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2018-2019 Incentive Grant Recipient

Final Report

June 17, 2019

## **Introduction**

This current research analyzes patient-reported information regarding response to levothyroxine in relation to consumption of selenium-containing foods or supplements. Healthcare professionals' knowledge of this information has the potential to shed further light on the effects of selenium on thyroid function, possibly paving the way for providers to titrate levothyroxine to the daily dose that best helps patients maintain a euthyroid state with minimal symptoms of hypothyroidism.

Related to increased hypothyroidism symptoms and poor quality-of-life is patient use of concomitant OTC supplements. In a 21-question survey administered to patients taking levothyroxine, 51.8% admitted to taking dietary supplements regularly.<sup>1</sup> Many of these supplements such as iron, calcium, and magnesium have been known to decrease the absorption of levothyroxine and therefore, negatively affect a patient's thyroid health. Research has recently shown that selenium supplementation may *positively* affect thyroid health.

Selenium content changes are of concern for patients with thyroid disease because selenium concentration in the body is highest in the thyroid gland. This concentration has been shown to be inversely related to thyroid tissue damage, goiter, and other thyroid complications.<sup>2</sup> Selenium is an essential element that plays a vital role in thyroid hormone synthesis and metabolism. Selenium also has antioxidant properties, fending off cancer and autoimmune pathologies. Patients with autoimmune thyroiditis require adequate selenium in the body to reduce production of anti-thyroid peroxidase antibodies. Thyroid peroxidase is an enzyme important to the thyroid gland because it functions to produce thyroid hormones. If anti-thyroid peroxidase antibodies are present, attack on normal thyroid tissue occurs.<sup>3</sup>

The recommended daily allowance of selenium for adults is 55 mcg which is a goal that has traditionally been met by eating a healthy diet. Deficiencies, however, have been reported in recent years due to environmental changes that have altered selenium content in the soil. This variance has affected selenium content found in locally-grown foods. Selenium is available as a stand-alone or combination daily supplement (multivitamin with minerals and fish oil) but is most often found in foods. Selenium is commonly found in bread, fish, eggs, meat, and poultry.

Many studies have implemented selenium supplements to aid in treating patients with thyroid disease. A trial in the United Kingdom, although inconclusive, suggests that participants from another geographic area where daily selenium intake might not be deemed adequate could show benefit to patients.<sup>4</sup> The CATALYST trial added a quality-of-life questionnaire to gain direct insight on patients' perspective on their treatment, and this will be incorporated into this current study with the same motive.

These existing trials have highlighted barriers to proper thyroid management and have gleaned patient assessment of quality-of-life based upon current regimens.<sup>5</sup> For this project, an additional piece was added to relate these documented observations to patient assessment of current intake of selenium-containing medications and/or foods to explore another possible area of intervention to better care for hypothyroid patients in the community.

## **Methods**

Following IRB approval and selection of four pharmacies based in Chicagoland, research was conducted in the following manner:

1. A questionnaire was created and questions (Appendix I) were imported into an online survey engine. A document was created with those same questions to use as a hardcopy of the questionnaire.
2. Copies of the questionnaire were distributed to four pharmacies in the Chicagoland area. A pilot was started a week prior to get an idea of usability and sustainability of distributing the questionnaire within workflow.
3. Attempts were made to partner with the American Thyroid Association (ATA) to increase validity and widespread support of the new research, but due to the relatively short time frame of about 3 months for data collection, research proceeded without the external participation.
4. Patients on levothyroxine were identified by running a national drug code (NDC) report and generating a list of patients on any strength of levothyroxine. Patients were contacted via phone about willingness to take the questionnaire. If willing, a copy of the survey was attached to items ready for pick-up for the patients, and the questionnaire administered when they visited the pharmacy. A questionnaire was also placed into prescription bags at the final pharmacist check if levothyroxine was one of the medications being checked. As part of the out-window counseling and sale process then, each patient was asked if they would be willing to take the questionnaire. For those patients who preferred to take an electronic version of the questionnaire, they were provided with the link to the online version.
5. Prior to answering the research-related questions, patients answered a series of questions to help determine if they would be included or excluded from taking the questionnaire. Inclusion and exclusion criteria were as follows:
  - a. Inclusion Criteria: 18+ years of age, documented hypothyroidism, current treatment with levothyroxine
  - b. Exclusion Criteria: Treatment with any other thyroid management agent, active malignancy, surgery within 6 months of study entry, s/p complete thyroidectomy, active bacterial or viral illness, severely immunocompromised (HIV/AIDS, chronic steroid use, transplant), impaired digestion and intestinal absorption (Crohn's, IBD, chronic diarrhea, colitis, extensive bowel or intestinal surgery)

- i. Were assessed and documented prior to consideration of questionnaire distribution
6. Completed questionnaires were collected and placed in a folder to be retained within the pharmacy. These questionnaires were gathered and analyzed collectively at the conclusion of the study.
7. Patients could elect to fill out a slip at the end of the questionnaire with their name, phone number and/or e-mail address to enter themselves in a raffle to win one of these four prizes for their participation:
  - a. Keurig
  - b. Portable Bluetooth speaker
  - c. \$100 VISA gift card
  - d. FitBit

Winners were anonymously drawn at the conclusion of data collection and contacted to claim their prizes. There were three winners drawn from the entire pool of participants across the four participating pharmacy sites.

