hours at T2. In the evening, caregivers collected saliva on average around 21.23 (\pm 1.05) hours at T1 and 21.20 (\pm 0.90) hours at T2.

Caregivers reported mild to moderate burden with a mean Zarit Burden score of 22.59 (\pm 16.56) at T1 and 26.90 (\pm 17.87) at T2. Caregivers reported reduced HRQOL at T2 with a mean EQ5D score of 6.58 (\pm 1.48) compared to 5.90 (\pm 1.12) at T1. On average, caregivers reported mild levels of depressive symptoms with a mean Patient Health Questionnaires (PHQ)-9 score of 6.67 (\pm 5.55) at T1 and 6.60 (\pm 5.96) at T2. At T1, 43% of caregivers and at T2 53% of caregivers reported no depressive symptoms.

Table 8

Summary of Main Study Variables at T1 and T2

Variable	T1 (N = 63)		T2 (N = 40)	
	<i>M</i> \pm <i>SD</i>	Minimum – Maximum	<i>M</i> \pm <i>SD</i>	Minimum – Maximum
Uncertainty	84.13 \pm 19.93	33–137	85.23 \pm 23.94	43–140
Perceived Stress	24.21 \pm 9.55	0–43	24.47 \pm 10.74	5–46
Salivary Cortisol AM	0.41 \pm 0.37 (N = 57)	0.03–2.30	0.33 \pm 0.21 (N = 38)	0.06–1.07
Salivary Cortisol PM	0.13 \pm 0.11 (N = 54)	0.02–0.58	0.12 \pm 0.10 (N = 38)	0.03–0.46
Burden	22.59 \pm 16.56	2–71	26.90 \pm 17.87	0–68
Health-Related Quality of Life	5.90 \pm 1.12	5–10	6.58 \pm 1.48	5–9
Depressive Symptoms	6.67 \pm 5.55	0–22	6.60 \pm 5.96	0–20

Note. *M* = mean; *SD* = standard deviation; Higher scores = greater uncertainty, higher perceived stress, greater burden, poorer health-related quality of life and greater depressive symptoms.

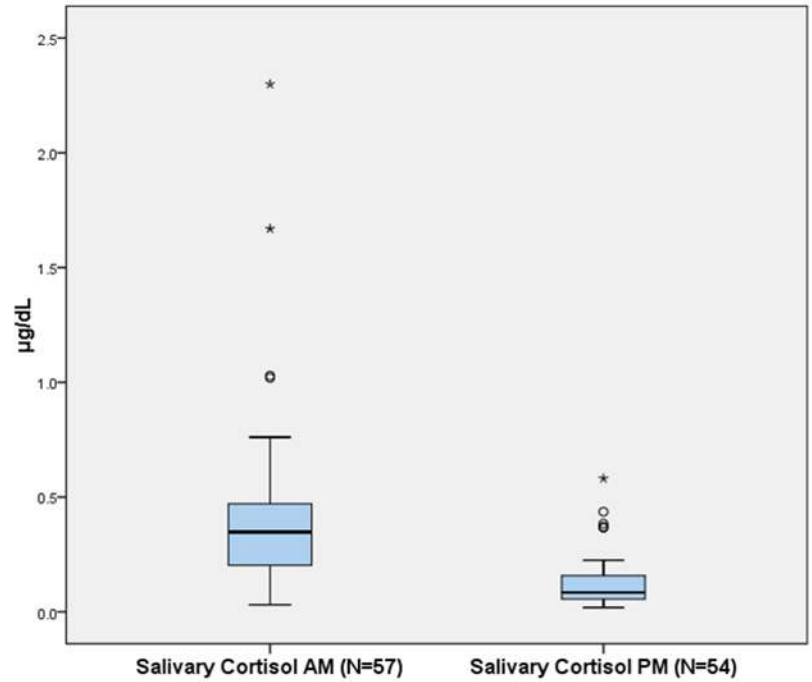


Figure 2. Diurnal salivary cortisol pattern at T1.

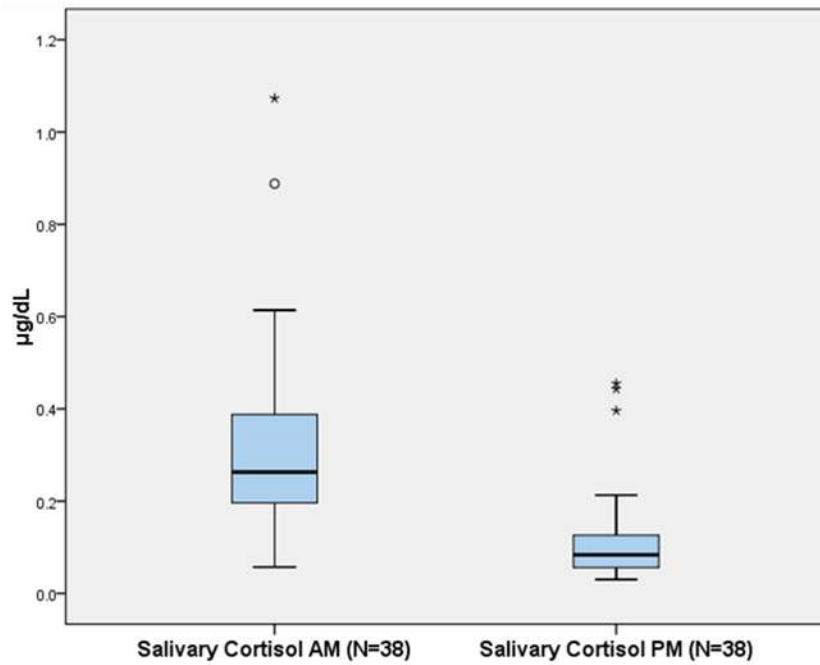


Figure 3. Diurnal salivary cortisol pattern at T2.

Comparisons of Study Variables at T1 and T2

Among the 40 participants with data at both T1 and T2, paired *t*-tests were used to examine T1–T2 differences in main study continuous variables (uncertainty, perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms) and continuous caregiver and stroke-survivor characteristics that were measured at both T1 and T2 (perceived quality of relationship with the stroke survivor, hours spent caring per day, perceived level of preparedness for caregiving, caregiver comorbidity, coping capacity and social support and stroke-survivor functional status). Fisher’s exact test was used to examine differences in the only categorical variable, other life events, that was measured at both time points.

Among the main study variables, salivary cortisol (at T1 and T2), burden (at T1), HRQOL (at T1 and T2) and depressive symptoms (at T1 and T2) were positively skewed due to variable floor effects. Thus, study variables at T1 and T2 were also compared using a Wilcoxon Signed Ranks Test. The results using paired *t*-tests and Wilcoxon Signed Ranks Test were similar; therefore, only the paired *t*-test results are reported.

Table 9 summarizes descriptive analysis and comparison of study variables measured at both time points among 40 participants who completed the study. Compared to T1, caregivers at T2 had poorer HRQOL ($t = -2.636, p = 0.012$), poorer health status ($t = 2.241, p = 0.031$), higher comorbidity scores ($t = -2.054, p = 0.047$), better coping capacity ($t = -2.061, p = 0.046$) and less social support ($t = 2.560, p = 0.014$). Functional status of the stroke survivors improved from T1 to T2 ($t = -3.266, p = 0.002$). There were no statistically significant differences between T1 and T2 for caregiver uncertainty, perceived stress, salivary cortisol (on waking and evening), burden, depressive symptoms,

perceived quality of relationship with the stroke survivor, hours spent caring per day, perceived level of preparedness for caregiving or other life events.

Table 9

Comparison of Study Variables between T1 and T2 (N=40)

Variable	<i>M</i> ± <i>SD</i> or <i>N</i> (%) at T1	<i>M</i> ± <i>SD</i> or <i>N</i> (%) at T2	<i>t</i> statistic	<i>p</i> value
Uncertainty	83.73 ± 23.47	85.23 ± 23.94	-0.713	0.480
Perceived Stress	24.38 ± 10.15	24.48 ± 10.74	-0.080	0.936
Salivary Cortisol AM (<i>N</i> = 38)	0.39 ± 0.23	0.33 ± 0.21	1.308	0.199
Salivary Cortisol PM (<i>N</i> = 37)	0.12 ± 0.10	0.12 ± 0.11	-0.061	0.952
Burden	23.0 ± 17.64	26.90 ± 17.87	-1.880	0.068
Health-Related Quality of Life	6.03 ± 1.25	6.58 ± 1.48	-2.636	0.012*
Depressive Symptoms	7.25 ± 5.84	6.60 ± 5.96	0.891	0.379
Perceived quality of relationship with the stroke survivor	1.28 ± 0.64	1.50 ± 0.75	-1.940	0.060
Hours spent caring per day	8.7 ± 6.29	7.6 ± 6.59	0.954	0.346
Perceived level of preparedness for caregiving	2.15 ± 0.98	2.25 ± 1.01	-0.561	0.578
Caregiver Comorbidity	5.65 ± 4.37	6.20 ± 4.69	-2.054	0.047*
Health Status	80.33 ± 12.68	74.68 ± 15.68	2.241	0.031*
Caregiver Coping Capacity	63.85 ± 12.52	67.25 ± 15.46	-2.061	0.046*
Caregiver Social Support	71.15 ± 13.14	63.88 ± 18.18	2.560	0.014*
Stroke-Survivor Functional Status	26.25 ± 28.83	43.75 ± 36.56	-3.266	0.002**
Other Life Event	17 (43%)	9 (23%)		0.134

Note. *M* = mean; *SD* = standard deviation; **p* < 0.05, two-tailed, ***p* < 0.01, two-tailed; Paired *t*-test was used for all variables except other life event for which Fisher's exact test was calculated; Caregivers had poorer health-related quality of life, more comorbidities, poorer health status, better coping capacity and less social support at T2; Stroke-survivor functional status improved from T1 to T2.

Bivariate Analysis

Correlations among the study variables. Correlations among caregiver or stroke-survivor characteristics and the main study variables at T1 were estimated. Pearson's correlation coefficient was calculated when two variables were normally distributed and Spearman's correlation coefficient was calculated when one of the variables was not normally distributed or was ordinal. Tables 10 and 11 report main study variables and characteristics of any statistically significant correlations. Variable correlations with each of the main variables are summarized here.

Uncertainty. At T1, greater uncertainty was significantly correlated with poorer coping capacity ($r = -0.424, p = 0.001$), less social support ($r = -0.307, p = 0.014$), poorer perceived quality of relationship with the stroke survivor ($r = 0.289, p = 0.022$), poorer stroke-survivor functional status ($r = -0.258, p = 0.041$), higher perceived stress ($r = 0.545, p < 0.001$), greater burden ($r = 0.439, p < 0.001$), poorer HRQOL ($r = 0.475, p < 0.001$), poorer health status ($r = -0.321, p = 0.01$) and greater depressive symptoms ($r = 0.487, p < 0.001$).

At T2, significant correlations persisted between greater uncertainty and the following variables: poorer coping capacity ($r = -0.560, p < 0.001$), poorer perceived quality of relationship with the stroke survivor ($r = 0.359, p = 0.023$), poorer stroke-survivor functional status ($r = -0.398, p = 0.011$), higher perceived stress ($r = 0.512, p = 0.001$), greater burden ($r = 0.586, p < 0.001$), poorer HRQOL ($r = 0.327, p = 0.039$), poorer health status ($r = -0.372, p = 0.018$) and greater depressive symptoms ($r = 0.413, p = 0.008$). Greater uncertainty was also statistically correlated with caregiver older age ($r = 0.350, p = 0.027$) and elevated salivary-cortisol level in the evening ($r = 0.418,$

$p = 0.009$). The correlation between uncertainty and social support, however, was no longer significant.

Perceived stress. At T1, higher perceived stress was significantly correlated with greater uncertainty ($r = 0.545, p < 0.001$), poorer coping capacity ($r = -0.543, p < 0.001$), greater burden ($r = 0.479, p < 0.001$), poorer HRQOL ($r = 0.573, p < 0.001$), poorer health status ($r = -0.421, p = 0.001$), greater depressive symptoms ($r = 0.590, p < 0.001$) and poorer stroke-survivor functional status ($r = -0.278, p = 0.027$). There was no significant correlation between perceived stress and salivary cortisol, either on waking or in the evening.

At T2, higher perceived stress remained significantly correlated with the following variables: greater uncertainty ($r = 0.512, p = 0.001$), poorer coping capacity ($r = -0.755, p < 0.001$), greater burden ($r = 0.680, p < 0.001$), poorer HRQOL ($r = 0.510, p = 0.001$), poorer health status ($r = -0.487, p = 0.001$), greater depressive symptoms ($r = 0.744, p < 0.001$) and poorer stroke-survivor functional status ($r = -0.419, p = 0.007$). Higher perceived stress was also significantly correlated with elevated salivary-cortisol level in the evening ($r = 0.520, p = 0.001$). The relationship of higher perceived stress and lower social support approached significance ($r = -0.310, p = 0.051$). The relationship of higher perceived stress and more caregiver comorbidities also approached significance ($r = 0.312, p = 0.050$). There was no significant correlation between perceived stress and salivary cortisol on waking.

Salivary cortisol. At T1, elevated salivary-cortisol level on waking was significantly correlated with greater burden ($r = 0.262, p = 0.049$), older caregiver age ($r = 0.370, p = 0.005$) and poorer perceived quality of relationship with the stroke

survivor ($r = 0.420, p = 0.001$). Salivary-cortisol level in the evening at T1 was not significantly correlated with any variable.

At T2, decreased salivary-cortisol level on waking was significantly correlated with poorer HRQOL ($r = -0.333, p = 0.041$) and poorer health status ($r = 0.383, p = 0.017$). The correlations between salivary-cortisol level on waking and burden, caregiver age or poorer perceived quality of relationship with the stroke survivor were no longer significant.

Elevated salivary-cortisol level in the evening at T2 was significantly correlated with higher uncertainty ($r = 0.418, p = 0.009$), poorer coping capacity ($r = -0.433, p = 0.007$), greater severity of stroke ($r = 0.426, p = 0.008$), higher perceived stress ($r = 0.520, p = 0.001$), poorer health status ($r = -0.370, p = 0.022$) and greater depressive symptoms ($r = 0.502, p = 0.001$). The relationship of elevated salivary-cortisol in the evening with poorer stroke-survivor functional status approached significance ($r = -0.319, p = 0.051$).

Burden. At T1, greater burden was significantly correlated with greater uncertainty ($r = 0.439, p < 0.001$), poorer coping capacity ($r = -0.427, p < 0.001$), more caregiver comorbidities ($r = 0.271, p = 0.032$), poorer perceived quality of relationship with the stroke survivor ($r = 0.403, p = 0.001$), poorer perceived level of preparedness for caregiving ($r = 0.411, p = 0.001$), higher perceived stress ($r = 0.479, p < 0.001$), elevated salivary-cortisol level on waking ($r = 0.262, p = 0.049$), poorer HRQOL ($r = 0.464, p < 0.001$), poorer health status ($r = -0.446, p < 0.001$) and greater depressive symptoms ($r = 0.474, p < 0.001$). There was no statistical correlation between burden and salivary cortisol in the evening.

At T2, greater burden was still significantly correlated with greater uncertainty ($r = 0.586, p < 0.001$), poorer coping capacity ($r = -0.650, p < 0.001$), higher perceived stress ($r = 0.680, p < 0.001$), poorer HRQOL ($r = 0.447, p = 0.004$), poorer health status ($r = -0.523, p = 0.001$) and greater depressive symptoms ($r = 0.558, p < 0.001$). At T2, however, burden failed to correlate significantly with caregiver comorbidity, perceived quality of relationship with stroke survivor, perceived level of preparedness for caregiving or salivary cortisol on waking.

Health-related quality of life. At T1, poorer HRQOL was significantly correlated with greater uncertainty ($r = 0.475, p < 0.001$), poorer coping capacity ($r = -0.470, p < 0.001$), more caregiver comorbidities ($r = 0.482, p < 0.001$), higher perceived stress ($r = 0.573, p < 0.001$), greater burden ($r = 0.464, p < 0.001$), poorer health status ($r = -0.646, p < 0.001$) and greater depressive symptoms ($r = 0.558, p < 0.001$).

At T2, poor HRQOL remained significantly correlated with greater uncertainty ($r = 0.327, p = 0.039$), poorer coping capacity ($r = -0.556, p < 0.001$), more caregiver comorbidities ($r = 0.586, p < 0.001$), higher perceived stress ($r = 0.510, p = 0.001$), greater burden ($r = 0.447, p = 0.004$), poorer health status ($r = -0.564, p < 0.001$) and greater depressive symptoms ($r = 0.489, p = 0.001$). In addition, poor HRQOL at T2 was statistically correlated with decreased salivary-cortisol level on waking ($r = -0.333, p = 0.041$) and more stroke survivor comorbidities ($r = 0.380, p = 0.016$).

Depressive symptoms. At T1, greater depressive symptoms were significantly correlated with greater uncertainty ($r = 0.487, p < 0.001$), poorer coping capacity ($r = -0.467, p < 0.001$), less social support ($r = -0.305, p = 0.015$), higher perceived stress ($r = 0.590, p < 0.001$), greater burden ($r = 0.474, p < 0.001$), poorer HRQOL ($r = 0.558,$

$p < 0.001$), poorer health status ($r = -0.447, p < 0.001$), poorer stroke-survivor functional status ($r = -0.249, p = 0.049$) and greater severity of stroke ($r = 0.297, p = 0.018$).

At T2, greater depressive symptoms were still significantly correlated with greater uncertainty ($r = 0.413, p = 0.008$), poorer coping capacity ($r = -0.744, p < 0.001$), higher perceived stress ($r = 0.744, p < 0.001$), greater burden ($r = 0.558, p < 0.001$), poorer HRQOL ($r = 0.489, p = 0.001$), poorer health status ($r = -0.409, p = 0.009$) and poorer stroke-survivor functional status ($r = -0.464, p = 0.003$). Greater depressive symptoms were also significantly correlated with the following variables: fewer close friends and relatives ($r = -0.406, p = 0.007$) and elevated salivary-cortisol level in the evening ($r = 0.502, p = 0.001$). At T2, however, depressive symptoms were no longer significantly correlated with social support or severity of stroke.

Table 10

Main Study Variables and Characteristics with Any Statistically Significant Correlations at T1 (N = 63)

Variables	1	2	3	4	5	6	7
1. Uncertainty		0.545**	0.172	0.070	0.439**	0.475**	0.487**
2. Perceived Stress	0.545**		0.131	-0.104	0.479**	0.573**	0.590**
3. Salivary Cortisol AM (N = 57)	0.172	0.131		0.113	0.262*	-0.016	0.125
4. Salivary Cortisol PM (N = 54)	0.070	-0.104	0.113		-0.157	-0.027	0.008
5. Burden	0.439**	0.479**	0.262*	-0.157		0.464**	0.474**
6. Health-Related Quality of Life	0.475**	0.573**	-0.016	-0.027	0.464**		0.558**
7. Depressive Symptoms	0.487**	0.590**	0.125	0.008	0.474**	0.558**	
8. CG Comorbidity	0.119	0.124	0.064	0.066	0.271*	0.482**	0.147
9. CG Health Status	-0.321*	-0.421**	0.043	0.240	-0.446**	-0.646**	-0.447**
10. CG Coping Capacity	-0.424**	-0.543**	-0.173	0.201	-0.427**	-0.470**	-0.467**
11. CG Social Support	-0.307*	-0.205	-0.159	0.108	-0.202	-0.168	-0.305*
12. CG Age	0.195	-0.105	0.370**	0.250	0.076	0.088	-0.116
13. Perceived Quality of Relationship with the SS	0.289*	0.176	0.420**	0.127	0.403**	0.185	0.125
14. Perceived Level of Preparedness for Caregiving	0.202	0.166	0.241	0.102	0.411**	0.180	0.120
15. SS Severity of Stroke	0.201	0.224	-0.238	-0.057	-0.014	0.224	0.297*
16. SS Functional Status	-0.258*	-0.278*	0.219	0.042	-0.040	-0.181	-0.249*

Note. * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed; CG = caregiver; SS = stroke survivor. Higher scores = greater uncertainty, higher perceived stress, greater burden, poorer health-related quality of life, greater depressive symptoms, more comorbidities, better health status, better coping capacity, better social support, poorer perceived quality of relationship with the stroke survivor, poorer perceived level of preparedness for caregiving, greater severity of stroke and better functional status.

