Review Article

Family Adaptation to Stroke: A Metasynthesis of Qualitative Research based on Double ABCX Model

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SUMMARY

Purpose: There is growing interest in synthesizing qualitative research. Stroke is a very common cause of disability often leaving stroke survivors dependent on their family. This study reports an interpretive review of research into subjective experience of families with stroke survivors based on the components of the Double ABCX Model including stressors, resources, perception, coping strategies, and adaptation of these families.

Methods: Metasynthesis was applied to review qualitative research looking at stroke family members’ experiences and responses to having a stroke survivor as a family member. Electronic database from 1990 to 2013 were searched and 18 separate studies were identified. Each study was evaluated using methodological criteria to provide a context for interpretation of substantive findings. Principal findings were extracted and synthesized under the Double ABCX Model elements.

Results: Loss of independence and uncertainty (as stressors), struggling with new phase of life (as perception), refocusing time and energy on elements of recovery process (as coping strategy), combined resources including personal, internal and external family support (as resources), and striking a balance (as adaptation) were identified as main categories. Family members of stroke survivor respond cognitively and practically and attempt to keep a balance between survivor’s and their own everyday lives.

Conclusions: The results of the study are in conformity with the tenets of the Double ABCX Model. Family adaptation is a dynamic process and the present study findings provide rich information on proper assessment and intervention to the practitioners working with families of stroke survivors.

Introduction

Annually, approximately 15 million people suffer from stroke worldwide [1,2]; Cerebrovascular accident or stroke is a serious health problem in the Western world [3,4]. Stroke patients frequently suffer decreased physical function (disability) [5]. Disability following stroke appears in the form of neurological dysfunctions (e.g., motor, sensory, visual) and limited ability to perform activities of daily living (ADLs) [6]. In Iran, based on different local studies, 33–327 persons in every 100,000 of the population are diagnosed with stroke each year making it the most prevalent cause of disability in adults [7,8]. However, according to a more accurate study, the annual incidence rate of stroke is 139 per 100,000 of population [9]. Stroke occurs suddenly, is traumatic, and leaves patients and families unprepared for dealing with its aftermath. It is a complex, life-changing experience for both stroke survivors and their family caregivers [10]. Thus, there is a growing interest in identifying compensatory mechanisms that can improve functional independence after stroke [11]. The role of the family is critical to stroke rehabilitation [12]. The family provides the most
critical resource for integrating and coordinating healthcare for its members [13]. It is a well-documented fact that the inclusion of family members in the caregiving process of stroke rehabilitation improves recovery [12]. Family caregivers of stroke patients are seriously in need of support. In both the short-term and long-term periods, many family caregivers report physical symptoms and psychological distress as a result of giving care [14]. The more severe a patient’s level of disability, the more likely the caregiver will experience higher levels of burden [10].

Family adaptation is a process in which families engage in direct responses to the extensive demands of a stressor and realize that systematic changes are needed within the family unit to restore factional stability and improve family satisfaction and well-being [15]. Informal family caregiving has been a focus of nursing research for more than 25 years [10], while caring for families is a growing part of nurses’ professional work in home care and in various healthcare settings [16]. Family nursing centers on the family as a unit of care, addressing family needs in response to a member’s illness or threat to health, rather than focusing on the individual [17]. Of the many approaches to family theory, family coping theory has been extensively tested and applied to families dealing with stress of traumatic and chronic illness [18]. Developed originally by Hill’s (1949), family stress theory called the ABCX postulates that a stressor (A) interacts with family resources for dealing with crises (B) and with the definition the family makes of the event (C) to produce crisis (X) [15,18,19]. The subsequent refinement of this model by McCubbin et al. treats coping as the central process in the family’s effort to adapt to a crisis and the A factor was expanded to include both the original and the pileup of stressors [15,18,20]. This model defines the process of adaptation to stressful situations as an interaction among four components. These components include the stressor (e.g., disease diagnosis, A), the internal and external resources one has to address the stressor (e.g., the support of family members, B), the appraisal of the stressor (e.g., seeing the stressor as a threat and challenge, C), and the coping strategies utilized to respond to the stressor (BC) [21–23]. The Double ABCX model of an adjustment and adaptation asserts that family outcomes following the impact of a stressor and crises are the by-products of multiple factors (A, B, C, and X) in interaction with each other [24]. The degree to which a family adapts after stroke can dramatically affect patient recovery [25]. Despite the high prevalence of stroke and the potentially high burden of family caregiving for the stroke survivors few studies have systematically addressed the consequences of stroke on family members [26]. Although the quantitative studies have provided valuable information about family members’ problems toward stroke survivors’ caregiving issues, in the past 20 years have there been very few qualitative research focused on describing and explaining family adaptation following stroke.

