

# Vital Link

The journal of the Canadian Association of Naturopathic Doctors

## Feature Articles

- Seniors in Motion; Effectiveness of Tai Chi on Fall Prevention
- Dysautonomia, Orthostatic Hypotension and Falls in the Elderly
- Polypharmacy; Are Seniors at Risk?
- The Influence of Age and Stress Related Factors on Hepatic Cytochrome p450 Enzyme Expression and Function
- Loneliness and Social Isolation as Factors in the Decline of Health in Seniors
- Considerations for Caregivers, Social Support and Cognitive Assessment

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Volume 23, Issue 1  
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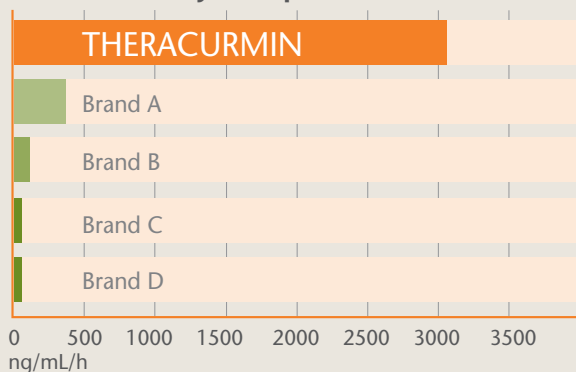


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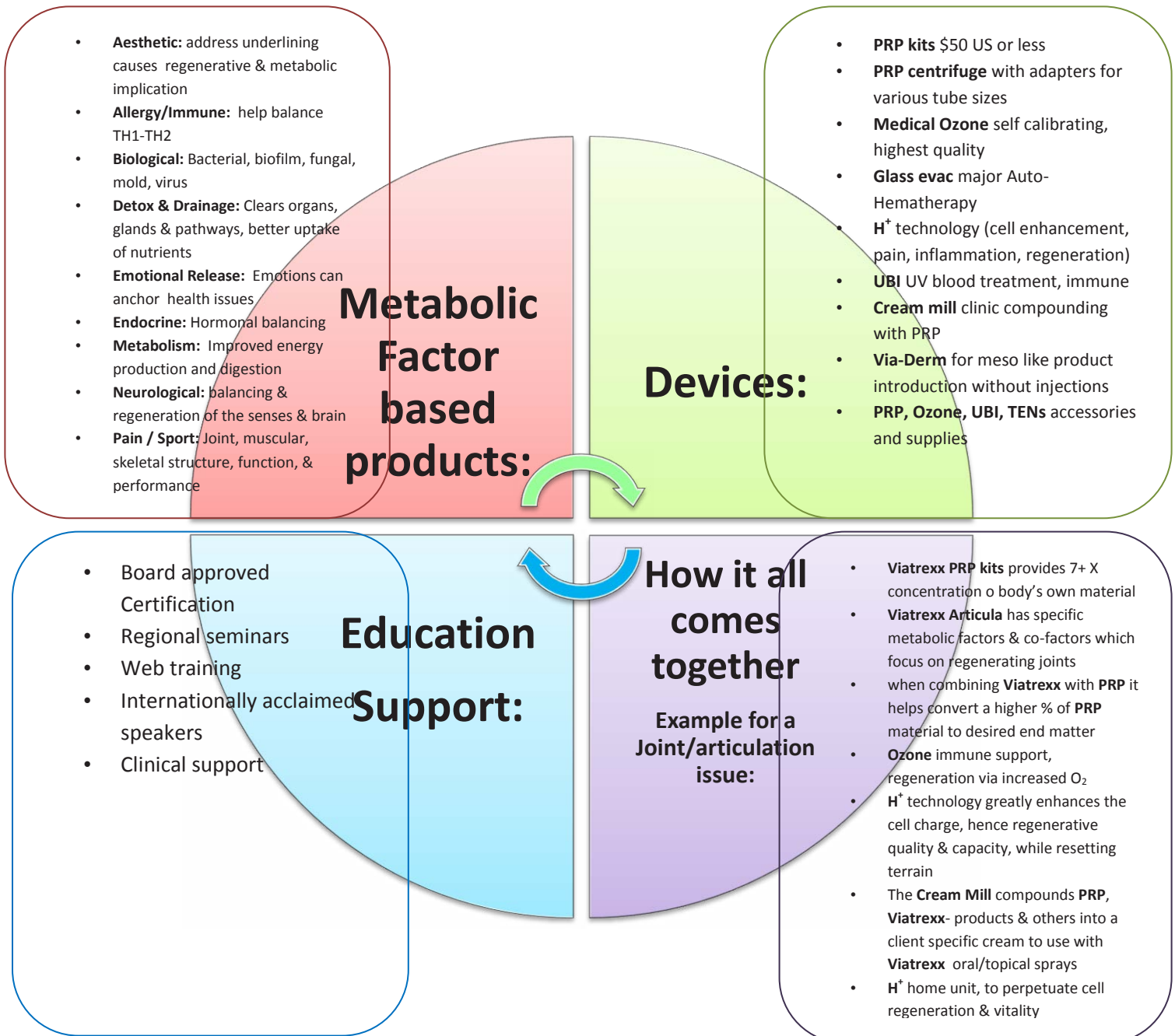
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# Vital Link

The journal of the Canadian Association of Naturopathic Doctors

**Volume 23, Issue 1, Spring 2016**

Improving Seniors' Health and Wellbeing

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# Naturopathic Notes

Dr. Iva Lloyd, BScH, ND

The challenges of growing old are often oversimplified and minimized. Working with the elderly requires a unique focus and intention. It is a fine dance between the limits of the physical body according to a person's vitality and understanding when to encourage someone to work harder to improve their health.

**A**s I pull my thoughts together for this article, I am reminded of a 70-year-old patient whom I was talking to about their change in health. After a moment of reflection he remarked, "I guess I have come to the point in my life where I go from being a user of my body to being a caregiver." There is a lot of wisdom in that statement – as there is in many statements that older patients make – and it is in those moments that we as NDs realize just how much we can learn from our patients.

As you age there is a time when the tide changes, when the awareness of getting old hits you and changes how you see life and how you see yourself within your own life. For some this awareness comes in their sixties, for others it comes in their eighties or later. As a naturopathic doctor it is important to know the science, the technical side of aging; but it is just as important to recognize that working with those that are aging is also about how they view and understand aging – what it means to them and how they experience aging.

Following are some common phrases I hear from elderly patients and some general guidelines I use:

### *"I feel invisible"*

This is one of the most common phrases I have heard when working with the elderly. It is not only what they say, but how they say it. You can hear and sense the feeling of being dismissed, the feeling that their words and actions are disregarded and ignored. They sense that life is moving forward and they are being left behind. People that are used to being in-charge, in positions of authority- people that were independent, strong and important – sense they are now invisible and feel like they don't matter.

Years ago, advice from elders was more likely to be valued and respected by younger generations. Prior generations saw parents

and grandparents as wise and experienced. Today, however, elderly people often seem to be spectators rather than participants in their own life. Too often, the role of the elderly is replaced by technology and by those with current education, rather than life experience. Although we may have more informational resources today than in years past, we would be wise to value the elderly; we learn from them and they in turn receive the respect they have earned.

### *"The world moves too fast"*

The pace of life, especially in urban settings, can be fast and impersonal. Whether you are grocery shopping, going to the bank, walking across the street or driving it is generally done quickly. Life in North America has been tailored to the young and the active. Many elderly feel that their inability to keep pace reflects poorly on them, when it could be more of a reflection of society not respecting the uniqueness of and how to accommodate the needs of the elderly.

Slowing down is a fact of aging. Generally speaking, as we age, cognitive processing and reaction times are slower, movement is more hampered and guarded and the overall pace of life changes. Often, I observe family members or caregivers trying to help the elderly by answering on their behalf. In both a therapeutic and family setting, elderly people are shut-down when those around them are too impatient to allow them to live their life at their new pace.

If you choose to work with the elderly, I encourage you to practice patience. Slow down and take the necessary time with each patient. Avoid answering for them or asking others to do so. Clarify the difference between a person not keeping up and the world not slowing down.

### *"I'm losing control"*

Loss is a common theme with aging; losing the ability to move as quickly as you use to, cognitive abilities and memories, sight or hearing, bladder or bowel control, and the list continues. Loss is often gradual, which can be painful and often contributes to feelings of helplessness and discouragement. As an ND, it is important to distinguish whether to provide treatment aimed to decrease the rate of loss, or to recognize when "the damage has been done" and to address the emotions associated with loss.

### *"I'm OK; I'm not OK"*

Whether an elderly individual feels they are alright or not correlates more with their state of mind than with their physical health.

One's level of contentment or satisfaction with one's life and one's expectations of aging have a lot to do with whether the aging process is embraced or fought. State of mind is extremely important as one ages and can override physical symptoms, both positive and negative. For example: a strong, positive mindset can override pain; whereas a negative mindset can worsen pain or another physical ailment.

Take the time to address both the physical and psychological aspect of a patient's health. Get a sense of which aspect is dominant and driving how a person is actually feeling and functioning.

### ***“Living is a chore”***

Ideally all elderly persons would age gracefully with full mobility, a strong mind, good eyesight and hearing. For many, though, that is not how life unfolds; there is pain, a loss of function, isolation, memory loss, and/or sensory changes. Some people reach a point where it feels as though living is a chore and they feel they cannot cope. When this happens it can contribute to a sense of helplessness or despair. If your patient should experience this state, I encourage you to put the emphasis of the treatment on how they are feeling. That might mean providing the correct homeopathic or herbal remedy; it could mean assisting your patient to find the support through an agency, or educating them or their caregivers about their state of health and options. Take the time to acknowledge the significance of their feelings and help find a way to their feeling the joy in even the little things in life.

### ***“I'm becoming a burden”***

A number of phrases that elderly patients use that are disconcerting, but one that pulls at my heart is when a person feels that they have become a burden to those who they love or to their caregivers. Pay attention to phrases like this and listen to what is being said and why. The patient may be astutely picking up the impatience or frustration of caregivers or loved ones

Finding ways to keep elderly patients engaged in their life is important both physically and mentally. Setting expectations, helping to educate the patient and providing coping tools are part of the treatment process. It is important to recognize the burden of caregivers; there is a stark reality to aging that many, including patients, caregivers, loved ones, family, and even practitioners, may not be prepared to handle.

## **General Guidelines for Working With the Elderly**

- ***Avoid helping too much.*** There is a fine line between helping someone and making them feel more helpless. I have watched many good-intentioned adult-children answer questions for their elderly parents that their parents were quite able to answer for themselves. Whether it is impatience or ignorance about aging, it happens often. Observe the level of engagement of each patient. Watch what they do when their answers are corrected, or someone else “helps” them because they are moving or speaking slowly. Many elderly people are more forgetful, are slower to respond, are slower to get around – but helping can sometimes worsen the problem.
- ***Transitions are often difficult.*** The aging process is not a steady decline. It tends to be more like stairs – you reach a plateau and then something happens and function steps down a notch – there is a new normal. Transitions, especially when associated with greater loss of function or worsening of a condition, are often difficult and require an adjustment period. Allow time for a person to adjust to their new reality; you may find that once an elderly patient comes to term with their new level of function things will improve. My dad, for example, had Parkinson's-like symptoms after a mild stroke that affected his vision. Once he adjusted to the decrease in vision the Parkinson's-like symptoms subsided.
- ***Know the difference between right and relevant.*** Changes in cognitive function show up in many different ways. For many it results in changes in reality and conscious time-frames. Elderly people – or anyone with memory loss – can mix up dates, or past and present. Encourage family members to listen without needing to correct the facts. It is interesting how elderly people re-sort information; I find it a reflection of how they have stored the information. Active listening lets a person know they are heard and not being judged for what they are saying.
- ***Familiarity is safe.*** The natural tendency of elderly people is to close down their world. They spend less time engaging with others. The more this happens, especially if there is cognitive decline or a decrease in vision or hearing, the more that they seek familiarity. It is important to encourage elderly individuals to stay active and engaged, but in a way with which they are familiar. Ask them what activities they wish to do and follow their lead.
- ***“How?” versus “when?”*** For loved-ones the focus is often on when will someone die, with mixed feelings of letting go to end suffering and hanging on to someone they love. For an elderly person how they will experience death is often the most important question. Many elderly people will say they would rather die in their sleep, while they still have their faculties and body functions than living longer in a compromised state

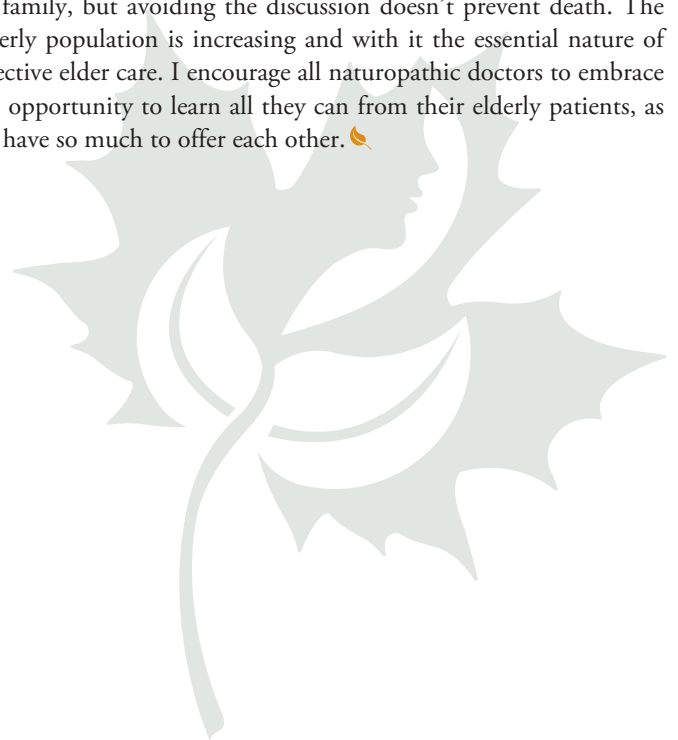


without the ability to participate in their world. The other day I asked a 73-year-old patient what she was most concerned about as she ages. She remarked she didn't want to have another stroke, as she believed a repeat would leave her with the inability to walk or speak. However, she was quite okay with having a stroke if the outcome was death; she just didn't want to have a "mild stroke." Often, knowing what a patient wants or doesn't want can make it easier to help them achieve their goals.

Working with elderly patients can be extremely rewarding, as seniors have much to share; so much wisdom and insight into what is important in life. These patients can remind us of the importance of truly listening with patience and interest in what they are saying and feeling. Taking time with the elderly, listening to their stories, hearing their concerns and their wishes is the essence of elder care.

The focus of naturopathic care on the whole person – the physical, mental, emotional and structural – makes it unique. Naturopathic therapies have a lot to offer the elderly. A well chosen homeopathic remedy can clarify the difference between depression and lack of vitality. Providing nutrients, whether through supplementation or IV therapy, can dramatically improve symptoms of fatigue or a lack of appetite. Herbal remedies can address pain when other medications are no longer as effective. I find that elderly patients respond quicker than most patients even with minimal supplementation.

Most importantly, talk to your elderly patients about aging, about their thoughts, expectations, fears and memories. Talk to your patients about dying, how they would like to die and what they wish to avoid. Too often the topic of death and dying is avoided by family, but avoiding the discussion doesn't prevent death. The elderly population is increasing and with it the essential nature of effective elder care. I encourage all naturopathic doctors to embrace the opportunity to learn all they can from their elderly patients, as we have so much to offer each other. 🍂



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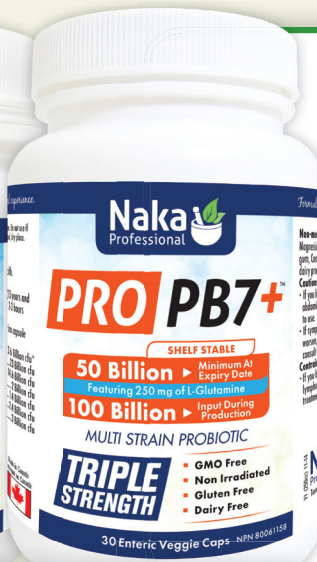
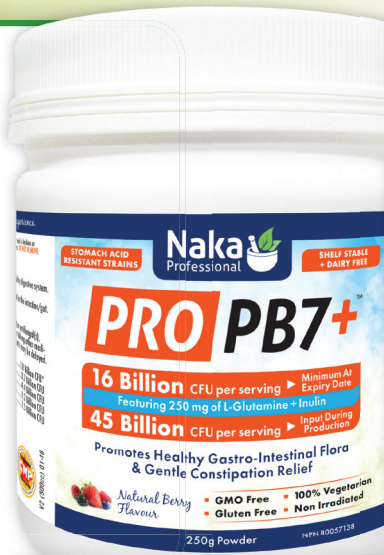
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# Seniors in Motion; Effectiveness of Tai Chi on Fall Prevention

Dr. Emily Rotella, ND

Falling is a growing health concern for seniors with one third experiencing at least one annually.<sup>1</sup> Each year approximately 30 percent of community-living seniors, aged 65 years and over, experience a fall.<sup>2</sup> This number increases to 45 percent when looking at those living in long-term care facilities.<sup>3</sup> Not only is the prevalence of falls among seniors significant but also the severity of resultant injuries.