Table 11

Main Study Variables and Characteristics with Any Statistically Significant Correlations at T2 (N = 40)

Variables	1	2	3	4	5	6	7
1. Uncertainty		0.512**	0.038	0.418**	0.586**	0.327*	0.413**
2. Perceived Stress	0.512**		-0.212	0.520**	0.680**	0.510**	0.744**
3. Salivary Cortisol AM (N = 38)	0.038	-0.212		0.072	-0.226	-0.333*	-0.207
4. Salivary Cortisol PM (N = 38)	0.418**	0.520**	0.072		0.205	0.267	0.502**
5. Burden	0.586**	0.680**	-0.226	0.205		0.447**	0.558**
6. Health-Related Quality of Life	0.327*	0.510**	-0.333*	0.267	0.447**		0.489**
7. Depressive Symptoms	0.413**	0.744**	-0.207	0.502**	0.558**	0.489**	
8. CG Comorbidity	0.248	0.312	-0.113	0.274	0.243	0.586**	0.112
9. CG Health Status	-0.372*	-0.487**	0.383*	-0.370*	-0.523**	-0.564**	-0.409**
10. CG Coping Capacity	-0.560**	-0.755**	0.244	-0.433**	-0.650**	-0.556**	-0.744**
11. CG Social Support	-0.034	-0.310	0.149	-0.052	-0.190	-0.194	-0.257
12. CG Age	0.350*	-0.088	0.135	-0.106	0.082	0.305	-0.102
13. Perceived Quality of Relationship with the SS	0.359*	0.199	0.159	-0.031	0.257	-0.010	0.089
14. Number of close friends and relatives	-0.056	-0.185	0.116	-0.106	-0.293	-0.162	-0.406**
15. SS Severity of Stroke	0.143	0.205	0.071	0.426**	-0.173	-0.007	0.248
16. SS Functional Status	-0.398*	-0.419**	-0.066	-0.319	-0.224	-0.193	-0.464**
17. SS Comorbidity	0.156	0.246	0.083	-0.083	0.005	0.380*	0.210

Note. * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed; CG = caregiver; SS = stroke survivor. Higher scores = greater uncertainty, higher perceived stress, greater burden, poorer health-related quality of life, greater depressive symptoms, more comorbidities, better health status, better coping capacity, better social support, poorer perceived quality of relationship with the stroke survivor, greater severity of stroke and better functional status.

Differences in main study variables by categories of caregiver and stroke-survivor characteristics. I explored differences in main study variables by category of caregiver and stroke-survivor characteristics. Two sample *t*-tests (for dichotomous variables) and one-way analysis of variance (ANOVA: for categorical variables having more than two levels) were used to examine differences in uncertainty and perceived stress between categories of caregiver and stroke-survivor characteristics. The variables salivary cortisol (T1 and T2), burden (T1), HRQOL (T1 and T2) and depressive symptoms were positively skewed, due to the floor effects. Thus, the Mann-Whitney *U* test (for dichotomous variables) and the Kruskal-Wallis test (for categorical variables on more than two levels) were used to compare differences in these characteristics.

Dichotomous/categorical variables and uncertainty. At T1, level of uncertainty differed significantly depending on stroke-survivor health insurance type ($t = 2.610$, $p = 0.011$; greater uncertainty found in those with private insurance/Medicare/Medicare + supplemental health insurance plans). At T2, uncertainty differed significantly by caregiver role (spouse vs. nonspouse; $t = -2.343$, $p = 0.024$), with greater uncertainty found among spousal caregivers.

Dichotomous/categorical variables and perceived stress. At T1, degree of perceived stress differed significantly, depending on stroke-survivor communicative ability ($t = -2.092$, $p = 0.041$; higher stress, less communicative ability) and stroke-survivor health insurance type ($t = 2.197$, $p = 0.032$; higher stress, private insurance/Medicare/Medicare + supplemental health insurance plans). At T2, perceived stress differed significantly depending on stroke-survivor gender ($t = 2.266$, $p = 0.029$ with higher stress in men) and stroke-survivor income ($F = 4.708$, $p = 0.015$; higher

stress found in caregivers with adequate vs. comfortable income levels).

Dichotomous/categorical variables and salivary cortisol. At T1, level of salivary cortisol on waking differed significantly depending on stroke-survivor health insurance type ($p = 0.040$; elevated salivary-cortisol level found in those with private insurance/Medicare/Medicare + supplemental health insurance plans) and other life events ($p = 0.015$; elevated salivary-cortisol level found in caregivers with no other life events). At T1, no statistically significant differences in salivary-cortisol level in the evening were found among categories of caregiver or stroke-survivor characteristics. At T1 and T2, the difference in level of salivary cortisol on waking among spousal and nonspousal caregivers approached significance ($p = 0.050$; elevated salivary-cortisol level in spouse at T1 and T2). At T2, salivary-cortisol level on waking differed significantly by caregiver race (elevated salivary-cortisol level in non-Hispanic White than non-White participants; $p = 0.047$) and salivary-cortisol level in the evening differed significantly by caregiver income ($p = 0.032$; elevated salivary-cortisol level found in caregivers with insufficient income compared with those reporting adequate or comfortable income).

Dichotomous/categorical variables and burden. At T1, level of burden differed significantly depending on stroke-survivor health insurance type ($p = 0.034$; greater burden found in those with private insurance/Medicare/Medicare + supplemental health insurance plans). No statistically significant differences in burden were found among categories of caregiver or stroke-survivor characteristics at T2.

Dichotomous/categorical variables and health-related quality of life. At T1 and T2, HRQOL differed significantly by caregiver income ($p = 0.029$ at T1 and $p = 0.011$ at T2; poorer HRQOL was found in caregivers with insufficient compared with comfortable

income).

Dichotomous/categorical variables and depressive symptoms. At T1, depressive symptoms differed significantly by caregiver income ($p = 0.014$; greater depressive symptoms in those with insufficient income compared with those reporting adequate or comfortable income), stroke-survivor income ($p = 0.041$; greater depressive symptoms in those with adequate income compared with those whose income is comfortable), caregiver race (greater depressive symptoms in non-White; $p = 0.015$) and stroke-survivor race (greater depressive symptoms in non-White; $p = 0.018$). At T2, no statistically significant differences in depressive symptoms were found among any categories of caregiver and stroke-survivor characteristics.

Multivariate Analysis

As discussed in Chapter 3, multivariate stepwise regression and a p -value cut off point of 0.05 were used to determine the effect of uncertainty on perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms at each time point (Aims 1, 2 and 3), controlling for covariates. Univariate or multivariate regression in each Baron and Kenny (1986) step was used in establishing the mediator effect of each perceived stress and salivary cortisol on the relationship between uncertainty and each psychological outcome (burden, HRQOL and depressive symptoms; Aim 4). The robust standard error was used to protect against violations in the homoscedasticity assumption in all analyses. Given the large number of covariates available and the limited sample size ($N = 63$ at T1 and $N = 40$ at T2), only caregiver and stroke-survivor characteristics that were identified from bivariate analysis on the basis of a p -value less than or equal to 0.05 were entered in the multivariate stepwise regression models to test Aims 1, 2 and 3.

Due to multicollinearity between caregiver comorbidity and health status, caregiver comorbidity was used as a covariate and health status was excluded from the regression models. For Aim 4, covariates, which remained in the final stepwise models for each Aim 1, 2 and 3, were entered in the multivariate regression models. For all analyses, a *p*-value of less than 0.05 in a two-sided test was considered statistically significant.

Aim 1: Determine at each time point if uncertainty (regarding stroke survivors' health outcomes and new caregiver role) predicts levels of caregivers' perceived stress.

H1: At each time point, greater uncertainty scores will be positively associated with higher levels of perceived stress.

At T1, uncertainty and the covariates—coping capacity, stroke-survivor functional status, stroke-survivor health insurance type and stroke-survivor communicative ability, as identified from bivariate analysis on the basis of a *p*-value less than or equal to 0.05—were entered in the multivariate stepwise regression model. In the final regression model, uncertainty and all covariates except stroke-survivor functional status and health insurance remained. At T1, 48% of the variance in perceived stress was explained by uncertainty, coping capacity and stroke survivor's inability to communicate. Greater uncertainty ($p < 0.001$), poorer coping capacity ($p < 0.001$) and stroke survivor's inability to communicate ($p = 0.025$) were associated with higher perceived stress (see Table 12).

Table 12

Multivariate Stepwise Regression of Perceived Stress at T1 (N = 63)

Predictors	β	Robust SE	<i>t</i> statistic	<i>p</i> value	95% CI
Uncertainty	0.163	0.042	3.89	< 0.001**	[0.079, 0.246]
Coping Capacity	-0.338	0.086	-3.94	< 0.001**	[-0.510, -0.166]
SS Communicative Ability	4.000	1.743	2.30	0.025*	[0.513, 7.487]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; SS = stroke survivor; $F(3, 59) = 29.98$; $\text{Prob} > F = 0.000$; $R\text{-squared} = 0.48$; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

At T2, uncertainty and the covariates—caregiver comorbidity, social support, stroke-survivor functional status, stroke-survivor gender and stroke-survivor income, as identified from bivariate analysis on the basis of a *p*-value less than or equal to 0.05—were entered in the multivariate stepwise regression model. Coping capacity mediated the relationship between uncertainty and perceived stress; thus, coping capacity was excluded from the model. In the final regression model, uncertainty and two covariates—caregiver social support and stroke-survivor income—remained, explaining 49% of the variance in perceived stress. Greater uncertainty ($p < 0.001$), lower social support ($p = 0.011$) and stroke survivors' adequate (compared to comfortable) income ($p = 0.005$) were associated with higher perceived stress (see Table 13).

Table 13

Multivariate Stepwise Regression of Perceived Stress at T2 (N = 40)

Predictors	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.211	0.051	4.14	< 0.001**	[0.107, 0.314]
Social Support	-0.170	0.063	-2.68	0.011*	[-0.299, -0.041]
SS Adequate Income#	8.000	2.681	2.98	0.005**	[2.554, 13.439]
SS Insufficient income#	9.080	6.163	1.47	0.150	[-3.432, 21.592]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; SS = stroke survivor; $F(4, 35) = 8.23$; Prob > $F = 0.0001$; R -squared = 0.49; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed; #Reference category was stroke survivor comfortable income.

At T1 and T2, greater uncertainty scores were positively associated with higher perceived stress, controlling for covariates (caregiver coping capacity and stroke survivor's inability to communicate at T1 and social support and stroke-survivor income at T2). Thus, Hypothesis 1 was supported.

Aim 2: Determine at each time point if uncertainty predicts levels of caregivers' physiological stress (salivary cortisol).

H2: At each time point, greater uncertainty scores will be positively associated with elevated levels of salivary cortisol.

Uncertainty and salivary cortisol on waking. At T1, in univariate regression analysis, uncertainty was not significantly associated with salivary cortisol on waking ($p = 0.103$; see Table 14).

Table 14

Univariate Regression of Salivary Cortisol on Waking at T1 (N = 57)

Predictor	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.003	0.002	1.66	0.103	[-0.001, 0.006]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(1, 55) = 2.75$; Prob > $F = 0.103$; R -squared = 0.024.

At T1, the variables identified from bivariate analysis on the basis of a p -value less than or equal to 0.05—caregiver age, relationship to the stroke survivor (spousal vs. nonspousal), perceived quality of relationship with the stroke survivor, other life events and stroke-survivor health insurance type—were entered in the multivariate stepwise regression model. In the final regression model, caregiver age and other life events remained whereas relationship to the stroke survivor, perceived quality of relationship with the stroke survivor and stroke-survivor health insurance were excluded. At T1, 10% of the variance in salivary cortisol on waking was explained by caregiver age and other life events. Older caregiver age ($p = 0.043$) and having no other events in the period since the stroke ($p = 0.048$) were associated with elevated salivary-cortisol level on waking (see Table 15).

Table 15

Multivariate Stepwise Regression of Salivary Cortisol on Waking at T1 (N = 57)

Predictors	β	Robust SE	t statistic	p value	95% CI
CG Age	0.005	0.002	2.07	0.043*	[0.000, 0.009]
Other Life Events	-0.176	0.087	-2.03	0.048*	[-0.351, -0.002]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; CG = caregiver; $F(2, 54) = 4.61$; Prob > $F = 0.01$; R -squared = 0.10; * $p < 0.05$, two-tailed.

At T2, in univariate regression analysis, uncertainty was not significantly associated with salivary cortisol on waking ($p = 0.570$; see Table 16).

Table 16

Univariate Regression of Salivary Cortisol on Waking at T2 (N = 38)

Predictor	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.001	0.002	0.57	0.570	[-0.002, 0.004]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(1, 36) = 0.33$; Prob > $F = 0.57$; R -squared = 0.012.

At T2, the variables identified from bivariate analysis on the basis of a p -value less than or equal to 0.05 were caregiver race (non-Hispanic White vs. non-White), relationship to the stroke survivor (spousal vs. non-spousal). Caregiver race and relationship to the stroke survivor were entered in the multivariate stepwise regression model. In the final regression model, relationship to the stroke survivor remained. At T2, 15% of the variance in the salivary-cortisol level on waking was explained by the relationship to the stroke survivor (see Table 17). A spousal relationship with the stroke survivor was associated with elevated salivary-cortisol level on waking ($p = 0.035$).

Table 17

Multivariate Stepwise Regression of Salivary Cortisol on Waking at T2 (N = 38)

Predictors	β	Robust SE	t statistic	p value	95% CI
Relationship to the SS	0.17	0.077	2.19	0.035*	[0.012, 0.326]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; SS = stroke survivor; $F(1, 36) = 4.78$; Prob > $F = 0.036$; R -squared = 0.15; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

Uncertainty and salivary cortisol in the evening. At T1, uncertainty was not significantly associated with salivary cortisol in the evening in univariate regression analysis ($p = 0.451$; see Table 18). Salivary-cortisol level in the evening was not significantly correlated with any variable. In addition, no statistically significant differences in salivary-cortisol level in the evening were found among categories of caregiver or stroke-survivor characteristics.

Table 18

Univariate Regression of Salivary Cortisol in the Evening at T1 (N = 54)

Predictor	β	Robust <i>SE</i>	<i>t</i> statistic	<i>p</i> value	95% CI
Uncertainty	0.000	0.001	0.76	0.451	[-0.001, 0.002]

Note. β = unstandardized slope coefficient; *SE* = standard error; CI = confidence interval; $F(1, 52) = 0.58$; Prob > $F = 0.451$; R -squared = 0.006.

In univariate regression analysis at T2, uncertainty was not significantly associated with salivary cortisol in the evening ($p = 0.055$; see Table 19). Uncertainty and the covariates—coping capacity, caregiver income, stroke-survivor functional status and severity of stroke, which were identified from bivariate analysis on the basis of a p -value less than or equal to 0.05—were entered in the multivariate regression model. No variables that were significantly associated with salivary cortisol in the evening remained in the final model.

Table 19

Univariate Regression of Salivary Cortisol in the Evening at T2 (N = 38)

Predictor	β	Robust <i>SE</i>	<i>t</i> statistic	<i>p</i> value	95% CI
Uncertainty	0.001	0.001	1.98	0.055	[-0.000, 0.002]

Note. β = unstandardized slope coefficient; *SE* = standard error; CI = confidence interval; $F(1, 36) = 3.93$; Prob > $F = 0.055$; R -squared = 0.072.

At neither T1 nor T2 was uncertainty significantly associated with salivary cortisol, either on waking or in the evening. Thus, Hypothesis 2 (which proposed that at each time point, greater uncertainty scores would be positively associated with elevated levels of salivary cortisol) was not supported.

Aim 3: Examine at each time point the relationship of uncertainty to psychological outcomes (burden, HRQOL and depressive symptoms).

At each time point, greater uncertainty scores will be positively associated with

H3: greater burden,

H4: poorer HRQOL and

H5: greater depressive symptoms.

Uncertainty and burden. At T1, uncertainty and the covariates—perceived quality of relationship with the stroke survivor, perceived level of preparedness for caregiving, coping capacity, caregiver comorbidity and stroke-survivor health insurance type, as identified from bivariate analysis on the basis of a *p*-value less than or equal to 0.05—were entered into the multivariate regression model. In the final regression model, uncertainty and the covariates perceived level of preparedness for caregiving and caregiver comorbidity remained; however, perceived quality of relationship with the stroke survivor, caregiver coping capacity and stroke-survivor health insurance were excluded. Of the variance in burden, 43% was explained by uncertainty, perceived level of preparedness for caregiving and caregiver comorbidity (see Table 20). Greater uncertainty (*p* < 0.001), less preparedness for caregiving (*p* = 0.009) and more caregiver comorbidities (*p* = 0.010) were associated with greater burden.

Table 20

Multivariate Stepwise Regression of Burden at T1 (N = 63)

Predictors	β	Robust <i>SE</i>	<i>t</i> statistic	<i>p</i> value	95% CI
Uncertainty	0.335	0.071	4.72	< 0.001**	[0.193, 0.477]
Preparedness for Caregiving	4.236	1.579	2.68	0.009**	[1.076, 7.395]
CG Comorbidity	1.026	0.384	2.67	0.010*	[0.258, 1.794]

Note. β = unstandardized slope coefficient; *SE* = standard error; CI = confidence interval; CG = caregiver; $F(3, 59) = 14.14$; Prob > *F* = 0.000; *R*-squared = 0.43; **p* < 0.05, two-tailed, ***p* < 0.01, two-tailed.

At T2, uncertainty and the covariate coping capacity as identified from bivariate analysis on the basis of a p -value less than or equal to 0.05 were entered into the multivariate regression model. Both uncertainty and coping capacity remained in the final model. Forty nine percent (49%) of the variance in burden was explained by uncertainty and coping capacity (Table 21). Greater uncertainty ($p = 0.031$) and poorer coping capacity ($p = 0.006$) were associated with greater burden.

Table 21

Multivariate Stepwise Regression of Burden at T2 (N = 40)

Predictors	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.242	0.108	2.24	0.031*	[0.023, 0.461]
Coping Capacity	-0.542	0.185	-2.93	0.006**	[-0.917, -0.167]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(2, 37) = 21.55$; Prob > $F = 0.000$; R -Squared = 0.49; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

At T1 and T2, greater uncertainty scores were positively associated with greater burden, controlling for covariates (perceived level of preparedness for caregiving and caregiver comorbidity at T1 and caregiver coping capacity at T2). Thus, Hypothesis 3 was supported.

Uncertainty and health-related quality of life. At T1, uncertainty and the covariates—caregiver coping capacity, comorbidity and income, as identified from bivariate analysis on the basis of a p -value less than or equal to 0.05—were entered into the multivariate stepwise regression model. In the final regression model, uncertainty and covariates caregiver coping capacity and comorbidity remained; caregiver income, however, was excluded. Of the variance in HRQOL, 54% was explained by uncertainty, caregiver coping capacity and caregiver comorbidity (see Table 22). Greater uncertainty

($p < 0.001$), poorer coping capacity ($p = 0.026$) and more caregiver comorbidities ($p < 0.001$) were associated with poorer HRQOL.

Table 22

Multivariate Stepwise Regression of Health-Related Quality of Life at T1 (N = 63)

Predictors	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.017	0.005	3.74	< 0.001**	[0.008, 0.026]
Coping Capacity	-0.019	0.008	-2.29	0.026*	[-0.036, -0.002]
CG Comorbidity	0.130	0.032	4.00	< 0.001**	[0.065, 0.195]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(3, 59) = 13.95$; Prob > F = 0.000; R-squared = 0.54; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

In the univariate regression model at T2, 11% of the variance in HRQOL was explained by uncertainty, and greater uncertainty ($p = 0.023$) was associated with poorer HRQOL (see Table 23). It was noted that coping capacity mediated the relationship between uncertainty and HRQOL. Thus, a multivariate stepwise regression model was conducted, omitting coping capacity to determine the effect of uncertainty on HRQOL, controlling for covariates (caregiver income, caregiver comorbidity and stroke-survivor comorbidity) identified from bivariate analysis on the basis of a p -value less than or equal to 0.05; uncertainty, however, failed to remain in the final model.

Table 23

Univariate Regression of Health-Related Quality of Life at T2 (N = 40)

Predictor	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.020	0.009	2.37	0.023*	[0.003, 0.038]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(1, 38) = 5.61$; Prob > F = 0.023; R-squared = 0.11; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

To further explore significant variables that might explain HRQOL at T2, HRQOL at T2 was regressed on the independent variables coping capacity, caregiver income, caregiver comorbidity and stroke-survivor comorbidity, as identified from bivariate analysis on the basis of a p -value less than or equal to 0.05 while omitting uncertainty. In the final regression model, all independent variables remained except stroke-survivor comorbidity. Of the variance in HRQOL, 57% was explained by coping capacity, caregiver comorbidity and caregiver income (see Table 24). Poorer coping capacity ($p = 0.004$), more caregiver comorbidities ($p < 0.001$) and caregivers' income ($p = 0.001$; insufficient rather than comfortable) were associated with poorer HRQOL.