Providing a richer understanding of an issue is not possible from the results of one study [27]. Qualitative metasynthesis is an emerging method for synthesis of the findings of qualitative studies [28]. Metasynthesis is defined as “the theories, grand narratives, generalizations, or interpretive translations produced from the integration or comparison of findings from qualitative studies” [29]. It is a method of blending a group of qualitative studies to discover the common essence in the data and translate that into a new understanding [30]. The aim of the present study was to firstly, bring together the voice of families with stroke survivors who participated in qualitative research, on the basis of adaptation to stroke survivors’ caregiving tasks, and secondly, to determine the extent to which stroke family members’ experiences can be accommodated within the Double ABCX Model of family crises.

### Methods

#### Study design

A synthesis of qualitative studies relating to stroke family members’ experience of having a stroke patient is proposed.

#### Data collection

An interdisciplinary online search was done from the databases of Medline, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), OVID Medline, Proquest, SID, Magiran, IRAN MEDEX, MEDLIB and IranDoc from January 1, 1990 to November 31, 2013. The Google Scholar search engine was used to generate articles as well. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were applied to select the studies [31]. Keywords such as family adaptation, stroke family, cerebrovascular accident, family, stroke informal caregivers, qualitative research, experience, themes, grounded theory, and phenomenology were used. The abstract of papers were retrieved by the first two authors to determine their appropriateness. Bibliographies of the retrieved papers were also examined carefully. The inclusion criteria of studies to be examined were the following: having a qualitative design and focusing on the community-dwelling stroke patients’ caregivers and their families. There was no restriction in the paper selection, regarding the stroke patients’ range of age or length of stroke disease. Only studies in the English language were included. Eighteen qualitative studies on the caregivers’ experience of having stroke survivors in the family and the family adaptation were retrieved finally.

#### Measurements

A consensus definition for each statement was developed to maximize consistency by the first two authors using standards for the systematic review of qualitative literature [32] (Table 1). The purpose of the quality appraisal was ascertaining the methodological quality of the studies included in the synthesis. If the studies inadequately focused on the topic, or were not actually qualitative (sometimes studies collected data using qualitative methods, but did not analyze the data qualitatively), they were excluded from the research. The exclusion process is summarized in Figure 1.

#### Data analysis

The study followed the broad principles of metasynthesis outlined earlier. In the first stage, two authors reviewed each paper alone to extract qualitative findings. No attempt was made to reanalyze primary data presented as quotations, as these were inevitably sparse and selective in relation to the totality of the data in any study [32]. In the second stage of the analysis, clustering and recoding the findings from individual studies under broader themes was performed through discussion and agreement in meetings with all the authors. The aims of the meetings were resolving the possible disagreement between the two authors over papers rejection or inclusion to the synthesis process as well as recognizing higher-order concepts. The Preliminary coding rubric was established by the research team based on the framework of the Double ABCX Model of family crisis [15] and were reviewed for congruence with the tenets of the model. Within the coding rubric, individual codes were grouped within the model domains of a stressor, resources, definition the family makes of the event, coping strategies, contextual characteristics and adaptation [15,18].

