

Domain Definitions for Neuro-QOL

The dominant model of multidimensional health status was first suggested in the 1940's by the charter of the World Health Organization (WHO). The WHO defined health as a "state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity."¹⁵⁶ Our collective experience in spinal cord injury, neuro-oncology, stroke, MS, and Parkinson's disease, and our review of the neurology HRQL literature suggest: a) the three dimensions of physical, mental and social well-being that are articulated in the basic WHO model are widely accepted in neurology HRQL research ; b) the majority of disease-specific HRQL instruments incorporate aspects of these 3 domains to some extent; and c) there are aspects of HRQL which, while subsumed under physical, mental or social well-being, are unique in content or scope to neurological conditions.

The development of a generic instrument that will be widely accepted as a measure of HRQL across the numerous and varied neurological conditions will require a consensus as to the domains to be evaluated. In preparation for the proposed patient and expert interviews to be conducted as part of this project, we attempted to identify a set of concepts that are relevant to the conditions we identified for this proposal. Beginning with the conceptual model in Figure 2-1, this step was informed by an examination of existing HRQL measures used in neurology, our review of the neurology literature above, and our own experience in the development of HRQL instruments.

First, existing neurology HRQL instruments were identified (see Appendix 1 for representative sample) and a comprehensive list of covered domains was made. This list can be found in the first column of Table 1-1, below. If at least one disease-specific instrument measured an HRQL domain, a specific Medline search was conducted in the other conditions. The search combined the domain description (e.g., pain) with the condition(s) in which it did not appear to be represented in HRQL questionnaires. If the literature indicated that the domain was important and/or likely to be affected by the disorder or its treatment, then an "X" was placed in that box. This process continued until it appeared that the majority of existing domains were listed. The resulting grid is shown in Table 1-1.

The next step was to conceptualize domains as common to these disorders or unique in occurrence or manifestation to a specific disorder. Using a cutoff, HRQL issues that were important to at least 80% of diseases were considered to be common ("generic"), while those that fell below that line were considered to be disease-specific. In addition, a domain such as "treatment effects" was considered to be unique, or disease-specific. That is, while people with any of these conditions are likely to experience treatment effects that impact their lives, the particular side effects are likely to vary significantly across diseases.

Table 1-1: Identification of HRQL domains across a subset of neurological conditions	Stroke	PD	MS	Epilepsy adult	Epilepsy child	AD	TBI	SCI	Brain tumor adult	Brain tumor child	Migraine	
Emotional Distress	X	X	X	X	X	X	X	X	X	X	X	100%
Cognitive Complaints	X	X	X	X	X	X	X		X	X	X	100%
Social Well-Being/Functioning	X	X	X	X	X	X	X	X	X	X	X	100%
Physical Functioning/Mobility	X	X	X	X	X	X	X	X	X	X		91%
Fatigue	X	X	X	X	X	X	X		X	X	X	91%
Pain	X	X	X	X	X		X	X	X	X	X	91%
Communication/ Language Difficulty	X	X		X	X	X	X	X	X	X		82%
Fine motor Function/Hand Function	X	X	X	X	X		X	X	X	X		82%
Spasticity	X	X	X	X	X		X	X		X		73%
Sensory Impairment	X	X	X			X	X	X	X	X	X	82%
Global HRQL/Life Fulfillment/Satisfaction with Life	X	X	X	X	X	X	X	X	X	X	X	100%
Ability to Work/School/Participate in Meaningful Activities	X	X	X	X	X	X	X	X	X	X	X	100%
Independence/Control/Mastery/Efficacy	X	X	X	X	X	X	X	X	X	X		92%
Sexual Function	X	X	X	X		X	X	X	X			89%
Bowel/Bladder Function	X	X	X			X	X	X	X	X		78%
Treatment Effects	X	X	X	X	X	X	X	X	X	X	X	100%