Table 24

Multivariate Stepwise Regression of Health-Related Quality of Life at T2 (N = 40)

Predictors	β	Robust SE	t statistic	p value	95% CI
Coping Capacity	-0.036	0.011	-3.12	0.004**	[-0.055, -0.012]
CG Comorbidity	0.129	0.028	4.68	< 0.001**	[0.073, 0.185]
CG Adequate Income#	0.636	0.392	1.62	0.114	[-0.160, 1.431]
CG Insufficient Income#	1.389	0.378	3.67	0.001**	[0.622, 2.157]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(4, 35) = 27.29$; Prob > $F = 0.0000$; R -squared = 0.57; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed ; #Reference category was caregiver comfortable income.

At T1, greater uncertainty scores were positively associated with poorer HRQOL, controlling for the covariates caregiver coping capacity and comorbidity. At T2, greater uncertainty scores were positively associated with poorer HRQOL only in the univariate regression model. Thus, Hypothesis 4 (that at each time point, greater uncertainty scores would be positively associated with poor HRQOL) was partially supported.

Uncertainty and depressive symptoms. At T1, uncertainty and the covariates—caregiver race, caregiver income, coping capacity, social support, stroke-survivor functional status and severity of stroke, as identified from bivariate analysis on the basis of a p -value less than or equal to 0.05—were entered in the multivariate stepwise regression model. In the bivariate analysis, depressive symptoms statistically differed depending on stroke-survivor race and stroke-survivor income. These variables, however, were excluded from the regression model due to multicollinearity between caregiver race and stroke-survivor race, as well as caregiver income and stroke-survivor income. In the final regression model, uncertainty and the covariates caregiver race and coping capacity remained, whereas caregiver income, social support, stroke-survivor functional status and severity of stroke were excluded. Of the variance in depressive symptoms, 40% was explained by uncertainty, coping capacity and caregiver race (see Table 25). Greater uncertainty ($p = 0.002$), poorer coping capacity ($p = 0.042$) and caregivers' race (non-White, $p = 0.009$) were associated with greater depressive symptoms.

Table 25

Multivariate Stepwise Regression of Depressive Symptoms at T1 (N = 63)

Predictors	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.111	0.033	3.31	0.002**	[0.044, 0.178]
Coping Capacity	-0.112	0.054	-2.08	0.042*	[-0.220, -0.004]
CG Race	3.454	1.271	2.72	0.009**	[0.911, 5.997]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; CG = caregiver; $F(3, 59) = 15.59$; Prob > $F = 0.000$; R -squared = 0.40; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

At T2, uncertainty and the covariate number of close friends and relatives, as identified from bivariate analysis on the basis of a p -value less than or equal to 0.05, were entered in the multivariate stepwise regression model. Depressive symptoms were also

statistically correlated with caregiver coping capacity and stroke-survivor functional status in bivariate analysis. Coping capacity, however, mediated the relationship between uncertainty and depressive symptoms when controlling for number of close friends and relatives, whereas uncertainty mediated the relationship between stroke-survivor functional status and depressive symptoms when controlling for number of close friends and relatives. Thus, coping capacity and stroke-survivor functional status were omitted from the regression model.

Of the variance in depressive symptoms, 22% was explained by uncertainty (see Table 26), and greater uncertainty was associated with greater depressive symptoms ($p = 0.002$). The number of close friends and relatives did not remain in the final model.

Table 26

Multivariate Stepwise Regression of Depressive Symptoms at T2 (N = 40)

Predictor	β	Robust SE	t statistic	p value	95% CI
Uncertainty	0.116	0.036	3.25	0.002**	[0.044, 0.189]

Note. β = unstandardized slope coefficient; SE = standard error; CI = confidence interval; $F(1, 38) = 10.59$; Prob > F = 0.002; R-squared = 0.22; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

At T1, greater uncertainty scores were positively associated with greater depressive symptoms, controlling for caregiver coping capacity and race. At T2, greater uncertainty scores were positively associated with greater depressive symptoms, whereas the covariate, number of close friends and relatives, did not remain in the final regression model. Thus, Hypothesis 5 (that at each time point, greater uncertainty scores would be positively associated with greater depressive symptoms) was supported.

Table 27 summarizes significant associations between uncertainty and perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms at T1 and T2.

Table 27

Significant Associations between Uncertainty and Perceived Stress, Salivary Cortisol, Burden, Health-Related Quality of Life and Depressive symptoms at T1 (N = 63) and T2 (N = 40)

	T1	T2
Perceived Stress	S (< 0.001**)	S (< 0.001**)
Salivary Cortisol AM	NS (0.103) in univariate analysis (N = 57)	NS (0.570) in univariate analysis (N = 38)
Salivary Cortisol PM	NS (0.451) in univariate analysis (N = 54)	NS (0.055) in univariate analysis (N = 38)
Burden	S (< 0.001**)	S (0.031*)
Health-Related Quality of Life	S (< 0.001**)	S (0.023*) in univariate analysis
Depressive Symptoms	S (0.002**)	S (0.002**)

Note. S = significant; NS = nonsignificant; * $p < 0.05$, two-tailed, ** $p < 0.01$, two-tailed.

Repeated-measures sensitivity analysis for Aims 1, 2 and 3. Separate bivariate linear mixed models with repeated measures of each dependent variable (perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms) were computed to further explore the overall effects of uncertainty or covariates on repeated measures of each dependent variable.

Sensitivity analysis revealed that uncertainty was associated with repeated measures of perceived stress, burden, HRQOL and depressive symptoms. Uncertainty, however, was not associated with repeated measures of salivary cortisol either on waking or in the evening. The interactions between uncertainty and time were not associated with repeated measures of perceived stress, salivary cortisol either on waking or in the evening,

burden, HRQOL or depressive symptoms.

The majority of covariates that remained in the final stepwise regression model at either at T1 and T2 were associated with repeated measures of each dependent variable. Stroke-survivor communication ability, which was associated with perceived stress at T1, was not significantly associated with repeated measures of perceived stress although it approached significance ($p = 0.062$). The relationship to the stroke survivor associated with salivary cortisol on waking at T2 was not significantly associated with repeated measures of salivary cortisol on waking ($p = 0.064$), but did approach significance. With these few exceptions, the results from the regression analysis at each time point were consistent with the findings from bivariate linear mixed models with repeated measures of each dependent variable.

Time was not associated with repeated measures of perceived stress, salivary cortisol on waking or in the evening or depressive symptoms. Time, however, was associated with repeated measures of burden and HRQOL. In other words, perceived stress, salivary cortisol on waking or in the evening and depressive symptoms did not change, whereas caregivers demonstrated greater burden and poorer HRQOL by 6 weeks poststroke. With the exception of the effect of time on burden, these results were consistent with the findings from the paired t -tests using subjects with complete data at both time points ($N = 40$). The paired t -test showed that, although not statistically significant, the differences between T1 and T2 for burden in that smaller sample approached significance at $p = 0.068$.

Aim 4: Explore at each time point the mediator effect of stress (perceived stress and physiological stress) on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms).

At each time point, perceived stress and salivary cortisol will mediate the relationship between uncertainty and

H6: burden,

H7: HRQOL and

H8: depressive symptoms.

Mediator effect of perceived stress on the relationship between uncertainty and burden. At T1, uncertainty was a significant determinant of burden ($\beta = 0.44$, $t = 5.14$, $p < 0.001$) and of perceived stress ($\beta = 0.26$, $t = 5.70$, $p < 0.001$). When uncertainty and perceived stress were simultaneously regressed on burden, while controlling for perceived level of preparedness for caregiving and caregiver comorbidity, these four variables together explained 47% of the variance in burden; perceived stress remained a significant determinant ($\beta = 0.43$, $t = 2.10$, $p = 0.040$), and the significant relationship of uncertainty to burden was reduced ($\beta = 0.23$, $t = 2.92$, $p = 0.005$), indicating a partial mediator effect.

Uncertainty ($p = 0.031$) and coping capacity ($p = 0.006$) were significant factors influencing burden at T2. Coping capacity mediated the relationship between uncertainty and stress; thus, coping capacity was excluded to test this aim, that is, the mediating effect of perceived stress in the relationship between uncertainty and burden. At T2, uncertainty was a significant determinant of burden ($\beta = 0.44$, $t = 4.54$, $p < 0.001$) and of perceived stress ($\beta = 0.23$, $t = 3.76$, $p = 0.001$). When uncertainty and perceived stress

were simultaneously regressed on burden, these two variables together explained 54% of the variance in burden; perceived stress remained a significant determinant ($\beta = 0.86$, $t = 3.78$, $p = 0.001$), and the significant relationship of uncertainty to burden was reduced ($\beta = 0.24$, $t = 2.56$, $p = 0.015$), indicating a partial mediator effect.

Mediator effect of perceived stress on the relationship between uncertainty and health-related quality of life. At T1, uncertainty was a significant determinant of HRQOL ($\beta = 0.029$, $t = 4.15$, $p < 0.001$) and of perceived stress ($\beta = 0.26$, $t = 5.70$, $p < 0.001$). When uncertainty and perceived stress were simultaneously regressed on HRQOL, while controlling for caregiver comorbidity and coping capacity, these four variables together explained 55% of the variance in HRQOL; perceived stress was not a significant determinant ($\beta = 0.017$, $t = 1.91$, $p = 0.062$), and the significant relationship of uncertainty to HRQOL remained ($\beta = 0.014$, $t = 2.85$, $p = 0.006$), indicating no mediator effect.

At T2, uncertainty was a significant determinant of HRQOL ($\beta = 0.02$, $t = 2.37$, $p = 0.023$) and of perceived stress ($\beta = 0.23$, $t = 3.76$, $p = 0.001$). When uncertainty and perceived stress were simultaneously regressed on HRQOL, the two variables explained 26% of the variance in HRQOL; perceived stress remained a significant determinant ($\beta = 0.06$, $t = 2.58$, $p = 0.014$), whereas uncertainty was no longer a significant determinant ($\beta = 0.01$, $t = 0.67$, $p = 0.505$), indicating a full mediator effect.

Mediator effect of perceived stress on the relationship between uncertainty and depressive symptoms. At T1, uncertainty was a significant determinant of depressive symptoms ($\beta = 0.14$, $t = 4.67$, $p < 0.001$) and perceived stress ($\beta = 0.26$, $t = 5.70$, $p < 0.001$). When uncertainty and perceived stress were simultaneously

regressed on depressive symptoms, while controlling for coping capacity and caregiver race, these four independent variables together explained 46% of the variance in depressive symptoms; perceived stress remained a significant determinant ($\beta = 0.19$, $t = 3.11$, $p = 0.003$), and the significant relationship of uncertainty to depressive symptoms was attenuated ($\beta = 0.08$, $t = 2.17$, $p = 0.034$), indicating a partial mediator effect.

At T2, uncertainty was a significant determinant of depressive symptoms ($\beta = 0.12$, $t = 3.25$, $p = 0.002$) and of perceived stress ($\beta = 0.23$, $t = 3.76$, $p = 0.001$). When uncertainty and perceived stress were simultaneously regressed on depressive symptoms, these two variables together explained 62% of the variance in depressive symptoms; perceived stress remained a significant determinant ($\beta = 0.41$, $t = 7.48$, $p < 0.001$), and the significant relationship of uncertainty to depressive symptoms became nonsignificant ($\beta = 0.02$, $t = 0.70$, $p = 0.489$), indicating a full mediator effect.

Mediator effect of salivary cortisol on the relationship between uncertainty and psychological outcomes (burden, HRQOL and depressive symptoms). At neither time point—T1 or T2—was uncertainty a significant determinant of salivary cortisol on either waking ($p = 0.103$ at T1 and $p = 0.570$ at T2) or in the evening ($p = 0.451$ at T1 and $p = 0.055$ at T2). Thus, there were no mediating effects of salivary cortisol on waking or in the evening on the relationship of uncertainty to psychological outcomes (burden, HRQOL and depressive symptoms).

Summary for Aim 4. Table 28 summarizes mediator effects of perceived stress on each relationship between uncertainty, burden, HRQOL and depressive symptoms. There was a partial mediator effect of perceived stress on the relationship between

uncertainty and burden, while controlling for perceived level of preparedness for caregiving and caregiver comorbidity at T1 and in univariate regression analysis without controlling for covariates at T2. There were, however, no mediating effects of salivary cortisol on waking or in the evening on the relationship of uncertainty to burden at either T1 or T2. Thus, Hypothesis 6 (that at each time point, perceived stress and salivary cortisol would each mediate the relationship between uncertainty and burden) was partially supported.

There was no mediator effect of perceived stress on the relationship between uncertainty and HRQOL at T1. By T2, there was a full mediator effect of perceived stress on the relationship of uncertainty to HRQOL in univariate regression analysis without controlling for covariates. Prior to testing the mediator effect of perceived stress on the relationship between uncertainty and HRQOL, the association between uncertainty and HRQOL, however, was not strong. There were, however, no mediating effects of salivary cortisol on waking or in the evening on the relationship of uncertainty to HRQOL at either T1 or T2. Thus, Hypothesis 7 (that at each time point, perceived stress and salivary cortisol would mediate the relationship between uncertainty and HRQOL) was partially supported.

There was a partial mediator effect of perceived stress on the relationship between uncertainty and depressive symptoms, while controlling for caregiver coping capacity and race at T1 and a full mediator effect of perceived stress on the relationship of uncertainty to depressive symptoms in univariate regression analysis without controlling for covariates at T2. There were, however, no mediating effects of salivary cortisol on waking or in the evening on the relationship of uncertainty to depressive symptoms at

both T1 and T2. Thus, Hypothesis 8 (that at each time point, perceived stress and salivary cortisol would mediate the relationship between uncertainty and depressive symptoms) was partially supported.

Table 28

Mediator Effects of Perceived Stress on the Relationship between Uncertainty, Burden, Health-Related Quality of Life and Depressive Symptoms at T1 (N = 63) and T2 (N = 40)

	T1	T2 (in univariate analysis)
Burden	Partial Mediation	Partial Mediation
Health-Related Quality of Life	No Mediation	Full Mediation
Depressive Symptoms	Partial Mediation	Full Mediation

CHAPTER 5: DISCUSSION

Introduction

I examined the effect of uncertainty on caregiver perceived and physiological stress and psychological outcomes (burden, health-related quality of life [HRQOL] and depressive symptoms) within the first 2 weeks (baseline) following a sudden health event (i.e., stroke) in a family member and again 4 weeks later (~6 weeks poststroke). In addition, I examined whether perceived or physiological stress influenced the relationship between uncertainty and psychological outcomes at each time point. This final chapter (a) summarizes principal findings, (b) discusses the meaning of study results and their relationship to existing literature, (c) identifies the strengths and limitations of the study, (d) specifies implications for clinical practice and health policy and (e) makes recommendations for future research.

Summary of Principal Findings

To the best of my knowledge, I believe I am the first to investigate the effect of uncertainty on perceived and physiological stress, burden, HRQOL or depressive symptoms in caregivers of stroke survivors in the very early phase poststroke. In addition, I explored the mediator effect of stress on the relationship between uncertainty and psychological outcome. Greater uncertainty was significantly associated with higher perceived stress in caregivers of stroke survivors, both immediately following the stroke and at 6 weeks poststroke. Uncertainty was not a significant predictor of physiological stress, however, at either time point. Greater uncertainty was significantly associated with greater burden, poorer HRQOL and greater depressive symptoms at both observations. By 6 weeks poststroke, however, uncertainty was significantly associated with poorer

HRQOL only in univariate analysis, indicating that the importance of uncertainty to HRQOL had waned. In addition, perceived stress partially mediated the relationship between uncertainty and depressive symptoms at baseline, and at 6 weeks poststroke it fully mediated that relationship; patients with greater uncertainty had more depressive symptoms as perceived stress levels increased. At both observations, perceived stress partially mediated the relationship between uncertainty and burden.

Comparison with Findings in Existing Literature

Uncertainty. The present study revealed that the level of uncertainty in caregivers of stroke survivors was consistent from baseline (Mean [*M*] ± Standard Deviation [*SD*]: 84.13 ± 19.93 , $N = 63$) to 6 weeks poststroke ($M \pm SD$: 85.23 ± 23.94 , $N = 40$); further, in the 40 caregivers with complete data at both time points, there was no statistically significant difference in level of uncertainty. The level was higher than that previously reported for several populations of family caregivers for persons living with, for example, dementia, prostate cancer and myocardial infarction (Mishel, 1997b). In addition, Mitchell and Courtney (2004) reported that average caregiver uncertainty levels, when a family member transferred from intensive care, ranged from 76.24 to 78.93. Nausser's (2010) study of uncertainty in caregivers for patients with heart failure, using only a 30-item version of the Perception of Uncertainty in Illness Scale for Family Member, also reported proportionally lower uncertainty scores than in the caregivers of stroke survivors in the present study. These findings suggest that caregivers of stroke survivors may have somewhat greater uncertainty. The average duration of providing care for patients with heart failure in the Nausser study was approximately 4 years, whereas the sampling interval for caregiving after stroke in the present study was shorter (within 2 weeks

poststroke to around 6 weeks poststroke). Caregivers of new stroke survivors must adjust to an altered relationship with their family member and also take on new responsibilities as informal caregivers; they may have great uncertainty in making meaning of their stroke survivors' potential health outcomes and their own new caregiver role.

Characteristics of caregivers or their stroke survivors that influence uncertainty in caregivers for stroke survivors have not been well documented in the existing literature. Although not the aim of the present study, it was notable that several of these were found related to uncertainty: caregiver coping capacity, caregiver health status, perceived quality of relationship with the stroke survivor and stroke-survivor functional status at both observations; and caregiver social support and stroke-survivor health-insurance type at baseline and caregiver age and relationship to the stroke survivor at 6 weeks poststroke. These observations add to the body of knowledge about factors that may influence caregiver uncertainty.

Stress.

Perceived stress. In this study, caregiver perceived stress was consistent from baseline ($M \pm SD$: 24.21 ± 9.55 , $N = 63$) to 6 weeks poststroke ($M \pm SD$: 24.47 ± 10.74 , $N = 40$), regardless of the current posthospital placement of the patient (rehabilitation hospital, nursing facility or other). By comparison, the mean perceived stress-scale levels in a probability sample of the United States ($N = 2,355$) was $19.62 (\pm 7.49)$; B. Cohen & Williamson, 1988) and $16.22 (\pm 8.73)$ in caregivers of older adults with heart failure (Schwarz & Dunphy, 2003). Average perceived stress levels in caregivers of stroke survivors in the present study were higher than those reported in these other studies, suggesting that stroke-survivor caregivers are at high risk for the development of stress-

related morbidity as found in the existing literature.

The finding that greater uncertainty was associated with higher perceived stress in caregivers of stroke survivors is supported by studies on uncertainty in other populations. Shannon and Lee (2008) reported that a mother's uncertainty about infant HIV serostatus was correlated with her perceived stress. In their study, however, there was no adjustment for other factors that may have influenced perceived stress, whereas in the present study, uncertainty was a main predictor for perceived stress when adjusting for other caregiver and stroke-survivor characteristics, both at baseline and at 6 weeks poststroke. These results indicate that caregiver uncertainty is likely a key factor associated with stress during the first 6 weeks of caregiving.

Previous research identified several factors affecting perceived stress: caregiver gender, age, health status, time since beginning to provide care for stroke survivors, coping strategies/capacity, social support, preparedness for caregiving, stroke-survivor functional status and severity of stroke (Ostwald et al., 2009). With the exception of coping capacity and social support, none of these factors was supported in the present study. One possible reason for these differences may be that the time period we explored, the first 6 weeks of caregiving, represents only a relatively early period of caregiving, whereas Ostwald et al. (2009) investigated perceived stress in caregivers on hospital discharge and then up to 12 months postdischarge. Another possibility affecting differences in study outcomes is the larger sample size in the Ostwald et al. study, which included 159 stroke survivors and their caregivers.

In the present study, in addition to uncertainty, factors associated with perceived stress were caregiver coping capacity and stroke survivor's inability to communicate at

baseline and social support and stroke survivor's income at 6 weeks poststroke. Of stroke survivors, 43% were unable to communicate verbally. Other researchers have reported that communication loss or aphasia was the most upsetting factor to caregivers and was related strongly to caregiver burden (Bakas, Kroenke, et al., 2006; Vincent et al., 2009). When stroke survivors were in the acute stage, their caregivers experienced stress from the stroke survivor's inability to communicate. At 6 weeks poststroke, caregivers reported significantly less perceived social support from family, friends and significant others compared to baseline. Although stroke survivors had recovered much function, other issues such as economic strain and reduction in perceived social support surfaced as important aspects affecting caregiver perceived stress. In addition, although caregivers spent significant time in caregiving during the first 6 weeks of caregiving, this factor did not affect perceived stress. Time spent per day in caregiving was consistent from 8.59 (± 6.64 , $N = 63$) at baseline to 7.60 (± 6.59 , $N = 40$) at 6 weeks poststroke. Tooth et al. (2005) reported that caregivers of stroke survivors spent approximately 4.6 hours per day at 6 months poststroke and approximately 3.6 hours per day at 12 months to assist patients with daily activities.