Based on the Hill’s classic family theory [33], the Double ABCX Model extended by MacCubbin and Patterson, to address the issue
Table 1: Consensus Definitions of Criteria to Include Qualitative Studies.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Consensus definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Illumination of subjective meaning</td>
<td>Does the research, as reported, illuminate the subjective meaning, actions, &amp; privileging of the subjective experience of family adaptation to stroke context of those being researched?</td>
</tr>
<tr>
<td>2. Adaptation responsiveness of research design</td>
<td>Is there evidence of the adaptation responsiveness of the research design to the circumstances issues of real-life social settings being met during the course of the study?</td>
</tr>
<tr>
<td>3. Sample size</td>
<td>Is the description provided detailed enough to allow the researcher or context of what is being researched?</td>
</tr>
<tr>
<td>4. Description of appropriate knowledge</td>
<td>Are the structures &amp; processes within which the individual or situations are focused on their knowledge in their own right?</td>
</tr>
<tr>
<td>5. Sources of knowledge compared or contrasted</td>
<td>Are subjective perceptions &amp; experience treated as evidence resulting from stroke induced disability, affected the</td>
</tr>
<tr>
<td>6. Shift from description to analysis interpretation</td>
<td>How does research move from a description of the data, through quotations or examples, to an analysis of their meaning &amp; significance?</td>
</tr>
<tr>
<td>7. Claims for generalizability</td>
<td>What claims are being made for the generalizability of the findings?</td>
</tr>
</tbody>
</table>

Ethical considerations

The Ethics Committee of The University of Social Welfare and Rehabilitation Sciences approved this study (registration no.: 92/801/A/2/7245) on July 1, 2013.

Results

Literature search and review of reference lists revealed 411 records and abstracts which were screened by two authors independently. Once duplicated studies were removed, the remaining 308 abstracts were checked. Following exclusions and removal the studies that were not qualitative, showed inadequate focus on the topic or insufficient methodological quality, a total of 18 articles and thesis published between 1993 and 2013 remained. Of the 12 published studies, 5 articles were in the discipline of nursing, 3 in psychology, 2 in public and health sciences and 2 in occupational therapy. Six unpublished dissertations were included, from the nursing discipline and one from the occupational therapy field. The studies were done in Iran (n = 2), the United States of America (n = 4), the United Kingdom (n = 4), Canada (n = 3), Taiwan (n = 1), Hong Kong (n = 1), Brazil (n = 1), Sweden (n = 1) and Thailand (n = 1). Data were preliminarily collected using individual semi-structured, unstructured or in-depth interviews. Only four studies [36–39] used other forms of data collection. Data analysis was the area that varied, most among the studies, and included various descriptions (Table 2).

Substantive findings

Family stresses and demands: Pileup (A A) component

The initial stressor (A) is defined as a life event or transition impacting the family unit, and which has the potential of producing change in the family social system [35]. Loss of independence and certainty. The most frequently discussed stressors were loss of independence and certainty. Stroke survivors’ loss is characterized in several areas. Loss of independence resulting from stroke induced disability, affected the
physical and functional health and normal patterns of ADLs in survivors [8,44]. The health-related changes caused undesirable consequences for both the survivors and their family caregivers. The stroke survivors’ loss of physical and functional ability caused their loss of or damaged personal identity and family-related roles and normal pattern of interdependence. These conditions lead to disability-associated experience, including anxiety, depression, anger, being hypercritical and emotional disturbance [38,40,44,45] which in turn had an impact on the immediate lives of family members [38] especially the life of the main caregiver. This impact is related to caregiving role responsibilities and challenges [47,51].

![Study exclusion flow diagram.](image)

Table 2 Characteristics of Qualitative Studies Included in Metasynthesis.