Between 2005 and 2013 the number of injuries related to falling increased by 54 percent with approximately 20 percent of those who fell requiring medical attention and ten percent sustaining a fracture.<sup>1,3</sup> This makes falls the leading cause of injury related hospitalizations among Canadian seniors.<sup>1</sup> The medical costs directly associated with these events were estimated at approximately two-billion dollars in 2004.<sup>1</sup>

Experiencing a fall in later life correlates not only with direct physiological consequences such as disability and decreased mobility but also with social and psychological consequences of loss of independence, depression, lack of self confidence, a subsequent fear of falling and an increased likelihood of nursing home admittance, which ultimately leads to an increased risk of premature death.<sup>1</sup> The largest proportion of fall related injuries, 45 percent, occur while walking on a flat surface other than snow or ice.<sup>1</sup> Physical activity may help individuals adapt to the functional changes associated with aging. In fact, the United States Surgeon General recommends 30 minutes of moderate intensity exercise per day, at least five times per week.<sup>4</sup> However, in 2003, less than 36 percent of those aged 65 years or older met these recommendations.<sup>4</sup> The lack of physical activity results in decreased muscle strength- an important risk factor for hip fractures.<sup>5</sup> Low compliance rates with exercise recommendations may be due to the fact that typically advocated activities are too high impact or difficult for the elderly to participate in.

Over the next 20 to 30 years naturopathic doctors will likely see an increase in the number of elderly patients seeking assistance for fall related injuries and for the associated desire to prevent a recurrence. Maintaining physical activity is a vital component in the overall treatment protocol for any elderly patient. The question,

however, is what is the best possible exercise protocol to improve physical functioning while, decrease fears associated with falling and create an overall improvement in well being? Tai Chi is an exercise that is becoming increasingly popular among seniors. It is a traditional Chinese exercise that incorporates deep breathing, mental concentration, and postural alignment with slow, fluid movements;<sup>6</sup> it teaches precise body movements while maintaining a tranquil and concentrated mind. The low-impact and gentle nature of this exercise makes it a promising and safe option for older adults. Tai Chi has generated much interest from the scientific community, resulting in the completion of many studies on its effectiveness. It has been shown to be an effective therapy for the prevention of falls among the elderly through the improvement of physiological function, reduction in fear, and improvement of self-efficacy in the performance of daily living activities.

The physical capabilities of an individual are an important factor in their risk of suffering from a fall, with poor muscle strength and balance being predictors of fall likelihood. This paper will review 12 relevant primary scientific research papers relating to Tai Chi and the elderly, as well as one meta-analysis. Eleven of the 12 primary papers demonstrated improvements in fitness or physiological capabilities from the practice of Tai Chi with five specifically noting improvements in muscle strength.<sup>3,4,6-11,13-15</sup> In all studies that compared Tai Chi to a control group that did not participate in any form of exercise, it showed significant improvements in physical function. One study examined the effects of a 12-week Tai Chi exercise program on knee and ankle strength, balance, flexibility and mobility, of 68 institutionalized seniors, demonstrating that a Tai Chi exercise program safety improved physical strength and reduce the risk of falls in this residential population.<sup>3</sup> In the meta-analysis four studies were examined that looked at the effects of Tai Chi on balance, when compared to a non-exercise control. Of these studies half showed significant positive effects however the other half showed non-statistically significant benefits.<sup>2</sup> When the meta-analysis looked at Tai Chi compared to an exercise control all the studies examined showed small but statistically significant improvements in balance.<sup>2</sup> Additionally, five of the primary papers compared Tai Chi to another form of exercise. In a particular study Tai Chi was compared to a low impact exercise that found no statistically significant difference between the two exercise forms in physical function but both were found to be statistically significant when compared to a negative control; measured by evaluating ability to stand from a chair, aerobic endurance via two-minute step test, upper body grip strength and balance.<sup>7</sup>



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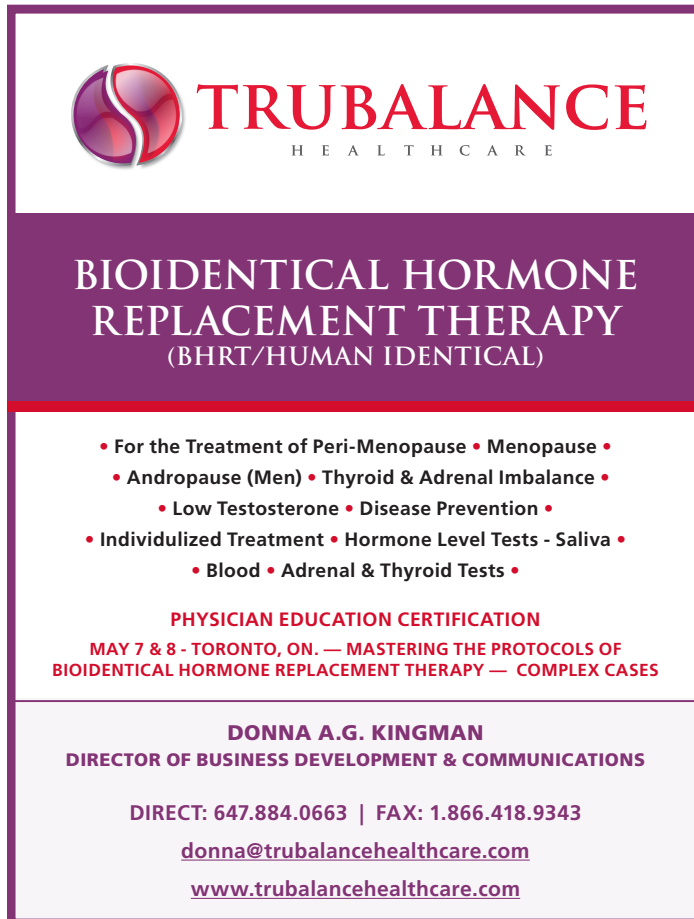
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However, the Tai Chi group reported statistically significant improvements in subjective health relative to the low impact exercise and negative control groups.<sup>7</sup> Additionally, a study comparing Tai Chi to lower limb strength exercises demonstrated equal benefits in strength and balance and a similar fall reduction rate over 17 months.<sup>8</sup> In a different study that had participants practice Tai Chi for one hour, three times per week, Tai Chi was more effective than brisk walking, a form of low impact exercise, in enhancing aerobic fitness (estimated by VO<sub>2</sub> max, knee extensor strength, flexibility and balance).<sup>9</sup> Additionally, Tai Chi was shown to reduce the incidence of falls to a larger degree than lower extremity training over a 12-month period.<sup>10</sup> Furthermore, Tai Chi was shown to be an effective alternative to physical therapy exercises for fall prevention in a group of community living seniors over a 12-month period.<sup>11</sup>

In contrast, a study to examine the effects of Tai Chi on bone mineral density, muscle strength, balance, and flexibility in community-living seniors showed no benefits to the practice of Tai Chi, when compared to resistance exercise.<sup>5</sup> This may be due to the fact that a strenuous form of resistance exercise was used, which may provide faster results, yet may also cause injuries or have a low compliance rate among elderly populations. The benefits demonstrated by these articles are directly correlated with a decreased likelihood of experiencing a fall because of an increase in muscle strength and balance. Tai Chi decreased the risk of multiple falls by 48 percent.<sup>7</sup>

Older adults who have experienced a fall may develop a fear of falling. A fear of falling is reported to be the top concern in the community-dwelling elderly.<sup>12</sup> This anxiety can cause people to self restrict their activity levels in an attempt to prevent future falls. They may begin to experience muscle loss and a decline in physical fitness by restricting such activities. This decline may in turn increase the risk of suffering an additional fall and decrease their independence level. Independence may be decreased if injuries are sustained during the fall and assistance is required to perform daily activities. Therefore, it is crucial to reduce this fear in the elderly in order to ensure their participation in daily activities that allow them to maintain their independence and continue to exercise.

Several of the studies confirmed that the regular practice of Tai Chi lead to a reported decrease in the level of fear towards falling among participants. In a meta-analysis of nine trials, 2,203 participants reported significant declines in these fears.<sup>13</sup> This decline in anxiety was noted in not only studies that compared Tai Chi to a non-exercise control but also to other forms of physical activity. One study investigated whether Tai Chi could decrease the fear of falling in seniors who had previously suffered a fall, better than an educational program.<sup>12</sup> After 48 weeks of participation the Tai Chi group exhibited significantly greater reductions in their fear levels, compared to the educational program.<sup>12</sup> The fear exhibited by seniors who have previously fallen may stem from a belief that they are unable to prevent falls while performing certain activities. Thus, seniors with a fear of falling have greater declines in their ability to perform activities of daily living.<sup>9</sup>



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Self-efficacy is defined as a “belief in one’s capabilities to organize and execute the courses of action required to produce a given attainment”.<sup>14</sup> If an elderly individual does not believe that they are able to perform daily activities or exercise because it may result in a fall, they would be considered to have low levels of self-efficacy. Often a fear of falling may be the result of a lack of confidence in performing certain activities. A lack of confidence in one’s own ability may lead to dependence, which is known to decrease quality of life. Therefore, it is crucial to increase the confidence that older individuals have in their abilities to perform certain activities. Assuming that if people are confident in their ability to maintain balance while performing an activity then their fear of suffering a fall will be reduced. A study designed to test whether Tai Chi is able to positively impact balance and thus increase confidence levels of seniors performing activities of daily living was done with 35 seniors.<sup>15</sup> In this study Tai Chi was shown to significantly increase their confidence with respect to balance while performing functional activities.<sup>15</sup> Four studies, in addition to the aforementioned experiment, demonstrated that through the regular practice of Tai Chi balance improved as well as confidence in the ability to perform activities of daily living.

Tai Chi has been shown to be a valuable tool in the prevention of falls among the elderly. Recent evidence suggests that Tai Chi may be able to decrease falls by addressing multiple causes. Since it is a gentle form of exercise, it allows seniors to safely increase strength, endurance, flexibility, and balance; thereby, increasing their physical fitness levels. It also affects seniors psychologically by decreasing their level of fear towards falling. This decrease in fear will lead to an increase in the activities that they participate in and therefore maintains physical fitness and helps prevent future falls. Finally, Tai Chi can increase older adults’ quality of life by improving their self-efficacy and hence increasing their self-reliance. Given that Tai Chi can improve balance, confidence, physical fitness, and decreases fear, it can be considered a therapeutic exercise to prevent falls in the face of declining functional and cognitive abilities in the elderly. 🍂

## About the Author

**Dr. Emily Rotella, ND** is a recent graduate of the Canadian College of Naturopathic Medicine. Prior to her studies in naturopathic medicine she completed an honours bachelor of science from the University of Toronto with a double major in health & disease and psychology. She currently practices in downtown Toronto with special interests in botanical medicine, women’s health and the endocrine system.

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# Dysautonomia, Orthostatic Hypotension and Falls in the Elderly

Dr. Dorothy Adamiak, ND

The prevalence of dysautonomia and its characteristic presentation as orthostatic hypotension is largely underestimated and current fall prevention strategies are usually limited to the use of assistive devices, pharmacological management of comorbid diseases, and environmental modification targeting prevention of accidents. This article brings awareness to dysautonomia and its role in falls in the elderly and recommends fall prevention strategies that utilize pertinent naturopathic modalities.

**R**ecognizing dysautonomia as a factor contributing to falls is an emerging opportunity for naturopathic doctors, as current intervention programs are insufficient. Between 2003 and 2010 fall-related injury in Canada increased from 47.2% to 57.5% per 1,000 falls. Fall-related deaths also experienced a statistically significant rise. Between 1997 and 1999 fall-related deaths jumped from 8.1 to 9.4 per 10,000 elderly.<sup>1</sup> Inclusion of naturopathic modalities can potentially reduce mortality, injury, and recurrences of falls through avenues not widely pursued. Recommendations to routinely screen for orthostatic hypotension, thoroughly identifying nutritional deficiencies, and assessing lifestyle factors that contribute to falls, such as lack of physical conditioning and gut dysbiosis, are not well highlighted in current Canadian fall-prevention guidelines.<sup>1</sup>

## Statistics for Falls in Seniors

Falls in the elderly are debilitating, serious, and costly. Falls cause anxiety, disrupt daily activities, restrict movement, limit independence, contribute to depression and despondence and seriously diminish quality of life; yet despite precautions, one in three seniors experience a fall each year.<sup>2</sup> The risk goes up with age reaching 50% in those over 80 years of age.<sup>2</sup> However, these statistics may represent only a fraction of the problem as a large number of falls are unreported due to fear of consequences for those who fall. Seventy-six percent of those who fall need emergency care and 24% require further hospitalization.<sup>3</sup> Falls account for 70% of accidental deaths in elderly and are associated with 27% risk of mortality within two years.<sup>4</sup> The financial cost associated with falls are estimated at \$2

billion CAD annually. Falls can be precipitated by variety of factors including poor gait, poor vision, cognitive impairment and muscle weakness, as well as acute and chronic illness, some of which may be secondary to dysautonomia.

## Dysautonomia

Dysautonomia, or autonomic nervous system failure, includes a family of disorders, such as postural orthostatic tachycardia syndrome (POTS), neurocardiogenic syncope, and multiple system atrophy. Dysautonomia occurs frequently in diabetes, alcoholism and Parkinson's disease.

Dysautonomia disrupts mechanisms that depend heavily on the autonomic nervous system, which include: muscular reflexes, sensory adjustments, cognitive abilities, and cardiovascular regulation, all of which are necessary for the body's adaptation to a changing environment.

Orthostatic hypotension is a key feature of dysautonomia. In seniors residing in institutions orthostatic hypotension is a contributing factor for about 55% of falls, syncope, dizziness that results in head injury from a fall, bone fractures or hospitalization.<sup>5</sup> In non-institutionalised population orthostatic hypotension is present in 20% of the older population.<sup>6</sup> However, this number appears to be understated; a study published in *Neurology 2006* revealed that 47% of patients reporting dizziness, light-headedness or syncope had orthostatic hypotension, 54% of whom experienced a blood pressure drop only after three minutes, which could not be diagnosed by orthostatic tests of shorter duration.<sup>7</sup>

## Hypotension Unawareness

Sporadic hypotensive events, with or without an orthostatic feature, are also more common than previously thought. A study published by *Journal of Human Hypertension* (2000) revealed that up to 49% of the general adult population is affected. Sporadic hypotension is especially common in "thin subjects", subjects with low creatinine levels and lower muscle mass.<sup>8</sup>

Research from 2009 pointed out that there is general hypotension unawareness even in severe orthostatic hypotension cases. A study published in *Am J Med* (2009) demonstrated that even in severe orthostatic hypotensive cases, where diastolic drop was greater than 60 mmHg from the baseline only 43% of subjects had typical symptoms (mainly light-headedness).<sup>9</sup> Twenty-



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four percent of patients had atypical symptoms and 33% were completely asymptomatic.<sup>10</sup> Other studies suggest that up to 80% of patients with a “lesser degree of orthostatic hypotension” may be asymptomatic.<sup>11</sup> Atypical symptoms such as fatigue, weakness, palpitations, back and neck pain, dizziness, precordial pain, seizures, hyperhidrosis, cognitive slowing, visual and hearing disturbances are features of delayed orthostatic hypotension.

Postprandial hypotension, which occurs within two hours of a meal is a common cause of syncope in elderly and reaches 67% of prevalence. Postprandial hypotension follows inadequate peripheral vasoconstriction and insufficient heart rate increase. It is frequently precipitated by ingesting hot meals, ingesting vasodilators, ingesting high carbohydrate meal, or sitting in a hot environment. Breakfast is the most common meal leading to syncope.<sup>12</sup> Post-meal syncope is considered an atypical presentation of orthostatic hypotension.<sup>11, 13</sup> Syncope requires systolic blood pressure to drop below 90 mmHg.

### Detection of Dysautonomia

There are many physiological reasons for the increased prevalence of orthostatic hypotension in the elderly. Among them are reduced arterial compliance and increased venous tortuosity, cardiac hypertrophy impairing diastolic filling, decreased renal sodium conservation, age-dependent decline in renin and angiotensin, reduced maximum heart rate during exercise, change in heart rate after hypotensive manoeuvres, and reduced cerebral blood flow.<sup>13</sup>

Current detection methods for autonomic system malfunction are cumbersome and not widely employed. Available tests that include autonomic reflex screen, thermoregulatory sweat test, supine compared to standing serum norepinephrine, and 24-hour urinary sodium tests are not part of routine physical examinations and blood pressure diaries recorded by patients are typically unreliable.

Heart rate variability (HRV) is currently investigated as a more clinic-friendly screening method for dysautonomia. Preliminary studies done by Brain Injury Rehabilitation Service, Westmead Hospital, Australia suggested that post-injury dysautonomia can be seen in HRV test as a large increase in sympathetic phase and reduced parasympathetic activity.<sup>14</sup> Another study on autonomic abnormalities published by *J Affect Discord* (2011) found that lower HRV was a frequent feature of depression and that depression was an independent predictor for developing systolic orthostatic hypertension.<sup>15</sup>

Absence of easily accessible and reliable clinical tests leaves a void and suggests that clinicians may find that pre-screening for dysautonomia through a more in-depth interview may be preferred. Nocturia, stress incontinence, erectile dysfunctions, bowel irregularities and changes to sweating pattern may be one of the earlier clues as to presence of autonomic dysfunction. Later stages of dysautonomia often presents with symptoms such as persistent weakness, post-exercise syncope, excessively fluctuating blood pressure, speech slurring and unsteady gait. Atypical presentation of autonomic nervous system failure may

## DEFINITIONS

**Hypotension** - Hypotension is defined as a blood pressure below 90/60 mmHg.

**Orthostatic Hypotension** - Orthostatic hypotension is defined as a systolic drop of at least 20 mmHg and/or at least 10 mmHg drop in diastolic value within three minutes of standing.

**Sarcopenia** - Sarcopenia is consistent with a gait speed of less than one metre/second and an objectively measured low muscle mass.

**Syncope** - Syncope is a sudden loss of consciousness characterised by immediate and spontaneous recovery that does not necessitate electrical or chemical cardiac rehabilitation. An average syncope lasts 12 seconds and is precipitated by cerebral hypoperfusion.