Poorer caregiver coping capacity was associated with higher perceived stress at baseline and mediated the relationship between uncertainty and stress at 6 weeks poststroke; it is noteworthy that coping capacity consistently influenced perceived stress during the first 6 weeks of caregiving. Even with a relatively small sample size at 6 weeks poststroke, uncertainty and coping capacity remained significant predictors of perceived stress. After the stroke survivor's discharge from the hospital, caregivers with greater uncertainty experienced higher levels of perceived stress, which may have

contributed to difficulty adjusting to their new role. Those with higher coping capacity at 6 weeks poststroke, however, had lower perceived stress.

Physiological stress. No studies investigating the relationship between uncertainty and physiological stress response were found in the current literature. In the present study, uncertainty was not a predictor of physiological stress at either time point. There was, however, a significant correlation between caregiver uncertainty and evening salivary-cortisol level at 6 weeks poststroke. Although caregivers were uncertain regarding the outcomes of the stroke and their new caregiver role at baseline, there was no measurable influence on physiological stress in the first few days after the stroke. Their greater uncertainty by 6 weeks poststroke, however, may have influenced their physiological regulatory mechanisms. At that same observation point, there was also a significant correlation between perceived stress and salivary-cortisol level in the evening, whereas this relationship was not significant at baseline. One possible explanation is that while physiologic homeostasis may have been maintained even in the face of perceived stress at baseline, the body's failure to compensate longer term led to a physiological stress response by 6 weeks poststroke.

In addition, acute stress response, which would be represented by an increase in salivary cortisol among caregivers of stroke survivors, may be more likely to be detected in salivary cortisol in the evening. Woods et al. (2008) also reported that cortisol dysregulation for residents with advanced dementia is more likely to be detected in the evening. In the present study, salivary-cortisol levels on waking, however, were not correlated with uncertainty or perceived stress at either time point. A 12-month self-management intervention in patients with irritable bowel syndrome, including cognitive-

behavioral strategies, reduced perceived stress over time, but did not diminish urinary salivary cortisol in the morning (Deechakawan, Cain, Jarrett, Burr, & Heitkemper, 2013).

In the present study, the mean salivary-cortisol levels on waking and in the evening at each time point were in normal ranges, based on the salivary cortisol expected ranges provided by the enzyme-linked immuno sorbent assay kit manufacturer, although salivary-cortisol levels in a few participants were above or below normal ranges. Further exploration is required with a larger sample size. One study reporting salivary-cortisol levels in female caregivers of stroke survivors found that younger age was associated with lower levels of cortisol on waking and 30 minutes postwaking (Saban et al., 2012). In the present study, at baseline, older caregiver age was associated with elevated salivary-cortisol level on waking, and experiencing other life events was associated with a lower salivary-cortisol level on waking; these significant associations had, however, disappeared by 6 weeks poststroke. Instead, at the second time point, a spousal relationship with stroke survivors was associated with elevated waking levels of salivary cortisol. The inconsistency found for study variables that were related to salivary-cortisol levels (correlations and associations) at both time points—and either on waking or in the evening—in the present study is puzzling and warrants further research on salivary cortisol with repeated measures in a larger sample to better understand the mixed results.

Saban et al. (2012) reported that salivary-cortisol levels were lower across the day in caregivers with higher versus lower depressive-symptom scores. Another study reported that patients with relapsed major depression had higher cortisol levels than patients in stable remission (Zobel et al., 2001). At 6 weeks poststroke in the present study, having greater depressive symptoms was correlated with elevated salivary-cortisol

level in the evening, but not with the levels on waking at either time period. The present study measured salivary-cortisol levels at two time points during the first 6 weeks of caregiving, whereas Saban et al. (2012) measured them at approximately 8 months of caregiving. One possible explanation for these differences may be that when caregivers initially are exposed to stressors, e.g., within 2 weeks poststroke, their physiologic homeostasis may have been maintained, as suggested previously. By 6 weeks poststroke, as in the present study, stressors had induced an increase in hypothalamic-pituitary-adrenal (HPA)-axis activity, which caused elevated cortisol level. By 8 months poststroke, however, HPA-axis activity may have decreased or overadjusted, resulting in lower levels of cortisol (Fries, Hesse, Hellhammer, & Hellhammer, 2005; Saban et al., 2012).

Another difference between the present study and that of Saban et al. (2012) is gender differences in the study samples; the present study included both male and female caregivers, whereas their study was limited to women. The present study, however, found no significant gender differences for salivary-cortisol levels. Women with irritable-bowel syndrome had slightly higher urinary cortisol levels than did men; however, this difference was not statistically significant (Deechakawan et al., 2013). Thus, gender differences between study samples would not likely be a reason affecting the relationship between salivary-cortisol levels and depressive symptoms.

Psychological outcomes.

Burden. In this study, caregivers reported mild to moderate burden on average during the first 6 weeks of caregiving; this observation is consistent with results of a study by Bugge et al. (1999) in which caregivers experienced “strain” at least 1 month poststroke. In the present study, 14% to 20% of caregivers experienced burden at

moderate-to-severe or severe levels. One possible reason for the inconsistent findings between the present study and the study by Tooth et al. (2005), in which 44% caregivers reported considerable burden at 6 months and 42% reported burden at 12 months poststroke, may be the effect of time on burden. I studied caregiver burden during the first 6 weeks of caregiving whereas Tooth et al. studied burden from 6 months to 12 months poststroke; the experience of burden may be cumulative and worsen over time and certainly burden in caregivers is reported to be at much higher levels at 1 year. Some studies reported that caregiver burden continued to increase from 2 months to 6 months (Ilse et al., 2008) or from 1 month to 6 months (Blake et al. 2003; Bugge et al., 1999). Two other studies, however, reported that burden of caregivers decreased over time, that is, baseline to 6 months (McCullagh et al., 2005; Vincent et al., 2009). Additional studies that encompass multiple measurements over longer periods from the stroke event to several years, as well as inclusion of comparable risk factors and measures, are required to understand the mixed results in the existing literature.

No previous studies were found that explored the direct relationship between uncertainty and burden in caregivers. In a study of caregivers for patients with Parkinson's disease, Sanders-Dewey et al. (2001) reported that uncertainty was a significant factor affecting psychological distress. In the present study, uncertainty was a significant predictor for burden. I found that burden in caregivers increased slightly from baseline (within 2 weeks poststroke) to 6 weeks poststroke, although there was no statistical difference based on paired *t*-tests in the smaller sample of those who completed the study. In addition, at both observations, perceived stress partially mediated the relationship between uncertainty and burden. Although the mediator effect of perceived

stress on the relationship between uncertainty and burden was weak, this result suggests that caregiver uncertainty may lead to a stressful caregiving situation, which eventually induces greater burden.

Uncertainty, perceived level of preparedness for caregiving and caregiver comorbidity at baseline, and uncertainty and caregiving coping capacity at 6 weeks poststroke were significant factors influencing burden in the present study. The findings that caregiver comorbidity was associated with burden at baseline and that coping capacity was associated with burden 6 weeks poststroke are supported by other studies (Cameron & Gignac, 2008; Van Puymbroeck & Rittman, 2005). Ostwald et al. (2009) reported that preparedness for caregiving influenced perceived stress in caregivers for stroke survivors. The significant effect of perceived level of preparedness for caregiving on burden found in the present study, however, has not been shown in previous studies. Another interesting finding in the present study was that perceived level of preparedness for caregiving was associated with burden only at baseline; further, there was no significant difference in perceived level of preparedness for caregiving at baseline and 6 weeks poststroke (from $M \pm SD$: 2.21 ± 1.11 , $N = 63$ to $M \pm SD$: 2.25 ± 1.01 , $N = 40$ on scale of 1 [*excellent*] to 4 [*poor*]), suggesting that although there was greater uncertainty among caregivers, time in caregiving experience did not affect sense of preparedness and average preparedness level did not improve. Perceived level of preparedness for caregiving may be an important factor in acute stages of stroke, such as within the first 2 weeks poststroke, but over time, other factors such as uncertainty and coping capacity may be more important influences on burden than preparedness for caregiving. This factor warrants further exploration.

Health-related quality of life. Northouse et al. (2002) reported that uncertainty was associated with mental health dimensions of HRQOL (while adjusting for caregiver and patient characteristics) in caregivers for persons with recurrent breast cancer. In the present study, uncertainty was associated with HRQOL at baseline. By 6 weeks poststroke, uncertainty had lost its significant association with HRQOL, while adjusting for other caregiver and stroke-survivor characteristics, although there was a significant association in univariate regression analysis. The study by Northouse et al. (2002) was a cross-sectional study with a sample of 189. In the present study, only 40 caregivers remained at 6 weeks poststroke to explore the relationship between uncertainty and HRQOL. Our dissimilar result could, thus, be related to the limited sample size; at 6 weeks poststroke, the 40 remaining caregivers, on average, had significantly poorer HRQOL and poorer health status than they had at baseline (based on a paired *t*-test with the sample of 40 caregivers), whereas uncertainty levels among these remaining caregivers was consistent over time. Another possibility is that a relatively lower reliability and fewer items (only 5) of the EQ5D instrument used to measure HRQOL may have impeded the detection of the effect of uncertainty on HRQOL. Although caregiver HRQOL and health status each declined from baseline to 6 weeks poststroke, other factors, including caregiver coping capacity and comorbidity, appeared to have a stronger influence on HRQOL than did uncertainty at 6 weeks poststroke. Neither age of caregiver nor that of stroke survivor influenced HRQOL or health status in caregivers in the short time period of the present study; it should be noted, however, that 30% of caregivers were aged 65 years or older, placing them at higher longer term risk for morbidity and mortality from caregiving.

Our finding of a continuous effect of caregiver coping capacity and comorbidity on HRQOL over time does support results of previous studies (Morimoto et al., 2003; Visser-Meily et al., 2009). McCullagh et al. (2005) revealed that increasing caregiver age and male gender were associated with their poorer quality of life, whereas these same caregiver characteristics were not associated with HRQOL in the present study. Possible explanations for this difference may include the variation between studies in operational definitions and measures for quality of life and HRQOL. The McCullagh et al. study used EQ-Visual-Analog Scale (VAS) to measure quality of life, whereas the present study used EQ5D to measure HRQOL. In addition, caregivers in this sample were much younger ($M \pm SD$: 56.92 ± 13.81 years) compared to those in the study by McCullagh et al. (2005; $M \pm SD$: 65.7 ± 12.5 years).

One of the noteworthy findings of the present study is that caregiver HRQOL, health status and comorbidity each got worse, even while stroke-survivor functional status improved. Caregiving outcomes in stroke survivors is reported to be related to physical and psychological health as well as related morbidities (Anderson et al., 1995; Bauer et al., 2000; Berg et al., 2005; Blake et al., 2003; Burman, 2001; Forsberg-Warley et al., 2002; McCullagh et al., 2005; Pierce et al., 2006; White et al., 2003). Stroke has a sudden onset. Thus, while caregivers were trying to adjust to their new caregiver role in the early weeks of caregiving, their own health status had already begun to deteriorate, underscoring the importance of monitoring caregivers during this critical period.

Perceived stress mediated the relationship between uncertainty and HRQOL at 6 weeks poststroke but not at baseline. This relationship is limited to univariate regression analysis without adjusting for other caregiver and stroke-survivor characteristics. In

addition, prior to testing the mediator effect, the association between uncertainty and HRQOL was not strong. This result, however, may be clinically meaningful. Uncertainty was associated with HRQOL in patients with cancer and their caregivers (Northouse et al., 2002) and patients with gynecological cancer (Padilla, Mishel, & Grant, 1992). Compared to noncaregivers, caregivers of patients with Alzheimer's disease had elevated allostatic load (measures of blood pressure, BMI, total/HDL, HDL cholesterol, plasma norepinephrine and epinephrine; Roepke et al., 2011). Uncertainty in caregivers of stroke survivors during the early weeks is likely a key factor associated with caregiver stress, leading to poorer HRQOL.

Depressive symptoms. Although in the present study caregivers, on average, reported mild levels of depressive symptoms, approximately 30% of caregivers had moderate, moderate-to-severe or severe depressive symptoms. This finding is consistent with previous reports that as many as 23% to 33% of caregivers experience depression during an 18-month poststroke follow-up period (Berg et al., 2005; Blake et al., 2003), yet is nearly twice as high as the 18% of caregivers with moderate, moderate-to-severe or severe depressive symptoms reported in the Bakas, Kroenke, et al. study (2006).

The finding of a significant effect of uncertainty on depressive symptoms is consistent with earlier findings of a correlation between uncertainty and depression in caregivers for persons with Parkinson's disease (Sanders-Dewey et al., 2001). In that study, however, other predictors that may influence caregiver depression were not analyzed, whereas in this study, uncertainty, caregiver coping capacity and race were each found to be associated with depressive symptoms at baseline. At 6 weeks poststroke, uncertainty and the covariate number of close friends and relatives were entered in the

multivariate stepwise regression model, but number of close friends and relatives did not remain in the final model. Thus, uncertainty itself was related to depressive symptoms. In the existing literature, a number of factors were found to influence depressive symptoms but mixed results between studies also have been reported. One result of the present study, that caregiver race and coping capacity were associated with depressive symptoms at baseline, is supported a study by Van Puymbroeck et al. (2008). Caregiver race was no longer associated with depressive symptoms at 6 weeks poststroke, but coping capacity mediated the relationship between uncertainty and depressive symptoms.

Although uncertainty and coping capacity were each significant predictors for depressive symptoms in caregivers for stroke survivors, over time the effect of coping capacity on depressive symptoms proved stronger than that of uncertainty. Caregivers may have mixed emotions about their caregiving situation because they may have daily caregiving tasks that disturb their own lifestyles or jobs. Chumbler, Rittman, and Wu (2008) reported that higher coping capacity was associated with lower levels of depression in caregivers of stroke survivors across 2 years of follow-up. They suggested that caregivers be encouraged to cope with their situations by finding meaning in caregiving rather than by focusing on negative demands or burden, and that this strategy may prevent depressive symptoms (Chumbler et al., 2008).

The current findings show that the degree of influence of perceived stress in the relationship between uncertainty and depressive symptoms was strengthened at 6 weeks poststroke. In other words, patients with greater uncertainty had greater depressive symptoms as perceived stress levels increased. In patients with multiple sclerosis, uncertainty about the illness was an important mediator of the relationship between the

present state of the illness and depression (Kroencke, Denney, & Lynch, 2001). Perceived stress as a mediator of the relationship between uncertainty and depressive symptoms is not clear in the current literature. Caregivers of stroke survivors may experience stress because they are not certain of the extent to which stroke survivors will worsen or recover, as well as how involved they will need to be in longer term care for the stroke survivor and the commensurate impacts on employment, economics, family life and so on. This uncertainty is highly associated with stress, which eventually leads to greater depressive symptoms. Stress-management behavioral therapy has been shown to decrease the prevalence of depression in patients with early-stage breast cancer (Antoni et al., 2001). Cognitive-behavioral therapies, including stress management related to uncertainty, may have utility in decreasing depressive symptoms in caregivers of stroke survivors as well.

Strengths of This Study

The present study exhibits several strengths. First, the prospective longitudinal design captured the effects of uncertainty on perceived and physiological stress, burden, HRQOL and depressive symptoms at two time points within the first 6 weeks poststroke: within 2 weeks poststroke and again at ~6 weeks poststroke. In addition, this is the first study to examine the role of uncertainty on these outcomes in caregivers of stroke survivors or to investigate caregiver experiences in the very early period poststroke. By including physiologic measures of stress, the early time period of caregiving was further illuminated. Although the follow-up period was relatively short, I was able to examine the influence of uncertainty on outcomes at each time point. As there was no intervention for caregivers between baseline and 6 weeks poststroke, I, thus, observed the “natural

history” of this relationship. The effects of uncertainty on perceived stress, burden, HRQOL and depressive symptoms were consistently important over time and explained a large amount of their variance. Different caregiver and stroke-survivor characteristics, however, affected outcomes at each time point: when stroke survivors were still in the hospital (baseline) and at 6 weeks poststroke (after discharge). These results are clinically meaningful because they facilitate the ability to target factors and key time points for potential intervention.

Second, I used multiple statistical methods to confirm the validity of the findings. I used either a parametric or nonparametric method for bivariate analysis based on distributions of the variables (Pearson’ correlation vs. Spearman’s correlation, two sample *t*-test vs. Mann-Whitney *U* test and analysis of variance [ANOVA] vs. Kruskal-Wallis test). The results from paired *t*-tests used to examine changes from baseline to 6 weeks poststroke in continuous variables among 40 participants were compared with those of Wilcoxon Signed ranks test. In addition, as sensitivity analyses, separate bivariate linear mixed models with repeated measures of each dependent variable to compare the effects of uncertainty or covariates were computed to affirm confidence in the results in the present study. The findings from the bivariate linear mixed models were very similar to those resulting from the conservative statistical analyses used to test the hypotheses, thereby increasing my confidence in the results.

Limitations of This Study

This study has some limitations that should be acknowledged. First, generalizability is potentially limited because of the study’s design, convenience sampling, single geographic region and relatively small sample size. For instance, the

present study did not include age/gender-matched noncaregivers or caregivers of persons with other conditions as control subjects. The literature on caregivers for patients with dementia, for example, indicates that they have elevated levels of salivary cortisol across the day and higher stress than do noncaregivers (Gallagher-Thompson et al., 2006). It would be difficult, however, to compare measures such as caregiver uncertainty or burden between caregivers and noncaregivers or even among those caring for persons with other conditions with nonacute onset; examining differences in perceived stress, salivary cortisol, HRQOL and depressive symptoms between caregivers for stroke survivors and either of these other groups, however, would increase current knowledge of stroke-survivor caregivers.

Furthermore, caregivers who did not agree to participate in the study or who were lost to follow up at 6 weeks poststroke may have had more caregiving responsibilities and higher stress levels. The main reason given for declining to participate in the study was “feeling overwhelmed with their current situation.” Some study participants who withdrew from the study expressed they could not continue to participate due to their caregiving situation and/or personal problems. Thus, there is a possibility that some caregivers with greater uncertainty or more severe levels of stress were not included in the present study. By 6 weeks poststroke, 13 stroke survivors had died and their caregiver data were excluded in analyses for that observation. Another 10 caregivers were lost to follow up or withdrew from the study. The majority of the baseline values in caregiver and stroke-survivor characteristics between these 23 caregivers who were not included in the data analysis at 6 weeks poststroke and 40 caregivers who completed the study were similar, pointing to overall homogeneity in the sample. The 40 caregivers who completed

the study, however, did report less social support at baseline than did the 23 who were excluded in the data analysis at 6 weeks poststroke; the sample of 40 caregivers at 6 weeks poststroke also contained a slightly larger proportion of non-White participants. Although these two differences were statistically significant, they are not believed to be clinically meaningful; however, there is a possibility that the findings at 6 weeks poststroke could be influenced by characteristics in the retained sample.

Second, the time period for follow up was limited. Extending the follow-up period to include multiple time points over a longer period of time after caregivers assume their caregiver role is required to further examine how uncertainty may change “naturally” and to determine its effect on long-term perceived stress, diurnal salivary cortisol and psychological outcomes. Still, the study results shed light on a previously unexplored period in the development of untoward caregiver outcomes.

Third, there is the possibility that participants were noncompliant with the protocol for saliva collection. Although caregivers were taught self-collection of saliva in a personal demonstration at baseline, I was unable to verify whether they actually followed directions. For example, some salivary-cortisol levels in the evening were higher than those on waking, an unusual finding that held even after reanalysis. It is possible that caregivers mislabeled the sample vials with an incorrect time of day. Salivary-cortisol levels in a few participants were similar between on waking and in the evening. A possible interpretation for these flatter salivary slope patterns in a few caregivers could be depression. Stroke-survivor caregivers with depression were found to have lower salivary levels across the day than did caregivers without depression (Saban et al., 2012).

Fourth, due to the small sample size and limited power in the present study, I chose as covariates to enter into the multivariate stepwise regression models for testing Aims 1, 2 and 3 only caregiver and stroke-survivor characteristics that were identified from bivariate analysis on the basis of a p -value less than or equal to 0.05. There is a possibility that some covariates that were not significant in the bivariate analysis could have been important factors affecting outcomes in a multivariate analysis. Because of the mediation effects between uncertainty and covariates, testing the mediator effect of perceived stress on the relationship between uncertainty and psychological outcomes including burden, HRQOL and depressive symptoms at 6 weeks poststroke was limited to univariate regression analysis. With a larger sample size, many more covariates could be controlled to better examine any mediating effect of stress on the relationship between uncertainty and psychological outcomes including burden, HRQOL and depressive symptoms.