An examination of Table 1-1 reveals the existence of domains that may be considered common. Some of these areas have considerable conceptual overlap, such as global quality of life and life satisfaction, and were combined into a single dimension. For spasticity, the patient experience can most likely be subsumed by pain, physical mobility, and hand function, so that a specific spasticity domain is not needed. The result of consultation with neurological and HRQL experts about the domains can be found in Table 1-2. This suggests that there may be 9 HRQL concepts that are common across these neurological disorders and 5 dimensions that can be considered unique or disease-specific. The latter term applies to areas that seem to be applicable to less than 80% of the identified conditions or whose manifestations vary widely across the conditions. **As noted above, this list is provisional and modifications will be made based on expert and patient input.**

		Provisional list of Generic (G) and Targeted (T) HRQL domains for neurological conditions	STROKE	PD	MS	EPILEPSY	AD	TBI	SCI	BRAIN TUMOR
G1	C1	Emotional Distress	X	X	X	X	X	X	X	X
G2	C2	Cognitive Complaints	X	X	X	X	X	X		X
G3	C3	Social Support, Functioning, Stigma & Sexual Functioning	X	X	X	X	X	X	X	X
G4	C4	Physical Functioning, Mobility, Self-care (Gross Motor Function)	X	X	X	X	X	X	X	X
G5	C5	Fatigue	X	X	X	X	X	X		X
G6	C6	Pain	X	X	X	X		X	X	X
G7	C7	Communication, Language Difficulty	X	X	X	X	X	X	X	X
G8	C8	Fine Motor Function/Hand Function	X	X	X	X		X	X	X
G9	C9	General well-being/life satisfaction	X	X	X	X	X	X	X	X
T1	U1	Sensory complaints	X	X	X		X	X	X	X
T3	U2	Bowel/bladder function	X	X	X		X	X	X	X
T4	U3	Sleep disturbance	X	X	X		X	X		X
T5	U4	Personality, behavioral changes	X	X	X		X	X		X

The following sections provide an overview of the definition and significance of the common (aka generic) and unique (aka targeted) HRQL domains identified above. As is detailed in Chapter 2, our group has created item banks in emotional distress, fatigue, pain, and physical functioning/mobility. These banks have been tested and calibrated with large samples of oncology patients. This previous work demonstrates the feasibility and acceptability of the item banking approach to HRQL assessment among patients and clinicians. It also provides a model from which to derive our current plan.

Physical Functioning

Drawing from Haley^{164; 165} and Wilson & Cleary,¹⁶⁶ we define PF as one's ability to carry out various activities, ranging from self-care (activities of daily living) to more challenging and vigorous activities that require increasing degrees of mobility, strength, or endurance. PF is an important aspect of health status and quality of life and its measurement is typically included in all HRQL assessments. The impact on PF can vary by diagnosis and treatment. Retaining optimal physical condition is often a personal goal of patients and supports optimal clinical response to therapy.^{167; 168} Routine assessment of PF can identify the trajectory of disability, thereby allowing early intervention that preserves independence and function.¹⁶⁹

People with neurological diseases may also experience loss of fine motor ability for a number of reasons including tremor (Parkinson Disease, MS), spasticity (cerebral palsy) or weakness or paralysis (spinal cord injury, stroke).¹⁹⁵ This loss of hand function often represents a major threat to independence. A person with diminished hand function faces the use mechanical adaptations or human assistance for performing personal care activities. It may affect their access to communication with others, as the ability to write or key-board is affected, and the ability to perform typical activities in the home or work place is compromised. Fine motor dysfunction may result in personal injury, as persons with weak hands may continue to use knives or other sharp implements.¹⁹⁶ Loss of hand function may also result in social isolation because an individual who can no longer use a knife or get a spoonful of food in his/her mouth avoids situations that involve eating. One of the most common regrets voiced by adults with fine motor impairments is their inability to interact actively or safely with children. They often avoid holding a new born or toddler for fear of dropping the child or express frustration that they are not able to engage in active play with their older children.