**VO(2Max)%** - maximal oxygen uptake is generally considered the best indicator of cardiorespiratory endurance and aerobic fitness.

also include: asymmetrical or oscillating feature, such as significant right/left blood pressure asymmetry, alternating unilateral nasal congestion, migraines or daily headaches, arrhythmia, sleep apnea, dysfunctional esophageal peristalsis, panic attacks and cravings for sweets and salt.<sup>16</sup>

### Causes of Dysautonomia

Dysautonomia can be caused by inherent nervous system disorders or degenerative neuropathies. However, recent research suggests that dysautonomia has several modifiable causes that are nutrition-, environmental-, and lifestyle-dependent. Although these causes are rarely addressed, they may constitute the most effective strategy to fall prevention. This concept is elaborated, below.

### Nutritional Deficiencies

Frequency of falls in elderly is dependent on nutritional status. Public Health Agency of Canada reported in 2014 that malnourished elderly who were treated by emergency care were more likely to report having fallen within the previous six months.<sup>1</sup>

Others studies indicated that nutritional deficiencies of specific vitamins and minerals can trigger or contribute to dysautonomia. Insufficiencies of thiamin (vitamin B1), magnesium, vitamin B12, and vitamin D are most commonly implicated.

#### Thiamin

Thiamin deficiency, known as beriberi, has been proposed as a prototype of functional dysautonomia. Its neurological symptoms



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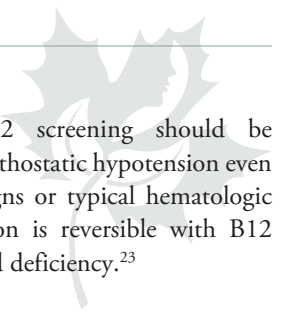


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including cardiac palpitations on mental or physical exertion, abnormal response to adrenalin, vagotonia/sympathicotonia, paresthesias and decreased proprioceptive perception are also features of autonomic nervous failure.

Beriberi is believed to be rare in developed countries and today few clinicians consider thiamin deficiency when assessing a patient. This belief has been recently questioned. Observations showed that thiamin deficiency does not occur only in visibly malnourished individuals, but can be present in robust patients without any signs of nutritional inadequacy.<sup>17</sup>

Thiamin is needed for phosphorylation of thiamin pyrophosphate (TPP) and synthesis of thiamin triphosphate (TTP). TPP and TTP are necessary to complete oxidative pathways during caloric metabolism. High-calorie diets carry a higher need for thiamin. The need for thiamine increases with ingestion of simple carbohydrate, thus it has been suggested that developed countries suffer widespread hidden deficiency of thiamine due to high sugar/high simple carbohydrate diet. It has been demonstrated that supplementation of thiamin in early stages reverses beriberi-like symptoms corrects previously noted autonomic system malfunctions.<sup>17</sup>

### **Magnesium**

Magnesium deficiency has been noted in relationship to mitral valve prolapse. Symptoms of mitral valve prolapse frequently overlap with symptoms of dysautonomia. Both can present with dyspnea, fatigue, dizziness, syncope, palpitations, resting bradycardia, poor exercise tolerance and orthostatic hypotension.

According to a paper presented by Gesell Institute of Human Development, New Haven, Conn, USA, supplementation of 300mg of magnesium lactate over 16 weeks produced significant improvement in serum magnesium as well as a marked improvement in symptoms listed above.

### **Vitamin B12**

It has been well-documented that proper function of the nervous system depends on adequate vitamin B12 levels.<sup>18</sup> Lack of B12 is responsible for defective sympathetic activation and even low-normal levels of this vitamin can produce changes in autonomic nervous system, result in orthostatic hypotension and syncope.<sup>19</sup> Vitamin B12 is necessary for release of noradrenaline. Its lack leads to failure of sympathetic nervous system, which results in orthostatic hypotension.<sup>20</sup>

*Clin Auton Res* (2004) reported that supplementation of vitamin B12 in deficient elderly produces statistically significant reduction in orthostatic hypotension. A marked decrease in blood pressure drop from 44/29 mmHg to 14/9 mmHg was seen after vitamin B12 supplementation.<sup>21</sup> It has been postulated that orthostatic hypotension may be one of the earlier signs of B12 insufficiency. Not surprisingly, many cases of orthostatic hypotension were found to be the first manifestation of pernicious anemia.<sup>22</sup>

Many investigators suggest that B12 screening should be implemented in everyone experiencing orthostatic hypotension even in the absence of clinical neurologic signs or typical hematologic manifestations.<sup>22</sup> Orthostatic hypotension is reversible with B12 supplementation in cases with established deficiency.<sup>23</sup>

### **Vitamin D**

Vitamin D is well-known for its value in increasing bone mineral density.<sup>24</sup> However, recently Public Health Agency of Canada started recommending it not only as a therapeutic adjunct for osteoporosis, but also for a valuable therapy in fall prevention. *J Intern Med* (2014) reported that orthostatic hypotension is common in vitamin-D-deficient women over 80 years old and can be reversed by vitamin D supplementation. The study demonstrated significant inverse linear association between 25-hydroxyvitamin D serum concentration and delayed orthostatic hypotension.<sup>25</sup> Vitamin D supplementation was shown to be effective in reduction of falls among elderly who were deficient.<sup>26</sup>

### **Physical deconditioning**

American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons stress that muscle weakness is the most important risk factor for falls, increasing the risk by four to five times.<sup>24</sup> Studies done on New Mexico population found that sarcopenia prevalence is 12% for persons 60 to 70 years of age and nearly 30% for persons over 80 years.<sup>27</sup>

Pharmacologic intervention to counteract sarcopenia has limited efficacy. Physical exercise is so far demonstrated to be the best intervention for maintaining and enhancing muscular strength.<sup>28</sup> According to Statistics Canada data pooled between 2007 and 2011, however, seniors do not exercise adequately. Only 11% seniors aged 60-79 meet Canada's physical activity guidelines.<sup>26</sup>

Lack of exercise not only contributes to sarcopenia, but also precipitates nervous system malfunction. The relationship between lack of exercise, physical deconditioning and dysautonomia has been addressed in a paper presented in *Neurology* (2012). A study done at Mayo Clinic between 2006 and 2011 demonstrated that orthostatic intolerance and VO(2max)% are inversely correlated. Reduced VO(2max)%, which is consistent with deconditioning, was present in almost all patients with orthostatic intolerance. This suggested that lack of exercise and subsequent deconditioning may play a central role in pathophysiology of dysautonomia.<sup>29</sup>

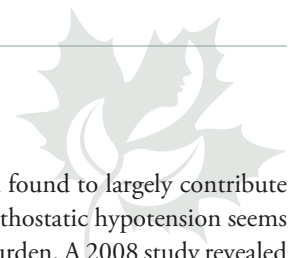
Attempts to improve nervous system function with exercise have been proven to be very effective in various types of dysautonomia. A three-month progressive endurance training caused remission in 71% of postural orthostatic tachycardia syndrome patients.<sup>30</sup> Eight-week strength training for elderly with orthostatic hypotension resulted in significant alteration of orthostatic response. A 1998 study presented by *J Cardiopulm Rehabil.* noted an average systolic increase of 9.7 mmHg and an average diastolic increase of 4.7 mmHg after intervention.<sup>31</sup>

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## Gut health and gut irritants

The effect of gut dysbiosis on general well-being has been long acknowledged by naturopathic medicine; however, recent research has provided more details on how gut health affects the autonomic nervous system.

The vagus, a long cranial nerve whose branches extend to digestive tract, contributes to regulation of heartbeat and blood pressure. It is worth mentioning that 90% of signals passing via vagus nerve go from the gut to the brain, not the other way around, therefore gut health is of prime interest in all nervous-system disturbances.<sup>32</sup>

The vagus nerve and its function are seldom taken into consideration by clinicians who assess the risk of falls. However, gut-ANS connection needs to always be taken into consideration given a large prevalence of digestive disturbances among seniors. Improper signals derived from the gut may cause over- or under-expression of various branches of autonomic nervous system.

Research indicates that 50% of patients with inflammatory bowel disease have some sort of autonomic system dysfunction.<sup>33</sup> Autonomic dysfunction has been found in 46% of patients with crohn's disease and 35% of patients with ulcerative colitis.<sup>34,35</sup> Digestive disturbances and falls have even a stronger correlation. Patients taking laxatives are two times more likely to experience falls than patients not using them.<sup>26</sup>

Dietary irritants are now being researched as a possible contributor to autonomic system dysregulation. Despite limited studies in this area gluten intolerance has already been implicated. A paper presented in *J Neurol Neurosurg Psychiatry* (2005) showed that 2.4% of symptomatic patients with idiopathic orthostatic hypotension had celiac disease confirmed by biopsy.<sup>36</sup>

Autonomic nervous system is in constant communication with enteric microbiota of the gut. Evidence exists that gut microbiota can alter autonomic nervous system function.<sup>37</sup> Recent research is suggestive that imbalanced gut microbiota plays an important part in variety of neurodegenerative conditions including MS, Guillain-Barre syndrome, Alzheimer's as well as Parkinson's disease.

Preliminary assessment showed that microbiota in Parkinson's disease has reduced abundance of the *Prevotellaceae* bacteria as compared with healthy controls and greater abundance of *Enterobacteriaceae*. This alteration is especially noted among patients with postural instability.<sup>38</sup> Small intestinal bacterial overgrowth (SIBO) is present in 54%-67% of Parkinson's patients and is correlated with pronounced motor symptoms. It has been postulated that Parkinson's disease does not start in the central nervous system, but originates in the gut and spreads via neuroendocrine, immunological and direct neural pathway to the brain.<sup>38</sup> It is worth noting that Parkinson's patients are three times more prone to falls than healthy controls.<sup>39</sup>

## Prescription Drugs

Prescription medications have also been found to largely contribute to dysautonomia.<sup>40</sup> The prevalence of orthostatic hypotension seems to be directly proportional to the drug burden. A 2008 study revealed that orthostatic hypotension is present in 35% of seniors who do not take any drugs, 58% in those who take one drug, 60% in those with two, and 65% in those who take three drugs. Medications identified to have the highest orthostatic effect are: hydrochlorothiazide (65%), lisinopril (60%), furosemide (56%), trazodone (58%), and terazosin (54%).<sup>41</sup>

Besides the obvious volume depletion caused by diuretics other drugs can also contribute to falls through different mechanisms. Elisabete Pinto in her article published in *Postgrad Med J*, mentioned that 11% of syncope in elderly is reported to be drug induced.<sup>12</sup> Among the drugs most implicated in falls are:

- Analgesics – due to reduced alertness and slow central processing
- Anti-arrhythmics – due to impaired cerebral perfusion
- Anticholinergics – due to confusion
- Antihypertensives – due to impaired cerebral perfusion
- Antipsychotics – due to antiadrenergic effects
- Psychoactive drugs – due to reduced alertness, slow central processing<sup>2</sup>

## Emerging opportunity for naturopathic doctors

Dysautonomia (and its feature, orthostatic hypotension) is much more prevalent than generally believed. It is also a condition not so much gene-dependent, but largely influenced by dietary choices and lifestyle habits. With better understanding of presentation as well as pathophysiology of dysautonomia we should no longer limit our intervention to proverbial “hydration, salt and incline”, but include restoration of nutritional reserves, digestive repair, physical conditioning, and communication with other key health care providers.

Naturopathic doctors are well-positioned to recognize early signs of dysautonomia, design a fall-preventing lifestyle plan for the patient, and educate patient-sharing clinicians on effects of drugs, causes of dysautonomia, and naturopathic alternatives.

Naturopathic doctors, besides being able to competently address dietary and lifestyle habits, are also uniquely positioned to treat dysautonomia as hydrotherapy<sup>42</sup>, homeopathy<sup>43</sup>, acupuncture<sup>44</sup> and breathing techniques<sup>45</sup> have been found capable of influencing autonomic nervous system. Incorporation of naturopathic wisdom and naturopathic modalities can prove to be one of the better and more comprehensive interventions for fall prevention in elderly.



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## About the Author

**Dr. Dorothy Adamiak (“DrD”), ND** has been in private practice ever since her graduation from Canadian College of Naturopathic Medicine in 1999. During that time she earned a diploma in bioregulatory medicine and was awarded an Honorary Fellowship from British Society for Bioregulatory Medicine in 2014.

For ten years she published two health magazines: LifePeak and ZdrowyStyl, but in 2010 she switched to blogging to lessen her environmental footprint. Today her site DrDNaturopath.com enjoys over half a million visitors a year. Her book *“The Ultimate Guide to Low & Fluctuating Blood Pressure”* earned five stars on Amazon. *“Revived! Proven Natural Solutions for Low Blood Pressure”*, another book she self-published, has just been made available as a download.

DrD is getting ready for a full-time career as a writer and a blogger. After refurbishing an old courier van and converting it into a motorhome she is about to let go of her busy practice and the city conveniences to instead pursue a nomadic minimalist lifestyle hoping to immodestly indulge in nature, passion, and freedom while teaching others the skills of health.

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# Polypharmacy; Are Seniors at Risk?

Dr. Jessica Burke Browman, ND, MPH

A 70-year-old man walks into his geriatrician's office for an initial visit. He reports that he has seen six specialists over the last 18 months. He is anxious and very confused by the varying advice he has received from these physicians. The geriatrician determines this man is taking over 12 medications, a number of them improperly, and suffers from various side effects and drug related interactions. No one has been observing him or coordinating his care.

## Polypharmacy Defined

It is well known in medical practice and research that prescription medication use increases with age. Polypharmacy is defined as the concurrent use of five or more prescription drugs and over-the-counter medications.<sup>1</sup> Overmedication is an extension of polypharmacy, and may be defined as the use of drugs that are not clinically indicated, or are incorrectly administered. Overmedication may result from age-related changes in pharmacokinetics, pharmacodynamics, inappropriate drug use, ignoring potential drug interactions, or prescribing a drug for the wrong diagnosis.<sup>2</sup> In addition to prescribed medications, a 2010 Ipsos-Reid survey found that 73% of Canadians regularly take natural health products including vitamins, minerals, herbal products, and homeopathic medicines.<sup>3</sup> These findings highlight the need for naturopathic doctors to closely monitor all forms of medication and treatment prescribed to their patients, particularly for those patients 65 and older. This issue has also been at the forefront of recent mainstream media attention and clearly must be addressed.<sup>4</sup>

## Aging Canadians

Like many industrialized countries, Canada is undergoing a demographic shift. The 2011 Canadian Census counted just under five-million people aged 65 and older. In that census, the population aged 60 to 64 experienced the fastest increase in growth (29.1%).<sup>5</sup> The trend towards a larger proportion of older adults will continue as the baby boom generation ages. In Ontario alone, the number of seniors aged 65 and over is expected to more than double from 1.8 million to 4.2 million by 2036, and will account for 23.4% of that province's population.<sup>6</sup>

The prevalence of chronic disease and disability is greater in seniors, those aged 65 and older. It is thus the number of seniors with chronic conditions, not age itself, that accounts for an increased use of primary health care services amongst this population.<sup>7</sup> Patients visiting physicians for treatment of one or more chronic conditions are likely to leave with a prescription. Prescription medications are the second most costly component of health care, accounting for almost 14% (\$29 billion) of Canada's annual healthcare spending in 2013.<sup>8</sup>

## Frequency & Origin of Polypharmacy

### Prescription Drug Use

Although there is acknowledgment of increased use of medications amongst seniors, Statistics Canada only recently conducted its first in depth analysis into prescription medication use by Canadians, aged six to 79. Prescription drug use increased with age, from 12% (six to 14 year-olds) to 83% (65 to 79 year-olds), while the number, or intensity (i.e., increased dosage frequency and amount of same drug), of prescription drug use rose from 3% to 70% in these same age categories respectively.<sup>8</sup> The presence and number of physical and mental health conditions was also found to be associated with prescription drug use. Almost all respondents who had four or more chronic conditions reported taking prescription drugs in the past two days. In that same time period, 90% of the respondents with at least three chronic conditions had taken medication, and for those with none of the selected chronic conditions, the figure was 22%.<sup>8</sup> Interestingly, the use of prescription drugs in Canada could not be explained by differences in socioeconomic status as had previously been suggested. As expected, prescriptions were highest in 65 to 79 year-olds, at approximately 30%.<sup>8</sup> Though it is clear that prescription drug use increases with age, a 2008 Canadian survey shows that chronic morbidity is a stronger predictor of polypharmacy than age alone (Table 1).<sup>9</sup>

It is important to note that the use of dietary supplements has also increased in the senior population. A US national population-based study of 57 to 85 year-olds, found that the prevalence of dietary supplements increased from 51.8% in 2005-2006 to 63.7% in 2010-2011.<sup>10</sup> Additionally, the concurrent use of two or more dietary supplements increased by 8.4%.<sup>10</sup> Multivitamins or mineral supplements, calcium, omega-3 fish oils and vitamin D were the most commonly used dietary supplements in 2010-2011.<sup>10</sup>

*continued page 27*

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– Dr. Pawa (West Coast Women’s Clinic)



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**Table 1: Average Number of prescription medications among seniors, by number of chronic conditions and age group<sup>9</sup>**

Age Group	Number of Chronic Conditions				Total
	0	1	2	3+	
65-74	1.1 (n = 432)	2.5 (n = 532)	3.6 (n = 385)	5.9 (n = 401)	3.0 (n = 1750)
75-84	1.8* (n = 226)	2.8 (n = 285)	4.0 (n = 261)	6.0 (n = 317)	3.8 (n = 1809)
85+	2.4* (n = 60)	3.0 (n = 67)	4.3 (n = 79)	5.8 (n = 87)	4.2 (n = 293)
<b>Total</b>	<b>1.3 (n = 718)</b>	<b>2.6 (n = 884)</b>	<b>3.8 (n = 725)</b>	<b>5.9 (n = 805)</b>	<b>3.3 (n = 3132)</b>

Chronic conditions include: arthritis, asthma, cancer, chronic pain, depression, diabetes, emphysema or chronic obstructive pulmonary disease, heart disease, high blood pressure, a mood disorder other than depression and stroke.

n = cohort sample size.

Sources: Canadian Survey of Experiences with Primary Health Care, 2008, Statistics Canada and Canadian Institute for Health Information.

\* CV is between 16.6% and 33.3%; interpret with caution because of high variability.