Finally, although not proposed for this study, sophisticated methods such as mixed models with repeated-measures analysis would be statistically more powerful because this analysis accounts for missing data if the data are missing at random. No previous studies, however, had examined the effect of uncertainty on perceived and physiological stress, burden, HRQOL and depressive symptoms in caregivers of stroke survivors. Therefore, as the first step, it was important in this study to explore whether uncertainty, as well as other caregiver and stroke-survivor characteristics, affect these outcomes at each time point—while stroke survivors are in the hospital and after discharge to home, rehabilitation hospitals or nursing facilities—using participants with complete data at each time point. Conducting separate regression analyses with complete

data at each time point in the present study was, thus, appropriate for the aims of the present study. Further, existing longitudinal studies on caregivers of stroke survivors have used a separate regression analysis to reveal factors that affected outcomes at each time point (Bugge et al., 1999; McCullagh et al., 2005; Tooth et al., 2005). Hence, my design permits important comparisons with existing reports and also fills gaps to contribute importantly to a story about the evolution of caregiver outcomes, including burden, over time.

Further, in the present study, there was no intervention for caregivers between baseline and 6 weeks poststroke. In a natural environment without any intervention and in the absence of previous study results, it is difficult to hypothesize whether perceived and physiological stress, burden, HRQOL and depressive symptoms change significantly or remain consistent over time. The paired *t*-tests using data from participants with complete datasets ($N = 40$) in the present study showed that perceived stress, salivary cortisol, burden and depressive symptoms were consistent from baseline to 6 weeks poststroke, whereas bivariate linear mixed models with repeated measures of each dependent variable using the entire available sample (63 at baseline, 53 [40 participants who completed the study and 13 participants whose stroke survivor died after baseline data collection] at 6 weeks poststroke) revealed that caregivers had greater burden and poorer HRQOL at 6 weeks poststroke compared to baseline. The difference from baseline to 6 weeks poststroke for burden based on the paired *t*-test in the present study approached statistical significance ($p = 0.068$), suggesting lack of power due to the small sample size at 6 weeks poststroke ($N = 40$). Using a larger sample size in future studies may reveal significant differences from baseline to 6 weeks poststroke. With a few exceptions (2

covariates [stroke-survivor communication ability for perceived stress at baseline and relationship to the stroke survivor for salivary cortisol on waking at 6 weeks poststroke] that approached significance in bivariate linear mixed models with repeated measures), the results from the regression analysis at each time point were consistent with the findings from bivariate linear mixed models with repeated measures of each dependent variable, adding further support for the study findings.

Implications for Clinical Practice and Health Policy

The findings from the current study have several implications for clinical practice with caregivers of stroke survivors. First, healthcare providers in neuroscience must become sensitized to caregiver uncertainty in the early period of caregiving. It is important for clinicians to help caregivers identify specific areas where they are uncertain (e.g., re: stroke-survivor outcome, the recovery process or caregiver role) and provide appropriate support. Using uncertainty as a predictor may help identify caregivers at risk for stress, burden, poor HRQOL or depressive symptoms—that is, those in need of additional support. In addition, the present study revealed that by 6 weeks poststroke, caregivers with greater uncertainty had greater depressive symptoms as perceived stress levels increased. Acting on these critical insights has the potential to improve clinical outcomes. Using early detection of uncertainty as a trigger to initiate caregiver intervention in the early period of caregiving, such as consultation or stress-management behavioral therapy, may lead to decreased depressive symptoms and reduced morbidity and mortality in this population.

Second, greater caregiver involvement in discharge planning for stroke survivors—by providing anticipatory guidance and information about care needs and care

options and enhancing caregiver preparedness—may also help reduce early uncertainty, support decision making in care planning and attenuate stress in the complex and often-alienating healthcare-delivery system during a critical period. Caregivers for patients with heart failure have better caregiving experiences and health outcomes when they are involved in hospital-discharge planning (Bull, Hansen, & Gross, 2000). The results from the present study indicated that caregiver uncertainty remained consistent from within 2 weeks poststroke to 6 weeks poststroke. Stroke-survivor functional status was correlated with uncertainty at both times in the present study. Stroke survivors who were discharged directly to home with their caregivers had had less severe strokes and fewer complications, but at 6 weeks poststroke, there was no difference in caregiver uncertainty regardless of posthospital discharge placement (i.e., rehabilitation hospital, nursing facility or homes) of the stroke survivor. Involvement in discharge planning, especially for stroke survivors who will be discharged directly home, could immeasurably help caregivers adjust to their new caregiver role, increase preparedness for caregiving and reduce their uncertainty. In the present study, less preparedness for caregiving in caregivers was associated with greater burden at baseline. In a related study (Ostwald et al., 2009), spousal caregivers who reframed their situation and prepared for caregiving had lower stress throughout the year after discharge.

Third, policymakers need to make better informed investments in caregivers to effectively reduce healthcare costs. The majority of new or recurring strokes occurs among the older population (Stephenson, 2001). The U.S. 65 years and older population comprised 35 million people in 2000 and will increase to 71 million by 2030 (U.S. Census Bureau, 2004); thus, it is expected that the numbers of caregivers for older adults

with stroke will increase commensurately. A policy improving informal family caregiving, especially for caregivers of stroke survivors, could result in cost savings in the formal long-term-care system. For example, in the present study, it was noted that caregivers reported lowered social support at 6 weeks poststroke compared to baseline. Social support (including instrumental and informational as well as emotional and companionship support) is an important buffer known to decrease stress in stroke survivors and their caregivers (Glass, Matchar, Belyea, & Feussner, 1993; Jonsson, Lindgren, Hallstrom, Norrving, & Lindgren, 2005; Ostwald et al., 2009; Pierce et al., 2004; Secrest, 2000). Efforts to enhance social support and discharge planning for stroke survivors and for their caregivers, as well as provide direct interventions for caregivers such as consultation or stress-management behavioral therapy, may prevent stress-related health problems in caregivers, decrease their burden and depressive symptoms and eventually reduce their healthcare costs by preventing or forestalling untoward outcomes. Therefore, provision of these services as a covered benefit under Medicare/Medicaid and other health insurances should be seriously considered.

Recommendations for Future Research

Replication studies are required that use a larger sample size in which many factors that have been viewed in previous studies as influencing outcomes can be successfully controlled. These include perceived stress, salivary cortisol, burden, HRQOL and depressive symptoms. Longitudinal designs that encompass longer periods (from the initial stroke event to several years poststroke) and multiple time points are also needed. Because of the relatively small sample size in the present study, it was difficult to examine the influence on outcomes of variables that changed over time. Such studies,

which can better employ multilevel mixed linear-regression analyses and explore the effects of time, interactions between time and uncertainty and interactions between time and other covariates, will further elucidate the overall effects of uncertainty on short- and long-term outcomes for caregivers. In the present study, salivary-cortisol levels were measured on waking and in the evening to decrease data-collection burden in caregivers. Longitudinal studies with saliva collection on waking, 30 minutes postawakening, afternoon and evening (4 measures per day) over 2 consecutive days at each measurement point would provide greater reliability and validity of the measure (Saban et al., 2012; Woods et al., 2008). Such longitudinal studies may reveal diurnal variation in salivary cortisol when caregivers for stroke survivors experience chronic stress. Further investigation is required to verify whether, over time, cortisol levels increase, similar to those in caregivers for patients with dementia (Bauer et al., 2000; Da Roza Davis & Cowen, 2001; de Vugt et al., 2005; Vedhara et al., 1999) or lower, similar to those in a previous study of caregivers for stroke survivors (Saban et al., 2012). In addition, daily self-reported stress reflecting how study participants feel when collecting saliva would enhance an interpretation regarding the finding of lack of correlation between perceived stress and salivary cortisol in the present study.

Future intervention studies that incorporate components of uncertainty into a problem-solving approach are required. In one study, social problem-solving telephone interventions with family caregivers of stroke survivors after hospital discharge enhanced mental health, caregiver preparedness and social functioning, and decreased depression, although there was no effect on burden (Grant, Elliott, Weaver, Bartolucci, & Giger, 2002). The steps for problem-solving therapy suggested by Grant et al. (2002) are to

(a) identify and define the problem, (b) decide what needs to be accomplished and list possible solutions to the problems, (c) choose and test best solution(s) and (d) evaluate outcomes of problem solving. Applying similar steps with caregivers to identify and define uncertainty for the individual; find possible solutions to resolve uncertainty; choose, test and evaluate the best problem-solving solutions and evaluate outcomes may increase effective communication between caregivers and healthcare providers to resolve uncertainty and enhance caregiver outcomes including stress, burden, HRQOL and depressive symptoms.

Conclusions

The purpose of the present study was to examine the effect of uncertainty on perceived and physiological stress, burden, HRQOL and depressive symptoms in caregivers of stroke survivors within 2 weeks and 6 weeks poststroke. The results of these analyses indicate that greater uncertainty was associated with higher perceived stress immediately following the stroke and also at 6 weeks poststroke. Uncertainty, however, was not a significant predictor of physiological stress at either time point. Overall, greater uncertainty was associated with greater burden, poorer HRQOL and greater depressive symptoms at both times. By 6 weeks poststroke, however, the influence of uncertainty on HRQOL had diminished. In addition, at 6 weeks poststroke, perceived stress fully mediated the relationship between uncertainty and depressive symptoms and mediated the effect of uncertainty on HRQOL. Prior to testing the mediator effect of perceived stress on the relationship between uncertainty and HRQOL, however, the association between uncertainty and HRQOL was not strong. At both times, perceived stress partially mediated the relationship between uncertainty and burden.

Healthcare providers in neuroscience must become sensitized to caregiver uncertainty in the early period of caregiving, helping them identify specific areas where they are uncertain (e.g., stroke-survivor outcome, the recovery process and/or caregiver role) and provide appropriate support. Further research on the observed rapid decline in caregiver health is warranted, and studies of the effect of uncertainty on long-term caregiving would be useful to explore its consequences over time.

APPENDIX A. SOCIODEMOGRAPHICS OF CAREGIVERS

Date: _____

Identification Number: _____

1. Age: _____(years)
2. Gender: a) Male b) Female
3. Race/Ethnicity:
a) Caucasian b) African American c) Asian d) Latino/Hispanic e) Other:
4. Native Language: a) English b) Spanish c) Other:
5. Relationship to the stroke survivor:
a) Spouse b) Child c) Grandchild d) Sibling e) Friend f) Other:
6. Perceived quality of relationship with the stroke survivor
on a scale of **1 = excellent, 4 = poor**

1	2	3	4
---	---	---	---
7. Duration of caregiving for the stroke survivor: prior to stroke _____days
since stroke _____days
8. Time spent caring per day: prior to stroke _____hours
since stroke _____hours
(It included time spent with stroke survivors in a hospital.)
9. Length of time since the stroke survivor was diagnosed with stroke: _____days
10. Perceived level of preparedness for caregiving
On a scale of **1 = well prepared, 4 = not at all prepared**

1	2	3	4
---	---	---	---
11. Your (caregiver) insurance including Medicare/Medicaid:
a) Private insurance b) Medicare c) Medicaid d) No Insurance e) Other:
12. Number of close friends and relatives: _____
13. Distance between the hospital (or facility) and your home:
_____miles or not applicable _____
14. Education (highest level of education completed):
a) Less than high school b) High school c) Vocational training d) College
e) Postgraduate
15. Employment Status:
a) Full-time work b) Part-time work c) Homemaker d) Unemployed e) Retired
f) Leave of Absence
16. Considering how well your household lives on its income, financially, would you say you are:
a) Comfortable, have more than enough to make ends meet
b) Adequate, have enough to make ends meet
c) Do Not have enough to make ends meet
17. Other life events in the past 3 months: e.g., death, moving, retirement, marriage
a) Yes, specify _____ b) No

Sociodemographics of Caregivers for the Second Interview

Date: _____

Identification Number: _____

1. Perceived quality of relationship with the stroke survivor
on a scale of **1=excellent, 4=poor**

1	2	3	4
---	---	---	---

2. Duration of caregiving for the stroke survivor: since stroke _____ days

3. Time spent caring per day: _____ since stroke _____ hours
(It includes time spent with your loved one with stroke in a hospital, rehabilitation center or nursing home.)

4. Length of time since the stroke survivor was diagnosed with stroke: _____ days

5. Perceived level of preparedness for caregiving
On a scale of **1= well prepared and 4 = not at all prepared**

1	2	3	4
---	---	---	---

6. Distance between the hospital or facility (rehabilitation center or nursing home) and your home: _____ miles or N/A _____

7. Other life events since the first interview: e.g., death, moving, retirement, marriage
a) Yes, specify _____ b) No

APPENDIX B. MISHEL UNCERTAINTY IN ILLNESS SCALE—FAMILY

MEMBER FORM

Date: _____

Identification Number: _____

INSTRUCTIONS:

Please read each statement. Take your time and think about what each statement says. Then place a “X” under the column that most closely measures how you are feeling about your family member TODAY. If you agree with a statement, then you would mark under either “Strongly Agree” or “Agree”. If you disagree with a statement, then mark under either “Strongly Disagree” or “Disagree”. If you are undecided about how you feel about him /her, then mark under “Undecided” for that statement. Please respond to every statement.

1. I don't know what is wrong with him/her.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

2. I have a lot of questions without answers.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

3. I am unsure if his/her illness is getting better or worse.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

4. It is unclear how bad his/her pain will be.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

5. The explanations they give about him/her seem hazy to me.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

6. The purpose of each treatment for him/her is clear to me.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

7. I do not know when to expect things will be done to him/her.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

8. His/her symptoms continue to change unpredictably.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

9. I understand everything explained to me.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

10. The doctors say things to me that could have many meanings.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

11. I can predict how long his/her illness will last.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

12. His/her treatment is too complex to figure out.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

13. It is difficult to know if the treatment or medications he/she is getting are helping.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

14. There are so many different types of staff; it's unclear who is responsible for what.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

15. Because of the unpredictability of his/her illness, I cannot plan for the future.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

16. The course of his/her illness keeps changing. He/she has good and bad days.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

17. It's vague to me how I will manage the care of him/her after he/she leaves the hospital.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

18. It is not clear what is going to happen to him/her.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

19. I usually know if he /she is going to have a good or bad day.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

20. The results of his/her test are inconsistent.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

21. The effectiveness of the treatment is undetermined.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

22. It is difficult to determine how long it will be before I can care for him/her by myself.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

23. I can generally predict the course of his/her illness.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

24. Because of the treatment, what he/she can do and cannot do keeps changing.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

25. I 'm certain they will not find anything else wrong with him/her.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

26. They have not given him/her a specific diagnosis.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

27. His/her physical distress is predictable; I know when it is going to get better or worse.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

28. His/her diagnosis is definite and will not change.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

29. I can depend on the nurses to be there when I need them.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

30. The seriousness of his/her illness has been determined.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

31. The doctors and nurses use everyday language so I can understand what they are saying.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
_____	_____	_____	_____	_____

APPENDIX C. PERCEIVED STRESS SCALE

Date: _____

Identification Number: _____

The questions in this scale ask you about your feelings and thoughts in the past day (24 hours) . In each case, you will be asked to indicate by circling how often you felt or thought a certain way.	0 = Never	1 = Almost Never	2 = Some- times	3 = Fairly Often	4 = Very Often
1. In the past day, how often have you been upset because of something that happened unexpectedly?					
2. In the past day, how often have you felt that you were unable to control the important things in your life?					
3. In the past day, how often have you felt nervous and “stressed”?					
4. In the past day, how often have you dealt successfully with irritating life hassles?					
5. In the past day, how often have you felt that you were effectively coping with important changes that were occurring in your life?					
6. In the past day, how often have you felt confident about your ability to handle your personal problems?					
7. In the past day, how often have you felt that things were going your way?					
8. In the past day, how often have you found that you could not cope with all the things that you had to do?					
9. In the past day, how often have you been able to control irritations in your life?					
10. In the past day, how often have you felt that you were on top of things?					
11. In the past day, how often have you been angered because of things that happened that were outside of your control?					
12. In the past day, how often have you found yourself thinking about things that you have to accomplish?					
13. In the past day, how often have you been able to control the way you spend your time?					
14. In the past day, how often have you felt difficulties were piling up so high that you could not overcome them?					

APPENDIX D. SALIVA COLLECTION INSTRUCTIONS

Supplies Needed: Swab, cap, storage tube and sample ID labels.

1. Do not eat food or drink liquid for 30 minutes before collecting saliva.
2. Do not brush your teeth for 30 minutes before collecting saliva.
3. Do not smoke for 60 minutes before collecting saliva.
4. Do not have any major dental work within 3 days before collecting saliva.
5. Using pre-prepared label, mark date and time.
6. Wash your hands.
7. Remove the oral swab from the tube (see the picture).
8. Put the oral swab under the tongue for 1 full minute. The oral swab can be moved around in the mouth to take advantage of saliva pooling under the tongue. This may help increase collection volume. If after 1 full minute the oral swab appears dry, then repeat the process.
9. Return the oral swab into tube insert and replace the cap.
10. Place the label on the storage tube.
11. Wash your hands.
12. After collecting each sample, please mark the time below.
(Dates will be marked on the form ahead time for you).
13. Place all two tubes in a plastic sealed bag and place in the freezer overnight.
14. After collecting samples, the research team members will pick up the samples.

Schedule for Salivary Cortisol Sampling

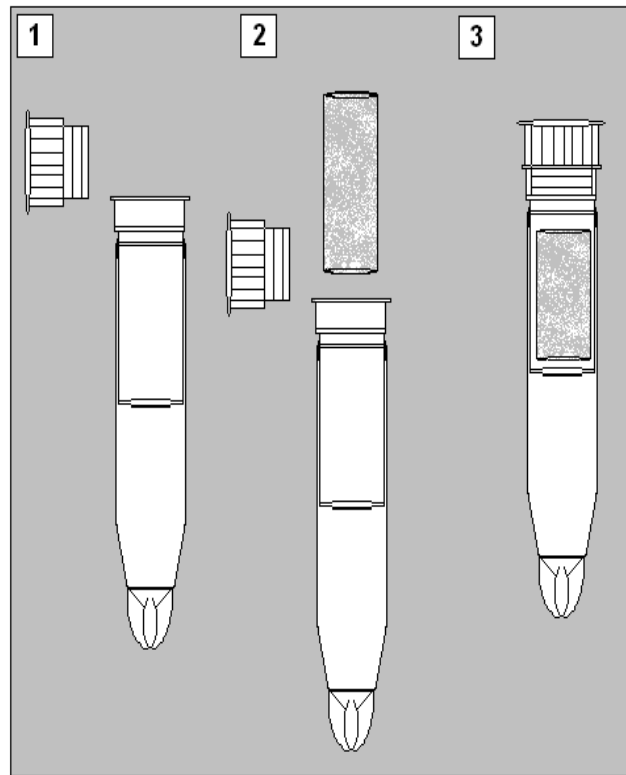
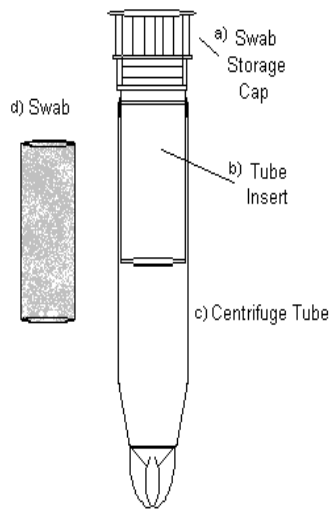
Collect 2 salivary samples per day after the first interview.

First Samples	
Date:	
Waking	9 pm
Actual Time:	Actual Time:

Collect 2 salivary samples per day before or after the second interview (1 month after the first interview).

Second Samples (1 month after the first interview)	
Date:	
Waking	9 pm
Actual Time:	Actual Time:

SAMPLE PREPARATION



APPENDIX E. ZARIT BURDEN INTERVIEW

Date: _____

Identification Number: _____

Please circle the response the best describes how you feel.