<table>
<thead>
<tr>
<th>First author of study, publication year</th>
<th>Place of study</th>
<th>Methodology (as reported by authors)</th>
<th>Data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jongbloed, 1994 [40]</td>
<td>Canada</td>
<td>Content analysis</td>
<td>Individual interview, observation</td>
</tr>
<tr>
<td>Shah, 2011 [41]</td>
<td>USA</td>
<td>Not stated</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Strudwick &amp; Morris, 2010 [42]</td>
<td>UK</td>
<td>Inductive thematic analysis</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Pierce et al, 2009 [39]</td>
<td>USA</td>
<td>Content analysis</td>
<td>Web based interview</td>
</tr>
<tr>
<td>Green &amp; King, 2009 [38]</td>
<td>Canada</td>
<td>Content analysis</td>
<td>Telephone interview</td>
</tr>
<tr>
<td>Subgranon, 1999 [43]</td>
<td>Thailand</td>
<td>Grounded theory</td>
<td>Individual interview, observation, field notes</td>
</tr>
<tr>
<td>Greenwood et al, 2009 [44]</td>
<td>UK</td>
<td>Not stated</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Backstrom &amp; Sundin, 2009 [45]</td>
<td>Sweden</td>
<td>Thematic content analysis</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Jongbloed, Stanton, &amp; Fousek, 1993 [46]</td>
<td>Canada</td>
<td>Ethnographic research</td>
<td>Individual interview, observation</td>
</tr>
<tr>
<td>Roecker et al, 2012 [47]</td>
<td>Brazil</td>
<td>Content analysis</td>
<td>Agency family records &amp; home visit documents</td>
</tr>
<tr>
<td>Dalvandi, 2011 [8]</td>
<td>Iran</td>
<td>Grounded theory</td>
<td>Individual interview &amp; focus group discussion</td>
</tr>
<tr>
<td>Eaves, 1997 [48]</td>
<td>USA</td>
<td>Grounded theory</td>
<td>Individual interview, observation</td>
</tr>
<tr>
<td>Dalvandi et al, 2011 [49]</td>
<td>Iran</td>
<td>Grounded theory</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Jones &amp; Morris, 2012 [50]</td>
<td>UK</td>
<td>Phenomenological analysis</td>
<td>Individual interview</td>
</tr>
<tr>
<td>Lawrence et al, 2010 [37]</td>
<td>UK</td>
<td>Thematic analysis</td>
<td>Focus group discussion</td>
</tr>
<tr>
<td>Wu, 2009 [51]</td>
<td>Taiwan</td>
<td>Content analysis</td>
<td>Interview, observation, public documents</td>
</tr>
<tr>
<td>Tong, 2005 [12]</td>
<td>Hong Kong</td>
<td>Grounded theory</td>
<td>Individual interview, observation, agency records</td>
</tr>
<tr>
<td>Pierce et al, 2004 [36]</td>
<td>USA</td>
<td>Not stated</td>
<td>Web based &amp; telephone interview</td>
</tr>
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</table>

Note. UK – the United Kingdom; USA – the United States of America.
Accepting caregiving-related roles by the family has the nature of hardship. This hardship includes loss of independence, autonomy and ability to plan daily living properly as well as loss of normal patterns of relationship with survivor, mutuality and role exchange [8,38,45,50]. These circumstances together with the loss of certainty about stroke outcomes in both the survivor’s and caregiver’s lives and future as well as the loss of confidence to cope with and suitably react to the these outcomes [12,40,44] consequently bring about negative psychological experiences for the family caregiver. These negative psychological experiences consist of anxiety, fear, emotional turmoil, insufficiency, helplessness, limitations, financial burden, stigmatization, insecurity, frustration, role strain, tension and fatigue [39,40,44–47,50].

**Family resources (bB factor)**

According to Mccubbin and Patterson (1981), the resources that a family may bring, to bear on the management of a crisis, consists of three basic kinds: the internal resources of an individual family member, the internal resources of the family, and the social support from resources external to the family [18].

Combined resources were realized as the main theme, which included the internal resources of a person to meet the demand of family; this consisted of the caregiver’s self-control skills and beliefs about caring for the stroke survivor. Other parts of these resources included beliefs about stroke, healthy lifestyle, caregiver’s own capacity and spirituality [12,37,41,45]. The internal resources of the family included the previous quality of the relationship between family caregiver and stroke survivor [48]. The external resources of family comprised multiple network of support from friends, home-care services and adequate social interaction [12,45].

**Family perceptions (cC factor)**

The cC factor refers to the meaning the family attributes to the crisis (x), the pile of stress and demands (aA), and their resources to deal with them (bB). These perceptions interact with the available resources to produce the coping response [18,52].

Entering to a new phase of life with continuous struggles with change was explored as a main theme under the family perception domain. Stroke induced stresses were perceived as a constant process [38] of struggle with the survivor’s functional disturbance [8]. These stresses may improve with time [36], or with the change of life plans result in loss of spontaneity in the action [45] which is perceived as struggle with a new phase in the family life.