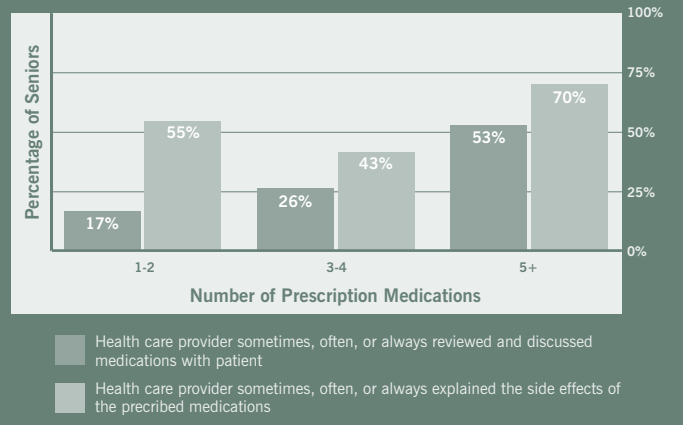
### Primary Health Care Providers & Communication

Seniors routinely visit several specialists, and may receive various prescriptions with little communication and coordination of care between these physicians. Findings from the 2009 Canadian Disease and Therapeutic Index showed that just over 80% of patients visiting their physician's office for treatment of hypertension or depression left with a prescription whereas only 2% of patients visiting a physician for a general medical exam or health check-up left with a script for a prescription medication.<sup>11</sup> The Canadian Survey of Experiences with Primary Health Care (CSE-PHC), co-funded by the Canadian Institute for Health Information and the Health Council of Canada, conducted computer assisted telephone interviews between April and June 2008, and results were analyzed by Statistics Canada.<sup>9</sup> This survey determined that more than three quarters of seniors have at least one chronic disease, and that 24% of Canadian seniors have three or more of the eleven most common chronic diseases. Although most seniors indicate that they had a primary health care provider, "less than half reported that their doctor reviewed their medications (48%) and explained potential side effects (47%) at least some of the time".<sup>9</sup> This gap in patient care leaves seniors susceptible to a variety of adverse drug events with outcomes ranging from physician visits, ambulatory care, hospitalization, to even death. Figure 1 illustrates the communication between patient and physician relative to the number of prescription medication being taken.

### Coordination of Care

There are many challenges coordinating care for seniors. The first is the lack of gerontologists. There are currently only 261 gerontologists in Canada, which is only one-fifth of the number needed.<sup>12</sup> A second issue arises from potential use of several pharmacies to fill prescriptions. Many patients believe their physicians are aware of what their other health care providers are prescribing, and in addition, incorrectly assume that pharmacies are able to vet all information electronically.

**Figure 1: Senior Patient & Health Care Provider Collaboration of Prescription Medications, Canada 2008<sup>9</sup>**



The first Canadian-wide, population-based study by Ramage-Morin (2009),<sup>13</sup> assessed the use of prescription and over-the-counter medication by Canadian seniors based on data from the 1996/1997 (institutional component) and 1998/1999 (household component) National Population Health Survey. In those aged 60-79, research found that pharmacists dispensed an average of 35 prescriptions per person in this age group, compared with an overall average of 14 prescriptions for younger Canadians. Polypharmacy was prevalent amongst 53% of seniors in medical and health care institutions and in 13% of those living in private residences. Analgesics and psycholeptics (sedatives, antipsychotics, anxiolytics, and hypnotics) were the most commonly prescribed, followed by digestive aids, diabetic and cardiovascular medications. No difference was noted in usage between men and women in either setting, which was further supported by the recent analysis into Canadians' prescription drug use.<sup>14</sup> An American study, however, cited 12% of women over the age of 65 taking 10 or more medications, and 23% taking a minimum of five prescription drugs.<sup>15</sup> Most significant in the Canadian study was the conclusion that polypharmacy was found to be associated with adverse drug events (ADE), including morbidity in Canadian seniors.<sup>13</sup> This finding has been the major focus in all related studies concerning polypharmacy and the elderly population in both Canada and abroad.

### **Consequences of Polypharmacy: Adverse Drug Events**

Overmedication is not limited to any one setting, but occurs in hospitals, clinical settings, and nursing homes. A consequence of multiple drug use includes adverse drug events (ADEs). An ADE is an unexpected and/or negative patient outcome resulting from any drug related medical intervention. ADEs may be caused by drug-drug, drug-disease, drug-natural health product, or drug-over the counter interactions, duplication, synergism, additive effect, discontinuation of therapy, dose alteration, skipping medications, and physiological antagonism.<sup>16,17</sup> A recent Canadian study found that ADEs are a significant concern in both in-patient and out-patient settings, with consequences ranging from morbidity to

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mortality.<sup>18</sup> The risk increases for seniors who take multiple medications, have a history of ADEs, or have a decreased capacity to eliminate drugs.<sup>16</sup> When seniors add non-prescription medications, including natural health products, there is an additional risk for ADEs. Research has established that seniors are the major consumers of non-prescription medications, taking on average one to 3.4 non-prescribed medications.<sup>16</sup> A study by Rutledge et al. (2004) concluded that patients taking both corticosteroids and NSAIDs had a 15 times greater risk for peptic ulcer disease compared to non-users of either medication.<sup>19</sup>

### **Emergency Room Visits**

ADEs are responsible for increased emergency room and physician visits, diagnostic tests, and hospitalization, with significant financial implications. One study found the increasing number of co-morbidities and medications was associated with a greater number of emergency room visits, with 42% of patients requiring hospitalization.<sup>18</sup> Approximately 29% of the ADEs/PADEs (potential adverse drug events) identified were considered to be preventable. The most common drug class found associated with the ADEs/PADEs were cardiovascular agents (37.4%).<sup>18</sup> In a meta-analysis of observational studies, Beijer and de Blaeij (2002) analyzed 68 studies cited in 64 different papers to determine the rate of hospital admissions due to ADEs.<sup>20</sup> Seventeen of the studies highlighted seniors (classified as age 65+) and ADEs. Figure 2 depicts the increased incidence of senior hospital admissions as a result of an ADE compared to that of non-seniors.<sup>20</sup> The meta-analysis concluded that ADEs, a consequence of polypharmacy, are a significant public health concern.

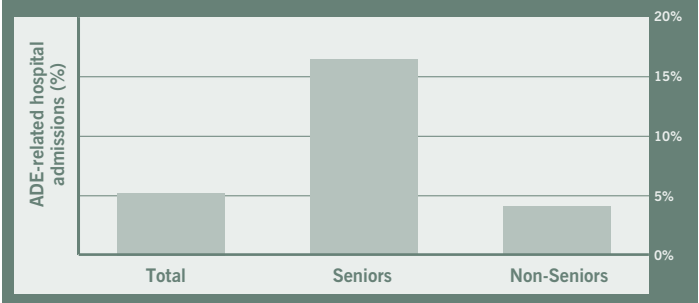
### **Cognitive Impairment & Falls**

Cognitive impairment, resulting from an ADE, increased more than ninefold for seniors taking a minimum of four medications.<sup>21</sup> Cognitive impairment, seen with both delirium and dementia, leaves seniors feeling dizzy and groggy, making them more vulnerable to serious falls.<sup>21</sup> A prospective cohort study of 294 seniors conducted by Jyrkkä et al found that 22% of patients taking five or less medications had cognitive impairment compared to 33% of patients taking six to nine medications, and 54% of patients taking 10 plus medications.<sup>22</sup> The increased incidence of falls, recurrent falls, and falls resulting in significant injuries, have all identified polypharmacy as a major risk factor, with increased incidence for patients taking four or more medications.<sup>21,23</sup>

### **Nutritional Deficiencies**

Of specific interest to naturopathic doctors is the impact of polypharmacy on the nutritional status of patients. Food-drug interactions are defined as 'alterations of pharmacokinetics or pharmacodynamics of a drug or nutritional element or a compromise in nutritional status as a result of the addition of a drug'.<sup>24</sup> The prospective study conducted by Jyrkkä et al concluded that a risk factor for malnourishment was the concurrent use of 10 or more medications.<sup>22</sup> As some diseases contribute to malnutrition, it must be noted that polypharmacy alone may not be responsible

**Figure 2: Seniors vs Non-Senior Hospital visits related to ADEs<sup>20</sup>**



for nutritional deficiencies. A cross-sectional study administered in 1100 community dwelling seniors found a statistically significant inverse correlation between increased number of medications and fibre intake.<sup>25</sup> Additionally, intake of cholesterol, glucose and sodium and increased medication use were found to be positively correlated. A lower intake of fat-soluble vitamins, B vitamins, carotenoids and minerals was also found in those taking multiple medications.<sup>25</sup>

### **Medication Compliance**

Medication compliance is also a major consequences of polypharmacy. Several studies have noted that although compliance is approximately 80% for acute medication use, this number drops significantly for long-term medication use, with compliance rates between 40-60%.<sup>26</sup>

## **Reducing Polypharmacy**

The medical literature has described several approaches to improve prescription medication use in seniors, and reduce ADEs. Recommendations include:

- *The Beers Criteria.* This criteria, first published in 1981, updated in 2015, lists potentially inappropriate medications that should be avoided or have their dose adjusted based on a patient's kidney function and select drug-drug interactions documented to be associated with adverse reactions in seniors.<sup>27</sup> Other tools to identify potentially inappropriate medications include McLeod and STOPP (Screening Tool of Older Persons' Potentially Inappropriate Prescriptions).<sup>28</sup>
- Centralize continuity of care by reducing the number of prescribing physicians for individual patients, health system changes, and policy reform. This may include support for e-prescribing.
- Engage in interactive, case-based, interdisciplinary meetings with multiple prescribers (appropriately trained pharmacists, clinical pharmacologists, and other regulated health care providers, including NDs).<sup>29</sup>
- Conduct routine medication reviews, including prescription medications, over the counter medications, and natural health products.
- Improve patient education and adherence.<sup>30</sup>
- Increase education to health care providers to promote safe, effective and evidence-based prescribing.

## Deprescribing


The number of concurrent medications being taken is the most important predictor of inappropriate prescribing and risk of ADEs, thus there is an established need to deprescribe. Deprescribing has been defined as ‘the process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes’.<sup>31</sup> Choosing Wisely Canada and Ontario Pharmacy Research Collaboration (OPEN) are two organizations developing evidence-based guidelines to identify unnecessary medications and help safely taper or eliminate certain medications in the elderly to reduce ADEs.<sup>32,33</sup> OPEN is specifically focused on providing feasible and evidence-based deprescribing guidelines specifically around the overuse and misuse of proton pump inhibitors, benzodiazepines, and antipsychotics. These guidelines will help support interdisciplinary teams in guiding the care of their senior population.<sup>32</sup>

## Naturopathic Doctors are Key Partners

It is clear that naturopathic doctors can play an important role in reducing polypharmacy among the senior population.

Steps that naturopathic doctors can take include:

- Identify all current medications. This process, medical reconciliation, is used in addition to identifying critical patient characteristics (mental, physical, social) that may place the patient at higher risk. It is often a first patient intake that reveals the concurrent use of prescription drugs, over the counter medications, and natural health products.
- Identify the multiple prescribers. It is important to determine all of the doctors who have prescribed medications to your shared patient to allow for engagement in open dialogue.
- Define the patient’s overall goals and values related to their health status and quality of life. This conversation involves discussion around current indications for medication use, magnitude of benefit versus harm, and most importantly an ongoing plan of shared communication and responsibility. If deprescribing or replacement of a prescription drug with a natural health product is indicated, then it is essential that naturopathic doctors work together with their patients’ medical doctors in the best interest of their mutual patients as NDs are not legally permitted to advise the removal of any prescription medication.
- Develop naturopathic interventions that are integrated and sustainable, involving a truly collaborative shared-care approach between primary care providers, specialists, and inter-professional healthcare providers.

These core themes of medical reconciliation, deprescribing, and patient centred-care fit well within the context of naturopathic medicine and most importantly remind us of our first guiding principal, First Do No Harm (*Primum non nocere*).

## About the Author

**Jessica Burke Browman, ND, MPH** is a 2004 graduate of the Canadian College of Naturopathic Medicine (CCNM). After several years of private practice in Toronto, she recognized that the principals of naturopathic medicine could be applied at the population level and decided to return to school to complete her Master of Public Health at the University of Waterloo. Jessica’s focus has been on public health and education. She has worked at Mt. Sinai Hospital in Community Development and currently teaches public health at CCNM in addition to continuing her private practice.

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# The Influence of Age and Stress Related Factors on Hepatic Cytochrome p450 Enzyme Expression and Function



Dr. Jennifer MacDonald, BSc, ND

In humans, xenobiotic biotransformation and metabolism depends on phase I and II enzymes.<sup>1</sup> Phase I consists primarily of cytochrome p450s (CYP) enzymes that metabolize many endogenous and exogenous chemicals.<sup>2</sup> CYPs are found in various tissues throughout the body and exist as different isoforms that can be divided into 18 families and 42 subfamilies.<sup>2</sup> These enzymes serve varied roles such as the metabolism of arachidonic acid and eicosanoids, cholesterol metabolism, steroid synthesis, vitamin D3 metabolism, and also the metabolism of xenobiotics.<sup>2</sup>

**F**or more information regarding the reactions catalyzed by the various CYP isoforms, refer to Table 2.

This paper focuses on the CYPs that are involved with botanical and drug transformation and not the detoxification of endogenous chemicals or environmental toxins. The majority of drugs are metabolized by the specific CYP isoforms: CYP2B6 and 7, CYP2C, CYP2D, CYP3A4 and CYP2C19.<sup>3</sup> CYP2C family is responsible for metabolizing around 20% of prescription drugs<sup>4</sup> and CYP3A4 metabolizes approximately 50%.<sup>5</sup> CYP3A4 is most abundant in the liver and small intestine, metabolizing the majority of xenobiotics metabolized in these organs.<sup>6</sup> The highest expressed isoforms in liver are CYPs 3A4, 2C9, 2C8, 2E1, and 1A2, while 2A6, 2D6, 2B6, 2C19 and 3A5 are less abundant.<sup>7</sup> CYPs are responsible for activating many of the beneficial compounds found within the diet and within botanicals. Many dietary compounds and natural health products (NHPs) can induce or inhibit the activity of important CYP isoforms.<sup>8</sup>

The phase II metabolizing or conjugating enzymes, consist of many different enzymes including UDP-glucuronosyltransferases (UGTs) and N-acetyltransferases (NATs).<sup>9</sup> While the liver is thought of as the predominate organ for biotransformation of substances, many CYPs reside in the gastrointestinal tract (GIT). Phase III transporters located within the GIT are also important for some

drug and herb metabolism.<sup>10</sup> This paper will focus primarily on phase I CYP enzymes, however the importance of phase II and III in the biotransformation of xenobiotics should be kept in mind.

**TABLE 1: KEY FACTS**

- Age related decline in pharmacokinetics is attributed to polypharmacy, liver and renal decline as well as the aging of cytochrome p450s
- In the majority of cases, stress up-regulates CYPs by glucocorticoids, catecholamine, and insulin
- Inflammation will lead to a reduction in CYP enzymes
- Oxidative stress can both up-regulate and down-regulate the expression of CYPs. Balancing this expression is important because under-expression of CYPs leads to accumulation and toxicity of xenobiotics, whereas over-expression can lead to the production of reactive oxygen species.

**TABLE 2: DIFFERENT CYP FAMILIES AND THEIR FUNCTION**

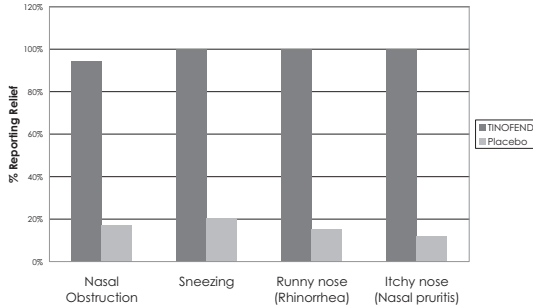
CYP1	Drug and steroid (especially estrogen) metabolism, benzo(a)pyrene toxification
CYP2	Drug and steroid metabolism
CYP3	Drug and steroid (including testosterone) metabolism
CYP4	Arachidonic acid or fatty acid metabolism
CYP5	Thromboxane A2 synthase
CYP7	Bile acid biosynthesis 7-alpha hydroxylase of steroid nucleus
CYP8	Varied
CYP11	Steroid biosynthesis
CYP11B1	Makes 11-beta-hydroxylase enzyme, helps produce hormones called cortisol and corticosterone.
CYP24	Vitamin D degradation
CYP26	Retinoic acid hydroxylase
CYP51	Cholesterol biosynthesis

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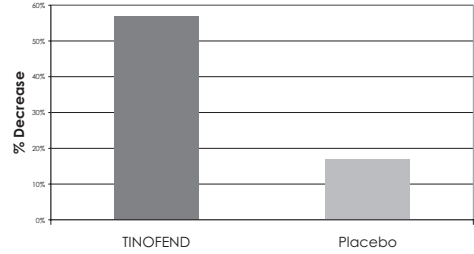
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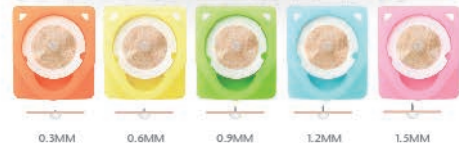
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## Dietary and Botanicals Substances

Numerous foods and natural health products will alter the expression and activity of CYPs, potentially leading to herb-drug interactions.<sup>8</sup> Grapefruit and grapefruit juice famously inhibit intestinal CYP3A4, increasing the bioavailability of drugs such as warfarin and quinidine that are metabolized by this enzyme<sup>11</sup> (Refer to reference<sup>12</sup> for an extensive Drug interaction chart) *Piper methysticum* (Kava-Kava) can inhibit CYP1A2 and CYP2E1, decreasing bioavailability of drugs metabolized by this enzyme.<sup>13</sup> It is possible for herbal components to be converted to toxic and carcinogenic metabolites by CYP.<sup>14</sup> Age specific CYP changes can occur, causing previously un-reactive substances to induce changes. A marginal inhibition of CYP2D6 was found in elderly subjects taking ginseng that was not found in younger subjects.<sup>15</sup> For additional NHP and drug interactions, refer to Table 3 as well as the Cytochrome P450 (CYP450) Enzyme Inducers Drug Reference Table.<sup>16</sup>

## Regulation of CYPs

The expression and activity of the CYPs are influenced by exogenous environmental factors, toxins, botanicals, dietary substances,<sup>8</sup> and drugs as well as by genetic factors, hormonal regulation, and the physiological and pathophysiological status of the organism.<sup>7</sup> The regulation of CYP enzymes is achieved through various mechanisms including gene transcription, protein translation, post-translational processing,<sup>17</sup> and epigenetic regulation.<sup>18</sup>

## Epigenetic

Epigenetics looks at changes to the phenotype that are caused by mechanisms other than the DNA sequence.<sup>19</sup> Epigenetic regulation of CYPs occurs by DNA methylation, both hypermethylation and hypomethylation, and histone modification.<sup>18</sup> Factors that affect DNA methylation include an individual's diet<sup>20</sup> as well as exposure to chemicals such as heavy metals, air pollution, and endocrine disruptors.<sup>21</sup> CYPs play an important role in carcinogenesis, therefore epigenetic changes in CYP genes lead to differences in cancer susceptibility.<sup>18</sup> Altered methylation of CYP1B1 is observed in colorectal and breast cancers, and nodular goiter.<sup>18</sup> Vitamin D deficiency and lowered response to supplementation has been associated with CYP2C11 and CYP241, with the regulation of these CYP isoforms also under epigenetic control.<sup>18</sup> Vitamin D plays an important role in the immune system, creating a connection between epigenetic CYP control, and the development of cancer and autoimmune diseases. Increased environmental exposure to toxins can lead to an accumulation of epigenetic changes that could account for altered CYP expression and impaired function as an individual ages. Epigenetics links increasing environmental exposures to altered changes in CYP enzymes, potentially impairing function as an individual ages.