	Never	Rarely	Sometimes	Quite Frequently	Nearly Always
1. Do you feel that your relative asks for more help than he/she needs?	0	1	2	3	4
2. Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?	0	1	2	3	4
3. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	0	1	2	3	4
4. Do you feel embarrassed over your relative's behavior?	0	1	2	3	4
5. Do you feel angry when you are around your relative?	0	1	2	3	4
6. Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?	0	1	2	3	4
7. Are you afraid what the future holds for your relative?	0	1	2	3	4
8. Do you feel your relative is dependent on you?	0	1	2	3	4
9. Do you feel strained when you are around your relative?	0	1	2	3	4
10. Do you feel your health has suffered because of your involvement with your relative?	0	1	2	3	4
11. Do you feel that you don't have as much privacy as you would like because of your relative?	0	1	2	3	4
12. Do you feel that your social life has suffered because you are caring for your relative?	0	1	2	3	4
13. Do you feel uncomfortable about having friends over because of your relative?	0	1	2	3	4

	Never	Rarely	Sometimes	Quite Frequently	Nearly Always
14. Do you feel that your relative seems to expect you to take care of him/her as if you were the only one he/she could depend on?	0	1	2	3	4
15. Do you feel that you don't have enough money to take care of your relative in addition to the rest of your expenses?	0	1	2	3	4
16. Do you feel that you will be unable to take care of your relative much longer?	0	1	2	3	4
17. Do you feel you have lost control of your life since your relative's illness?	0	1	2	3	4
18. Do you wish you could leave the care of your relative to someone else?	0	1	2	3	4
19. Do you feel uncertain about what to do about your relative?	0	1	2	3	4
20. Do you feel you should be doing more for your relative?	0	1	2	3	4
21. Do you feel you could do a better job in caring for your relative?	0	1	2	3	4
22. Overall, how burdened do you feel in caring for your relative?	0	1	2	3	4

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APPENDIX F. EUROQOL

Date: _____

Identification Number: _____

A. EQ5D

By placing a checkmark in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual Activities (*e.g. work, study, housework, family or leisure activities*)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/Discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression

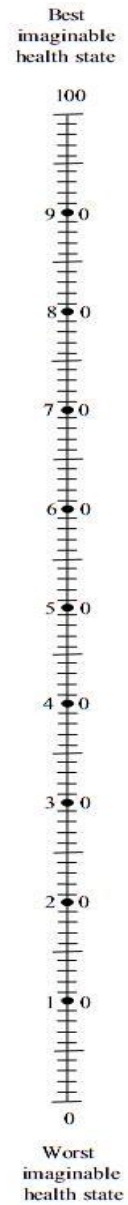
- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

B. EuroQol-VAS (visual-analog scale)

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

**Your own
health state
today**



APPENDIX G. PATIENT HEALTH QUESTIONNAIRE

Date: _____

Identification Number: _____

Over the <i>last 2 weeks</i> , how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things.				
2. Feeling down, depressed, or hopeless.				
3. Trouble falling or staying asleep, or sleeping too much.				
4. Feeling tired or having little energy.				
5. Poor appetite or overeating.				
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down.				
7. Trouble concentrating on things, such as reading the newspaper or watching television.				
8. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.				
9. Thoughts that you would be better off dead or of hurting yourself in some way.				

10. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all Somewhat difficult Very difficult Extremely difficult

APPENDIX H. CUMULATIVE ILLNESS RATING SCALE

Date: _____

Identification Number: _____

- 0: No problem
- 1: Current mild problem or past significant problem
- 2: Moderate disability or morbidity / requires “first line” therapy
- 3: Severe / constant significant disability / “uncontrollable” chronic problems
- 4: Extremely severe / immediate treatment required / end organ failure / severe impairment of function

Score Notes: Conditions, treatments, etc.

- 1: Heart
- 2: Vascular
 2a: Hypertension
- 3: Hematopoieric
- 4: Respiratory
- 5: Eyes, ears, nose, throat,
 and larynx
- 6: Upper gastrointestinal.....
- 7: Lower gastrointestinal.....
- 8: Liver and biliary
- 9: Renal
- 10: Genito-urinary
- 11: Musculo-skeletal /
 integument
- 12: Neurological
- 13: Endocrine/metabolic
 and breast.....
- 14: Psychiatric

APPENDIX I. SHORT-FORM VERSION OF SENSE OF COHERENCE

Date: _____

Identification Number: _____

Here is a series of questions relating to various aspects of your lives. Each question has seven possible answers. Please mark the number, which expresses your answer, with number 1 and 7 being the extreme answers. If the words under 1 are right for you, circle 1; if the words under 7 are right for you, circle 7. If you feel differently, circle the number which best expresses your feeling. Please give only one answer to each question.

1. Do you have feeling that you don't really care about what goes on around you?

1	2	3	4	5	6	7
very seldom or never						very often

2. Has it happened in the past that you were surprised by the behavior of people whom you thought you knew well?

1	2	3	4	5	6	7
never happened						always happened

3. Has it happened that people whom you counted on disappointed you?

1	2	3	4	5	6	7
never happened						always happened

4. Until now your life has had:

1	2	3	4	5	6	7
no clear goals or purpose at all						very clear goals and purpose

5. Do you have the feeling that you're being treated unfairly?

1	2	3	4	5	6	7
very often						very seldom or never

6. Do you have the feeling that you are in an unfamiliar situation and don't know what to do?

1	2	3	4	5	6	7
very often						very seldom or never

7. Doing the thing you do every day is:

1	2	3	4	5	6	7
a source of deep pleasure and satisfaction						a source of pain and boredom

8. Do you have very mixed-up feelings and ideas?

1	2	3	4	5	6	7
very often						very seldom or never

9. Does it happen that you have feelings inside you would rather not feel?

1	2	3	4	5	6	7
very often						very seldom or never

10. Many people – even those with a strong character – sometimes feel like sad sacks (losers) in certain situations. How often have you felt this way in the past?

1	2	3	4	5	6	7
never						very often

11. When something happened, have you generally found that:

1	2	3	4	5	6	7
you overestimated or underestimated its importance						you saw things in the right proportion

12. How often do you have the feeling that there's little meaning in the things you do in your daily life?

1	2	3	4	5	6	7
very often						very seldom or never

13. How often do you have feelings that you're not sure you can keep under control?

1	2	3	4	5	6	7
very often						very seldom or never

**APPENDIX J. MULTIDIMENSIONAL SCALE OF PERCEIVED SOCIAL
SUPPORT**

Date: _____
 Identification Number: _____

I am going to read several statements about how much help you receive from others. Please use the following scale to indicate how much you agree or disagree with each statement. The responses range from **very strongly disagree** to **very strongly agree**, with **neither agree nor disagree** in the middle. You can answer with either a number or the words.

very strongly disagree	strongly disagree	mildly disagree	neutral	mildly agree	strongly agree	very strongly agree
1	2	3	4	5	6	7

	1	2	3	4	5	6	7
1. There is a special person who is around when I am in need.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. There is a special person with whom I can share my joys and sorrows.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. My family really tries to help me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. I get the emotional help and support I need from my family.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I have a special person who is a real source of comfort to me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. My friends really try to help me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. I can count on my friends when things go wrong.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. I can talk about my problems with my family.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. I have friends with whom I can share my joys and sorrows.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. There is a special person in my life who cares about my feelings.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. My family is willing to help me make decisions.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. I can talk about my problems with my friends.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

APPENDIX K. SOCIODEMOGRAPHICS OF STROKE SURVIVORS

Date: _____

Identification Number: _____

1. Age: _____(years)
2. Gender: a) Male b) Female
3. Race/Ethnicity:
a) Caucasian b) African American c) Asian d) Latino/Hispanic e) Other:
4. Education (highest level of education completed):
a) Less than high school b) High school c) Vocational training d) College
e) Postgraduate
5. Employment Status:
a) Full-time work b) Part-time work c) Homemaker d) Unemployed e) Retired
f) Leave of Absence
6. Considering how well your household lives on its income, financially, would you say you are:
a) Comfortable, have more than enough to make ends meet
b) Adequate, have enough to make ends meet
c) Do Not have enough to make ends meet
7. Insurance including Medicare/Medicaid:
a) Private insurance b) Medicare c) Medicaid d) No Insurance e) Other:
8. Time since admission to hospital _____days

Sociodemographics of Stroke Survivors for the Second Interview

Date: _____

Identification Number: _____

1. A facility or home where a stroke survivor was initially placed **after hospital discharge**

a) Rehabilitation center b) Nursing Home c) Home d) Other: _____

Time since admission to facility _____ days

Or

Time since discharge to home _____ days

2. A facility or home **where a stroke survivor is now currently placed**

a) Rehabilitation center b) Nursing Home c) Home d) Other: _____

Time since admission to facility _____ days

Or

Time since discharge to home _____ days

3. Duration of rehabilitation including Inpatient _____ days

Outpatient _____ days

APPENDIX L. NIH STROKE SCALE & DESCRIPTION OF STROKE

Date: _____

Identification Number: _____

Instructions	Scale definition	Score
<p>1a. Level of Consciousness: The investigator must choose a response, even if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.</p>	<p>0 = Alert; keenly responsive. 1 = Not alert, but arousable by minor stimulation to obey, answer, or respond. 2 = Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.</p>	
<p>1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct—there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not “help” the patient with verbal or non-verbal cues.</p>	<p>0 = Answers both questions correctly. 1 = Answers one question correctly. 2 = Answers neither question correctly.</p>	
<p>1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to them (pantomime) and score the result (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.</p>	<p>0 = Performs both tasks correctly. 1 = Performs one task correctly. 2 = Performs neither task correctly.</p>	

Table continues

Instructions	Scale definition	Score
<p>2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve palsy (CN III, IV or VI) score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness or other disorder of visual acuity or fields should be tested with reflexive movements and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.</p>	<p>0 = Normal 1 = Partial gaze palsy. This score is given when gaze is abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present. 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.</p>	
<p>3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat as appropriate. Patient must be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia is found. If patient is blind from any cause score 3. Double simultaneous stimulation is performed at this point. If there is extinction patient receives a 1 and the results are used to answer question 11.</p>	<p>0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (blind including cortical blindness)</p>	
<p>4. Facial Palsy: Ask, or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barrier obscures the face, these should be removed to the extent possible.</p>	<p>0 = Normal symmetrical movement 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face)</p>	

Table continues

Instructions	Scale definition	Score
<p>5 & 6. Motor Arm and Leg: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine) and the leg 30 degrees (always tested supine). Drift is scored if the arm falls before 10 seconds or the leg before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder or hip may the score be “9” and the examiner must clearly write the explanation for scoring as a “9”.</p>	<p>0 = No drift, limb holds 90 (or 45) degrees for full 10 seconds. 1 = Drift, Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = No effort against gravity, limb falls. 4 = No movement 9 = Amputation, joint fusion, explain</p> <hr/> <p>5a. Left Arm 5b. Right Arm</p>	
	<p>0 = No drift, leg holds 30 degrees position for full 5 seconds. 1 = Drift, leg falls by the end of the 5 second period but does not hit bed. 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. 3 = No effort against gravity, leg falls to bed immediately. 4 = No movement 9 = Amputation, joint fusion, explain</p> <hr/> <p>6a. Left Leg 6b. Right Leg</p>	
<p>7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, insure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion may the item be scored “9”, and the examiner must clearly write the explanation for not scoring. In case of blindness test by touching nose from extended arm position.</p>	<p>0 = Absent 1 = Present in one limb 2 = Present in two limbs If present, is ataxia in Right arm 1 = Yes 2 = No 9 = amputation or joint fusion, explain</p> <hr/> <p>Left arm 1 = Yes 2 = No 9 = amputation or joint fusion, explain</p> <hr/> <p>Right leg 1 = Yes 2 = No 9 = amputation or joint fusion, explain</p> <hr/> <p>Left leg 1 = Yes 2 = No 9 = amputation or joint fusion, explain</p>	

Table continues

Instructions	Scale definition	Score
<p>8. Sensory: Sensation or grimace to pin prick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas [arms (not hands), legs, trunk, face] as needed to accurately check for hemisensory loss. A score of 2, “severe or total,” should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will therefore probably score 1 or 0. The patient with brain stem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic score 2. Patients in coma (item 1a=3) are arbitrarily given a 2 on this item.</p>	<p>0 = Normal; no sensory loss. 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware he/she is being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.</p>	
<p>9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. The patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet, and to read from the attached list of sentences. Comprehension is judged from responses here as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma (question 1a=3) will arbitrarily score 3 on this item. The examiner must choose a score in the patient with stupor or limited cooperation but a score of 3 should be used only if the patient is mute and follows no one step commands.</p>	<p>0 = No aphasia, normal 1 = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided material difficult or impossible. For example in conversation about provided materials examiner can identify picture or naming card from patient’s response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory comprehension.</p>	
<p>10. Dysarthria: If patient is thought to be normal an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barrier to producing speech, may the item be scored “9”, and the examiner must clearly write an explanation for not scoring. Do not tell the patient why he/she is being tested.</p>	<p>0 = Normal 1 = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe; patient’s speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. 9 = Intubated or other physical barrier, explain</p>	

Table continues

Instructions	Scale definition	Score
<p>11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.</p>	<p>0 = No abnormality. 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.</p>	

Description of Stroke

1. Type of stroke:
 - a) Ischemic _____
 - b) Intracerebral Hemorrhage _____
 - c) Subarachnoid Hemorrhage _____
 - d) Unclassified _____
2. Area of stroke:
 - a) Right _____
 - b) Left _____
 - c) Cerebellar _____
 - d) Brain Stem _____
 - e) Other _____
 - f) Unclassified _____
3. Communication disability: a) Yes _____ b) No _____ c) Unclassified _____
4. Time poststroke: _____ days

APPENDIX M. BARTHEL INDEX

Date: _____

Identification Number: _____

Instructions: Choose the scoring point for the statement that most closely corresponds to the patient's current level of ability for each of following 10 items. Record actual, not potential, functioning.

Activity Score	Scores
FEEDING 0 = unable 5 = needs help cutting, spreading butter, etc., or requires modified diet 10 = independent	
BATHING 0 = dependent 5 = independent (or in shower)	
GROOMING 0 = needs to help with personal care 5 = independent face/hair/teeth/shaving (implements provided)	
DRESSING 0 = dependent 5 = needs help but can do about half unaided 10 = independent (including buttons, zips, laces, etc.)	
BOWELS 0 = incontinent (or needs to be given enemas) 5 = occasional accident 10 = continent	
BLADDER 0 = incontinent, or catheterized and unable to manage alone 5 = occasional accident 10 = continent	
TOILET USE 0 = dependent 5 = needs some help, but can do something alone 10 = independent (on and off, dressing, wiping)	
TRANSFERS (BED TO CHAIR AND BACK) 0 = unable, no sitting balance 5 = major help (one or two people, physical), can sit 10 = minor help (verbal or physical) 15 = independent	
MOBILITY (ON LEVEL SURFACES) 0 = immobile or < 50 yards 5 = wheelchair independent, including corners, > 50 yards 10 = walks with help of one person (verbal or physical) > 50 yards 15 = independent (but may use any aid; for example, stick) > 50 yards	
STAIRS 0 = unable 5 = needs help (verbal, physical, carrying aid) 10 = independent	

APPENDIX N. CONSENT CAPACITY GUIDE FOR CAREGIVERS

Identification Number: _____

Interviewer: I am going to ask you some true/false questions now.

Before each statement state: True or False read statement	Correct	
	Yes	No
1) The goal of this study is to describe caregiver experience in response to a loved one's health event. (T)	Yes	No
2) If I do not participate in this study, my relative or friend's medical care will still be provided. (T)	Yes	No
3) If I participate in this study, it will cost me a lot of money. (F)	Yes	No
4) I can decide I do not want to participate at any time. (T)	Yes	No
5) If I participate, I will have to answer questions about how I am feeling and collect saliva samples to measure level of stress. (T)	Yes	No

Assessment: _____

Considering the risks and benefits we have discussed, what have you decided about participating in this study?

_____ to participate _____ not to participate-

why?: _____

A subject must have a perfect score of 5 for being eligible to provide informed consent for this study. If a subject gets a lower score, the information on the items missed may be repeated, and the specific question/s asked again. This may be done for a total of 3 trials. If a subject fails to obtain a score of 5 after 3 such attempts, he/she is not eligible to participate in the study.

Does Does not demonstrate adequate decision-making capacity.

 Printed name of assessor Signature of assessor Date

APPENDIX O. MACCAT-CR RECORD FORM FOR STROKE SURVIVORS

Understanding (Each item is rated 2–0)

Understanding Rating

2: Subject recalls the content of the item and offers a fairly clear version of it.

1: Subject shows some recollection of the item content, but describes it in a way that renders understanding uncertain, even after the interviewer has made efforts to obtain clarification from the subject.

0: Subject (a) does not recall the content of the item, or (b) describes it in a way that is clearly inaccurate, or (c) describes it in a way that seriously distorts its meaning, even after the interviewer has made efforts to obtain clarification from the subject, or offers a response that is unrelated to the question or is unintelligible.

1. Nature of project

Description and Interview Questions: “The purpose of the research project is to learn more about the experience of caregivers of older adults with stroke in the first 6 weeks of caregiving. You are being asked to participate in this study because you have been diagnosed with stroke and your family caregiver is participating in the study. The entire study is expected to be completed within one year. Your agreement to allow us to review your hospital records will be a one-time permission to get information about your health and stroke. You will not be asked to do anything. A member of the research team will review your hospital medical record to get selected information about your health, type of stroke, and severity of stroke.” Can you tell me your understanding of what I just said? [If subject fails to mention spontaneously, ask:]

a) What is the purpose of the research project I described to you?

Expected Answer: To learn more about the experience of caregivers of older adults with stroke in the first 6 weeks of caregiving.

b) How long will the research project last?

Expected Answer: The entire study is expected to be completed within one year. My agreement to allow us to review my hospital records will be a one-time permission to get information about my health and stroke.

c) What sorts of things will be done with people who agree to be in the study?

Expected Answer: I will not be asked to do anything. A member of the research team will review my hospital medical record to get selected information about my health and stroke.

Score

a) _____

b) _____

c) _____

Subtotal: _____

2. Primary purpose is research

Description and Interview Questions: “It is important for you to understand that the project in which you have been asked to participate is a research project. This study is not treatment. The main purpose of the study is to help researchers figure out caregiver experiences in response to a loved one’s stroke.” Can you tell me your understanding of what I just said?

Expected Answer: The project in which I have been asked to participate is for research, and not treatment/care.

Score

Subtotal: _____

3. Effects on individualized care

Description and Interview Questions:

a) “If you do not choose to participate in the research study, your medical care will still be provided.” Can you tell me your understanding of what I just said?

Expected Answer: If I do not participate in this study, my medical care will still be provided.

b) “What will you be asked to do if you agree to participate in this research project?”

Expected Answer: If I participate in this study, a member of the research team will review my hospital record. I will not need to do anything.

Score

a) _____

b) _____

Subtotal: _____

4. Benefits and risks/discomfort

Description and Interview Questions: “No major risks are anticipated from this study and your privacy and confidentiality will be protected. An identification code number will be assigned to you and the number, and not your name, will be used to identify all the information. There is no benefit to you. This study will guide future research and promote improved clinical practice and education for caregivers of survivors.” Can you tell me your understanding of what I just said? [If subject fails to mention spontaneously, ask:]

a) What are the risks?

Expected Answer: No major risks are anticipated from this study.

b) Will confidentially be maintained and your privacy be protected?
Expected Answer: My privacy and confidentiality will be protected. An identification code number will be assigned to me.

c) How will you benefit from the study?
Expected Answer: There is no benefit to me.

c) Will this study guide future research and promote improved clinical practice and education for caregivers of survivors?
Expected Answer: This study will guide future research and promote improved clinical practice and education for caregivers of survivors.

Score

- a) _____
- b) _____
- c) _____
- d) _____

Subtotal: _____

5. Ability to withdraw

Description and Interview Questions: “No one has to be in this study. People who agree to be in this research project can change their minds at any time. You can leave the study before the study ends. Nothing will happen to you, if you decide not to be in the study.” Can you tell me your understanding of what I just said?

Expected Answer: If I change my mind, I can withdraw at any time.

Score

Subtotal: _____

Total Understanding Score (22–0): _____

Appreciation (Each item is rated 2–0)

1. Object not personal benefit

Interview Questions: Earlier, we discussed benefits and risks of participation in this study. Do you believe that you have been asked to be in this study primarily for your personal benefit? [If yes, then:] What makes you believe that this is the reason you were asked?

Rating

2: Subject acknowledges that he or she is being recruited for a valid reason unrelated to potential benefit from being in the study (e.g., because he or she has had a stroke and has a caregiver who is willing to participate).

1: Subject acknowledges being recruited for reasons both related to and unrelated to potential personal benefit. Or, subject maintains being recruited for a reason related to only to potential personal benefit, but has a plausible explanation for why this is the case.

0: Subject maintains he or she is being recruited for a reason related only to potential personal benefit, but does not have a plausible explanation for why this is the case. Or, subject offers response that is unrelated to the question or unintelligible.

Score: _____

2. Withdrawal possible

Interview Questions: What do you believe would happen if you decided not to be in this study?

Expected Answer: If I do not participate in this study, my medical care will still be provided.

Rating

2: Subject acknowledges that failure to participate or later withdrawal will not adversely affect him or her (in particular, in the context of a treatment setting, that subject can continue to receive ordinary care, assuming that this in the case).

1: Subjects is uncertain whether failure to participate or later withdraw will adversely affect him or her. Or, subject believes failure to participate or later withdrawal will adversely affect him or her and has a plausible explanation for why this is the case.

0: Subject believes failure to participate or later withdrawal will adversely affect him or her and dose not have a plausible explanation for why this is the case. Or, subject offers response that is unrelated to the question or unintelligible.