Sensory complaints are also prominent in patients with neurological disorders. MS patients complain of vague and poorly characterized paresthesias, which may appear and remit in a rapid time course (<24 hours).²⁰⁰ Some patients complain of a sensation of “squeezing,” “burning,” or “pressure” in a band-like distribution around the thorax. In other cases, patients experience numbness or paresthesia in the face or extremities.^{198; 200} Loss of proprioception (i.e., knowledge of position of body parts) and joint sensation is frequently accompanied by edema of the limb or feelings of constriction. Fifty percent of MS patients develop objective sensory loss (position, vibration, shape, texture). Although not as often associated with Parkinson’s disease, sensory symptoms can be very disabling and distressing. The most common sensory complaint is that of a feeling of inner restlessness, presumed to be a form of “dopa-deficient akathisia.” Aching pain and discomfort in the extremities may also be present. Such pain may persist in persons with neurological disorders who experience continuous mechanical distress for reasons of poor posture or abnormal gait. Neuropathic pain, in contrast, is a symptom resulting from neural injury to a portion of the pain transmission system. It is often severe and of a burning or electrical quality. It often remains on-going even after the source of the pain process has resolved.¹⁹³ Intermittent or chronic neurogenic pain also results in significant emotional distress and often causes depression. In addition to negatively affecting one’s concentration, pain disrupts sleep patterns as well as family, work and social responsibilities. Sensory deficits in stroke patients may include visual deficits (e.g., double vision, decreased visual acuity, loss of vision in half of visual field), absent or diminished response to superficial sensation (touch, pain, pressure, heat/cold) and/or proprioception.¹⁹⁸ Perceptual deficits may include disorientation, apraxia, agnosia, right-left disorientation, and others.

Emotional Distress

Emotional Distress is a term used to describe unpleasant feelings or emotions that may interfere with the ability to cope with a disease, its physical symptoms, and its treatment. This includes emotional distress and covers a wide range of feelings, including worry, powerlessness, sadness, fear, depression, anxiety and panic (Schag et al, 1994; Lawton, Parmelee, Katz & Nesselrode, 1996; van’t Spijker, et al, 1997; Bottomley, 1998a; 1998b; Stark, et al, 2002). Negative Affect is correlated with, but distinct from, major depression. Patients often experience substantial and sustained emotional distress following the diagnosis and treatment of a neurological disease or injury.^{157; 158} A significant minority (16-50%) of patients experience distress severe enough to warrant psychiatric diagnosis during the course of their illness, most commonly major depression.^{157; 159-162} Even when subsyndromal, clinically significant symptoms of psychological distress necessitating intervention are present in as many as 40% of neurological patients.^{102; 158; 163} Greater levels of distress are generally associated with greater severity of disease and disability and cognitive deficits.¹⁶²

An important issue is whether affect is a state or trait, or both. The concept of negative affectivity (Watson & Clark, 1984) has been defined as a propensity to report dissatisfaction and distress, regardless of external reality. The concept has been measured by scales which relate to self-reported pessimism, self-blame, worry, lack of self-confidence and dissatisfaction. Recent findings by Lawton and colleagues (1996) show that indicators of negative affect can vary among depressed individuals on a daily basis. Thus, negative affective symptoms (which may be caused by depression or by negative events) are considered to be more state-like in that different indicators may change in response to external stimuli.

It may also be useful to measure externalizing problems, e.g., substance abuse, anger, aggression, and other expressions of behavioral dyscontrol.

Positive Psychological Functioning

Positive psychological functioning embodies aspects of a person’s quality of life that relates to a sense of well-being, satisfaction with life or overall sense of purpose or meaning. It has been characterized as happiness, contentment, high energy and interest (Watson & Tellegen, 1985). General Well-Being/Life Satisfaction may be a more stable or trait-like construct, although evidence suggests that certain aspects are amenable to change based on environmental interventions (Lawton, VanHaitsma, Klapper, Kleban, Katz & Corn, 1998).