## Inflammation

Inflammation affects the expression of CYPs and in general suppresses metabolism of drugs.<sup>22</sup> Hepatic CYP genes are suppressed

**TABLE 3: NHP EFFECTS ON CYP AND DRUG INTERACTIONS**

Compound	Active component	CYP affected*	Drug Interaction**
St. John's Wort <sup>8</sup>	Hyperiforin	Induces CYP3A4	Reduced bioavailability of nifedipine, omeprazole, oral contraceptives, quazepam, warfarin
Kava <sup>8</sup>	Kavalactones	Inhibit CYP1A2 and CYP2E1	Increases levels of CYP2E1 drugs such as chlorzoxazone
Ginseng <sup>8</sup>		CYP2D6	Marginally inhibits CYP2D6 drugs such as alprenolol, fluoxetine
Grapefruit <sup>11</sup>	6',7'-dihydroxybergamottin (DHB) and bergamottin (BG)	Inhibits CYP3A4	Increases bioavailability of CYP3A4 drugs such as erythromycin, clonazepam, warfarin, etc
Cruciferous vegetables <sup>104</sup>	Isothiocyanates	Induces CYP1A1 and CYP1A2	Decreases drugs such as haloperidol and maproxen
Licorice root <sup>105</sup>	Glabridin	Inhibits CYP2B6	
Garlic <sup>105</sup>	Diallyl sulfide	Inhibits CYP2E1	Increases levels of acetaminophen, and anaesthetics such as isoflurane
Grapes <sup>106</sup>	Resveratrol	Inactivates CYP3A4	Increases levels of many calcium channel blockers, benzodiazapenes and tamoxifen

\*Refer to reference 16 for the Enzyme Inducer and Inhibitor Table for extended CYP herb and drug interactions (<http://www.ebmconsult.com/content/pages/medications-herbs-cytochrome-p450-cyp-inducers>)

\*\*Refer to reference 12 for a Drug Interaction Table, listed by specific CYP isoforms (<http://medicine.iupui.edu/clinpharm/ddis/clinical-table/>)

during acute and chronic inflammation.<sup>23,24</sup> Several studies have demonstrated pro-inflammatory cytokines interleukin-1-alpha and beta (IL-1 $\alpha$  and IL- $\beta$ ), interleukin-6 (IL-6), interferon (IFN) $\gamma$ , and tumor necrosis factor alpha (TNF- $\alpha$ ) down-regulate CYP genes expression in the liver, reducing available CYP enzymes.<sup>22-24</sup> NF- $\kappa$ B is an important regulator of the immune and inflammatory response and can directly regulate the expression of CYP1A1, CYP2B1/2, CYP2C11, CYP2D5, CYP2E1, CYP3A7, and CYP27B1 through binding to the promoter region of these genes, suppressing transcription, and reducing expression of these enzymes.<sup>25,26</sup> There is therefore a connection between inflammatory diseases and the efficiency of the breakdown of xenobiotic substances. Indeed an alteration of CYP enzyme expression is found in chronic inflammatory conditions such as inflammatory bowel disease (IBD), and rheumatoid arthritis.<sup>26</sup> CYP enzyme levels are lowered by acute stress and also by chronic inflammatory diseases, impacting their ability to detoxify xenobiotics.

Other physiological impacts may occur as a result of inflammatory changes altering the expression of CYPs. Low 25(OH)D may be a consequence rather than a cause of chronic inflammatory diseases, resulting from a complex interaction of factors from intracellular bacteria to altered CYP expression.<sup>27</sup> Obesity causes subclinical inflammation that can impact hormone production, particularly of interest in hormone receptor positive breast cancer.<sup>28</sup> Cyclooxygenase (COX)-2 derived pro-inflammatory prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), activates CYP19 transcription, resulting in increased aromatase expression and elevated progesterone receptor levels in breast tissues.<sup>28</sup>

## Oxidative stress

Oxidative stress occurs when the production of free radicals exceeds the ability of the body to detoxify or neutralize these free radicals and repair the damage.<sup>29</sup> Two primary regulators of the response to oxidative stress are nuclear factor erythroid 2-like factor 2 (Nrf2) and NF- $\kappa$ B.<sup>30,31</sup> Free radicals are reactive molecules able to damage other molecules by making them unstable as well. In biological systems, reactive oxygen species (ROS) are free radicals that cause harmful effects such as lipid peroxidation and oxidative modification of proteins and nucleic acids.<sup>32</sup> Endogenous oxidants are produced by the electron transport chain within the mitochondria, inflammatory enzymes, and cytochrome p450 enzymes.<sup>30</sup> The production of oxidants from these sources varies with the pathophysiological situation, and has a tendency to increase with age.<sup>33</sup> Individuals with steatosis and nonalcoholic steatohepatitis have higher levels of ROS production.<sup>33</sup>

Oxidative stress represses the expression of the CYP1A1 gene at the transcriptional level.<sup>34-36</sup> The activity of the CYP1A1 gene promoter is negatively regulated by hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) or by depletion of the antioxidant glutathione (GSH), decreasing the expression of the genes encoding CYP quantity.<sup>36</sup> The repression of CYP1A1 could be beneficial because this isoform can transform and therefore create potentially mutagenic compounds.<sup>36</sup>

Whereas suppression of CYP enzymes can reduce drug transformation, excessive and uncontrolled expression of CYP enzymes may also be detrimental. Cytochrome p450s reduce oxygen to produce pro-oxidant species, which, if not countered by antioxidants and antioxidant enzymes, create oxidative stress.<sup>33</sup> Up-regulation of CYPs has been linked to ROS production<sup>37</sup> in the absence of inadequate phase II metabolism. CYP2E1, involved in lipid peroxidation, is prone to producing ROS, particularly superoxide anions, hydroxyl radicals, and H<sub>2</sub>O<sub>2</sub>.<sup>33</sup> Oxidative stress causes two conflicting responses, both the adaptive response of up-regulation of antioxidant defense systems and ROS producing CYPs such as CYP1A1.<sup>35</sup>

## Age and the Microbiome

With advancing age there are changes in nutrition and increased use of medication that modify the composition of the microbial community of the gastrointestinal tract.<sup>38</sup> The use of nonsteroidal anti-inflammatory drugs (NSAIDs) can lead to mucosal damage.<sup>38</sup> Broad spectrum antibiotics can increase pathogenic bacteria such as *Clostridia difficile* in the colon.<sup>38</sup> Proton pump inhibitors used to treat peptic ulcers may lead to bacterial overgrowth in the small intestine<sup>39</sup> and can increase the presence of *C difficile* in the GIT.<sup>40</sup> While some studies demonstrate disrupted microbial flora as a result of PPI use, others found no connection.<sup>41</sup> In the GIT, the microbial species changes with age; *Bifidobacteria*, Firmicutes, and *Fecalibacterium prausnitzii* decrease and *E. coli*, *Proteobacteria* and *Staphylococcus* increase.<sup>42</sup>

While this paper focuses on the effect of CYPs on exogenous substances, the intestinal microbiome is also involved with the metabolism of drugs, dietary compounds and botanical substances.<sup>43</sup> Numerous drugs can be substrates for bacteria and human gut microflora exert metabolic activities on various dietary compounds, such as isoflavones, influencing bioavailability and bioactivity.<sup>44,45</sup> The increased GIT population of pathogenic bacteria such as clostridia can cause inflammation in the digestive system, altering CYP expression and function.<sup>46</sup> Therefore, it is important to consider the health of the microbiome and microbial metabolism as an important variable in determining the level of drug and botanical activity affecting the failure or success of treatment.

## Age and Cytochrome Enzymes

Numerous studies demonstrate reduced clearance of drugs in the elderly.<sup>19,15,47,48</sup> Factors affecting the pharmacokinetics of drugs include: liver volume, liver blood flow, kidney function, and hepatic enzymes. Cytochrome enzymes conduct the majority of the drug metabolism and clearance.<sup>48</sup>

Multiple animal studies have tried to determine whether the reduced clearance of drugs in the elderly is due to cytochrome enzyme changes that result from aging.<sup>46,47</sup> In rats, increasing age causes significant alterations in hepatic expression and activity of some, but not all CYP enzymes.<sup>49-51</sup> The activity of CYP2B, CYP3A have

demonstrated an age-related decline, whereas no changes in activities of CYP1A2 were found.<sup>51</sup>

When examining human data, there is some controversy in the literature regarding age-related declines in CYP content, and activity. Several studies concluded that there isn't a decline in human CYP with age.<sup>52-54</sup> On the other hand, it is estimated that metabolic clearance by cytochrome P450 enzymes (CYP) is approximately 30–50% lower in older compared with younger people.<sup>48</sup> Other studies have found age-related reductions in clearance of CYP substrates and the metabolism of certain CYPs.<sup>52,53</sup> For example, a reduction of CYP27B1 and CYP2D6 substrates was associated with increasing age.<sup>52,53</sup> Another study found 30% decrease in CYPs in patients over 70 years of age.<sup>47</sup> Age related decline in CYPs that have been found in *in vitro* and *in vivo* studies correlates with declines in CYPs observed as a result of inflammation and oxidative stress, often associated with aging. The conflicting data that have been found may result from the fact that ageing is associated with increased inflammation, and inflammation affects the expression of CYPs. While phase I enzymes are affected in the elderly, phase II appears to be relatively preserved.<sup>52</sup>

Though not necessarily a result of normal aging, the risk of developing liver disease does increase with increasing age. Normal liver function is an important determinant of the activity of CYPs, especially CYP3A4, which metabolizes a large number of widely used pharmaceuticals.<sup>55</sup> It is an enzyme that is highly susceptible to liver disease.<sup>56</sup> In contrast, CYP2D6 is relatively unaffected by liver disease.<sup>56</sup> The susceptibility of other major CYP drug-metabolizing enzymes appears to range between less susceptible than CYP3A4 and more susceptible than CYP2D6.<sup>56</sup>

Frailty is an inevitable decline in abilities usually associated with physical aspects of aging.<sup>58</sup> Markers for frailty include IL-6, associated with chronic inflammatory disease,<sup>57</sup> low serum albumin, and iron.<sup>58</sup> Practitioners treating frail individuals should use caution recommending substances that will require CYP metabolism.

## Other Age-related Factors affecting Pharmacokinetics

Age-associated physiological and pathophysiological changes can affect the clearance of xenobiotics. Aging increases the likelihood of organ dysfunction, diseases, and resulting medication used to treat these disease.<sup>59</sup> Polypharmacy increases with age and affects drug clearance.<sup>60</sup> With polypharmacy, drugs taken simultaneously may interact with medications inhibiting or inducing CYPs, leading to altered metabolism with concurrently taken drugs.<sup>59,60</sup> Several drugs, such as amiodarone, omeprazole, losartane, fluconazole, sulfaphenazole and cimetidine act as inhibitors of CYP2C isoenzymes, leading to decreased metabolism of other drugs, such as warfarin, causing potentially life-threatening consequences for patients.<sup>61</sup> Other drugs such as verapamil, ketoconazole, erythromycin, and nifedipine inhibit CYP3A expression, resulting in reduced metabolism of the CYP3A substrates and subsequent high drug concentration.<sup>61</sup>

Changes to body composition in the elderly, decreased muscle mass and increased adipose tissue lead to altered drug distribution and increased clearance of non-polar drugs.<sup>59,62</sup> Non-polar compounds tend to be lipid-soluble and so their distribution in the body increases with age, resulting in drug retention and as a result, increased half-life.<sup>62</sup>

Aging is associated with both a decrease in kidney mass and the number of glomeruli from 20–30%.<sup>62</sup> As a result, there is a decline in the renal glomerular filtration rate, decreasing renal drug metabolism and drug metabolite clearance.<sup>63</sup> The likelihood of developing deteriorating kidney function also increases with increasing age. Animal studies in chronic renal failure have shown a major down-regulation (40–85%) of hepatic cytochrome P450-mediated metabolism by specific CYP enzymes.<sup>59</sup> Patients with deteriorating renal function demonstrate reduced activity of the CYP3A and CYPD6 enzyme pathway.<sup>64,65</sup> Albumin levels tend to decline in elderly patients as kidney function decreases.<sup>66</sup> The reduced serum albumin concentration can affect pharmacologic activity of drugs that tend to bind albumin, increasing the concentrations of available drug beyond what would be anticipated. Low level exposure to bisphenol A, polyfluorinated alkyl acids, dioxins and furans, polycyclic aromatic hydrocarbons and polychlorinated biphenyls can all negatively impact renal function.<sup>67</sup> The most important pharmacokinetic change in the elderly is the reduction in renal drug elimination, emphasizing the importance of considering a patient's renal function with case management.<sup>68</sup>

The ability of the hepatocytes to metabolize xenobiotics depends on the capacity to extract the substrates from the blood and on the amount of available blood. Blood flow reduces by an estimated 20-50% with aging.<sup>62</sup> Decreased hepatic mass, structural changes such as pseudocapillarisation, and reduced blood flow through the liver may all decrease phase I metabolism by CYP enzymes.<sup>69</sup> The ability of the hepatocytes to extract xenobiotics from the blood is dependent on transporter proteins located within the liver.<sup>70</sup> Pseudocapillarisation can occur with aging and impede the transfer of various substrates onto CYP enzymes.<sup>69</sup> Specifically sinusoidal changes that occur in pseudocapillarisation contribute to hepatocyte hypoxia, thus reducing available oxygen for the CYP enzymes that are oxygen-dependent.<sup>69</sup>

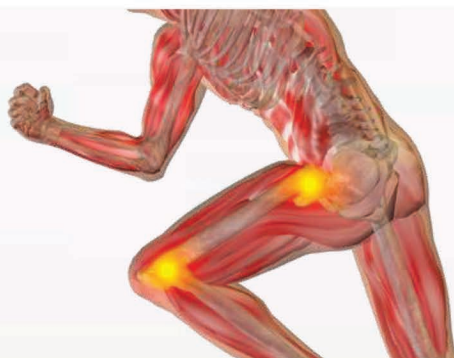
## Stress Response

Stressors that affect health arise from both physical and emotional sources, and are considered to be physiologically stressful because the adrenals are stimulated in response and release hormones. Stressors include emotional events, calorie restriction,<sup>71</sup> pathogens and toxins,<sup>17</sup> surgery,<sup>72</sup> sleep deprivation, infection and excessive exercise.<sup>73</sup> Psychological stressors are among the most potent activators of the hypothalamo-pituitary-adrenal (HPA) axis.<sup>74</sup> A variety of molecules are involved in the regulation of the HPA axis and stress including: corticotropin-releasing hormone, vasopressin, glucocorticoids, catecholamines (norepinephrine, epinephrine, and dopamine), cytokines, and adrenocorticotrophic hormone (ACTH).<sup>75</sup> Glucocorticoids, catecholamines, and cytokines impact xenobiotic metabolism.<sup>76</sup>



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## Psychological stress

Psychological stressors may indirectly modify the absorption and disposition of a xenobiotic through physiological changes, such as increased stress hormones, increased blood pressure, modifications in the cardiovascular, respiratory and gastrointestinal functions etc.<sup>77</sup> The acute stress response tends to shift blood flow towards the essential organs and away from the liver, small intestine, and kidneys, thus decreasing drug metabolism and elimination.<sup>77</sup> Psychological stress hormones such as glucocorticoids and catecholamines will directly regulate drug metabolism through regulation of CYPs.