Score: _____

Total Appreciation Score (4–0): _____

Reasoning (Each item is rated 2–0)

1. Consequential reasoning

Interview Question: Do you think that you are more likely to want to participate in the study or not participate in the study?

Expected Answer: Yes or No.

Rating

2: Subject states a choice.

1: Subject states more than one choice, seems ambivalent.

0: Subject does not state a choice.

Score: _____

2. Comparative reasoning

Interview Question: Tell me what it is that makes that your [option named by patient] better than [option not chosen by patient]?

Rating

2: Subject offers at least one statement in the form of a comparison at least two options, with the comparison including a statement of at least one specific difference. For example: “I’d prefer not to take part in the study, because I am not comfortable someone who is not involved in my care to see my medical record.”

1: Subject makes comparison statement, but does not include a statement of a specific consequence. For example, “It will be better if I stay out of the study”.

0: Subject makes no comparative statements.

Score: _____

3. Generating consequences

Description and Interview Questions: “If you agree to participate in this research project, a member of the research team will review your hospital record. You will not be asked to do anything.” What are some ways that participating in the study could affect your everyday activities?

Expected Answer: My participation will not affect my everyday activities.

Rating

2: Subject recalls the content of the item and offers a fairly clear version of it.

1: Subject shows some recollection of the item content, but describes it in a way that renders understanding uncertain, even after the interviewer has made efforts to obtain clarification from the subject.

0: Subject (a) does not recall the content of the item; or (b) describes it in a way that is clearly inaccurate, or (c) describe it in a way that seriously distorts its meaning, even after the interviewer has made efforts to obtain clarification from the subjects; or offers a response that is unrelated to the question or unintelligible.

Score: _____

4. Logical consistency of choice

There are no specific questions. The interviewer will determine whether participant's statements have been consistently logical, thus, signifying ability to provide informed consent.

Rating

2: Subject's final choice (in Expressing a Choice) follows logically from the subject's own reasoning, as explained by the subject in response to the three previous subparts.

1: It is not clear whether the choice follows logically from the subject's own reasoning.

0: Subject's choice clearly does not follow logically from subject's own reasoning.

Score: _____

Total Reasoning Score (8–0): _____

Expressing a Choice (Rate 2–0)

Description and Interview Questions: "As you know, you have been invited to participate in a research project to describe caregiver experience in response a loved one's health event, that is, a stroke." Do you think you are more likely to want to participate or not to want to participate?

Expected Answer: Yes, I would like to participate in the study. Or, no, I would not like to participate in this study.

Rating

2: Subject states a choice.

1: Subject states more than one choice, seems ambivalent.

0: Subject does not state a choice.

Score: _____

Total Expressing a Choice Score (2–0): _____

Total Scores (0–36): _____ **(Cut off score: 13)**

**APPENDIX P. UNIVERSITY OF PENNSYLVANIA INFORMED CONSENT
FORM (CAREGIVERS)**

Title of the Research Study: The effect of early uncertainty on caregiver stress and psychological outcomes: The case of stroke survivor caregivers

Protocol Number: 813927

Principal Investigator: Lois K. Evans, PhD, RN, FAAN,
van Ameringen Professor in Nursing Excellence, University of Pennsylvania School of Nursing, 418 Curie Boulevard, Room 419, Philadelphia, PA, 19104-4217, Telephone: 215-898-2140. Email: evans@nursing.upenn.edu

Co-investigator: Eeeseung Byun, MSN, RN, ACNP-BC, Doctoral Student, University of Pennsylvania School of Nursing, 418 Curie Boulevard, Room 310H, Philadelphia, PA, 19104-4217, Telephone: 215-746-4454. Email: eeeseung@nursing.upenn.edu

Emergency Contact: (name, address, phone and email) Eeeseung Byun, MSN, RN, ACNP-BC, Telephone: 215-746-4454. Email: eeeseung@nursing.upenn.edu

You are being asked to take part in a research study. This is not a form of treatment or therapy. It is not supposed to detect a disease or find something wrong. Your participation is voluntary which means you can choose whether or not to participate. If you decide to participate or not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you make a decision, you will need to know the purpose of the study, the possible risks and benefits of being in the study and what you will have to do if you decide to participate. As the researcher, I will talk with you about the study and give you this consent form to read. You do not have to make a decision now; you can take the consent form home and share it with your family, friends, or family doctor and family.

If you do not understand what you are reading, do not sign it. Please ask me, the researcher, to explain anything you do not understand, including any language contained in this form. If you decide to participate, you will be asked to sign this form and a copy will be given to you. Keep this form; in it you will find contact information and answers to questions about the study. You may ask to have this form read to you.

What is the purpose of the study?

The purpose of the study is to learn more about the feelings and experiences of caregivers of older adults with stroke in the first 6 weeks of caregiving. The study is a doctoral dissertation in the School of Nursing, University of Pennsylvania.

Why was I asked to participate in the study?

You are being asked to join this study because you (a) are a family member or friend of an older adult (age 65 or older) who was diagnosed with new or recurrent stroke within the past 2 weeks, (b) expect to be the primary caregiver for this older adult with stroke, (c) can communicate in English, (d) are able to demonstrate capacity for informed consent and (e) are age 21 or older.

How long will I be in the study? How many other people will be in the study?

If you decide to participate in the study, you will be involved for about four weeks. You will be interviewed in-person two times: within two weeks after the older person's stroke while they are still in the hospital and again four weeks later. This will take about 40–50 minutes for the first interview and 30–40 minutes for the second interview.

On a day following each interview, you will be also asked to collect your saliva (spit) using a sponge that you will place in your mouth for one minute twice in the same day. Collecting and labeling each saliva (spit) sample will take up to 5 minutes.

With the permission from your older adult with stroke, we will also review their hospital medical record to get information about his/her health, the type of stroke he/she has had and the severity of his/her stroke.

You will be one of 230 participants (115 caregivers and 115 stroke survivors) in the study. The entire study is expected to be completed within one year.

Where will the study take place?

Depending on your preference, you will be interviewed for the first time at hospital, your home, or another convenient location. For the second interview [four weeks later] you can be interviewed at home or another convenient location.

You will collect your own saliva (spit) sample at home.

What will I be asked to do?

You will be asked to respond to questions asked by the researcher who will read the questions aloud and record your answers. You will be given a written copy of the questions to view at the same time. This will take about 40–50 minutes for the first interview and 30–40 minutes for the second interview. The interview questions include information about you (for example, your age, gender, education, caregiving experience); questions about your feelings of uncertainty, stress, depression and caregiving burden, as well as your quality of life, health, ways of coping, and social support. You will be also asked about your older adults' functional status and characteristics (for example, age,

gender, education). If any of the information is missing, you will be re-contacted by investigator over the phone in an attempt to complete the information.

You will be also asked to collect your saliva (spit) to assess your biologic stress level (salivary cortisol) using a sponge that you will place in your mouth for one minute twice in the same day: 1) within 2 weeks after stroke and 2) 4 weeks after the first interview. Collecting each saliva sample will take up to 5 minutes. You will place the samples in a plastic bag and keep them in your freezer overnight. The researcher will pick up the saliva samples or you will place the bag in a pre-paid FedEx clinical envelope and mail it to the researcher.

What are the risks?

No major risks are expected from this study. You, however, may become tired while answering the interview questions or you may feel upset discussing your experience in taking care of your older adult family member/friend with a stroke. If you become tired, you may stop and complete the interview later. If you experience uncomfortable feelings and upset during the interview, you may take a break in the interview. The investigator is prepared to be sensitive and respectful if you decide not to participate or not to answer some of the questions. You may withdraw from the study at any time. You will not be asked to answer any questions that you do not wish to answer. To protect your privacy, a quiet place will be provided for an interview that is held in the hospital or another healthcare facility, with permission of the facility.

If you feel severely distressed during the hospital-based interview at the hospital, the investigator will contact a hospital-based psychiatric counseling service for your assistance. If you should develop this response during the interview at your home or other location, the investigator will help you contact emergency psychiatric services for your assistance.

All information including completed interview tools and coded computerized information will be cared for in a manner to protect your privacy and confidentiality. An identification code number will be assigned to you, and will be used to identify all the information you provide so that your name will not be placed at risk for identification. To ensure confidentiality, all research information will be kept in a locked filing cabinet in a secure area at the University of Pennsylvania School of Nursing and only the researchers will be allowed to see your personal data. In addition, all information in computerized files will be stored using a special protection tool specifically for research studies. No individual identifying information will be made public in any presentations or publications of the results of this study.

How will I benefit from the study?

There is no benefit to you. Your participation could help us understand the caregiving experience for older family members or friends with stroke, however, which can benefit

you indirectly. This study will guide future research and promote improved clinical practice and education for caregivers of stroke survivors. You may feel satisfaction from having had the opportunity to participate in the study and contribute to increased knowledge in science.

What other choices do I have?

Your alternative to being in the study is to not be in the study.

What happens if I do not choose to join the research study?

You may choose to join the study or you may choose not to join the study. Your participation is voluntary.

If you choose not to join the research study, you will lose no benefits or advantages that are now coming to you, or would come to you in the future. Neither will this decision affect the care for your older family member or friend with stroke. His or her health care providers will not be upset with your decision either way.

When is the study over? Can I leave the study before it ends?

The study is expected to end after all participants have completed all interviews and provided saliva samples. Your role in the study is complete after your second interview and return of the second set of saliva samples. The overall study may be stopped without your consent for the following reasons:

- The investigators, the sponsor or the Office of Regulatory Affairs at the University of Pennsylvania can stop the study anytime

You have the right to drop out of the study at any time during your participation. There is no loss of benefits to which you are otherwise entitled if you decide to do so. Withdrawal will not interfere with your future care.

If you no longer wish to be in the research study, please contact Eeeseung Byun at 215-746-4454 and talk with her directly or leave a message regarding your wish to voluntarily withdraw from the study.

How will confidentiality be maintained and my privacy be protected?

The researcher will make every effort to keep all the information you share during the study strictly confidential, as required by law. The Institutional Review Board (IRB) at the University of Pennsylvania is responsible for protecting the rights and welfare of research volunteers like you. The IRB has access to study information. Any forms you sign where you can be identified by name will be kept in a locked drawer in a safe area at the University of Pennsylvania School of Nursing. These forms will be kept confidential.

All these forms will be destroyed when the study is over.

Will I have to pay for anything?

There are no costs associated with participating in the study.

Will I be paid for being in this study?

You will receive a \$10 gift card upon completion of the quantitative interview and collection of saliva samples for each of two times: 1) within 2 weeks after stroke and 2) 4 weeks after the first interview (a total maximum value of \$20).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a she or the researcher cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study. If you have any questions or there is something you do not understand, please ask. You will receive a copy of this consent form.

_____ Signature of Participant	_____ Date
_____ Print Name of Participant	_____ Date
_____ Signature of Investigator	_____ Date
_____ Print Name of Investigator	_____ Date

**APPENDIX Q. UNIVERSITY OF PENNSYLVANIA INFORMED CONSENT
AND HIPAA AUTHORIZATION FORM (STROKE SURVIVORS)**

Title of the Research Study: The effect of early uncertainty on caregiver stress and psychological outcomes: The case of stroke survivor caregivers

Protocol Number: 813927

Principal Investigator: Lois K. Evans, PhD, RN, FAAN,
van Ameringen Professor in Nursing Excellence, University of Pennsylvania School of Nursing, 418 Curie Boulevard, Room 419, Philadelphia PA 19104-4217, Telephone: 215-898-2140. Email: evans@nursing.upenn.edu

Co-investigator: Eeeseung Byun, MSN, RN, ACNP-BC, Doctoral Student, University of Pennsylvania School of Nursing, 418 Curie Boulevard, Room 310H, Philadelphia, PA, 19104-4217, Telephone: 215-746-4454. Email: eeeseung@nursing.upenn.edu

Emergency Contact: Eeeseung Byun, MSN, RN, ACNP-BC, Telephone: 215-746-4454. Email: eeeseung@nursing.upenn.edu

You are being asked help with a research study by allowing us to see your hospital medical record information. This is not a form of treatment or therapy. It is not supposed to detect a disease or find something wrong. Your agreement is voluntary which means you can choose whether or not to allow us to see your hospital medical record. If you decide not to allow us to see your hospital medical record, there will be no loss of benefits to which you are otherwise entitled. Before you make a decision you will need to know the purpose of the research study, the possible risks and benefits of sharing your hospital medical record information and what you will have to do if you agree. The researcher is going to talk with you about the study and give you this consent form to read. You do not have to make a decision now; you can keep the consent form and discuss it with your family, friends and health care providers.

If you do not understand what you are reading, do not sign it. Please ask the researcher to explain anything you do not understand, including any language contained in this form. If you decide allow us to use your hospital medical record information, you will be asked to sign this form and a copy will be given to you. Keep this form; in it you will find contact information and answers to questions about the study. You may ask to have this form read to you.

What is the purpose of the study?

The purpose of the study is to learn more about the experience of caregivers of older adults with stroke in the first 6 weeks of caregiving. This is a doctoral dissertation study being conducted at the School of Nursing, University of Pennsylvania.

Why was I asked to participate in the study?

You are being asked to allow us to see your hospital medical record because (a) your family or friend caregiver is participating in the study, (b) you have been diagnosed with new or recurrent stroke, (c) you are within the first 2 weeks after having had the stroke, (d) you are age 65 or older, and (e) you can communicate in English.

How long will I be in the study? How many other people will be in the study?

The entire study is expected to be completed within one year. Your agreement to allow us to review your hospital medical record will be a one time to get information about your health, the type of stroke you have had and the severity of your stroke.

You will be one of 230 participants (115 caregivers and 115 stroke survivors) in the study.

Where will the study take place?

If you agree, the researcher will review your hospital medical record at the hospital.

What will I be asked to do?

You will not be asked to do anything. The researcher will review your hospital medical record to get selected information about your health, type of stroke and severity of stroke.

What are the risks?

No major risks are anticipated from this study.

The form onto which the information from your hospital medical record is written and the computerized file will be handled and processed in a way to protect your privacy and confidentiality. An identification code number will be assigned to your caregiver who is participating in the study, and will be used to identify all the information including the information from your hospital medical record. No personal names will be attached in order to prevent your identification. To ensure confidentiality, all research information will be kept in a locked filing cabinet in a secure area at University of Pennsylvania School of Nursing and only the investigator will be allowed to access the information. In addition, all computerized information will be stored using a special secure tool for research studies. No individual identifying information will be shared in scientific presentations or published papers in which study results are presented.

How will I benefit from the study?

There is no benefit to you. Your agreement to allow us see your hospital medical record could help us understand the caregiving experience for older adults with stroke, however, which can benefit you indirectly. This study will guide future research and promote improved clinical practice and education for caregivers of stroke survivors. You may feel satisfaction from having had the opportunity to participate in the study and contribute to increased knowledge in science.

What other choices do I have?

Your alternative to agreeing to allow the researcher to review your hospital medical record is to not agree.

What happens if I do not choose to join the research study?

You may choose to allow the researcher to review your hospital medical record or you may choose not to. Your participation is voluntary.

If you choose not to allow the researcher to review your hospital medical record, you will lose no benefits or advantages that are now coming to you, or would come to you in the future, nor will it affect the care you receive at the hospital. Your health care providers will not be upset with your decision.

When is the study over? Can I leave the study before it ends?

Your hospital medical record will be reviewed only once while you are still in the hospital to get information about your health, the type of stroke you have had and the severity of your stroke. No further information regarding your medical condition will be collected. The entire study with 230 participants (115 caregivers and 115 stroke survivors) is expected to end after all the information from caregivers and the stroke survivors for whom they care has been collected. The study may be stopped at any time without consent of the caregiver participants by the researchers, the sponsor or the Office of Regulatory Affairs at the University of Pennsylvania.

You have the right to ask that your hospital medical record information be removed from the research study at any time during your caregiver participation. There is no loss of benefits to which you are otherwise entitled if you decide to do so. Withdrawal will not interfere with your future care.

If you no longer wish your hospital medical record information to be included in the study, please contact Eeeseung Byun at 215-746-4454 and talk with her directly or leave a message regarding your wish.

How will confidentiality be maintained and my privacy be protected?

The research team will make every effort to keep all the information we review from your hospital medical record for this study strictly confidential, as required by law. The Institutional Review Board (IRB) at the University of Pennsylvania is responsible for protecting the rights and welfare of research volunteers like you. The IRB has access to study information. Any forms you sign where you can be identified by name will be kept in a locked drawer in secure area at the University of Pennsylvania School of Nursing. These forms will be kept confidential. All of these forms will be destroyed when the study is over.

Will I have to pay for anything?

There are no costs associated with allowing the researcher to review your hospital medical record.

Will I be paid for being in this study?

Your caregiver who is participating in the study will receive a gift card for each of the two times s/he is interviewed.

Who can see or use my information? How will my personal information be protected?

A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your health information. The Privacy Rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Researchers covered by this regulation are required to get your permission to use and share with others any health information that could identify you. If you sign this informed consent form, you are giving permission for the use and disclosure of your health information for purposes of this research study. You do not have to give this permission. We will do our best to make sure that the personal information from your hospital medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

What information about me may be collected, used or shared with others?

The study team will record the information regarding your health, type and severity of stroke on study forms. Your name will not appear on the study forms. Instead, subject identification number assigned to your caregiver will be written on your forms. Representatives from the groups identified below may need to look at your hospital medical records to make sure that the information on the study forms is correct or that the study was conducted properly. Reviews like that will take place at the study center or

where the hospital medical records are stored and can take place after the study is over.

Why is my information being used?

Your information will be used to:

- do the research
- oversee the research
- to see if the research was done right.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The principal investigator (researcher) for the study and her faculty mentor
- Other authorized personnel at University of Pennsylvania

Who, outside of the School of Medicine, might receive my information?

Your personal health information may be shared with the following people or groups:

- University of Pennsylvania School of Nursing
- The institutional review board (ethics committee) that approved this study and any other committees responsible for overseeing the research
- Government health agencies in the US or other countries.

Representatives from these groups may receive information from your caregiver's study forms or may review your medical records (as described above) or both. Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations. The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. Your personal health information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to disclose and use your health information. You do this by contacting Eeeseung Byun at 215-746-4454 and talking with her directly or leaving a message regarding your wish to voluntarily withdraw from the study. If you withdraw your permission, your information will not be used.

What if I decide not to give permission to use and give out my health information?

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. By signing this document you are permitting the School of Nursing to use and disclose personal health information collected about you for research purposes as described above.

How will confidentiality be maintained and my privacy be protected?

The researcher will make every effort to keep all the information you give us during the study strictly confidential, as required by law. The Institutional Review Board (IRB) at the University of Pennsylvania is responsible for protecting the rights and welfare of research volunteers. Your personal information may be shared with others if required by law. The IRB has access to study information.

Since this is a study about your caregiver, we will assign an identification number to your caregiver when consents are obtained. All related data we collect about you from your hospital medical record will carry that code rather than your name, social security number or hospital record number. The researcher who collects the information will have access to private information about you as an individual. All information will be stored in a locked office in a locked cabinet. Any forms you sign where you can be identified by name will be kept in a locked drawer in a locked office. These forms will be kept confidential. All the documents will be destroyed when the study is over.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding sharing your personal information as part of this research study or if you have any questions about your rights in sharing such information, you should speak with the Principal Investigator listed on the first page of this form. If she or the researcher cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

APPENDIX R. PATIENT AGREEMENT FORM
AGREEMENT TO PARTICIPATE IN RESEARCH

[Experience of caregivers for older adults with stroke]

My name is Eeeseung Byun. I am a graduate student at the School of Nursing, University of Pennsylvania. I am studying the experience of caregivers for older adults with stroke.

I am talking with you today because I am trying to learn more about the experience of caregivers for older adults with stroke in the first 6 weeks of caregiving, and your family/friend caregiver has agreed to be a join in this study.

If you agree, I will see your hospital medical record to get information about your health, the type of stroke you have had, and severity of the stroke. You will not need to do anything.

No major risks are expected from your allowing me to look at your hospital medical record as part of this study.

The form onto which the information from your hospital medical record will be written and the computerized research file will be handled and kept safely in a way to protect your privacy.

There is no benefit to you. Having being able to use your health information could help us understand the caregiving experience for older adults with stroke, however, which can benefit you indirectly.

Please talk this over with your family, friend or health care providers before you decide whether or not to agree. We will also ask your family or friend to give their permission to allow us to look at your hospital medical record. But even if your family or friend says “yes,” you can still decide not to allow it.

If you don’t want your medical record information to be used in this study, you do not have to agree. Remember, sharing this information is up to you and no one will be mad if you don’t want to participate or even if you change your mind later and want to stop.

You can ask any questions that you have about this study. If you have a question later that you didn’t think of now, you can call me (215-746-4454) or ask me the next time you see me.