Perceived Cognitive Functioning

Cognitive impairments may be experienced as deficits in attention, memory, concentration, or language (Ahles & Saykin, 2001; Brezden, Phillips, Abdolell, et al, 2000; Schagen, van Dam, Muller, et al, 1999). Cognitive complaints or distress might be considered a sub-domain of Cognitive Health or Cognitive Function. In general, cognitive functioning is often better measured by other methods, rather than self-report. Neurological disorders, by virtue of their involvement of the brain, spinal cord and/or peripheral nerves, may have highly specific or widely diffuse consequences.¹⁷⁰ One of those consequences, cognitive impairment, may be mild and limited in the number of cognitive dimensions affected, or severe and multidimensional. Cognitive dysfunction has been singled out as the most disabling aspect of neurological illness.¹⁷⁰ Intellectual functioning can be compromised with damage to the cerebral

cortex, basal ganglia, thalamus, or limbic system. Diffuse encephalopathies, such as Alzheimer's disease, produces more global cognitive deterioration, more commonly referred to as dementia. Depression is also common with diffuse encephalopathies such as Parkinson's disease.¹⁷¹ Neurologic lesions also produce affective changes, including disinhibition, depression, hypomania, or hallucinations, all of which have the capacity to negatively affect quality of life. In addition to those listed above and depending on the nature, location, and size of the lesion/injury, neurological disorders may produce deficits in attention, concentration, memory, orientation, language, perception, apraxia, and problem-solving. To the degree an individual is aware of his/her cognitive impairment, dysfunction in any one of many cognitive domains may negatively impact that individual's quality of life. Consequently, cognitive functioning is a relevant and important domain to include in a quality of life measure for such disorders.

Social Functioning

Although social well-being has long been recognized as an integral component of health,¹⁵⁶ it is often not included in HRQL instruments.^{172; 173} Assessing social adjustment in neurological disorders is important since the disease and its treatment can affect the quality of marital relationships, parental responsibilities, work abilities and social activities. Our review and preliminary research suggests several sub-domains of social well-being, of which we will focus on role participation in the context of work and family activities and relationships. Role participation refers to involvement in and satisfaction with one's usual social roles. This has also been referred to as social adjustment¹⁷⁴ and can include communication with others and feelings of belonging and trust (McDowell & Newell, 1996; Larson, 1993). This includes the existence of, and interconnections between, social ties, e.g., marital status, relationships with others, contacts with friends and relatives, memberships to organizations and volunteer participation (Wills, 1985). Finally, concern about social stigma, or fear of being perceived negatively by others, is reported frequently by individuals with neurological disorders.^{29; 30; 180; 181} Some of the neurological conditions have symptoms that make a person appear or move differently than usual (e.g., dyskinesias in Parkinson's; hemiparalysis in stroke). Both children and adults with epilepsy often live with the fear that they will be embarrassed by having a seizure in an "unsafe" place, such as when in the company of others who will ridicule them.¹⁸²⁻¹⁸⁷ The use of assistive devices such as canes or wheelchairs can also raise concerns of being socially stigmatized.

Sexual Functioning

Sexual functioning and intimacy have also been identified as important components of HRQL frequently affected by neurological diseases and their treatment.^{139; 175-179} Problems are often associated with sexual desire, arousal, orgasm and pain and can include anorgasmia, hyporgasmia, diminished vaginal lubrication and decreased libido in females and erectile dysfunction, ejaculatory dysfunction and diminished libido in males (Zorzon et al, 2001).

Fatigue

Fatigue is an overwhelming, debilitating and sustained sense of exhaustion that decreases one's capacity for physical and mental work.¹⁸⁸ It is a generalized level of tiredness beyond what is normally experienced by many healthy adults and can result from the disease itself or from treatment (e.g. radiation for brain tumors or interferon for MS).¹⁸⁹ Patients are often distressed by the experience of fatigue, as it diminishes one's ability to work effectively and to function at one's usual level in family or social roles. Untreated, fatigue contributes to emotional distress^{190; 191} and to a worsening of physical function through deconditioning.^{169; 192} Early identification of fatigue through rapid, accurate assessment will help providers identify the problem and more quickly initiate treatment or referral.