Data was analyzed using SPSS software, generating frequency and correlation data.

## **Results and Discussion**

Of the participants who completed the questionnaire (n=64), sixteen patients were eliminated due to a variety of reasons, in alignment with the exclusion criteria.

<b>Number of Patients Excluded</b>	<b>Reason for Exclusion</b>
2	Active malignancy
8	Taking an additional thyroid medication
4	Got a piece of thyroid removed
2	Pregnant or planning to become pregnant

Frequencies were generated to show details about participants' levothyroxine use and thyroid management.

- The average daily dose of levothyroxine taken was 99 mcg
- The strengths of levothyroxine most represented in this study were 100 mcg, 88 mcg, and 50 mcg
- The average number of years participants reported taking levothyroxine was 10.46 years or ~10 years
- A chi-square analysis of food sources with highest selenium content (brazil nuts and pork) in relation to quality-of-life (QOL) was significant (P<0.049)
  - 0-1 servings or 2+ servings per week of these foods were compared to participant-reported QOL (low vs. high)

- Though not statistically significant, nearly half (43.7%) of participants labeled their QOL a 0 (very poor), 1 (poor), or 2 (neutral)

Participant behaviors surrounding their thyroid therapy were assessed to see if there was correlation between these behaviors or these feelings and consumption of selenium-containing supplements or foods. Previous studies analyzed these types of behaviors strictly for those participants taking levothyroxine to gauge whether the medication seemed to be working to reduce hypothyroid symptoms, even with the addition of a regular selenium supplement. This research took it a step further to see if participants would report the same types of behaviors and feelings in relation to food servings containing selenium.

Results were not statistically significant other than the correlation between 0-1 or 2+ servings of the foods containing the highest amount of selenium (pork and brazil nuts). This was a bit unexpected but is attributed by the investigators to the smaller usable sample size than anticipated (n=48). This smaller sample size was a limitation of the study, in addition to the following:

- Findings were gleaned from patient-reported answers on the survey; ranking was based solely on patient interpretation
- Many factors can play into quality-of-life, but continued presence of symptoms and numerous doctor visits play a role
- Anticipated partnership with certified online forums/boards was not able to be acquired to provide a way for a mass amount of participants to complete the questionnaire electronically

## **Conclusions**

Due to sample size (n=48), it is unclear whether consumption of food with higher selenium content directly affects patient satisfaction with their levothyroxine therapy, though a number of participants stated they are symptomatic and frequently change strengths. All participants admitted that they know very little about the role of selenium in thyroid function making this is an area for educational growth, so this may be a potential area of opportunity and research in future studies.

The number of doctor visits, number of strength changes, and continued presence of symptoms can negatively affect quality-of-life for patients, all of which were assessed as a part of the survey administered. It may be worthwhile in future studies to use a validated quality-of-life questionnaire in order to pinpoint exactly what components of the participants' lifestyles and drug therapy directly affect quality-of-life measurements.

Data from this research suggests regular consumption of higher selenium-containing foods may have an impact on a patient's perception of overall QOL based upon the statistical significance calculated from responses of those participants who reported 0-1 or 2+ servings weekly of these foods.

## **Updates from Interim**

My project was finished prior to interim being submitted, other than the presentation of the poster at APhA. I thoroughly enjoyed presenting my poster and got a lot of questions about future study regarding the foods that contain the highest selenium (Brazil nuts and Pork). As the researcher studying foods that may affect thyroid function, I would love to see progression and extension of this project in the realm of consistency with servings of the highest selenium-containing foods. I think knowing the affect of these

foods on the thyroid and patient management of the thyroid has the potential to alter practice surrounding thyroid conditions.

## **References**

- <sup>1</sup>McMillian M, Rotenberg K, Vora K, et al. Comorbidities, concomitant medications, and diet as factors affecting levothyroxine therapy: results of the CONTROL surveillance project. *Drugs R D*. CrossMark, 2015.
- <sup>2</sup>National Institutes of Health. Selenium fact sheet for health professionals. <https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/> (accessed 23 July 2018).
- <sup>3</sup>Ventura M, Melo M, and Carrilho F. Selenium and thyroid disease: from pathophysiology to treatment. *Int J Endocrinol*;2017:1-7.
- <sup>4</sup>Rayman M, Thompson A, Bekaert B. Randomized control trial of the effect of selenium supplementation on thyroid function in the elderly in the United Kingdom. *Am J Clin Nutr*;87:370-378.
- <sup>5</sup>Winther K, Watt T, Bjorner J, et al. The chronic autoimmune thyroiditis quality of life selenium trial (CATALYST): study protocol for a randomized controlled trial. *Trials*;15(115).