**Coping strategies (BC)**

Coping becomes much more complex by shifting from the individual level to the family level. Family coping is defined as an active process where the family uses existing family resources and develops new behaviors and supplies to strengthen the family unit and reduce the impact of stressful life events [15].

Refocusing of time and energy on the elements of the recovery process. Fight with health-related impacts of stroke in the family through refocusing time and energy on the elements of recovery [38] was the main explored theme. Family members focus on the internal family elements of recovery within the family system. These elements include redefining new role patterns, getting organized with house chores [40,47] and sharing care [42,44]. More family recovery elements were found to be helping or relying on one another and the established coping strategies [44], being familiar with new routines [45,47] and letting off steam to the family [44]. Other elements of family recovery found included monitoring of stroke survivor and consequence of caring, filtering communication and interaction with the survivor [38], and making changes in the physical environment [41].

At the caregiver’s (personal) level, the main coping strategies consist of three parts including behavioral, cognitive and avoidance. Behavioral coping strategies consist of having accommodation for the survivor and avoiding institutionalized care [42,45,51] and using experience and knowledge through trial and error [51]. Other behavioral coping strategies are providing hygiene [39], organizing a new pattern of interdependence [40], and arranging actions into patterns and routines [41] by using a regular schedule and timetable [44]. Cognitive coping strategies comprised refocusing on the meaning of family and mutual relationship [38], preserving self-worth [8], ensuring the patient’s quality of care, reconstructing ordinary life and maintaining optimism [39,45] through comparing one’s present situation to others’ conditions who were worse off [44,45].

Cognitive coping also included leaving fear and guilt behind [45], learning key aspect of the care [12], managing unexpected situations, having confidence in other people’s assistance, entrusting the survivor’s own ability to take action [45] as well as keeping a sense of humor and laughter [39,44]. Other components of this strategy involved appreciation and acceptance of what had transpired in the new phase of life [38], being sensitive and taking into consideration the survivor’s need [39] and being assertive with community services [42]. Avoidance coping strategies encompassed avoiding what had transpired in the new phase of lives [38], avoiding thinking about the future [44], abandoning the idea that everything could go back to the way that life had been before the occurrence of stroke [45].

Social level coping strategies involved seeking help from other people [51], seeking information, learning stroke care [8,44,51] and being open to healthcare professionals’ and friends’ possible services [41,45]. Other social level coping strategies included requesting assistance to manage daily task [39], receiving support from stroke caregivers group and friends as well as sharing thoughts and feelings with them [36,40].

**Family adaptation (xX factor)**

The xX factor is the final product of the Double ABCX Model [18]. Family adaptation is the central concept of the Double ABCX Model that describes the outcome of a family effort to achieve a new balance in family functioning. This outcome ranged from positive adaptation to maladaptation [35].

Striking a balance was a main theme identified from the studies as a positive outcome [48,53]. The family continued to survive despite uncertainty [51] and achieved a balance in everyday life through integrating stroke into the family life [45] so that its intactness was maintained [38] and the survivors could regain their normal functions and roles [40]. Negative outcome (maladaptation) was identified as a family being drained of energy to go on and being an outsider as well as unsuccessful role playing [45].

**Contextual characteristics**

Context is a set of conditions in which problems or a situation arises, and to which people respond to [54]. Shortcomings in the rehabilitation and home care service indicate segregated health services identified to be the main theme. Lack of continuity of rehabilitation at home and in the community [8,49] and shortcomings in home care services and organization lead to lack of proper planning for survivor’s rehabilitation [43], which were identified as contextual characteristics.

**Discussion**

The aim of the metasynthesis in the present study was to determine the common experience of families with stroke survivors who participated in different qualitative research. This research helps to identify the theoretical foundation of family members’ experience of adapting to stroke survivors’ caregiving tasks in agreement with the
Double ABCX Model of family crises. The result of the present metasynthesis offers considerable support for the model.

The themes related to family stresses and demands were the loss of independence and uncertainty, which were approved as the main stressors for the stroke family. Stroke survivors’ state of discontinuity of the body, self and roles, and the resulting uncertainty were found to be the major theme in the metasynthesis study of Satink and colleagues [55]. They also reported that regaining the lost roles was one of the main themes of their study [55]. Greenwood and Mackenzie in their study found that loss of autonomy and uncertainty were the two main experiences of stroke caregivers [3]. The family stressors were shown to have direct effects on family adaptation and indirect effects through family perception [18] (Figure 2).