Glucocorticoids and catecholamines play primary roles in stress-mediated regulation of several drug-metabolizing CYPs by altering CYP gene expression, transcription, and translation.<sup>78-80</sup> The transcriptional mechanisms by which glucocorticoids control the expression of CYPs involve direct and indirect binding of the CYP genes.<sup>6</sup> The quantity of glucocorticoids can affect the modulation of certain CYP genes. Glucocorticoids at low concentrations act as inducers of CYP2C and CYP3A, whereas at high concentrations, they have an inhibiting effect.<sup>81</sup> In general, stress will up-regulate CYP3A, CYP2A, CYP2C, CYP2D, CYP1A, CYP2J5 and down-regulate CYP2B and CYP2E1.<sup>17,55,61,81</sup>

The catecholamines epinephrine and norepinephrine bind to adrenergic receptors (AR) on hepatocytes, immune cells, and on pancreatic cells.<sup>81</sup> Binding of catecholamines to immune cells promotes the secretion of a number of inflammatory cytokines including TNF- $\alpha$ , IL-1 and IL-6. TNF- $\alpha$ , IL-1 and IL-6 induce the expression of CYP2C11 and CYP2D1/2.<sup>17</sup> Catecholamines bind to AR on pancreatic cells and stimulate the release of insulin. Insulin stimulates insulin receptors (IR) on hepatocytes, leading to the activation of intermediates that will affect CYP gene expression.<sup>81</sup> Both insulin and glucagon control the expression of CYP2, favouring down-regulation.<sup>22</sup> Therefore, both chronic (glucocorticoid mediated) and acute stress (epinephrine and norepinephrine mediated) will impact the expression of CYPs.

Psychological stress increases the release of inflammatory mediators IL-1, IL-6, and TNF- $\alpha$ ,<sup>76</sup> down-regulating CYP enzyme production. Psychological stress also leads to oxidative stress and subsequently activated NF-kB, which modifies CYP regulation at a post-transcriptional level.<sup>26</sup>

There are some similarities between the psychophysiological modulation of CYP genes between different species, but overall the changes are species specific. Therefore, animal studies cannot be reliably used to determine the CYP changes that result from psychological stress.<sup>82</sup>

## Management

Naturopathic doctors are in a unique position to address root causes and offer comprehensive dietary and lifestyle counselling for elderly patients and their caregivers. Understanding and applying

knowledge of the cytochrome changes that occur with stress and aging to practice management can help prevent and reduce adverse drug reactions and ensure patients are metabolizing pharmaceutical as well as natural products optimally. Caution needs to be taken when utilizing animal studies because modulation and expression of CYPs can be species specific.

Altered microbial composition in the elderly can be managed by supplementing with prebiotics and probiotics. Supplementation with inulin<sup>83</sup> and short chain fructooligosaccharides (FOS) increase bifidobacteria and can decrease the quantity of enterococci.<sup>84</sup> Supplementation with strains of *Bifidobacterium longum* and *Lactobacillus fermentum* have been shown to increase the quantity of bifidobacteria.<sup>85</sup> Patients should be educated regarding the negative impact that NSAIDs, antacids, and PPIs have on the microbial community composition. The establishment of a healthy intestinal microbiome may be an appropriate therapeutic goal in treating the elderly population.

With a decrease in smell and taste with aging, eating patterns change and dehydration is a common occurrence. The changes of blood volume and blood flow and the impacts on xenobiotic metabolism illustrate the importance of counselling elderly patients to maintain hydration. This is especially important given many older individuals are taking diuretics.

The biotransformation of xenobiotics is dependent on the proper function of the kidneys and liver, organs that decline in function with age. Liver support with hepatoprotective botanicals such as *Silybum marianum* could benefit elderly patients; one study reported benefit with 140mg of silymarin a day.<sup>86</sup> Supplementation with Coenzyme Q-10 may help manage the oxidative stress experienced by individuals with kidney failure.<sup>87</sup> Counselling the patient to reduce their exposure to kidney damaging environmental chemicals such as bisphenol A and polycyclic aromatic hydrocarbons could potentially slow down renal decline.<sup>88</sup> Refer to Table 4 for chemical sources of these renal toxins.

Management of epigenetic changes is not straightforward. Reducing exposure to compounds, such as alcohol and fried food, which cause epigenetic changes, is advisable. To combat oxidative stress, supplement with glutathione or N-acetyl cysteine, taurine, and selenium, which can support glutathione synthesis.<sup>89</sup>

Naturopathic doctors frequently employ gentle, lifestyle modifications such as deep breathing exercises, meditation, and counselling to address underlying stress within their patients. These non-pharmaceutical interventions are excellent therapies given polypharmacy is a frequent occurrence among the elderly population. As stress levels decrease, the stress induced modification of the cytochrome enzymes will change, altering the pharmacodynamics and pharmacokinetics.<sup>33</sup> Given the demonstrated effects of the glucocorticoid cortisol on CYP enzymes, cortisol modulators could improve patient outcomes by normalizing CYP expression.

Supplementation is still a consideration for healthy patients, following examination of current medications and potential interactions. Plant sterols can reduce physically induced cortisol peaks.<sup>90</sup> Phosphatidylserine might counteract the stress induced activation of HPA axis because it buffers the overproduction of cortisol and ACTH.<sup>91</sup> Administration of phosphatidylserine has demonstrated benefits in modulating the response to both physical stress as well as psychological stress.<sup>88,91</sup> In one study a dose of 400mg of phosphatidylserine blunted serum ACTH and led to a decrease of serum and salivary cortisol.<sup>92</sup>

An anti-inflammatory diet may help lessen the inflammatory mediated CYP changes, potentially lessening the adverse drug and botanical reactions that can occur. More specific interventions could be utilized on an individual basis. Antioxidants, such as vitamin E, help to protect against free radicals and combat oxidative stress.<sup>56</sup> Activation of Nrf2 by botanical compounds such as curcumin and sulforaphane may subsequently activate antioxidant enzymes and anti-inflammatory products to inhibit overactive CYP enzymes.<sup>98,102</sup> The activation of Nrf2 helps to mitigate oxidative stress, reducing the pathophysiology these oxidants cause including the inappropriate control of CYP enzymes.<sup>103</sup> Consumption of curcumin and sulforaphane either as food or supplements could prove useful to protect the CYP enzymes from oxidative stress.<sup>102</sup> Refer to Table 4 for additional management suggestions.

**TABLE 4: SOURCES OF CONTAMINATION OF ENVIRONMENTAL CHEMICALS<sup>88</sup>**

Environmental Toxin	Source
Phthalates	Shampoos, cosmetics, personal hygiene products, vinyl plastics, food packaging, intravenous tubing
Bisphenol A	Polycarbonate plastics, epoxy resins, intravenous tubing
Perfluoroalkyl acids	Electrochemical fluorination, telomerization, surface protection agents, sealants, surfactants, food packaging, non-stick cooking surfaces, stain-resistant sprays, fire-retarding foams
Dioxins and Furans	Pesticides, bleaching of wood pulp, waste incineration
Polycyclic aromatic hydrocarbons	Incomplete combustion of coal, oil, and gas; tobacco smoke, charbroiled meat

**TABLE 5: MANAGEMENT OF AGE AND STRESS EFFECTS ON CYP**

Compounds	Dose	Mechanism	Drug Interaction Examples and Other Effects <sup>12</sup>
Curcumin <sup>93</sup>	50 and 100 mg/kg	Inducer of the Nrf2 pathway, induces CYP3A4	Benzodiazapines alprazolam and midazolam
Urtica Dioica <sup>94</sup>	400mg/kg	Antioxidant mechanisms	
Rosemary officinalis <sup>95</sup>	Diet of 0.5% rosemary extract	Induce CYP2B2, Inducer of the Nrf2 pathway	Helps to reduce oxidative stress
N-acetyl cysteine (NAC) <sup>96</sup>	25 mg/kg and 50 mg/kg	CYP2E1 inhibitor	Affects conversion of several anesthetics, ethanol, and benzene
Phosphatidylserine <sup>97</sup>	200mg a day	Might counteract the stress induced activation of HPA axis. Buffers overproduction of cortisol and ACTH	Reduces stress response
Sulforaphane <sup>98</sup>	0.5 mg/kg/d	Inducer of the Nrf2 pathway	Helps to reduce oxidative stress
Ellagic acid <sup>99</sup>	10 and 30 mg/kg/d	Inhibits CYP2, inducer of the Nrf2 pathway	Affects a wide variety of drugs such as beta blockers, oral hypoglycemics, and antipsychotics. Helps to reduce oxidative stress
Indole-3-carbinol <sup>100</sup>	500 mg/d	Induces CYP1	Affects a variety of drugs such as haloperidol, clozapine, and olanzapine
Quercetin <sup>101</sup>	500 mg/day	Inhibits CYP1A1	CYP1E1 activates environmental carcinogens: polycyclic aromatic hydrocarbons and arylamines.







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# Loneliness and Social Isolation as Factors in the Decline of Health in Seniors

Katherine Chung, BSc, BA, ND (Cand.)



Isolation and loneliness are both terms used interchangeably and subjectively. However, it is important to differentiate the two terms to ensure proper clinical assessment and appropriate treatment intervention. When looking at isolation, we must differentiate between social isolation (which has objective components)<sup>1</sup> and perceived isolation (which has been shown to be a more important determinant of deleterious outcomes,<sup>2,1</sup> specifically depression).<sup>3</sup> It is important to note that social isolation and loneliness are not highly correlated with one another, meaning that social isolation does not necessarily mean that the patient feels lonely.<sup>1</sup>

When looking at loneliness, we must differentiate between social loneliness and emotional loneliness. Social loneliness is caused by a lack of social integration and participation (i.e. due to isolation) whereas emotional loneliness occurs when there is an absence of connection.<sup>4</sup> In this instance, connection is seen as either intrapersonal (i.e. the mind-body connection and/or self-awareness) or extrapersonal (i.e. interpersonal relationships and/or relationship with the transcendent).<sup>5</sup> It is important to screen and differentiate between these experiences in the elderly population because of their increased susceptibility to depression<sup>4,6</sup> and medically fragile state; putting this patient population at an imminent health risk and increased risk of death.

One way of approaching loneliness is through the biopsychosocial-spiritual model in which loneliness can be due to a biological predisposition (potentially related to inherited personality traits), psychological precipitating factors (such as grief and depression), objective social isolation,<sup>4</sup> and spirituality. Note that the definition of spirituality is also a subjective term and often used synonymously with religiosity. It is important to differentiate the two, not only for our clinical assessment (i.e. framing interview questions towards connection, rather than using theological terms that some patients may be hesitant to speak about) but also as a potential treatment intervention (i.e. mindfulness-based practices or providing resources/outreach to faith-based communities).

According to Sulmasy,<sup>5</sup> spirituality is an umbrella term for connection in which religiosity/religious practices fall under. Spirituality is defined as an individual's/group's relationship with the transcendent<sup>5</sup> (i.e. life after death or meaning of life) whereas religion/religious practice is an expression of one's spirituality, *generally* focused on a belief in a deity. Given this definition, we can then begin to change to the mind frame of spirituality – shifting our view from solely a religious practice towards the broader concept of connection with the outer world. In doing so, we can then see that spirituality can be expressed either through one's relationship with their religious practice *or* through nature, music, art, a set of philosophical beliefs, or interpersonal relationships.<sup>5</sup>

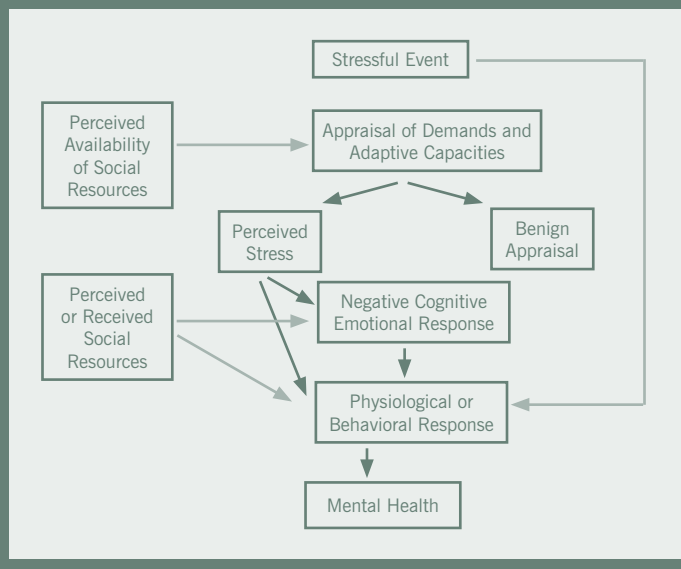
The biopsychosocial-spiritual approach of loneliness is advantageous for naturopathic clinical practice because it allows NDs to integrate an assessment method that encompasses all the naturopathic principles that we operate through. This approach provides a clear and holistic outline for our assessment of the senior population. This leads to a more in-depth and clear picture of the experience of loneliness, allowing naturopathic physicians to choose appropriate and individualized therapeutic interventions. Given the *general* nature of our clinical practices (i.e. longer initial visits, holistic and systematic approach to healing), we have a unique advantage to perform a more thorough assessment of this population and prevent the negative health outcomes loneliness and isolation cause – which will be discussed below.

## Mechanisms/Models relating social isolation and health outcomes

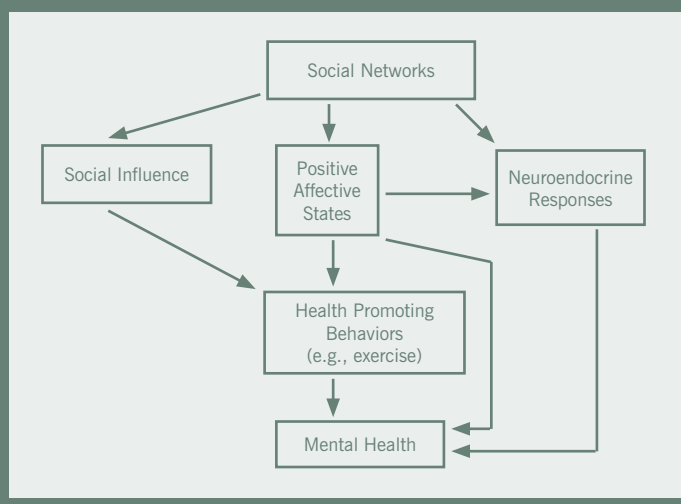
Research has shown that the relationship between social interaction and health outcomes is complex.<sup>7</sup> To determine appropriate clinical interventions and assessment methods, appropriate theories on how social relationships are linked to health outcomes is of utmost importance. There are two models proposed by Cohen et al:<sup>7</sup> stress-buffering model (Figure 1) and main effect model (Figure 2).

The stress-buffering model (Figure 1) hypothesizes that social support prevents and/or modulates stressful responses that have negative consequences to health outcomes.<sup>1,8,9</sup> It posits that the functional aspects of social relationships (e.g. perceived support) operate through this model.<sup>8</sup> Perceived isolation plays an important role in this model, as it has a strong influence on the cascade of negative emotional and behavioural responses to stressful events,<sup>1,8</sup> thus creating a downward spiral that would lead this patient population into a vicious cycle of negative health outcomes.

**Figure 1: Stress-buffering model-positing the effects of social relationships on health outcomes<sup>11</sup>**



**Figure 2: Main effect model positing the effects of social relationships on health outcomes<sup>11</sup>**



From a physiological perspective, this state can disrupt the Hypothalamus-Pituitary-Adrenal (HPA) axis<sup>1</sup> cascading down to an immunocompromised state and an increase in cardiovascular reactivity in response to stress.<sup>14</sup>

The main effect model (Figure 2) hypothesizes that there are several pathways in which participation in one's social network influences health outcomes.<sup>11,8</sup> In this model, social influences refer to the way in which members of the society obtain guidance (positive or negative) on health-related behavior (e.g. dealing with grief, finding purpose in life, or increasing physical activity). This model also posits that the structural aspects of social relationships (e.g. social participation) operate through this model.<sup>8</sup> Unlike the stress-buffering model, this implicates that positive social relationships have a beneficial effect on health outcomes regardless if the person is under stress or not.

The importance of social integration in this model lies in the positive psychological states felt (i.e. sense of purpose, belonging, and self-worth) leading to an increase of motivation for self-care, and modulation of neuroendocrine responses to stressful events.<sup>8</sup> This leads to healthier diets, more physical activity, emotional resilience in the face of loss, and positive health behaviours, such as social participation and treatment compliance.<sup>12,14</sup>

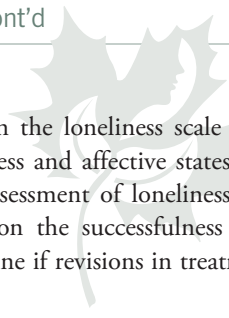
### Physiological effects of isolation/loneliness

Social disconnectedness has been associated with worsening physical health regardless of whether or not it prompts the feelings of loneliness or perceived isolation.<sup>3</sup> Those who suffer through social disconnectedness have been shown to experience systolic hypertension, poor sleep, and abnormal stress responses<sup>13,2,1,4,14</sup> and have increased C-reactive protein (CRP) and fibrinogen.<sup>14</sup> Objectively socially isolated patients in particular have been shown to have poorer recovery of systolic blood pressure and a greater increase in total: HDL cholesterol ratio.<sup>14</sup> However, if we look specifically at perceived isolation it predicts greater vascular resistance, elevated blood pressure, morning rise in cortisol, less restful sleep, and a sedentary lifestyle.<sup>2</sup>

Interestingly enough, a 2007 genome-wide study revealed that socially isolated persons had an under-expression of the anti-inflammatory glucocorticoid receptor pathway and an over-expression of pro-inflammatory NF-kB/rel transcription pathway.<sup>11,2,14</sup> Human and animal studies suggest that glucocorticoid resistant states, chronic sympathetic tonus, oxidative stress, and HPA activation has been secondary to perceived isolation.<sup>2</sup> This means that the patient did not have to be *objectively* isolated from society; as long as they *subjectively* felt isolated this negative physiological health outcome can occur. These physiological changes can have an immense impact on cognitive function and rate of cognitive decline. Studies have shown that the combination of APOE4, elevated ionized serum calcium, and objective/subjective loneliness were strong predictors of cognitive decline.<sup>11</sup> This further supports the theory that objective and subjective social isolation play equally important roles in the determinant of deleterious physiological and cognitive health outcomes.