Communication & Language Difficulty

The ability to communicate through written and spoken language is "the medium of all delicate interpersonal transactions (p.499).¹⁹⁴ Arising almost solely from trauma or disease of the brain, dysfunction in this arena is common across neurological disorders. The type and extent of communication problems are determined by the location and extent of the injury or lesion. Such problems include aphasia, which is impairment of receptive or expressive language; dysarthria, or articulation difficulty without impairment in language comprehension; and more general speech and language disturbance resulting from global impairment of higher mental functioning, such as in dementia.

Bowel and Bladder Functioning

The two major components of bladder and bowel functioning are storage and emptying. The loss of both functions in adults with neurological conditions is commonplace and is a source of embarrassment and frustration. Bladder dysfunction is one of the initial symptoms of MS and is also common in patients with spinal cord injury, brain tumors, head injuries and dementia, and those whose frontal lobes have been assaulted by stroke. Bladder dysfunction is a symptom of Parkinson's disease but typically occurs during later stages of the disease and may be secondary to prostatic disease.¹⁹⁷

Bowel dysfunction, which can cause incontinence or constipation, occurs in the above conditions at much lower frequency than bladder dysfunction, but is arguably even more profound in its impact on HRQL. Due to embarrassment caused by incontinence, patients frequently fail to report the problem to their health care providers, and the condition goes untreated. Concerns about loss of bladder or bowel control strike at the essence of individuals' self-confidence. Fear of loss of control often interferes with sexual intimacy, which then leads to more general relationship discord. There are few social stigmas of greater significance than having "accidents" in public, and concern about having quick access to a bathroom causes people to be afraid to leave their homes. The HRQL issues for bowel and bladder function are sufficiently different that we have created one item bank for each.

Personality and Behavioral Changes

Several neurological disorders are characterized by changes in personality and behavior. With head injury, the site of brain injury, extent of injury, patient's premorbid personality and environment are all contributing factors.¹⁹⁸ Personality changes may include self-centeredness, inability to show empathy, impatience, and impulsiveness. Frontal lobe injuries, whether due to trauma or stroke, are associated with specific behaviors, such as decreased drive and initiative, flat affect, disinhibition, disregard for social protocols, apathy, lethargy, lack of goal-directed behavior, impulsive control difficulties, and impaired sense of self-identity.¹⁹⁹ Lesions of the temporal lobe are characterized by episodes of violent behavior and possibly seizure disorders. Patients with MS may demonstrate disease-related euphoria, irritability and apathy.¹⁹⁸ Behavioral changes attributable to the disease or its treatment(s) are also noted in Parkinson's disease.²⁰⁰

Sleep Disturbance

Many neurological disorders adversely affect patients' total amount and patterns of sleep.¹⁹⁴ Convulsive seizures often occur during sleep, especially in children. This occurs mainly in stage 4 of non-REM sleep or in REM sleep, but they are also common during the first hour after awakening.¹⁹⁴ Conversely, sleep deprivation may be conducive to seizures. Depending on the location of the brain lesion, stroke patients may experience hypersomnia, diminished non-REM and REM sleep, sleep apnea, or daytime drowsiness. Major head injury is a significant cause of sleep disturbance, which may persist for months or years; organized sleep activity is absent in virtually all types of coma resulting from anatomic trauma to the brain. Parkinson's disease is associated with fragmented and unrestful sleep, particularly in the early morning hours. Sleep may be disrupted by the nighttime re-emergence of bradykinesia and rigidity, tremor or involuntary movements or medication-induced vivid dreams and hallucinations. Patients with epilepsy and Alzheimer's disease are also known to have sleep-related complaints.

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