The family resources (bB) deal with the crises and contribute largely to the family’s adaptation [18]. Combined family resources may be obtained from three possible sources: caregiver’s attributes, the family system, and the community [56]. The internal resources of a person include physical and emotional health, education, personality characteristics of individual family members and high self-efficacy. Mutual support and open communication were found to be of important family resources [52]; the community resources consisted of formal services, such as home care programs and community-based social services [56].

The cC factor refers to the meanings the family assigns to the crisis (xX) and the accumulation of stressors and demands (aA), as well as the resources to deal with the crisis and stressors (bB). These perceptions interact with available resources to produce the coping response [52]. The perceptions of family stressors were identified as one of the strongest predictors of negative caregiving outcomes [56]. In the stroke patients’ family at least some of the impacts of family stresses and demands (aA) on perceptions of the crisis (cC) may be challenged through family resources (bB) [18].

Family coping (cC) is an active process where the family utilizes existing family resources and develops new behaviors and fresh resources that strengthens the family unit and reduce the impact of stressful life events [15]. Farhood emphasized the role of coping behaviors in decreasing the presence of vulnerability [24]. There is a discrepancy between “coping” and “strategies”. Coping is a cognitive process where a person learns how to put up with the effects of illness. It involves preserving a feeling of personal worth and a sense of coherence in the face of the disruption caused by illness and acts as a buffer against the stressors. In contrast, the term “strategies” focus on the actions that mobilize resources and maximize outcomes rather than on the adapted attitudes [3].

Another way to view family coping is to consider whether the coping strategies come from within the family or rely on the support and resources outside the family [15]. These distinctions were adapted here as an examination of the themes under the notion of “coping strategies” as a general term for both. Refocusing of time and energy on the elements of the recovery process emerged from our analysis, which indicates that the elements of recovery in stroke patients require more attention in the area of family coping. Vanhook in her study explains three main domains and six categories as the fields of recovery from stroke: physical (cognition and function), psychological (self-concept and health perception) and social domains (role identity and relationships) [57].
Family adaptation (xX) factor is the ultimate product of the Double ABCX Model [18]. Family adaptation is a process in which families engage in direct response to the extensive demands of a stressor and realize that systematic changes are needed within the family unit [15]. Family adaptation is a positive response to family stressor (s) through using effective coping strategies [52]. There have been isolated attempts to describe the process by which families reach adaptation to the disability caused by stroke [18]. Striking a balance is the recognized theme which shows that family adaptation is the result of family efforts to bring a new level of balance, harmony and coherence to a family following a crisis. Positive family adaptation is a balance in the family system that facilitates its organization and unity [58].

From the view of both ecological approaches and family systems theories, consideration of family adaptation includes the family’s relationship to other social structures [34]. Social structures influence the family in the chronic illness context and relates to effective adaptation [59]. Several social factors have been reported in the literature that intervenes in the stress–illness relationship. They mediate the effect of stress on the individual and the family. A high-level of social support helps protect the individual against the negative consequences of stressors [24]. Integrated social support, especially health services have a strong positive impact on family adaptation to stroke.

Conclusion

The present research has revealed the utility of synthesized findings of qualitative research to provide greater insight into the factors that contribute to family adaptation; it provides more understanding of the family caregivers’ experiences. This metasynthesis study uncovered several areas for further nursing research and education, notably the need to further develop methods for helping the families affected by stroke to gain balance. Working with families of stroke survivor can be challenging for medical practitioners. The Double ABCX Model provides a proper format for examining the contributing factors of family adaptation to a stroke survivor. This metasynthesis has thereby added substantially to the previous research the main factors contributing to family adaptations to stroke, for which comprehensive evidence has not been available. The value of this model is its emphasis on family functioning as a dynamic and interrelated system rather than a static, isolated unit that helps the clinical practitioners get more accurate perspectives when working with stroke families. In addition, the Double ABCX Model helps link the assessment and interventions through ongoing evaluation of the family’s needs and making changes in coping strategies whenever necessary.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Acknowledgments

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