Signing your name below means that you agree to for your hospital medical record information to be used in this study. You and your family or friend caregiver will be given a copy of this form after you sign it.

**APPENDIX S. THOMAS JEFFERSON UNIVERSITY INFORMED CONSENT
DOCUMENT FOR HUMAN-SUBJECTS RESEARCH (CAREGIVERS)**

Department: Nursing

Principal Investigator: Meg Bourbonniere, PhD, RN

Telephone: 215-503-6122

Co-Investigator(s): Lois Evans, PhD, RN, FAAN

Telephone: 215-898-2140

Co-Investigator(s): Eeeseung Byun, PhD(c), MSN, RN, ACNP-BC

Telephone: 215-746-4454

Nursing Study Title: The effect of early uncertainty on caregiver stress and psychological outcomes: The case of stroke survivor caregivers

Lay Study Title: Experience of Caregivers for Older Adults with Stroke

What Is Informed Consent?

You are being asked to take part in a nursing research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans. Before you can make a knowledgeable decision about whether to participate, you should understand the possible risks and benefits related to this study. This process of learning and thinking about a study before you make a decision is known as *informed consent* and includes:

- Receiving detailed information about this research study;
- Being asked to read, sign and date this consent form, once you understand the study and have decided to participate. If you don't understand something about the study or if you have questions, you should ask for an explanation before signing this form;
- Being given a copy of the signed and dated consent form to keep for your own records.

What is the purpose of this study?

The purpose of the study is to learn more about the feelings and experiences of caregivers of older adults with stroke in the first 6 weeks of caregiving. The study is a doctoral dissertation in the School of Nursing, University of Pennsylvania.

Why was I asked to participate in the study?

You are being asked to join this study because you (a) are a family member or friend of an older adult (age 65 or older) who was diagnosed with new or another stroke within the past 2 weeks, (b) expect to be the primary caregiver for this older adult with stroke, (c) can communicate in English, (d) are able to demonstrate an understanding of the informed consent and (e) are age 21 or older.

How many individuals will participate in the study and how long will the study last?

230 participants (115 caregivers and 115 stroke survivors) from the Thomas Jefferson University Hospitals and University of Pennsylvania Health System will participate in the study. We hope to enroll at least 130 participants (65 caregivers and 65 stroke survivors) at Jefferson. Your involvement in the study will last about 6 weeks. The entire study will take about 12 months to complete.

What will I have to do during the study?

You will be asked to respond to questions asked by the researcher who will read the questions aloud and record your answers. You will be given a written copy of the questions to view at the same time. This will take about 40–50 minutes for the first interview and 30–40 minutes for the second interview. The interview questions include information about you (for example, your age, sex, education, caregiving experience); questions about your feelings of uncertainty, stress, depression and caregiving burden, as well as your quality of life, health, ways of coping, and social support. You will be also asked about your older adults' functional status and characteristics (for example, age, sex, education). If any of the information is missing, you will be re-contacted by the investigator over the phone in an attempt to complete the information.

You will also be asked to collect your saliva (spit) to assess your biologic stress by measuring a substance in saliva (salivary cortisol) using a sponge that you will place in your mouth for one minute twice in the same day: 1) within 2 weeks after stroke and 2) 4 weeks after the first interview. Collecting each saliva sample will take up to 5 minutes. You will place the samples in a plastic bag and keep them in your freezer overnight. The researcher will pick up the saliva samples or you will place the bag in a pre-paid FedEx clinical envelope and mail it to the researcher.

What are the risks or discomforts involved?

No major risks are expected from this study. You may become tired while answering the interview questions or you may feel upset discussing your experience in taking care of your older adult family member/friend with a stroke. If you become tired, you may stop and complete the interview later. If you experience uncomfortable feelings and upset during the interview, you may take a break in the interview. The investigator is prepared to be sensitive and respectful if you decide not to participate or not to answer some of the

questions. You may withdraw from the study at any time. You will not be asked to answer any questions that you do not wish to answer. To protect your privacy, a quiet place will be provided for an interview that is held in the hospital or another healthcare facility, with permission of the facility.

If you feel severely distressed during the interview at the hospital, and if you agree, the investigator will contact a hospital-based psychiatric counseling service for your assistance. If you should develop this response during the interview at your home or other location, the investigator will help you contact emergency psychiatric services for your assistance.

Are there alternatives to being in the study?

Your alternative to being in the study is to not be in the study.

How will privacy and confidentiality (identity) be protected?

All information including completed interview results and coded computerized information will be cared for in a manner to protect your privacy and confidentiality. An identification code number will be assigned to you, and will be used to identify all the information you provide so that your name will not be placed at risk for identification. To ensure confidentiality, all research information will be kept in a locked filing cabinet in a secure area at the University of Pennsylvania School of Nursing and only the researchers will be allowed to see your personal data. In addition, all information in computerized files will be stored using a special protection program specifically for research studies. No individual identifying information will be made public in any presentations or publications of the results of this study.

The researcher will make every effort to keep all the information you share during the study strictly confidential, as required by law. The Institutional Review Board (IRB) is responsible for protecting the rights and welfare of research volunteers like you. The IRB has access to study information. Any forms you sign where you can be identified by name will be kept separate from your questionnaires in a locked drawer in a safe area at the University of Pennsylvania School of Nursing. These forms will be kept confidential. All these forms will be destroyed when the study is over.

The information from this study may be published in scientific journals or presented at scientific meetings but you will not be personally identified in these publications and presentations.

Will I benefit from being in this study?

There is no benefit to you. Your participation could help us understand the caregiving experience for older family members or friends with stroke, however, which can benefit you indirectly. We hope this study will guide future research and promote improved

clinical practice and education for caregivers of stroke survivors. You may feel satisfaction from having had the opportunity to participate in the study and contribute to increased knowledge in science.

Will I be paid for being in this study?

You will receive a \$10 gift card upon completion of the quantitative interview and collection of saliva samples for each of two times: 1) within 2 weeks after stroke and 2) 4 weeks after the first interview (a total maximum value of \$20).

Will I be told about any new findings?

You will not receive the study results or other data about the study. However, this study will guide future research and promote improved clinical practice and education for caregivers of stroke survivors.

Are there costs related to being in this study?

There are no costs associated with participating in the study.

Can I be removed from the study or quit the study?

Your decision to participate in this research study is entirely voluntary. You have been told what being in this study will involve, including the possible risks and benefits.

Your participation in this research project may be terminated by the researcher for any reason.

You may refuse to participate in this investigation or withdraw consent and quit this study without penalty and without affecting the care for your older family member or friend with stroke at the Thomas Jefferson University. His or her health care providers will not be upset with your decision either way. If you no longer wish to be in the research study, please contact Eeseung Byun at 215-746-4454 (or Dr. Meg Bourbonniere at 215-503-6122) and talk with her directly or leave a message regarding your wish to voluntarily withdraw from the study.

CONTACT INFORMATION

Telephone number for questions about your rights as a research participant	The Jefferson Institutional Review Board	215-503-8966
For questions, concerns or complaints about the research, or if you suspect a research-related injury	The Principal Investigator, Dr. Meg Bourbonniere Co-investigators, Dr. Lois Evans Eeeseung Byun	215-503-6122 215-898-2140 215-746-4454
If you have difficulty contacting the study staff	Call the Jefferson Office of Human Research	215-503-0203

If you want more information about the Jefferson Institutional Review Board or Jefferson’s Human Research Protection Program, please visit our website at http://www.jefferson.edu/human_research/irb/index.cfm.

Non-Waiver of Legal Rights Statement

By your agreement to participate in this study, and by signing this consent form, you are not waiving any of your legal rights.

In order to be in this research study, you must sign this consent form.

You affirm that you have read this consent form. You have been told that you will receive a copy.

Signatures:

Your Name (Please print or type)

Date

Your Signature

Date

Name of Person Conducting Consent Interview

Date

Signature of Person Conducting Consent Interview

Date

Signature of Principal Investigator or Co-Investigator

Date

**APPENDIX T. THOMAS JEFFERSON UNIVERSITY INFORMED CONSENT
DOCUMENT FOR HUMAN-SUBJECTS RESEARCH (STROKE SURVIVORS)**

Department: Nursing

Principal Investigator: Meg Bourbonniere, PhD, RN

Telephone: 215-503-6122

Co-Investigator(s): Lois Evans, PhD, RN, FAAN

Telephone: 215-898-2140

Co-Investigator(s): Eeeseung Byun, PhD(c), MSN, RN, ACNP-BC

Telephone: 215-746-4454

Nursing Study Title: The effect of early uncertainty on caregiver stress and psychological outcomes: The case of stroke survivor caregivers

Lay Study Title: Experience of Caregivers for Older Adults with Stroke

What Is Informed Consent?

You are being asked to take part in a nursing research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans. Before you can make a knowledgeable decision about whether to participate, you should understand the possible risks and benefits related to this study. This process of learning and thinking about a study before you make a decision is known as *informed consent* and includes:

- Receiving detailed information about this research study;
- Being asked to read, sign and date this consent form, once you understand the study and have decided to participate. If you don't understand something about the study or if you have questions, you should ask for an explanation before signing this form;
- Being given a copy of the signed and dated consent form to keep for your own records.

What is the purpose of this study?

The purpose of the study is to learn more about the feelings and experiences of caregivers of older adults with stroke in the first 6 weeks of caregiving. The study is a doctoral dissertation in the School of Nursing, University of Pennsylvania.

Why was I asked to participate in the study?

You are being asked to allow us to see your hospital medical record because (a) your family or friend caregiver is participating in the study, (b) you have been diagnosed with new or another stroke, (c) you are within the first 2 weeks after having had the stroke, (d) you are age 65 or older, and (e) you can communicate in English.

How many individuals will participate in the study and how long will the study last?

230 participants (115 caregivers and 115 stroke survivors) from the Thomas Jefferson University Hospitals and University of Pennsylvania Health System will participate in the study. We hope to enroll at least 130 participants (65 caregivers and 65 stroke survivors) at Jefferson. Your involvement in the study will last about 6 weeks. The entire study will take about 12 months to complete.

What will I have to do during the study?

You will not be asked to do anything. The researcher will review your hospital medical record to get selected information about your health, type of stroke and severity of stroke.

What are the risks or discomforts involved?

No major risks are anticipated from this study.

Are there alternatives to being in the study?

Your alternative to agreeing to allow the researcher to review your hospital medical record is to not agree.

How will privacy and confidentiality (identity) be protected?

The form onto which the information from your hospital medical record is written and the computerized file will be handled and processed in a way to protect your privacy and confidentiality. An identification code number will be assigned to your caregiver who is participating in the study, and will be used to identify all the information including the information from your hospital medical record. No personal names will be attached in order to prevent your identification. To ensure confidentiality, all research information will be kept in a locked filing cabinet in a secure area at University of Pennsylvania School of Nursing and only the investigator will be allowed to access the information. In addition, all computerized information will be stored using a special secure program for research studies. No individual identifying information will be shared in scientific presentations or published papers in which study results are presented.

Federal regulations require that certain information about individuals be kept confidential. This information is called “protected health information” (PHI). PHI includes

information that identifies you personally such as name, address and social security number, or any medical or mental health record, or test result, that may have this sort of information on it. The laws state that you may see and review your TJU or Thomas Jefferson University Hospital medical records at any time.

If you sign this informed consent form, you are giving permission for the use and disclosure of your PHI for purposes of this research study. You do not have to give this permission. The following individuals or entities may have access to your PHI and by law must protect it. These include investigators listed on this consent form and other personnel of Thomas Jefferson University and Thomas Jefferson University Hospitals, Inc. involved in this specific study, the University's Division of Human Subjects Protection and the Institutional Review Board (IRB). It may also be provided to other people or groups as follows:

- Authorized personnel at University of Pennsylvania.

Your PHI may also be shared with the following entities that, while not obligated by law to protect PHI, will protect it to the best of their ability:

- University of Pennsylvania School of Nursing
- University of Pennsylvania Institutional review board (ethics committee) that approved this study and any other committees responsible for overseeing the research
- Government health agencies in the US or other countries
- Any person or agency required by law.

The following information will be provided to the study sponsor and other entities noted above:

Your health, the type of stroke you have had and the severity of your stroke.

The information from this study may be published in scientific journals or presented at scientific meetings but you will not be personally identified in these publications and presentations.

You may withdraw or take away your permission to disclose and use your PHI. You do this by contacting Eeeseung Byun at 215-746-4454 (or Dr. Meg Bourbonniere at 215-503-6122) and talking with her directly or leaving a message regarding your wish to voluntarily withdraw from the study. If you withdraw your permission, your information will not be used.

Will I benefit from being in this study?

There is no benefit to you. Your agreement to allow us see your hospital medical record could help us understand the caregiving experience for older adults with stroke, however,

which can benefit you indirectly. We hope this study will guide future research and promote improved clinical practice and education for caregivers of stroke survivors. You may feel satisfaction from having had the opportunity to participate in the study and contribute to increased knowledge in science.

Will I be paid for being in this study?

Your caregiver who is participating in the study will receive a gift card for each of the two times s/he is interviewed.

Will I be told about any new findings?

You will not receive the study results or other data about the study. However, this study will guide future research and promote improved clinical practice and education for caregivers of stroke survivors.

Are there costs related to being in this study?

There are no costs associated with participating in the study.

Can I be removed from the study or quit the study?

You may choose to allow the researcher to review your hospital medical record or you may choose not to. Your participation is voluntary.

If you choose not to allow the researcher to review your hospital medical record, you will lose no benefits or advantages that are now coming to you, or would come to you in the future, nor will it affect the care you receive at the hospital. Your health care providers will not be upset with your decision.

You may withdraw or take away your permission to disclose and use your hospital record by contacting Eeeseung Byun at 215-746-4454 (or Dr. Meg Bourbonniere at 215-503-6122) and talking with her directly or leaving a message regarding your wish to voluntarily withdraw from the study.

**APPENDIX U. THOMAS JEFFERSON UNIVERSITY SURROGATE CONSENT
FOR A RESEARCH PROTOCOL**

Department: Nursing

Principal Investigator: Meg Bourbonniere, PhD, RN

Telephone: 215-503-6122

Co-Investigator(s): Lois Evans, PhD, RN, FAAN

Telephone: 215-898-2140

Co-Investigator(s): Eeeseung Byun, PhD(c), MSN, RN, ACNP-BC

Telephone: 215-746-4454

Nursing Study Title: The effect of early uncertainty on caregiver stress and psychological outcomes: The case of stroke survivor caregivers

Lay Study Title: Experience of Caregivers for Older Adults with Stroke

Name of Subject: _____

COMPLETE SECTIONS “A,” “B” AND “C” BELOW.

A. REASON FOR SURROGATE CONSENT:

_____ The subject is unable to give informed consent.

- Reason for Subject’s Inability To Give Informed Consent:¹

B. SURROGATE INFORMATION:

_____ COURT ORDER AUTHORIZING GUARDIAN CONSENT

Date of Order: _____ Name of Guardian: _____

_____ POWER OF ATTORNEY Name: _____

¹ Examples of evidence to consider include indications in the medical record concerning whether the subject was oriented times three, whether the subject was alert and communicating with others, whether the subject was able to write messages on paper, and whether the subject was able to adequately respond to questioning regarding his or her participation in the research. Other considerations include the subject’s baseline cognitive status and the administration of medications that might impair mental capacity.

_____ SPOUSE Name: _____

_____ PARENT Name: _____

_____ ADULT CHILD Name: _____

_____ ADULT BROTHER/SISTER Name: _____

_____ OTHER ADULT RELATIVE Name: _____
Relationship: _____

C. PATIENT'S ASSENT TO PARTICIPATE:

_____ The subject's assent to inclusion in the study was sought and obtained.

_____ The subject's assent to inclusion in the study was sought and denied.

_____ The subject's assent was not sought.

- Reason for Subject's Inability to Assent: _____

Signatures:

_____(Date)

Surrogate's Signature

_____(Date)

Name of Person Conducting Consent Interview

_____(Date)

Signature of Person Conducting Consent Interview

_____(Date)

Signature of Principal Investigator or
Co-Investigator

APPENDIX V. RECRUITMENT SCRIPT

Hello, my name is _____, and I am a nurse here at the University of Pennsylvania. I am also a PhD student in the School of Nursing (I am Research Assistant in the School of Nursing). I am working with Dr. XX and the nurses here on the unit, and we are worried about the amount of stress that families have/experience when their loved one has had a stroke. So our project is to learn more about family caregiver stress.

Could I talk with you for a few minutes now about the project? [If this is not a good time for you, would you mind my coming back later? etc....].

The study is about feelings and experiences when taking care of, or helping care for, an older family member in the first few weeks after stroke, when they first begin to provide care for their loved ones.

I am going to give you a general picture of the study. There are several survey questions that I will ask you or read to you. Answering the questions will take a maximum of 40–50 minutes. Questions are related to how members of the family feel and what they experience from their caregiving.

The next day after the interview, we will ask you collect your saliva on a cotton sponge that we will provide and collect from you. The saliva will be used to measure the stress level of family caregivers. Then, one month later, we will meet with you for the second interview and again ask you to collect your saliva.

Let me explain how to collect your saliva. You will collect saliva after waking up and then around 9 pm before you go to bed. Basically, each time you will put a cotton sponge under your tongue for a minute, take it out and place it in the tube we will give you, and then keep it in a plastic bag in your freezer overnight. The research team will pick up the two tubes or arrange a time and place to pick them up from you. We provide a \$10 gift certificate for the first interview and saliva collection and another \$10 one month later for the second interview and saliva collection.

Would you like to participate in this study?

{If the person indicates that they do not wish to collect saliva}: If you are not comfortable collecting your saliva, we can do only the survey questions. Would you be able to do only the survey questions? {If the person indicates they are too busy to meet us for the second interview}: If you are too busy to meet for the second interview, we can give you a copy of the survey questions to take home and then we can do the second interview over the phone while you are reading the questions and answering them at the same time.

APPENDIX W. PHONE SCRIPT TEMPLATE

Hello, my name is _____, and I am a nurse at the University of Pennsylvania. I am also a research assistant in the School of Nursing. I am working with Dr. Meg Bourbonniere and the nurses here on the unit at the Thomas Jefferson University Hospital, and we are interested in studying the amount of stress that families have/experience when their loved one has had a stroke. So our project is to learn more about family caregiver stress.

Is this good time to talk with you? If you do not have time now, can I call you back later?

The study is about feelings and experiences when taking care of, or helping care for, an older family member in the first few weeks after stroke, when they first begin to provide care for their loved ones.

I am going to give you a general picture of the study. There are several survey questions that I will ask you or read to you. Answering the questions will take up to 40–50 minutes. Questions are related to how members of the family feel and what they experience from their caregiving.

The next day after the interview, we will ask you collect your saliva on a cotton sponge that we will provide and collect from you. The saliva will be used to measure chemicals that indicate your stress level as a family caregiver. Then, one month later, we will meet with you for the second interview and again ask you to collect your saliva for a repeat of the test.

Let me explain how to collect your saliva. You will collect saliva after waking up and then around 9 pm before you go to bed. Basically, each time you will put a cotton sponge under your tongue for a minute, take it out and place it in the tube we will give you, and then keep it in a plastic bag in your freezer overnight. The research team will arrange a time and place to pick up the saliva samples from you or you will place the bag in a pre-paid FedEx clinical envelope and mail it to the researcher.

We provide a \$10 gift certificate for the first interview and saliva collection and another \$10 one month later for the second interview and saliva collection.

Your participation in this study is entirely voluntary, and you can refuse to participate or stop your participation at any time without penalty or loss of benefits to which you are otherwise entitled, and without affecting your loved one or their care at Jefferson.

Would you like to participate in this study?

{If the person indicates that they do not wish to collect saliva}: If you are not comfortable collecting your saliva, we can do only the survey questions. Would you be able to do only the survey questions? {If the person indicates they are too busy to meet us for the second interview}: If you are too busy to meet for the second interview, we can

give you a copy of the survey questions to take home and then we can do the second interview over the phone while you are reading the questions and answering them at the same time.

(If no) Thank you for your time. I won't call you again.

(If yes) When would be good time for you to meet?

APPENDIX X. FLYER



Care to change the world.™

School of Nursing
Claire M. Fagin Hall
418 Curie Boulevard
Philadelphia, PA 19104 - 4217



Research Study Seeks Family Caregivers for Older Adults with Stroke

You May be Eligible if You:

1. Are a family member or friend of an older adult (age 65 or older) who had a stroke or brain hemorrhage within the past 2 weeks.
2. Expect to be the primary caregiver for the older adult with a stroke or brain hemorrhage.
3. Can communicate in English.
4. Are age 21 or over.

Qualified Participants will:

1. Take part in two interviews about caregiving and collect samples of saliva.

Participants will be compensated with gift cards worth up to \$20 for their time and effort.

For more information about this study call 215-746-4454.

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