### Cognitive effects of isolation/loneliness

Not only is objective/subjective social isolation associated with worsening physiological health, there is also a strong association of perceived isolation with the decline in mental health.<sup>3</sup> Studies from 1996 – 2001 have shown that social participation and social networks delay the incidence of cognitive decline in both men and women over the age of 65,<sup>15,16,17,12</sup> whereas higher levels of loneliness are associated with increased levels of depressive symptoms, independent of effects of age, gender, ethnicity, education, income, marital status, social support, and perceived stress.<sup>4</sup> This is because loneliness is associated with increased feelings of anxiety, anger, and negative mood.<sup>11</sup>



Although loneliness on its own has not been shown to affect mortality rate in seniors, mortality rates significantly increases when it appears in conjunction with depressive symptoms<sup>4</sup> potentially due to the altered immune and physiological responses. Perceived isolation has also been associated with heightened accessibility of negative social information,<sup>11,2</sup> meaning these patients are more prone to interpret or expect negative outcomes in a social situation. This, as one study reveals, may be because social isolation predicted weaker activation of the ventral *striatum* (a key component of the mesolimbic dopamine system<sup>11,2</sup>) to pleasant pictures of people than of equally pleasant pictures of objects.<sup>2</sup> Because of its impact on the ventral striatum, perceived isolation is also deemed a risk and contributing factor to overall cognitive performance, rate of cognitive decline, worsened executive function, negativity and depressed cognition, and heightened sensitivity to social threats.<sup>11</sup>

When looking at specific cognitive diseases, such as Alzheimer’s and various forms of dementia, loneliness has been associated with substantially increasing rates and progression of both pathologies.<sup>11,2,9,4</sup> In fact, the strength of association between social isolation and the incidence of dementia is comparable with other well-established risk factors, such as late-life depression, decreased physical activity, and low education levels.<sup>9</sup> This is also compounded by the findings that loneliness may increase the risk of clinical expression of dementia at the same degree as Alzheimer’s neuropathology does.<sup>9</sup>

### Assessing and monitoring for isolation

There are several approaches and/or methods to assess and monitor for isolation in the elderly. It is important to determine in what capacity the patient is experiencing isolation and/or loneliness (i.e. perceived or objective) to apply appropriate interventions and to monitor the success of that intervention.

The simplest way of assessing for loneliness is asking the patient if they feel lonely. This simple question asks directly about the feeling of being lonely.<sup>4</sup> However, the simplicity of this assessment method is also its Achilles’ heel. This method presumes an understanding of the concept of loneliness,<sup>4</sup> which we have discovered is not an objective concept and has no universally accepted definition, and does not integrate the biopsychosocial-spiritual understanding of loneliness. This method also fails to differentiate between social and emotional loneliness, which we have also learnt is important to determine for it allows for an appropriate intervention.

To overcome these issues, screening tools for social isolation/loneliness should measure several factors, including the number of contacts, feeling of belonging, fulfilling relationships, engagement of others and quality of network members.<sup>12</sup> One comprehensive and specific, assessment method is the UCLA Loneliness Scale (Figure 3). This is a 20-item questionnaire, which rates each item from 1 to 4 (1 = never; 4 = often). This scale is most commonly used and preferred by researchers and clinical practitioners (especially in a psychiatric clinical setting).<sup>4</sup> This assessment method is that it has high internal consistency, which is its strength. Studies using

this method have shown that scores on the loneliness scale were validated by other indicators of loneliness and affective states.<sup>18</sup> It also provides a more comprehensive assessment of loneliness and allows for a more in-depth feedback on the successfulness of a chosen intervention method (to determine if revisions in treatment protocols are required).

**Figure 3: The Revised UCLA Loneliness Scale**

**Directions: Indicate how often you feel the way described in each of the following statements. Circle one number for each.**

Statement	Never	Rarely	Sometimes	Often
1. I feel in tune with the people around me	1	2	3	4
2. I lack companionship	1	2	3	4
3. There is no one I can turn to	1	2	3	4
4. I do not feel alone	1	2	3	4
5. I feel part of a group of friends	1	2	3	4
6. I have a lot in common with the people around me	1	2	3	4
7. I am no longer close to anyone	1	2	3	4
8. My interests and ideas are not shared by those around me	1	2	3	4
9. I am an outgoing person	1	2	3	4
10. There are people I feel close to	1	2	3	4
11. I feel left out	1	2	3	4
12. My social relationships are superficial	1	2	3	4
13. No one really knows me well	1	2	3	4
14. I feel isolated from others	1	2	3	4
15. I can find companionship when I want it	1	2	3	4
16. There are people who really understand me	1	2	3	4
17. I am unhappy being so withdrawn	1	2	3	4
18. People are around me but not with me	1	2	3	4
19. There are people I can talk to	1	2	3	4
20. There are people I can turn to	1	2	3	4

**Note. The total score is the sum of all 20 items**

Both of these screening tools do not take into spiritual practices of an individual. According to Sulmasy,<sup>5</sup> initial research demonstrates that at least 41% of patients want their physicians to address their spiritual concerns, whether they identify as being religious/spiritual or not. Hodge et al. identified that many seniors indicated that their relationship with the transcendent was a central component of their lives and spiritual practices emerged as the most prominent spiritual need of this demographic.<sup>19</sup> Clinically, NDs should assess patients’ current manner of spiritual coping, their relationship with the transcendent<sup>5</sup> and their views on the meaning of life. Not only is it important to determine the positive effects of spiritual beliefs, it is imperative to determine how these beliefs are serving the patient (i.e. does this belief have a positive or negative impact in their worldview).

The effects of spirituality and religion on the perception of loneliness and isolation is complex; thorough discussion is required to understand the true impact spiritual beliefs have on the health outcomes of the senior population and is beyond the scope of this paper. However, it is clear that properly assessing and monitoring isolation/spiritual coping mechanism in the elderly population is extremely important. Not only does it circumvent the perpetuation of negative health behaviours and decrease the risk of isolation-related health decline, it also provides an opportunity for clinicians to facilitate social integration of their elderly patients. This can be through connecting them with faith-based communities, volunteer organizations that teach the elderly computer skills, or other community – based organizations that maintain (and potentially increase) their social connectedness – as discussed below.

### Barriers to the clinical assessment of loneliness and isolation

There are several barriers that complicate the clinical assessment of loneliness and isolation in the elderly population, one of which is language. In this instance, language can mean one of two things. The first is the most obvious which is not sharing a common language, but the second is commonly overlooked when assessing for spiritual practices, which is using language that is specific to a particular spiritual/religious practice (i.e. God or prayer or meditation) before the patient introduces these terms first. This is a barrier because spiritual/religious language does not necessarily resonate with some patient's worldviews and in many cases, patient's relationships with the transcendent or meaning of life is beyond the traditional confines of religious/spiritual beliefs.<sup>20</sup> By using an implicit spiritual assessment (i.e. more neutral terms such as connection or framing questions around what the patient does to cope with stress or to put them at ease), it will demonstrate in what capacity they express their spirituality (based on the definition discussed in the introduction) or what type of connection they need (which aids in choosing appropriate treatment interventions). This approach allows clinicians an avenue to assess patients who do not identify with being religious/spiritual or hesitate to overtly speak about their spiritual/religious beliefs.<sup>20</sup> For a non-exhaustive list of Implicit Spiritual Assessment Questions that assesses a patient's past, present and future spirituality, refer to page 227 of David Hodge's "Implicit Spiritual Assessment: An Alternative Approach for Assessing Client Spirituality".<sup>20</sup>

Other barriers that are not specific to the assessment of isolation/loneliness but play a major role in the assessment of the geriatric population are patients who are already cognitively impaired, patients who have decreased hearing/sight, and patients who normalize/down play their negative experiences due to their belief that it is part of the aging process and should just be accepted. Unfortunately, there are no assessment tools for loneliness that can be used for patients who have dementia or other cognitive impairment. This is unlike the assessment for patients with dementia who suffer from depression, in which case the Cornell Scale for Depression in Dementia was created and is used in many clinical settings.

### How can Naturopathic Doctors help?

With patients suffering from isolation, an appropriate therapeutic intervention should be implemented to minimize the risks of loneliness and/or social isolation and thereby improve health outcomes. Research has shown the complex relationship between social interaction and health outcomes<sup>21</sup> and there has been mixed success in different intervention methods.<sup>21</sup> This could be due to the fact that most proposed interventions focus on the social type of loneliness;<sup>4</sup> as we have discovered from the comprehensive literature presented, perceived isolation is actually a more important determinant of deleterious outcomes.<sup>2,1</sup>

A seven-point guideline proposed by Shearer and Davidhizar<sup>22</sup> provides a general overview of appropriate clinical interventions. Although this guideline was proposed to support the spouses of an elderly patient, it can also be applied to the patients themselves. This guideline also reflects the concurrent effects social isolation has on health outcomes while encompassing the comprehensive view of loneliness via the biopsychosocial-spiritual model.

These seven points are:

- 1) Assess (spouse) for loneliness
- 2) Offer support through active listening
- 3) Promote development of positive relationships
- 4) Facilitate maintaining relationships with others (including faith-based communities)
- 5) Assist positive reminiscing
- 6) Assist (patient) to deal with changes
- 7) Promote involvement in activities

Adding an assessment of spirituality (based on the framework discussed above) would be of added benefit and provides not only a holistic view of the patient but could also encompass more novel treatment interventions such as meditation, music therapy, and art therapy.

Although guidelines are available to aid in determining an appropriate therapeutic treatment protocol for lonely/socially isolated elderly patients, no standard of care has been proposed. There have been several intervention methods proposed in which clinicians can use to individualize a treatment protocol where the psycho-social aspect of the patient can be targeted clinically. These intervention methods can be used to enhance the patient's natural networks (ex: support groups or one-on-one support), increase emotional support, or address the cognitive and/or behavioural barriers to forming rewarding interpersonal relationships (ex: Mindfulness Based Cognitive Behavioural Therapy).<sup>21,8</sup> However, novel interventions are beginning to roll out and incorporating the use of technology (i.e. Skype, social media)<sup>4</sup> to assist in connection and social integration as it provides a medium for patients to receive audio and visual connection when friends/family cannot be

physically present. Although more literature is needed to support the use of these novel interventions, it is important to keep them in our toolbox considering the increase in tech-savvy nature of certain elderly populations and as the Generation-X group begin entering into this demographic.

The best approach to the prevention of negative health outcomes from social isolation, perceived isolation, or loneliness is an integrative approach. By mixing all of the different intervention methods, we maintain the naturopathic principle of *Tolle Totum* and ensure all pathways that are leading towards objective and subjective feelings of isolation are being addressed.

## Conclusion

Comprehensive literature and research has been done for decades and exemplifies the intimate relationship between social isolation, perceived isolation, and loneliness; and physical and psychological health outcomes. Currently, there is a plethora of research and theories proposing therapeutic interventions for those that are socially isolated and lonely. This demonstrated the importance of providing additional support (in the form of physical, psychological, and spiritual interventions) to isolated elderly patients, especially those who are experiencing marital or physical transition or death,<sup>14</sup> and that only regular interactions-rather than a large social network-are needed to stimulate the brain, release stress, and contribute to healthy behavior.<sup>9</sup> Supporting literature shows that social support can encourage older adults to seek preventative or appropriate medical treatment leading to better adherence to medications/treatment plans and participate in less negative health behaviour.<sup>1</sup> The most important conclusion to be gained from this research is that loneliness and isolation should be sought for in any medical/psychiatric assessment<sup>4</sup> in the geriatric population to keep to our naturopathic principles of *Tolle Causam, Tolle Totum, and Praevenire.* 🍂

## About the Author

**Katherine Chung, BSc, BA, ND (Cand. 2016)** is a current student and TA of traditional Chinese medicine at the Boucher Institute of Naturopathic Medicine (BINM) and a copywriter for Professional Health Systems. She completed her undergraduate degrees in biology and cultural and spiritual psychology from the University of Calgary. Upon graduation from BINM in June 2016, Katherine aims to integrate both her science and arts background into her naturopathic practice, with a special interest in mental illness. Katherine Chung resides in Vancouver, BC and aims to practice in the Lower Mainland and complete the residency program at BINM.

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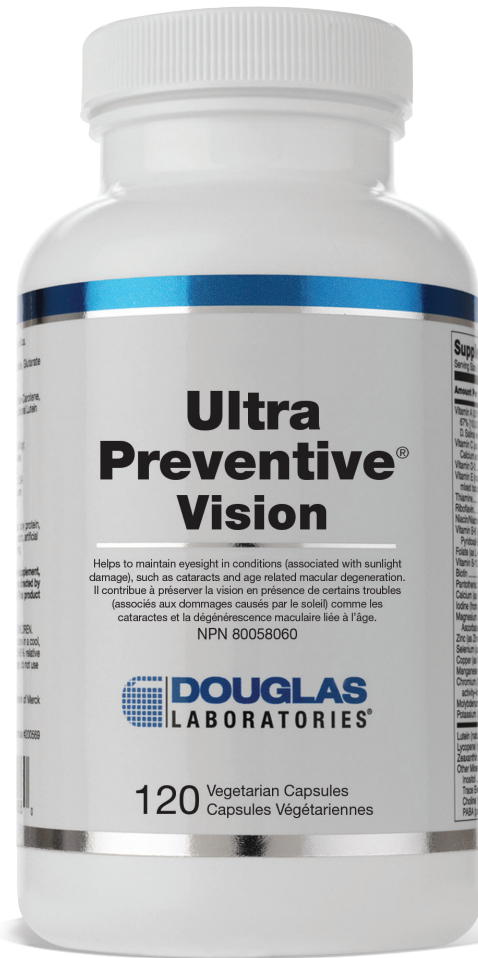


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# Considerations for Caregivers, Social Support and Cognitive Assessment

Dr. Laura Belus, ND, Dr. Jessa Landman, ND, Dr. Ellen Wong, ND

With a rapidly aging demographic, naturopathic doctors need to be aware of the changing landscape of older adult care. This includes the critical role of caregivers, the quantitative and qualitative aspects of social support, as well as the cognitive assessment tools for prevention and disease progression.

As healthcare practitioners focused on all facets of well-being, the importance of a complete care model, including gathering specific information, developing an assessment and making a diagnosis, is paramount to a naturopathic doctor. This article aims to highlight undervalued areas of older adult health and how naturopathic doctors can participate in improving outcomes for this population.

## The Rewards and Challenges of Caregiving

The changing population demographics in Canada mean that an aging population will require more caregiving than possibly ever before. The health issues that may cause a patient to require a caregiver ranges from cancer and dementia, to chronic renal or heart failure. As practitioners, we need to inquire about the health status of our patient's family members and identify those who may be in a caregiver role. The reasons for this are many, and include the unfortunate reality that caregivers often have a poor quality of life, and are often displeased with the support they receive from the mainstream health care system.<sup>1</sup>

Caregivers can be parents, spouses, siblings, children or friends. The tasks for caregivers are numerous, and include helping with personal care, transportation to and from appointments, housework, management and coordination of medical care, administration of medication, emotional support, navigating social services, managing money, tending to insurance matters, grocery shopping and meal preparation. More than half of caregivers in one study reported having more tasks than they could deal with.<sup>1</sup> In addition to daily medical and living demands, caregivers may find themselves faced with the extra tasks of learning about the disease, learning new medical terms, and making sure the patient has all the information they need to make decisions about their care, such as information about suggested treatment and available complementary care.

In many instances caregivers may experience a slow but escalating list of responsibilities and demand on time, such as in the case of a slowly progressing disorder (e.g., dementia), or may be suddenly thrown into the role without any prior training or experience due to an acute emergency (e.g., stroke). Regardless of the situation, caregivers will better adapt if they have higher self-efficacy. Self-efficacy is conceptually defined as the belief that one can perform confidently and capably in a given situation.<sup>2</sup> It is an important determinant of emotional and behavioural responses to stress. Research has demonstrated that low self-efficacy corresponds to negative outcomes in caring, such as increased rates of depression, lack of ability to respond to disruptive behaviour, inability to control upsetting thoughts and increased levels of perceived stress.<sup>3</sup>

Caregiver burden is defined as the extent to which caregivers feel that their emotional or physical health, social life, and financial status have suffered as a result of this role.<sup>2</sup> Caregiving often requires a large time commitment, and may involve intense physical exertion (e.g., transferring patients from beds to wheelchairs), declining social engagements due to feelings of worry or guilt about leaving a loved one, and unpaid time off work.

Research has identified factors that influence the level of perceived caregiver burden. Dementia is a common condition that requires some level of caregiving, and as many as 80% of those with dementia are cared for in their homes by family members.<sup>1</sup> The level of burden perceived by the family caregiver, quite surprisingly, does not demonstrate any correlation with the duration of time spent as a caregiver nor with the progression of memory loss.<sup>1</sup> However, caregiver burden increases when the patient exhibits more severe behavioural and emotional problems, including depression.<sup>4</sup> Active coping skills, management strategies, firmness in directing behaviour, and greater family and social support are associated with lower levels of caregiver burden.<sup>4</sup>

Other conditions requiring care may have disease specific challenges that contribute to caregiver burden. For example, caregivers of those with amyotrophic lateral sclerosis (ALS) have been shown to experience an increased level of burden when worsening symptoms of respiratory failure require ventilation,<sup>5</sup> likely related to the caregiver's responsibility for the maintenance of equipment and the stability of the patient, both significant stressors. Caregivers of patients with chronic obstructive pulmonary disorder are often spouses, and worsening burden is associated with strains on the marital relationship due to declining energy for sexual intercourse, coughing interfering with intimacy, and lack of social life due to fatigue and dyspnea.<sup>6</sup>

In general, caregivers of patients diagnosed with a condition of a progressive nature (except dementia) tend to experience increased strain as the condition worsens. For those caregivers of patients with advanced COPD, more symptoms of anxiety and depression were noted, and self-rated health was significantly worse when compared with caregivers of patients of early COPD.<sup>7</sup> Likewise, caregivers of patients with a cancer diagnosis who were receiving palliative care reported greater impairment in physical functioning and general health when compared to caregivers of patients with a diagnosis receiving active treatment.<sup>2</sup>

Caregiver burden can manifest as chronic fatigue, a sense of frustration, guilt, depressive symptoms, excessive distress and loss of control.<sup>8</sup> Recognizing 'caregiver neglect' as a level of caregiver burden is important as this 'neglect' can negatively affect the patient's progression of the disease and the risk of the need for a care facility earlier than later.<sup>9</sup> Addressing caregiver burden early on can promote the health of both the caregiver and the patient.

The importance of recognizing and addressing a caregiver's state of health cannot be overstated. Advanced levels of caregiver burden correlate with higher morbidity and mortality in caregivers.<sup>1</sup> A recent review found that the most prevalent physical problems reported by caregivers included sleep disturbance, fatigue, pain, loss of physical strength, loss of appetite and weight loss.<sup>9</sup> Fatigue was reported to affect relationships and impact mood, and to result in decreased motivation, ability to concentrate, and ability to perform usual activities. In studies of cancer patients and their caregivers, anxiety and depression rates among caregivers ranged from 16% to 56%, and in some studies, exceeded patients' levels.<sup>10</sup> Other studies have reported that the rates of post-traumatic stress disorder were found to be about 4%.<sup>11</sup>

As health care physicians, it is important to know how to screen for caregiver burden. The Zarit Burden Interview is the most widely used scale to assess caregiver burden, and can be obtained free of charge. It is also important to identify risk factors for those who are at increased risk of anxiety and depression. It has been found that caregivers at increased risk of depressive symptoms include younger females, those reporting lower socioeconomic status and lower education levels, unmarried caregivers living with the patient, those with pre-existing health conditions, caregivers of older patients or those with advanced disease, and caregivers with less social support are at increased risk of developing depression.<sup>8</sup>

Despite the stressors and possible health issues that may arise as a result of caregiver burden, it is important to inform patients of the positive aspects of caregiving as well. For instance, patients with COPD who have a caregiver are less likely to smoke, have a better exercise capacity, have better adherence to medications and report less frequent emergency room visits.<sup>7</sup> Rewards of caregiving for the caregiver may be the self-discovery of strength in hard times, a sense of self-worth and personal growth, feeling closer to the patient,<sup>12</sup> helping the patient to stay at home for as long as they can,<sup>7</sup> a sense

of accomplishment,<sup>3</sup> and happiness over quality of time spent with the patient. Caring for the patient may also help caregivers to accept the death of the patient and work through their grief.<sup>8</sup>

## Considerations for Older Adult Social Support

Social support has a strong impact on older adult's health and is an independent risk factor in later life. Lack of social support has been correlated with many chronic diseases and for mortality, comparable to other well-established risk factors such as blood pressure, weight and overall nutritional status.<sup>14,15</sup> In the elderly demographic specifically, medical and social factors have a complex interplay that affects important health measures such as cognitive function, levels of distress and overall quality of life.<sup>16</sup>

The effect of social support on individual health outcomes is complex and multifaceted. Understanding the variables of social support is critical to providing appropriate care. Initial research in social support for the older adult population dates back to the mid-1970s, and has since provided valuable information with respect to mental and physical health and illness, in addition to public health concerns, such as long-term care facilities, public programs and health insurance spending.<sup>14,17-19</sup> Notwithstanding these advancements, there remains a lack of universal acceptance of the full definition of social support. This article aims to more clearly define the components of social support, the health outcomes with which it is associated and the validated measurement tools for the naturopathic clinician.

There exist several wide-ranging variations of the term social support. Broadly speaking, social support can be divided into two components: structural and functional. These components distinguish between the number of connections – known as structural – and their associated meaning to the individual – known as functional. We will examine each of their effects on various health outcomes. First, structural social support is the most commonly measured component in research studies as it pertains to types of networks and number of social connections. It follows a very sociological perspective and examines the interconnectedness of social ties towards one another. For example, belonging to a community club and a religious group are both structural types of support that allow an older adult to connect with members of their local community based on common interest. Second, in contrast, the functional component of social support looks at the specific significance that each particular relationship serves. This is more of a psychological view as it examines *how* the associations personally affect the individual.<sup>21</sup> Using the previous example, the community club may encourage the older adult to feel a sense of purpose, while the religious group may foster feelings of belonging and friendship. The functional meaning of social support differs based upon the individual and needs to be assessed as such. This aspect is often overlooked in older adults, as many clinicians falsely assume a greater number of networks translates to improve health outcomes. Instead it is the meaning and feelings behind social support connections that are most valuable at evaluating their benefits.

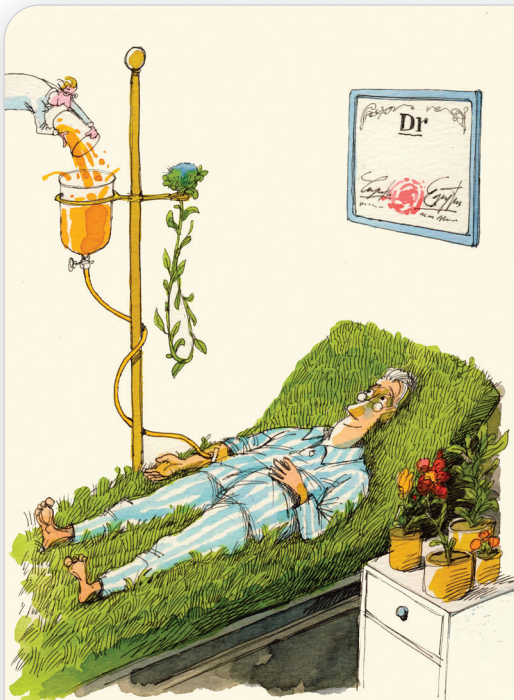
In 1986, one of the most comprehensive definitions of social support, proposed by Barrera,<sup>22</sup> suggested that social support is comprised of three subtypes that are inter-related. His concept of social support categories includes embeddedness, received support, and perceived support.

- **Social embeddedness** assesses the frequency of contacts between an individual and their social network. A person who is embedded socially would voluntarily belong to and interact with numerous organizations or social groups. A lack of social embeddedness can contribute to feelings of social isolation and is also associated with symptoms of loneliness and depression.<sup>23</sup> Caution is advised when clinicians research “social isolation” as distinct from simple “embeddedness” in studies to be referenced for patient care.
- **Received support** is defined as the amount of tangible help received, as from a caregiver, healthcare practitioner or friend. It is a useful reference point when measuring effects of caregiving on patient outcomes. Received support highlights an important quantitative measure of social support in relation to public health policy and long-term care programs.
- **Perceived support** measures the extent to which an individual experiences having or receiving support from others. Although it is a subjective measure, it has been shown to be the strongest predictor of clinical health outcomes such as decreased mortality, reduced cognitive decline and reduced severity of depression compared to examining the other two facets of social support.<sup>14,20,24</sup>

More recently in 2007, Dr. Neil Krause, a researcher in older adult health at the University of Michigan, further divided support into three types: enacted support, negative interaction, and anticipated support.<sup>25</sup> Each of these types describes how an individual builds, maintains and feels about their social ties.

- **Enacted support** describes feeling esteemed and valued by the use of emotional, tangible and informational methods.
- **Negative interaction** pertains to conflict and disagreements that accompany some social relationships. When this occurs, expected biases towards negative interaction persist among new and potentially supportive relations in different contexts. This leads to a weakened belief in the benefit of social support.
- **Anticipated support** ties in with the idea of perceived support; as one develops a strong, positive association with a friend or partner and feels a sense of security, that individual has hope and positive regard for the future, should they need assistance of any kind.<sup>25</sup> Paradoxically, it has been shown that a strong sense of perceived support provides older adults with the coping skills needed to reduce their reliance on their support networks.<sup>20,26</sup> These findings support the concept that a strong psychological belief system is directly related to positive, more independent behavioural outcomes with far-reaching practical applications in utilizing cognitive tools to improve health measures.

The connection between a strong social support network and positive health outcomes is not a new idea. In fact, it has been well documented that social support is positively associated with



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reduced cardiovascular disease, depression, improved quality of life for individuals with diabetes, even improved oral health (reduced risk of edentation, tooth & root decay).<sup>27</sup> However the mechanisms contributing to reduced mortality through social support are poorly understood. Lyyra and Heikkinen described the pathways by which aspects of social support contribute to increased longevity in 2006, in a study of over ten years' duration with female adults over 80 years of age. They concluded that those women with the highest ratings of *non-assistance* perceived support (reassurance of worth, emotional closeness and sense of belonging) had a 2.5-time lower likelihood of death than those with the lowest ratings.<sup>14</sup> They utilized the Social Provisions Scale (SPS), a comprehensive measure which classifies perceived support into assistance and non-assistance based subscales. This highlights which aspects of social support older adults choose to weigh most heavily regarding improved health. It appears that the mere feeling of inclusion and worth are much stronger predictors of longevity than the comfort of knowing a support system is present and available.

Although there are many instruments to measure social networks, there are fewer tools that truly encompass social support in its entirety. In order to serve as a clinical screening tool with maximal utility, the scale should include all areas of social support. Both quantitative (structural) and qualitative (functional) measures of support should be noted. This allows a practitioner to assess areas of concern, improvement, and greatness clinical utility.

As mentioned earlier, the Social Provisions Scale (SPS) is a 24-item scale based on the pioneering work of Weiss, outlining the six categories of social relationships: attachment, social integration, reassurance of worth, opportunity for nurturance, guidance, and reliable alliance.<sup>14,17</sup> This self-administered, perceived support measure has been examined for convergent and divergent validity, and has shown a strong reliability of 0.92.<sup>14,28</sup> It is important to note that the SPS does not assess for particular sources of structural support, but rather, how their support network contributes to overall perceived social support – or functional support.

Social support is a multifaceted concept. Most research fails to either clearly define this idea, or selects only a single proponent of it when tracking its measurements. More comprehensive measures are needed in order to social support and to improve clinical outcomes, especially in older adults. Most notably, the idea of perceived social support, a qualitative measure, rather than number of connections, a quantitative measure, holds a strong presence in reducing all-cause mortality and should not be overlooked when assessing older patients. The concept of social support in its entirety needs further study regarding the psychological and coping skills of the older adult.

## Considerations for Cognitive Assessment

At present, preliminary assessment of cognitive decline begins with either caregiver concern, patient inquiry or healthcare provider suspicion. However, at the early stages of cognitive impairment, signs and symptoms can be masked by either denial or coping by

both the patient and the patient's family.<sup>1</sup> A delay in diagnosis can also be due to some symptoms of cognitive impairment mimicking those of other conditions including: normal age-associated memory changes, depression, drug reactions, vision and hearing decline.<sup>29</sup>

The National Institute of Neurological, Communicative Disorders and Stroke-Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) classifies Alzheimer's disease as definite (clinical diagnosis and histologic confirmation), probable (clinical diagnosis without histologic confirmation), or possible (atypical clinical features not due to other diagnosis and no histologic confirmation).<sup>30,31</sup> While there have been new developments in research, there are still no brain imaging techniques or laboratory measures that can definitively help with the diagnosis of mild cognitive impairment or Alzheimer's disease. It is therefore important for primary healthcare providers to recognize early risk factors and warning signs, apply appropriate screening tools, and assess daily functioning, behavioural symptoms and co-morbidities.

Upon initial suspicion of cognitive decline, a healthcare practitioner should note and/or inquire about risk factors that include age, female gender, history of head trauma, limited education, family history of Alzheimer's Disease, history of smoking, obesity and history of cardiovascular diseases (stroke, hyperlipidemia, hypertension, diabetes, hyperinsulinemia).<sup>29</sup> The medical evaluation should include screening for conditions that mimic Alzheimer's disease and inquiry about recent illnesses or injuries (including epilepsy), new over-the-counter medications, new prescription medications (benzodiazepines and anti-cholinergics can mimic memory loss), change in supplements, use or exposures to illicit drugs and current or historic exposure to environmental toxins. Laboratory tests that can help rule out conditions mimicking Alzheimer's disease include CBC (anemia or infection), glucose, thyroid, liver and renal function, electrolytes and vitamin B12 levels. Practitioners should also be mindful of screening and monitoring common comorbidities that may include cardiovascular disease, infections, pulmonary conditions, renal insufficiency and arthritis.<sup>32</sup>

Following risk factor inquiry and ruling out other potential conditions, a healthcare practitioner should consider warning signs of Alzheimer's disease. According to the Alzheimer's Association, the following are ten key warning signs:

- memory loss
- difficulty performing familiar tasks
- problems with language
- disorientation to time and place
- poor or decreased judgment
- problems with abstract thought
- misplacing things
- changes in mood or behaviour
- changes in personality and loss of initiative.<sup>32</sup>

After identifying possible risk factors and warning sign, use validated screening tools to further identify the possibility of Alzheimer's diagnosis. Although no validated screening tool is both 100% sensitive and 100% specific, they can provide reasonable evidence that impairment exists and further action can be discussed with the patient. Widely used cognitive assessments are the Mini-Mental State Examination (MMSE), the Mini-Cog, and the Montreal Cognitive Assessment (MoCA).

The MMSE assesses six areas of cognitive function, including orientation, registration, attention/calculation, recall, language and ability to copy a figure. There are 30 items, requiring approximately 10 minutes for a total of 30 points in which a score of less than 23 indicates cognitive impairment. The MMSE is fairly quick to administer, with a sensitivity of 79% and a specificity of 78%.<sup>29</sup> It can be used to track progression over time but is not a good assessment for early Alzheimer's Disease.<sup>33</sup> Results can also be biased from age, race, education and socioeconomic status.<sup>34</sup>

The Mini-Cog combines a 3-item recall test and a recall distractor with a sensitivity of 76%, specificity of 89%<sup>1</sup> and can be a powerful indicator if activities of daily living are impaired.<sup>35</sup> It's easier and quicker to administer than the MMSE (2 items with a total score of 5 and in approximately 3 minutes), with less bias on those with low socioeconomic status or less education than the MMSE. It may also be easier to administer to non-English speaking populations.<sup>34</sup>

MoCA is another tool that is often used in a primary care setting to determine mild cognitive impairment, especially frontal lobe and executive dysfunction. It does not seem to be biased for various cultural and educational differences.<sup>36</sup> In those who score within the normal range on the MMSE, the MoCA appears to have high sensitivity of 90% for mild cognitive impairment and 100% of mild Alzheimer's disease.<sup>37</sup>

After employing screening tools, the next step is to assess how this condition affects the patient's and caregiver's life. Using validated tools to examine daily function is instrumental in tracking the burden on both patient and the caregiver. While a preliminary interview can indicate basic day-to-day functions such as eating or use of the bathroom, the IADL (daily functioning assessment tool) is the most widely used tool to measure more complex areas of activities such as using the telephone, traveling, shopping, preparing meals, housework, taking medication and managing money. The scale is rated by both the patient and the caregiver and is based on the scale of I (independent), A (requires assistance) or D (dependent).<sup>38,39</sup> This tool takes approximately 10-15 minutes to administer.<sup>29</sup> The Functional Assessment Questionnaire (FAQ) was developed from the IADL in which the patient is scored from 0 (independent) to 30 (dependent). The range of areas surveyed include ability to write cheques or pay bills, assemble tax records or business affairs, shop for clothes, household items or groceries, play games such as bridge or chess or work on a hobby, heat liquids or turning off stove,

prepare a balanced meal, keep track of current events, pay attention and understand TV, book or magazine, remember appointments, occasions, and medications, and travel out of current neighbourhood by driving or arranging public transport.<sup>29</sup>

Following assessment of activities of daily living, the healthcare practitioner then assesses behavioural symptoms such as anxiety, agitation, depression or apathy as over 80% of patients with Alzheimer's disease will experience these at some time during the course of their illness.<sup>29,40</sup> Either the Neuropsychiatric Inventory Questionnaire (NPI) or the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) can be used, although these questionnaires tend to be more utilized in observational and research settings.<sup>29</sup>

Lastly, caregiver burden should be assessed. Family caregivers are often increasingly responsible for caring for the patient as his or her skills deteriorate. The caregiver may be fully responsible for administering medications, performing activities of daily living and maintaining the patient's contact with various healthcare providers. Due to the added responsibility and the knowledge that Alzheimer's Disease is likely to cause deterioration of skills, caregivers often experience higher rates of depression and physical illness themselves.<sup>41</sup> Ensuring that the caregiver receives adequate support and rest is crucial for both the well-being of the caregiver and the patient.

## Summary

- Due to the aging nature of our population, caregivers will be required more than ever. It is extremely important to recognize and address caregiver burden in clinical practice, as caregivers often have a negative quality of life.
- Perceived support (by the patient) has been shown to be the strongest predictor of clinical health outcomes such as decreased mortality, reduced cognitive decline and reduced severity of depression
- Clinical measurement tools such as the 24-item Social Provisions Scale (SPS) for social support and the Montreal Cognitive Assessment (MoCA) for both mild cognitive impairment and early Alzheimer's disease should be utilized as assessment tools

## Future Direction

An aging population presents several areas to be aware of for any naturopathic practice. These include obtaining a thorough, objective patient assessment, understanding the social ties and their individual significance to the patient, and the role of supportive caregivers who acknowledge the health challenges involved. These considerations of older adult care are vital to all healthcare practitioners, in particular naturopathic doctors, who should strive to both educate and empower elder patients and their families to bring about long lasting vitality and improved quality of life. 🌱

## About the Authors

**Dr. Laura Belus, ND** is a graduate from the Canadian College of Naturopathic Medicine and is passionate about cardiovascular health, stress management and aging well. To further these interests she has worked with New York City's integrative cardiologist Dr. H. Schwartz and has spoken at the 2014 & 2015 annual Older Adults Centres' Association of Ontario conferences. Dr. Belus, ND, continues to provide educational seminars in her local community of practice in Burlington, Ontario.

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